Mapping of conformational epitopes in dust mite allergens Der f 1 and Der p 1

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The Group 1 mite allergens, Der f 1 and Der p 1, are potent allergens excreted by Dermatophagoides farinae and Dermatophagoides pteronyssinus, respectively. Monoclonal antibody-based epitope mapping studies identified multiple species-specific epitopes on the Group 1 mite allergens, and a unique cross-reactive epitope defined by mAb 4C1. Binding of 4C1 to this epitope inhibits human IgE binding to both allergens. In order to determine the molecular basis of the cross-reactivity, the crystal structures of Der f 1 and Der p 1, both in complex with 4C1, were elucidated. Structural data reveal the epitope that is common to both Der f 1 and Der p 1. In both allergens the epitope is not only formed by the same amino acids, but the conformations of the epitope forming residues are very similar. Moreover these amino acids have the same conformations whether the allergens are complexed with antibody or not, in the case of both Der f 1 and Der p 1. The crystal structure of 4C1 alone shows that the CDR regions of the antibody do not significantly change in conformation upon allergen binding. Identification of the key amino acids involved in the unique cross-reactive epitope on the Group 1 mite allergens in combination with site-directed mutagenesis will facilitate identification of IgE-binding epitopes. This approach will lead to design of modified allergen molecules that could be used in recombinant vaccines for the treatment of dust mite allergy.