

Allergens

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What makes an antigen an allergen? This question has been at the core of much research regarding the basic mechanisms of allergy as well as the development of diagnostic and therapeutic allergen products. Great strides have been made since Kjell Aas asked this question in his classic review in *Allergy* (1), but we appear no closer to the answer.

The mechanisms leading to allergic reactions have been well described in recent years and our understanding of it at the molecular level has greatly improved. Conversely, the molecular structures responsible for these allergic reactions are not as well understood. Techniques for the isolation, identification, and epitope mapping of allergens have greatly enhanced our ability to test old and new ideas about what makes an antigen an allergen. We continue to search for “major allergens,” and when we identify them, we hope to delineate “allergenic determinants” and “immunodominant epitopes.” Even now, unique structural motifs or determinants responsible for

allergenicity have not yet been identified, and we will probably never find them.

At the same time, however, we have strong evidence that allergenic crossreactivity depends on shared structural features (protein folding) that are detectable at the level of primary and tertiary structure. Knowledge of the structural and functional characteristics of allergens is also critical in designing new forms of immunotherapy, assessing the safety of newly introduced proteins in genetically modified foods, and, ultimately, in understanding what makes an allergen an allergen (2–4). The article by Dr. Verdino addresses how modern methods for elucidating the structure of allergens can help decipher the determinants of allergenicity.

Any antigen is potentially allergenic if its presentation in the context of the major histocompatibility complex class II pathway induces a switch to the production of antigen-specific immunoglobulin E antibodies and if it establishes memory B-cells capable of sustaining the sensitized state. It has become generally

accepted that CD4⁺ T-cells producing the T-helper (Th)2-type cytokines interleukin (IL)-4, IL-5, IL-9, and IL-13 play an important role in promoting atopic allergy. Indeed, successful allergen immunotherapy could be explained in terms of downregulation of allergen-specific Th2 responses through immune deviation or immune suppression (5,6). Therefore, the detailed analysis of the T-cell response to allergens and the identification of T-cell epitopes of allergens may lead to novel approaches for allergen-specific treatment. This may be especially important with food allergens, because conventional immunotherapeutic approaches have not yielded positive results. Dr. Bohle addresses this in her article.

Stinging insect venoms are probably the best-characterized allergen products derived from natural sources and used for specific immunotherapy. Nearly all of the allergens from these sources have been either sequenced or cloned, and the allergenic properties of these proteins have been extensively studied. The article by Dr. Hoffman, who has made significant contributions to our knowledge of hymenoptera venom allergens over the last 20 yr, reviews the approaches used for their isolation, characterization, and analysis.

Allergenicity is not an inherent property of an antigen. There is a growing body of evidence that the nonallergenic components derived

from environmental allergen sources such as proteases from mites and molds may amplify the response to allergens (7). At the same time, vaccine manufacturers use adjuvants to modify the immune response to allergens (8). Therefore, allergenicity should be viewed in the context of a complex network of innate immune responses, Th1, Th2, and T_{reg} cells responding to not just the allergen itself but also to their nonallergenic counterparts. The article by Dr. Kauffman provides a strong case for studying the interaction of the innate receptor families with environmental allergen sources to shed some light on this complex network.

References

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