Allergens from house dust and storage mites

Susanne Vrtala

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Summary

House dust mites are among the most important allergy triggers worldwide. While mites of the genus Dermatophagoides occur almost worldwide, the tropical mite Blomia tropicalis and storage mites are only of importance for certain areas or groups of people. The most important allergens of Dermatophagoides pteronyssinus are Der p 1, Der p 2, and Der p 23 with immunoglobulin E (IgE)-binding frequencies of more than 70% and high allergenic activity. Also of importance are Der p 5, Der p 7, and Der p 21, which have IgE-binding frequencies of about 30%. According to the current state of knowledge, these six allergens are the allergens of clinical relevance which are also required for diagnosis and immunotherapy with individual components.

Keywords

Dermatophagoides · Blomia tropicalis · Major allergens · Component-specific diagnosis · Clinically relevant allergens

Abbreviations

HDM House dust mites
IgE Immunoglobulin E
IUIS International Union of Immunological Societies
LPS Lipopolysaccharides
MW Molecular weight
TLR4 Toll-like receptor 4
WHO World Health Organization

Introduction

House dust mites (HDM) are one of the most important allergen sources in the home and are widespread worldwide except in very cold and dry regions [1]. In HDM-populated areas, more than 50% of allergic patients are sensitized to HDM and it is estimated that approximately 65–130 million people worldwide suffer from HDM allergy [2, 3]. HDM allergic patients show symptoms such as allergic rhinitis or atopic dermatitis, and untreated HDM allergy is also a major risk factor for the development of asthma [4]. The HDM species Dermatophagoides pteronyssinus and D. farinae are considered the most important triggers of HDM allergy worldwide and are highly homologous and cross-reactive [5, 6]. In tropical and subtropical countries, the tropical mite Blomia tropicalis is predominant, but the two Dermatophagoides species are also found there [7]. Although Blomia tropicalis and Dermatophagoides contain homologous allergens, little IgE cross-reactivity is shown between the two species [8, 9]. Therefore, in regions colonized by Blomia tropicalis, allergic patients often suffer from two different mite allergies, which are difficult to differentiate diagnostically and need to be treated differently. In addition, in very humid housing conditions, storage mites of the species Lepidoglyphus destructor, Tyrophagus putrescentiae, and Glycyphagus domesticus are often found in house dust, but storage mites are predominantly considered a hazard of some occupational groups (e.g., farmers, bakers), where they represent an important risk factor for the development of occupational asthma [10–12]. While storage mites are cross-reactive with each other, IgE cross-reactivity between storage mites and HDM is very low [13]. Therefore, an accurate diagnosis is required to identify the allergenic mite species and to target therapy to patients. Mite extracts are often not
suitable for making an accurate diagnosis because they cannot distinguish between co-sensitization and cross-sensitization. In addition, mite extracts are difficult to standardize, have different allergen contents, and sometimes important allergens are missing from the extracts, which means that not all mite allergic patients can be diagnosed with the available extracts [14]. Therefore, it is important to produce the single allergens of the mites, either in the form of natural allergens purified from the mites or in the form of recombinant allergens produced in prokaryotic or eukaryotic expression systems. With the help of these single allergens, it is possible to determine the exact IgE sensitization pattern of a patient and to distinguish between co-sensitizations and cross-sensitizations. This also allows the success of an immunotherapy with mite extracts to be estimated in advance.

**The allergens of HDM and their significance**

Currently, 39 allergens of the house dust mite genus *Dermatophagoides* have already been recognized by the Allergen Nomenclature Subcommittee of the World Health Organization (WHO) and the International Union of Immunological Societies (IUIS) [15]. Depending on the mite species (*Dermatophagoides pteronyssinus* or *Dermatophagoides farinae*), allergens

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### Table 1  The allergens of the house dust mite species *Dermatophagoides pteronyssinus* (Der p) and *Dermatophagoides farinae* (Der f)

| Group | Biological function | MW (kDa) | Der p | Der f | % IgE binding | Clinical importance |
|-------|---------------------|----------|-------|-------|---------------|---------------------|
| 1     | Cysteine protease   | 24       | x     | x     | 64–100        | High               |
| 2     | ML domain lipid-binding protein | 14 | x | x | 63–100 | High |
| 3     | Trypsin             | 28       | x     | x     | 7–97          | Low                |
| 4     | Alpha-amylase       | 57       | x     | x     | 28–74         | Medium             |
| 5     | Unknown             | 15       | x     | x     | 30–40         | Medium             |
| 6     | Chymotrypsin        | 25       | x     | x     | 41–65         | Low                |
| 7     | Lipid-binding protein | 22 | x | x | 30–40 | Medium |
| 8     | Glutathione S-transferase | 27 | x | x | 4–96 | Low |
| 9     | Serine protease     | 24       | x     | x     | 92            | Low                |
| 10    | Tropomyosin         | 33       | x     | x     | 2–81          | Low                |
| 11    | Paramyosin          | 103      | x     | x     | 7–82          | Low                |
| 13    | Fatty-acid binding protein | 15 | | x | 6 | Low |
| 14    | Apolipophorin       | 190      | x     | x     | 2–84          | Low                |
| 15    | Chitinase           | 61       | x     | x     | 8–70          | Low                |
| 16    | Gelosolin           | 53       | –     | x     | 47            | Low                |
| 17    | EF hand binding protein | 53 | | x | 35 | Low |
| 18    | Chitinase-like protein | 49 | x | x | 38–63 | Low |
| 20    | Arginine kinase     | 40       | x     | x     | 7–44          | Low                |
| 21    | Unknown             | 15       | x     | x     | 30–40         | Medium             |
| 22    | Unknown             | 17       | –     | x     | Unknown       | Low                |
| 23    | Peritrophin         | 8        | x     | x     | 70–86         | High               |
| 24    | Troponin C          | 18       | x     | x     | 11            | Low                |
| 25    | Triosephosphate isomerase | 27 | x | x | 75 | Unknown |
| 26    | Myosin              | 18       | x     | x     | 25            | Unknown            |
| 27    | Serpin              | 48       | –     | x     | 42            | Unknown            |
| 28    | Heat shock protein 70 | 71 | x | x | 68 | Unknown |
| 29    | Peptidyl-prolyl cis-trans isomerase | 18 | x | x | 40 | Unknown |
| 30    | Ferritin            | 20       | x     | x     | 40            | Unknown            |
| 31    | Coflin              | 17       | x     | x     | 30            | Unknown            |
| 32    | Pyrophosphatase     | 34       | x     | x     | 40            | Unknown            |
| 33    | Tubulin             | 44       | x     | x     | 25            | Unknown            |
| 34    | Enamine-imine deaminases | 16 | | x | 70 | Unknown |
| 35    | Unknown             | 14       | –     | x     | 50            | Unknown            |
| 36    | Unknown             | 23       | x     | x     | 40            | Unknown            |
| 37    | Petrotrophic-like protein | 30 | x | x | 20–30 | Low |
| 38    | Bacterial lytic enzyme | 15 | x | – | 70 | Unknown |
| 39    | Calcium-binding protein | 18 | – | x | 10 | Unknown |
Allergens with high relevance

