



Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Short Communication

In-vitro diagnosis of allergic diseases

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The diagnosis of allergic diseases has traditionally been based on detection of specific IgE to relevant allergens either by skin testing or by determination in serum using enzyme linked immunosorbent assay (EISA), CAP system fluorescence enzyme labeled assay (FEIA) and UniCAP based methodologies. Both of these methods are performed using whole allergenic molecules that contain both non-relevant allergenic components and additional undefined non-allergenic components and therefore pose associated problems with standardization. In addition, the fact that several plant foods contain proteins that are homologous to plant aeroallergens contributes to the over-diagnosis of food allergies because of cross-reactivity as it results in positive tests that may not be clinically relevant. An ideal test should also be able to distinguish between sensitization and clinical reactivity and between the varying degrees of abilities of specific epitopes to trigger allergic reactions. There is still an unmet need for a laboratory test to fulfill these criteria.

Recent years have witnessed major changes in the clinical and diagnostic approaches especially to patients with type I, IgE mediated food allergies. Quantitative determination of specific IgE to whole food allergens still remains to be the most useful clinical tool to predict individual reaction to food allergens. Food specific IgE levels that predict clinical reactivity at various degrees of specificity, sensitivity, and positive and negative predictive values have been published and these tables have proved to be very useful adjuncts in the clinical decision making in food challenges. We have recently shown that some sIgE levels and STAT6 gene variants may be important determinants to predict longer persistence of CMA.

In recent years, component resolved diagnosis (CRD) has been introduced as a novel methodology to be useful especially in patients with food allergy and studies investigating its usefulness in various areas have started to appear in the medical literature. CRD is based on detecting specific IgE to purified natural or recombinant allergens using microarray techniques. With this method one is able to detect specific IgE to components of an allergen rather than the whole allergen.

Nicolau et al. have examined the role of CRD in differentiating between sensitization and allergy to peanut. In this study, of the 110 children who were sensitized to peanut, 66 have produced no reactions on

oral food challenge and 19 were considered to be allergic to peanut. Specific IgE to Ara h2 was most predictive of the outcome. In a more recent study, Masthoff et al. have shown that IgE levels ≥ 1 kUA/L to nCor a 9 in children and adults or ≥ 5 kUA/L to rCor a 14 in children and ≥ 1 kUA/L in adults had a specificity of $>90\%$ for severe allergy to hazelnut. However, it should be noted that patients from different geographical regions may not show the same pattern of specific IgE to allergen components and therefore the results of a single study may not be universally applicable. The usefulness of component testing for animal food allergens such as milk and egg is less well established and studies have produced varying and often conflicting results.

The purposes of using CRD and future aims can be summarized as follows:

- To determine specific IgE to single component of natural or recombinant allergen
- To plan individual specific therapies according to the specific protein component
- To investigate the clinical response at the molecular level
- To define clinical risks for the individual patient
- To define possible cross reactions
- To predict the outcome of oral food challenges and ideally negate the need for them
- To aid in selecting patients for allergen specific immunotherapy.

Allergen epitope profiling

This method is based on the hypothesis that individuals who have IgE antibodies recognizing a greater number or a specific pattern of sequential epitopes are more likely to have clinical allergy rather than asymptomatic IgE sensitization. Studies regarding its role in predicting clinical reactivity have produced conflicting results.

Basophil activation test

The value of this test in differentiating between clinical reactivity and sensitivity, and as an aid in differentiating cross reactivity using both whole allergenic molecules and recombinant allergens is under current investigation. Available data suggest that this test is comparable to food specific IgE and skin prick testing.

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In spite of these advances in recent years, type I allergy, specifically food allergy, still possesses many unknowns and ideal methods in clearly differentiating sensitization from allergy, in predicting severity especially anaphylaxis and in predicting persistence and prognosis remain to be discovered.

Q2 Uncited references

[1,2,3,4]

References

- [1] Masthoff LJ, Mattsson L, Zuidmeer-Jonghean L, Lidholm J, et al. Sensitization to cor a 9 and cor a 14 is highly specific for a hazelnut allergy with objective symptoms in Dutch children and adults. *J Allergy Clin Immunol* 2013 Aug;132(2):393–9. 90
- [2] Nicolaou N, Poorafshar M, Murray C, Simpson A, et al. Allergy or tolerance in children sensitized to peanut: prevalence and differentiation using component-resolved diagnostics. *J Allergy Clin Immunol* 2010;125(1):191. 92
- [3] Sicherer SH, Sampson HA. Food allergy: epidemiology, pathogenesis, diagnosis, and treatment. *J Allergy Clin Immunol* 2014;133:291–307. 93
- [4] Yavuz ST, Buyuktiyaki B, Sahiner UM, Birben E, et al. Factors that predict the clinical reactivity and tolerance in children with cow's milk allergy. *Ann Allergy Asthma Immunol* 2013;110:284–9. 94