Der p 23 – clinical relevance of molecular monosensitisation in House Dust Mite allergy

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.18176/jiaci.0392
House dust mite (HDM) induced allergic diseases affect approximately 2% of the world’s population, thereby being a cause of major healthcare and economic burden[1]. Component-resolved diagnostics offers the possibility of a higher diagnostic precision and allows better management of each patient[2]. Specific immunotherapy (SIT) is an effective therapeutic approach in sensitised individuals with allergic respiratory disease. However, in comparison with SIT for grass or birch pollen, SIT for HDM shows significantly lower therapeutic success[3]. This reduced efficacy might be explained by poor standardisation of most of the commercially available HDM SIT extracts. Variable amounts of the main HDM allergens (Der p 1, Der p 2, Der p 23) or even absence of important components in the different commercial extracts may underlie insufficient therapeutic results in some groups of HDM allergic patients[4].

Recently Der p 23, a peritrophin-like protein, was identified as a new major Dermatophagoides pteronyssinus allergen[5], recognised by approximately 75% of patients. It was shown to induce IgE-dependent basophil activation, thus having high allergenic activity. A recent study in sera of 722 participants of the German Multicenter Allergy Study showed that IgE to Der p 23 at 5 years of age or less was a predictive factor of asthma at school age[6]. Nevertheless, data concerning the clinical relevance of Der p 23 are still lacking. Its recent commercial availability for diagnostics allowed us to identify a new group of patients sensitised only to Der p 23 and not to other major HDM allergens. Thus, the aim of the present study was to analyse the relationship between sensitisation to Der p 23 and clinical symptoms of allergic diseases in sensitised patients.

Patient data were selected from the database of the Department of Allergy and Immunology of Hospital de São Bernardo, Centro Hospitalar de Setúbal E.P.E., in Portugal. The study was approved by the local ethics committee and the national data protection commission. The database was scanned for patients with perennial allergy to HDM who were referred to our institution between 2010 and 2018. Patient selection was based on the following criteria: (1)
History of perennial allergic symptoms; (2) Positive skin prick test to *Dermatophagoides pteronyssinus* (wheal ≥ 3mm); (3) specific IgE to total extract of *Dermatophagoides pteronyssinus* ≥ 0.35 kUA/l (ImmunoCAP, Thermo Fisher Scientific); (4) specific IgE to Der p 1 and Der p 2 ≤ 0.35 kUA/l and to Der p 23 ≥ 0.35 kUA/l (ImmunoCAP, Thermo Fisher Scientific), all analysed in May 2017, using frozen sera stored in our biobank.

Patients’ sera were transferred to the Department of Pathophysiology and Allergy Research, Medical University of Vienna, Austria, for MeDALL chip analysis[7], which is based on microarray technology for diagnosis and monitoring of IgE and IgG reactivity profiles towards a wide-ranging variety of allergens. The chip contains a panel of 13 components from *Dermatophagoides pteronyssinus* (Der p 1, Der p 2, Der p 4, Der p 5, Der p 7, Der p 10, Der p 11, Der p 14, Der p 15, Der p 18, Der p 21, and Der p 23 and clone 16-encoded allergen).

From the initial database of 144 HDM allergic patients with measured levels of IgE specific to *Dermatophagoides pteronyssinus* and to Der p 1, Der p 2 and Der p 23, 7 patients (4.9%) met the criteria mentioned above and were analysed using MeDALL chip (Table 1). All of these 7 patients had symptoms of perennial rhinitis and three of them also had asthma, but none of the patients had ever received any SIT.

We found that 6 out of the 7 patients were only sensitised to Der p 23, whereas no sensitisation to other HDM allergens present on the chip were detected.

Regarding other perennial sensitisations, none of the tested sera had IgE reactivity to major allergen components of *Dermatophagoides farinae* (Der f 1 and Der f 2), but three patients were sensitised to pet allergens, and two of those patients were also sensitised to *Lepidoglyphus destructor* (Lep d 2) (Table 1).

The importance of Der p 23 as a new major HDM allergen is supported by numerous research groups[8]. However, only few data have been published concerning monosensitisation to this new major allergen. Recently, Sven Becker, at al[9] described a similar group of 5 HDM allergic patients tested with MeDALL chip that was shown to be positive for Der p 23, whereas other HDM allergen components were negative. Thus, from a molecular point of view, those patients were regarded as being truly monosensitised to this allergen.