Group 1, 2 and 23 allergens of HDM are called major allergens because they have high IgE binding frequency and high allergenic activity [16, 17]. Der p 1 is a cysteine protease with a molecular weight of 24 kDa, which is produced as a proform and becomes biologically active by posttranslational cleavage of the propeptide [18]. The protease activity of Der p 1 can cut the transmembrane molecules occludin and claudin, destroying the barrier of the bronchial epithelium [19]. Group 1 allergens are found in large amounts in house dust and about 80–90% of all mite allergy sufferers are sensitized to group 1 allergens [16, 20]. Group 2 allergens contain an MD-2-related lipid recognition domain that can bind lipopolysaccharides (LPS), allowing them to activate Toll-like receptor4 (TLR4) [21]. Der p 2 has a molecular weight of 14 kDa, which is localized in the intestine and feces of mites, and is recognized by 80–100% of mite allergic individuals [16, 22]. Der p 21 is a peritrophin-like protein that contains a chitin-binding domain in the sequence but does not bind chitin [17, 23]. Approximately 70–80% of HDM-allergic patients are sensitized to Der p 23, which has a molecular weight of 8 kDa [17]. All three major allergens (Der p 1, Der p 2, Der p 23) cause severe allergic symptoms and are, thus, of great clinical significance [24]. Moreover, it has been shown that childhood sensitization to HDM starts with the development of IgE antibodies to these three allergens [25].

Allergens with medium relevance

The group 5, 7 and 21 allergens of HDM are referred to as allergens of medium importance. All three have an IgE-binding frequency of about 30% and are thus not major allergens, but they have high allergenic activity [24]. Der p 5 and Der p 21 are proteins with a molecular weight of 15 kDa whose biological function is still largely unknown. Sequence homologies exist between the two allergens but no cross-reactivity; thus, they are two independent allergens [26]. Der p 7 has a molecular weight of 22 kDa and shows structural similarities with LPS-binding proteins [27]. Divergent data exist for Der p 24, which is recognized by 20–30% of HDM-allergic patients in some studies, but weakly binds IgE in most populations [25, 28]. The divergent data for Der p 24 may be due to cross-reactivity, but this has only been partially explored [29].

Allergens with low relevance

According to the current state of knowledge, the other allergens of HDM are only of minor importance or are only relevant for certain patient groups. Der p 11, the paramyosin of the mite, is of minor relevance for patients with respiratory symptoms, whereas for patients with atopic dermatitis, it is a major allergen with an IgE-binding frequency of more than 50% [30]. It is suggested that in patients with atopic dermatitis this allergen, as well as others present only in the mite body but not in the mite feces, may lead to sensitization via the skin [30]. For two other allergens (Der p 20, Der p 37), it has been shown that patients who react to these allergens suffer more frequently from asthma [31, 32]. Der p 10, mite tropomyosin, is recognized by only about 10% of mite allergic patients, but shows...
high sequence homology to tropomyosins of other invertebrates (e.g., shellfish, cockroaches, parasites, and mosquitoes) [33]. Therefore, a high cross-reactivity between tropomyosins from invertebrates can be found. Tropomyosin is the major allergen in crustaceans, where it can cause severe symptoms in allergic individuals [34].

The allergens of the storage mites and the tropical mite Blomia tropicalis

Far less well studied than HDM of the genus Dermatophagoides are the allergens of storage mites and Blomia tropicalis. Although a number of allergens have already been described in these species, little is known about their clinical significance (Tables 1 and 3). The described allergens show homologies to the corresponding groups of HDM allergens, but little cross-reactivity [8]. As with HDM, group 2 allergen is a major allergen in storage mites [35]. Interestingly, Blo t 5 and Blo t 21 have been described as the major allergens in Blomia tropicalis, but little is known about the importance of Blo t 1 and Blo t 2, and a group 23 allergen of Blomia tropicalis has not yet been described [36].

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Conflict of interest S. Vrtala declares that she has no competing interests.

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