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Focus onPeanut Allergens

Peanut allergy affects 1% of the population and is associated with the most fatal foodrelated anaphylactic reactions ⁽¹⁾. While many types of food allergies are outgrown, peanut allergy tends to develop early in life and persists in 80% of affected individuals through adult life ⁽²⁾.

Sensitization to peanut occurs to a number of peanut allergens and mono-sensitization to a single peanut allergen is relatively rare ⁽³⁾.

Eleven peanut allergens are recognized by the WHO/IUIS Allergen Nomenclature subcommittee (www.allergen.org):

Ara h 1 is a member of the 7/8 globulins (vicilins) of seed storage proteins that belong to the cupin superfamily ⁽⁴⁾.

Ara h 2, Ara h 6 and Ara h 7 are members of the 2S albumins (conglutin) that belong to the prolamin superfamily $^{(4)}$.

Ara h 3 and Ara h 4 are considered the same allergens and are members of the 11S globulins (legumins/glycinins) that belong to the cupin superfamily ⁽⁵⁾.

Ara h 5 is a profilin and Ara h 8 a Bet v 1 homologue, which is of relevance for peanut-allergic patients with birch pollen allergy $^{(6)}$.

Ara h 9 is a lipid transfer protein (LTP) and an important allergen in peanut allergic patients from the Mediterranean region. In this area, a strong association between sensitization to peanut and peach lipid transfer protein was observed with high cross-reactivity between Pru p 3 and Ara h 9^{(7) (8) (9)}.

The clinical relevance of the oleosins Ara h 10 and 11 is still under investigation.

Peanut allergy has diverse clinical and immunological patterns in different geographical areas around the world. American patients frequently have antibodies to Ara h 1, Ara h 2 and Ara h 3 (56.7-90%) while Spanish patients recognize these three allergens less frequently (16-42%) and are more often sensitized to Ara h 9, most likely as a result of sensitization to Pru p 3 ^{(10) (8;11-13)}.

A body of evidence suggests that IgE responses to Ara h 2 may be a useful marker for predicting peanut allergy, however additional allergenic components, such as Ara h 9, may be necessary ⁽¹⁴⁾.

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The crystal structures of peanut allergens Ara h 1 and Ara h 2 have recently been solved.



The major allergen Ara h 1 is a 64 kD protein that comprises 12-16% of the total peanut protein. Chruszcz et al showed that the crystal structure of the Ara h 1 core (residues 170-586) has a bicupin fold, which consists of two core β -barrels, each associated with a loop domain of α -helices, very similar to the reported structure of other vicilins (Fig.1). While natural Ara h 1 forms higher molecular weight aggregates in solution, in its crystalline state, the core region of Ara h 1 forms trimeric assemblies ⁽¹⁵⁾.

Fig.1: Ara h 1 trimer. Chruszcz et al, 2011

The crystal structure of major peanut allergen Ara h 2 was determined by Mueller et al. The structure is a five-helix bundle held together by four di-sulfide bonds ⁽¹⁶⁾. It is similar to other prolamin family members, particularly Ara h 6, which shares 59% sequence identity (Fig.2). Ara h 2 and Ara h 6 have similar immunoreactivity in chimeric IgE ELISA



and are considered the most potent peanut allergens accounting for the majority of effector activity in peanut extracts ^(17,18) (^{19;20)}. For use in molecular diagnostics the combined results of IgE reactivity to Ara h 2 and Ara h 6 yielded the highest diagnostic sensitivity and specificity for detecting clinically evident peanut allergy in a French patient cohort ⁽¹²⁾.

Fig. 2: Superposition of Ara h 2 (green) and Ara h 6 (cyan). Mueller et al, 2011

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