

EDITORIAL

***Blomia tropicalis*: more than just another source of mite allergens**

Ramos et al. describe highly allergenic fragments of the paramyosin allergen, Blo t 11 from *Blomia tropicalis* [1]. This might at first appear a little esoteric but in fact it is an important and timely direction for allergy research. *B. tropicalis* is the most important allergen for allergic diseases in many tropical and subtropical regions [2, 3]. These include highly populated countries in Asia and South America. The inhabitants of these regions are rapidly adopting many aspects of Western housing and lifestyle so an asthma epidemic associated with these changes can be expected. Although the reasons for the changes are not understood, an increased incidence of asthma has already been demonstrated following urbanization in Kenya [4] and increased bronchial hyper-reactivity has been found in Estonia following the end of Soviet government [5]. The geographical range of *B. tropicalis* is also larger than initially appreciated. Tawain for example has a well-defined winter season but it is now recognized that it has a high degree of infestation and sensitization to *B. tropicalis*, albeit lower than tropical regions like Singapore [6]. It is also a problem in Western regions such as Florida, USA. *B. tropicalis* is thus already an important allergen and is likely to become one of the world's largest causes of allergic sensitization.

There are over 50 000 species of mites but *B. tropicalis* has been considered as an adjunct to the highly documented infestations of the pyroglyphid mites *Dermatophagoides pteronyssinus*, *D. farinae* and *Euroglyphus maynei*. *B. tropicalis* is a glycyphagid mite and although they have a passing resemblance to *Dermatophagoides* (Fig. 1) they are very different organisms. The amino acid sequences of the homologous proteins from these families are about 40% identical which is the same as that between *Dermatophagoides* and mammals and insects (*c.* 45% identity for trypsin and 35% for chymotrypsin). Not unexpectedly only a few of the allergens have any antigenic cross-reactivity [3, 7]. There are some exceptions and as discussed below this presents a problem in diagnosis. Not only are the homologous proteins of *B. tropicalis* for the most part antigenically different to the pyroglyphid mites but it appears that the biochemical spectra of the allergens of *B. tropicalis* and *Dermatophagoides* mites are also different. This is well documented for the group 5 allergens. These proteins of unknown biochemical function are of intermediate allergenicity for *D. pteronyssinus*, as shown by IgE antibody responses, but are major allergens for responses to *B. tropicalis* with 70% of allergic subjects recognizing these allergens [7, 8]. The IgE-binding data has only been presented in arbitrary units so it would be of interest to determine whether or not anti-Blo t 5 titres are as high as those induced by the major group 1 and 2 allergens of *Dermatophagoides*. Data on the group 1 and 2 allergens, which constitute the known major allergens of pyroglyphid mites, have not been published for *B. tropicalis*. The group 1 and 2 allergens of these species are both highly abundant and highly allergenic so the absence or paucity of these allergens in *B. tropicalis* extracts suggests either a fundamental difference in the biology of the organisms or point to properties which

influence the allergenicity of different proteins. Clearly there is a priority to determine if homologues of the group 1 and 2 allergens exist and if so whether they are major specificities. A cysteine protease with a high IgE-binding activity was recently entered in the International Union of Immunological Societies (IUIS) allergen database (www.allergen.org) by Cheung, Lee and Chua so the information could be forthcoming. A similar mystery exists for the closely related storage mite *Lepidoglyphus destructor*. Despite a large body of work investigating the allergens of this mite, no cysteine protease allergen has been identified [9]. *L. destructor* does however, have a highly allergenic group 2 allergen Lep d 2 and Johansson et al. have presented serological evidence for an IgE-binding protein with a cross-reaction to Lep d 2 in *B. tropicalis* extracts [10].