According to studies of prevalence of IgE recognition and allergen-specific IgE levels, Der p 1, 2, 5, 7, 21, and 23 appear to be the clinically most relevant HDM allergens and all are represented on the MeDALL chip, in addition to others. However, despite the comprehensive panel of molecular components, the possibility still remains that these patients might have IgE reactivity to other HDM allergens not represented on the chip[10].
Our results showed that three patients also had sensitisation to pet-derived allergens. Two of these pet allergic patients were sensitised to *Lepidoglyphus destructor*, an important storage mite in Mediterranean areas. Therefore, we cannot exclude the possibility that IgE reactivity to both of these groups of allergens might be a cause of the perennial rhinitis and asthma. However, the remaining four patients had clinical symptoms of respiratory allergy that were most probably due to sensitisation to Der p 23, thereby highlighting the clinical relevance of this allergen. This is important since different HDM molecular compositions have been previously shown to differentially associate with asthma in sensitised adults, in a study carried out in Spain, in 384 HDM-allergic individuals [11].

Our results regarding Der p 23 are interesting but should be interpreted with caution. Firstly, monosensitisation to Der p 23 seems to be a rare event. Secondly, our sample size is small. Thirdly, relationships between serum levels of specific HDM allergens and clinical relevance as detected by target-organ provocation tests is not always clear [12]. Nevertheless, although Der p 23 is only present in low amounts in house dust and also in HDM extracts, it has previously been shown to be able to induce high IgE titers [13]. In addition, the presence of clinical symptoms of HDM allergy in our group of Der p 23-monosensitised patients suggests that this allergen has clinical relevance by itself. Although more studies are warranted to further clarify the clinical relevance of Der p 23, our study suggests that this allergen should probably have to be considered in terms of HDM SIT extract composition.

**Source of support:**
Recipient of an EAACI Research Fellowship 2018 – 10 000 Eur - 6 months at Center for Pathophysiology, Infectology and Immunology, Dept. of Pathophysiology and Allergy Research / Division of Immunopathology, Medical University of Vienna

**Conflicts of Interest:**
The authors declare that they have no conflicts of interest, financial or otherwise.
References


13- Thomas WR. Hierarchy and molecular properties of house dust mite allergens. Allergol Int. 2015;64:304-11. Doi: 10.1016/j.alit.2015.05.004.
Table 1. Detailed evaluation of the 7 HDM allergic patients who were negative for Der p 1 and Der p 2, and positive for Der p 23 by conventional IgE serology (ImmunoCAP).

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex</th>
<th>Age (y)</th>
<th>Resp. allergy</th>
<th>sIgE D. pter. (kUA/l)</th>
<th>sIgE Der p 23 (kUA/l)</th>
<th>MeDALL Der p 23 (ISU)</th>
<th>MeDALL other components of D. pter.</th>
<th>MeDALL other perennial sensitisations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>26</td>
<td>Rhinitis</td>
<td>1.74</td>
<td>4.16</td>
<td>7.11</td>
<td>Negative</td>
<td>Can f 5</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>43</td>
<td>Rhinitis</td>
<td>0.98</td>
<td>1.02</td>
<td>1.75</td>
<td>Negative</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>7</td>
<td>Rhinitis</td>
<td>31.0</td>
<td>15.7</td>
<td>16.7</td>
<td>Der p 5, Der p 7, Der p 18</td>
<td>Fel d 1, Fel d 2, Lep d 2</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>10</td>
<td>Rhinitis</td>
<td>4.22</td>
<td>5.54</td>
<td>0.65</td>
<td>Negative</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>13</td>
<td>Rhinitis</td>
<td>2.02</td>
<td>4.43</td>
<td>3.65</td>
<td>Negative</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>36</td>
<td>Rhinitis</td>
<td>18.5</td>
<td>4.55</td>
<td>0.97</td>
<td>Negative</td>
<td>Can f 5, Lep d 2</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>35</td>
<td>Rhinitis</td>
<td>22.6</td>
<td>30.9</td>
<td>17.9</td>
<td>Negative</td>
<td>-</td>
</tr>
</tbody>
</table>

M = male; F = female; y = years; Resp. allergy = Respiratory allergy; D. pter. = Dermatophagoides pteronyssinus; L. destructor = Lepidoglyphus destructor; sIgE = specific IgE; - = none