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Mutational analysis of major IgE-binding epitopes of recombinant bovine αS1-casein

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Background

Cow's milk allergy (CMA) is one of the most widespread human allergies, especially in very young children. One of the main bovine milk allergen is αS1-casein which is considered as intrinsically unfolded protein. Its epitope determinants have been partially characterized using synthetic peptides and crucial amino acid residues for IgE-binding have been identified. However, this very useful approach for epitope characterization neglects local interactions or local structures formed in the full-length protein and their impact on the accessibility of epitopes for IgE.

Methods

The importance of amino acids previously identified as crucial for IgE-binding was evaluated in the context of the whole protein. The binding of αS1-casein specific IgE from 14 patients with CMA on recombinant αS1-casein and two mutant forms in which critical amino acid residues for IgE-binding have been mutated was measured by indirect ELISA and competitive ELISA.

Results

For the majority of the patients, mutation reduced significantly IgE-binding but did not suppress it completely. Thus, most of the patients likely produce IgE directed against epitopes, until now, considered as minor. Nevertheless, we observed a great variability in patient responses. For some patients, the complete suppression of IgE-binding was achieved.

Conclusions

Such recombinant mutated αS1-caseins with reduced IgE-binding ability can be useful for the development of CMA immunotherapy.

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