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Commentary

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Assessment of allergen cross-reactivity

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Abstract

The prediction of allergen cross-reactivity is currently largely based on linear sequence data, but will soon include 3D information on homology among surface exposed residues. To evaluate procedures for these predictions, we need ways to quantitatively assess actual cross-reactivity between two allergens. Three parameters are mentioned: 1) the fraction of the epitopes that is cross-reactive; 2) the fraction of IgE that is cross-reactive; 3) the relative affinity of the interaction between IgE and the two allergens. This editorial briefly compares direct binding protocols with the often more appropriate reciprocal inhibition protocols. The latter type of protocol provides information on symmetric versus asymmetric cross-reactivity, and thus on the distinction between complete (= sensitising) allergens versus incomplete, cross-reacting allergens. The need to define the affinity threshold of the assay and a caveat on the use of serum pools are also discussed.

In a paper recently published in this Journal, the question was raised whether a fungus considered for biological pest control (Beauvaria bassiana) could elicit allergic reactions due to cross-reactive IgE antibodies induced by allergens from known allergenic fungi [1]. Based on homology in the amino acid sequence, four potentially cross-reactive proteins were cloned, expressed in E coli and tested for IgE (cross)reactivity using sera from patients with known fungal allergies. Support for (cross)reactivity was found for two of these four proteins. The two (cross)reactive proteins had the highest sequence homology to known allergens: the enolase was 85% sequence-identical to the Alternaria enolase known as Alt a 6 and the aldehyde dehydrogenase was 71% sequence-identical to the Alternaria dehydrogenase Alt a 10. The two proteins with no demonstrable (cross)reactivity had sequence identities of 51 and 60% to two Aspergillus fumigatus proteins. It is tempting to conclude that this result supports the notion that sequence identity is a useful predictor of cross-reactivity.

A few comments on the prediction on cross-reactivity as illustrated by this study. As the authors point out, the number of sera used to test for cross-reactivity was small (N = 20, tested as 10 pools of 2; a caveat on the use of serum pools will be discussed later). Moreover, the clinical history of the patients is not specified, which is particularly relevant in view of the quite distinct modes of allergen exposure in case of invasive aspergillosis as compared to airborne Alternaria. IgE reactivity was investigated by immunoblotting of crude E. coli extracts as the source of the recombinant proteins, which is useful but not ideal since it is known to be inefficient for some allergens. Lastly, as discussed in more detail below, cross-reac-