f424 rAra h 3

rAra h 3 from peanut (*Arachis hypogaea*)

Possible Clinical Utility

Allergen components have a wide variety of uses, from the diagnosis and management of allergic disease to the development of immunotherapy, standardisation of diagnostic tests and as tools in molecular allergology. Recombinant Ara h 3 serves as a marker for sensitization to peanut glycinin, with potential cross-reactivity to glycinins from other leguminous foods which may elicit clinical food reactions.

Allergen Description

Peanut is an annual plant belonging to the *Fabaceae* or legume family. It grows close to the ground and produces its fruit, the actual peanut, below the soil surface. A characteristic feature of leguminous seeds, such as peanuts, is that the nutrient storage tissue is formed by the enlarged cotyledons which have the biological role of supporting the germination and initial growth of the seedling. This is in contrast to the so-called tree nuts, including walnut, brazil nut and hazelnut, which are botanically unrelated to peanut.

Peanuts contain three major types of seed storage protein: vicilin, conglutin and glycinin (1). Members of these protein families have traditionally been characterized and named with respect to their sedimentation rate in ultracentrifugation and their solubility in different salt conditions. By these criteria, vicilin belongs to the 7S globulin family, conglutin to the 2S albumin family and glycinin to the 11S globulin family (2-5).

Vicilin, conglutin and glycinin comprise three major allergens of peanut, designated Ara h 1, Ara h 2 and Ara h 3, respectively. Other described peanut allergens include Ara h 4, which is closely related to Ara h 3; Ara h 5 (profilin); Ara h 6 and Ara h 7, which are both closely related to Ara h 2; Ara h 8, which belongs to the PR-10 protein family, typified by the major birch pollen allergen Bet v 1; and Ara h 9, a lipid transfer protein related to the major peach allergen Pru p 3.

Assessment of IgE sensitization using natural peanut extract is affected by cross-reactivity with a range of other plant-derived allergen sources. For example, IgE reactivity to Ara h 8 is likely to result from cross-reactive birch pollen (Bet v 1) sensitization while IgE reactivity to Ara h 9 may be caused by primary sensitization to peach LTP (Pru p 3) or some pollen LTP. In contrast, IgE antibody reactivity to rAra h 1, rAra h 2 or rAra h 3 is likely to indicate primary sensitization to peanut which makes them useful as more specific markers in the investigation of suspected peanut allergy.

Ara h 3 is a glycinin, a member of the 11S globulin family, and may also function as a trypsin inhibitor (4, 6-13). Ara h 3 is first produced as a precursor consisting of a single polypeptide chain which is processed to form several polypeptides ranging from approximately 14 to 45 kDa in size which make up the mature Ara h 3 protein. The subunit organization of Ara h 3 is similar to that of soy glycinin.

Potential Cross-Reactivity

While total peanut extract contains a variety of potentially cross-reactive IgE-binding determinants, Ara h 3 shares sequence similarity and possible cross-reactivity only with other members of the glycinin protein family.

A sequence similarity between Ara h 3 and the glycinins in soybean and pea of 62% to 72% has been reported (14). Sin a 2, a major allergen from yellow mustard seed, was shown to have a sequence identity with other allergenic 11S globulins ranging between 27% and 38%. Three peptides described as epitopes in Ara h 3 were moderately conserved in Sin a 2 (15). Similarly, IgE-binding epitopes of Ara h 3 exhibited some structural homology among different tree nut allergens (Jug r 4 of walnut, Cor a 9 of hazelnut, Ana o 2 cashew nut), accounting for in vitro cross-reactivity observed. IgE-binding epitopes similar to those found in 11S globulin allergens do not apparently occur in other allergens with the cupin fold such as Ara h 1 from peanut, Jug r 2 from walnut, Cor a 11 of hazelnut or Ana o 1 from cashew nut (16).

Clinical Experience

Sensitization to Peanut occurs with a high degree of heterogeneity to a number of Peanut allergens. Mono-sensitization to a single peanut allergen is relatively rare (17).

In an evaluation of recombinant allergens, Ara h 1, Ara h 2, and Ara h 3, using sera of 77 Peanut-allergic patients, seven different patterns of sensitization were identified to these allergens. The majority of patients (97%) had specific IgE to at least one of the recombinant allergens (Ara h 1, Ara h 2, and Ara h 3), and 77%, 75% and 77% recognized rAra h1, rAra h 2 and rAra h 3 respectively. High epitope diversity was found in patients with a history of more severe allergic reactions (17).

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Phadia

Phadia AB. P O Box 6460, SE-751 37 Uppsala, Sweden
Tel +46 18 16 50 00. www.phadia.com

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