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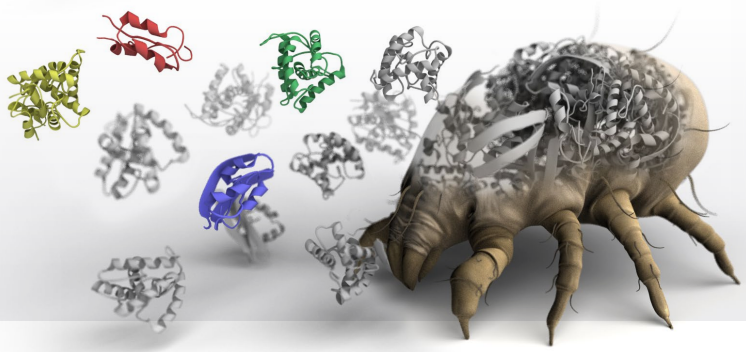
The relevance of Der p 23 in mite allergy



Mite allergy

Allergy to house dust mites (HDM) is a main cause of respiratory allergies, and exposure to HDM is a major trigger of asthma exacerbations[1]. Treatment strategies for HDM-induced rhinitis and asthma include medication and allergen avoidance and in certain cases allergen specific immunotherapy (AIT).

Patient clinical history with symptom expression upon mite exposure, together with the detection of mite specific IgE, form the basis for diagnosing HDM allergy. Generally, extract based tests are used as the first step to confirm sensitization to HDM. In patients that will undergo mite specific AIT, however, it is recommendable to identify the relevant sensitizer(s) on the component-resolved level in order to select the optimal treatment[1-3].

Dermatophagoides pteronyssinus and *Dermatophagoides farinae* are the most common HDM species in temperate zone, both containing the two major allergens - group 1 and 2 proteins, from mite bodies and feces, respectively. Together Der p 1 and Der p 2 will identify between 63 and 97% of patients sensitized to *D. pteronyssinus* extracts, as shown in studies from Europe, North America and Japan[4]. Thus, a significant proportion of house dust mite sensitized patients may be missed by the use of only group 1 and group 2 allergens in the diagnostic work up.

Der p 23 – a major and potent allergen

To date, eighteen allergens in addition to Der p 1 and Der p 2 from *D. pteronyssinus* are registered in the WHO/IUIS database (http://www.allergen.org). Of these, Der p 23 appears to be of particular high clinical relevance, as demonstrated by recent studies. This allergenic protein is present on the surface of mite fecal particles, which is the major airborne form of mite allergens that also carries Der p 1, while Der p 2 is found mainly in the mite bodies (Platts-Mills and Caraballo in[3]). Up to 74% of *D. pteronyssinus* allergic patients are sensitized to Der p 23, which is close to the frequency of sensitization to that of Der p 1 and Der p 2[2, 5]. Although levels of sIgE to Der p 23 is on average 5 times lower than to Der p 1 and Der p 2 in HDM allergic patients[6] it appears to be ten times more potent than Der p 1 in activating mast cells[5]. Thus, Der p 23 appears both highly allergenic and a frequent sensitizer, i.e. it is a major HDM allergen, which together support/suggest a relevant role of this allergen in the immune response.

Potential cross-reactivity

The amino acid sequence identity of Der p 23 and the corresponding *D. farinae* homologue, Der f 23, is 87%. Structural studies of Der p 23 and subsequent modelling of Der f 23 on its structure, suggest that considerable cross-reactivity may occur between the two proteins[6], although this remains to be demonstrated.

Der p 23 as a marker of HDM induced respiratory diseases/asthma

It is well known that HDM allergy is a major risk factor for asthma, and that early HDM sensitization has a significant effect on lung function[7]. The severity of asthma correlates with both the number of sensitizations as well as with sIgE levels[8, 9].

Also on the molecular level, the number of component-specific sensitizations correlate with disease severity, and sensitizations appear years before diseases development, as demonstrated in grass allergic children[10]. Similar results for HDM sensitization and allergic respiratory diseases were demonstrated in the MAS cohort, where number of HDM-component specific sensitizations increased with disease severity, as well as with age. Importantly, sensitization to Der p 1 and Der p 23 before the age of five was predictive of asthma at school-age[11].

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Children with both HDM allergy and asthma were shown to be sensitized to more mite allergen components than non-asthmatic children with mite allergy. Furthermore, the IgE levels to Der p 1, Der p 2 and Der p 23 were higher in the asthmatic children than in non-asthmatic children[12].

Taken together the available studies indicate that sIgE to Der p 23 can add important information on the disease progression, and may serve as a severity marker for asthma in HDM allergy.

The relevance of Der p 23 for AIT

The sensitization rate to D. pteronyssinus differs between populations, but on average, more than 10% of HDM allergic adults and children lack sIgE to Der p 1 or Der p 2. Approximately half of these can be expected to be sensitized to Der p 23, as supported by studies in which patients were negative to several other HDM allergens investigated[12-15]. Overall, available studies suggest that among HDM allergic patients 4-6% may be mono-sensitized to Der p 23.

The unique sensitization profile of a patient is important to understand before selecting optimal AIT treatment[1, 2]. Therapeutic HDM extracts differ greatly in relative content of Der p 1 and Der p 2[16-18], although a standardized HDM tablet for sub-lingual immunotherapy, with a relation of Der p 1:Der p 2 close to one[4, 19], was recently introduced. However, as treatment success depends on the matching of the patient sIgE profile with the allergen content of the therapeutic extract, treatment success may be low when these differ significantly or extracts are lacking in relevant components.

The amount of Der p 23 in both mite fecal particles and bodies is rather low, and therapeutic extracts may be low in content of, or even lack this allergen[5]. Consequently, Der p 23 mono-sensitized patients, or patients with substantial sensitization to Der p 23, may run the risk of less efficacious AIT than if predominantly sensitized to Der p 1/Der p 2.

In conclusion, Der p 23 can aid in identifying up to 5% more HDM extract sensitized patients than by using only Der p 1 and Der p 2. Furthermore, patients with a considerable or even predominant Der p 23 sensitization can be identified, enabling a better-informed judgement of the potential for successful AIT treatment and/or choice of extract.

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