

f423 rAra h 2

rAra h 2 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 2 is a marker for sensitization to peanut 2S albumin (a storage protein) and often associated with systemic and more severe reactions. Recombinant allergens have a wide variety of uses, from the diagnosis and management of allergic patients to the development of immunotherapy to the standardisation of allergenic test products as tools in molecular allergology. Recombinant allergens are particularly useful for investigations of allergies manifesting wide crossreactivity.

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 2 is homologous to and functions as a trypsin inhibitor, and is related to the 2S albumin family of seed storage proteins (2, 3, 4-15). It is also known as conglutin (3). Ara h 2 contributes up to 9% of the total protein content in peanut extracts (2). Ara h 2 is a 17.5 kDa protein and has a 30% homology with 2S albumins, but appears to have the closest homology with conglutin from lupin. Ara h 2 has eight cysteine residues that could form up to four disulfide bonds (16).

Potential Cross-Reactivity

Ara h 2 has a 30% homology with 2S albumins, but appears to have the closest homology with conglutin from lupin (18). Cross-reactivity may therefore occur between Ara a 2 and other foods containing 2S albumins, dependent on the degree of homology. Ara h 2 has been shown to share common IgE-binding epitopes with almond and brazil nut allergens (18).

Ara h 6 has homology to Ara h 2, especially in the middle part and at the C-terminal part of the protein. Inhibition studies demonstrate that at least parts of the epitopes of Ara h 6 are cross-reactive with epitopes on Ara h 2 (19). However, Ara h 2 appears to be the more potent allergen (9).

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 (21).

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 h 1, rAra h 2 and rAra h 3 respectively. High epitope diversity was found in patients with a history of more severe allergic reactions (17).

A British study, evaluating sera of 40 Peanut-allergic individuals, of 18 allergens identified, 8 were bound by >50% of patients and the total number of bands per patient correlated significantly with challenge score and serum-IgE. Ara h 2 was recognized by 71% of sera (20).

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