

Editorial

Component-resolved diagnosis in food allergy, are micro-array assays helpful to the clinician?

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Only a few tools have opened new horizons in the diagnosis of food allergy. In the first half of the 20th century, skin prick tests have allowed identifying sensitization to suspected foods. In the second half of last century, clinicians had started to establish standardized food challenge protocols to distinguish between sensitization and true food allergy, and in the late 1960s, the discovery of IgE antibodies had opened up new fields for specific IgE measurements. IgE measurement techniques commonly used today apply modified enzyme-linked immunosorbent assay (ELISA) techniques. The quantity of serum needed for each allergen tested is a common limitation, in particular when testing children. In this regard, micro-array assays opened a new technological field allowing testing large number of allergens with a minimal amount of serum.

At bedside, it is essential that analytical methods are validated against clinical outcomes, i.e. standardized food challenges. In this regard, the concept of specific IgE antibody levels providing cut-off values for clinical reactivity has emerged in the last 10 years. After the initial reports by Sampson (1, 2), numerous publications have shown that specific IgE antibody titers to various foods can provide a clear help to the physician for the diagnosis of food allergy (3–6). In addition, the study of specific IgE profiles to various epitopes or protein fractions have proven to be helpful to predict the natural history of food allergy (7–9). However, it has recently become clear that defined IgE titers mainly depend on various characteristics of the patient groups studied by the different investigators (10).

The study published by Ott et al. (11) in this issue of *Allergy* investigates the usefulness of micro-array-based IgE detection in a well-characterized population of children with hen's egg and cow's milk allergy. In order to do this, micro-array results were compared to 'classic' IgE measurement methods, skin prick tests and the outcome of double-blind placebo control food challenges. The study included 130 children suspected with hen's egg or cow's milk allergy. All children had standardized food challenges, and skin prick tests and *in vitro* test results were compared to the outcome of the food challenges. In the same method in line with the previously published studies determining IgE cut-off titers for clinical reactivity, the authors performed receiver operating characteristic (ROC) curve analyses and determined the predictive value of the different diagnostic methods. Overall, they found that, by analyzing the combined major allergens of cow's milk or hen's egg by micro-array, the accuracy of this test was comparable to the CAP-FEIA *in vitro* specific IgE measurement system (Phadia, Uppsala, Sweden) or skin prick test method. They concluded that the micro-array technique is similar to the current standards (skin prick test or *in vitro* IgE antibody measurement); however, by using far less blood and allowing to test more antigens or antigenic fractions.

Few other investigators have tested so far micro-array techniques for the diagnosis of food allergy. Shreffler et al. (12) have shown that the combined measurement of antibodies to Ara h 1, Ara h 2 and Ara h 3 can provide prognostic information about patients with food allergy. Noh et al. (13) and Flinterman et al. (14) have both

shown, in separate studies, that micro-array allows measuring accurately IgE and IgG4 antibodies in food allergic patients.

Micro-array analysis definitively opens up new options in the diagnosis of food allergy, not by measuring new proteins, but by allowing measurement of much larger number of proteins for a given patient. However, in this advantage of the technique lies also the major drawback of micro-array.

Our current knowledge of the significance of positive results to many proteins is limited and largely population related. It has been well established by other IgE measurement techniques such as SPOT membranes that specific antibody response profiles can predict the natural outcome of food allergy. However, the more tests are

performed, the more difficult becomes the interpretation of the result. Thus, the major task for a good usage of micro-array techniques in the diagnosis of food allergy will be to establish micro-array profile results in relation to the patients' specific clinical profiles. In addition, proper interpretation of the large number of information provided by micro-arrays will unfortunately not be available to most nonspecialized physician in charge of patients with food allergy. Or in other words, too much information is not good information.

Finally, as stated by the authors of the article, standardized food challenges will still be necessary in many patients for the diagnosis of a suspected food allergy, or for the follow-up of an already diagnosed food allergy.

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