Like the *Dermatophagoides* mites, *B. tropicalis* produces a large number of allergens. Over 20 IgE-binding bands have been shown by Western blotting and by crossed radioimmuno-electrophoresis [3, 10], and several allergens have been biochemically characterized (Table 1). The allergens which have been well characterized are Blo t 5 [8], the tropomyosin Blo t 10 [11], the major Blo t 11 paramyosin allergen and the allergen Blo t 12 and 13. Blo t 12 is a protein without any known sequence homology but has a 50% IgE-binding frequency [12], and Blo t 13 is a member of a well-defined family of fatty acid binding proteins but with weak allergenicity [13]. The paramyosin allergen Blo t 11 was originally reported to bind IgE in 52% of *B. tropicalis* subjects but the present study of Ramos et al. has shown a quantitatively different result. In this different sample a recombinant peptide from Blo t 11 bound IgE in 58% of sera while the reactivity of the whole molecule was only 24% [1]. The important result here is the markedly increased reactivity of a particular peptide (336–557) and this could be useful for more definitive serology. The higher reactivity of the peptides could result from problems with the stability of natural paramyosin and with the production of fully antigenic recombinant paramyosin. This may also be reflected in the different IgE-binding frequencies in different studies. It is also possible that the real allergens in the environment are indeed peptides from degraded paramyosin [14]. Other allergens which have not been described by publication, but have recently been included in the IUIS database, are the trypsin, Blo t 3; amylase Blo t 4; the chymotrypsin Blo t 6, and another weak allergen Blo t 19, which is an anti-microbial peptide. The group 11 and 12 allergens have only been described for the *Glycyphagoidae*. The group 7 allergens have been described for *L. destructor* [9] so it is likely this protein is also allergenic in *B. tropicalis*.

The Blo t 11 paramyosin allergen examined by Ramos et al. [1] is reportedly the second most important allergen of *B. tropicalis*. This is not unexpected because paramyosin, as shown for Der f 11, is also an important allergen of the pyroglyphid mites. Der f 11 has been shown to bind IgE in 80% of sera from patients allergic to *Dermatophagoides* and it corresponds to the 95–100 000 high molecular bands noted by many investigators in Western blotting [15]. While the presence of high

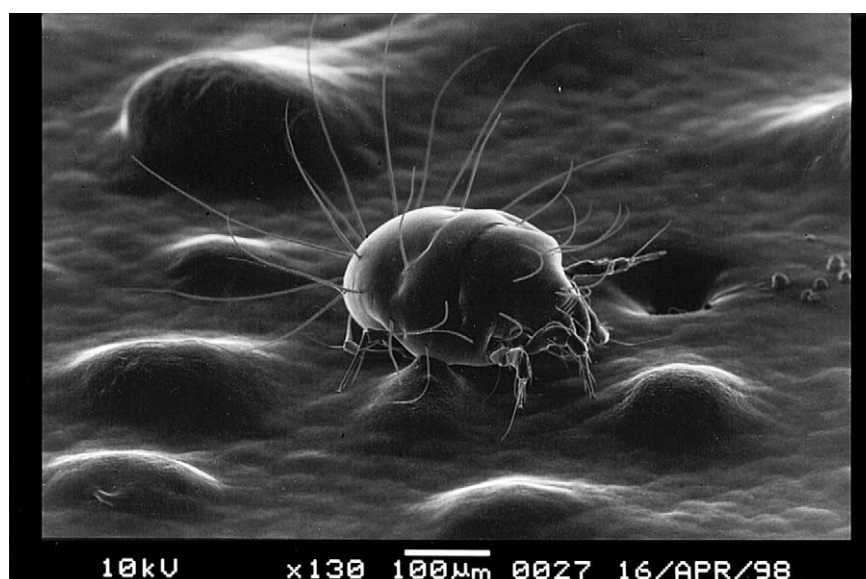


Fig. 1. Scanning electron micrograph of *Blomia tropicalis*. The mites are approximately 250 µm in length.

Table 1. Allergens of *Blomia tropicalis**

Allergen	Size (kDa)	Biochemical identity	% IgE-binding**
Blo t 5	13.9	Unknown	70
Blo t 10	33	Tropomyosin	30
Blo t 11	102	Paramyosin	57
Blo t 12	14.2	Unknown	50
Blo t 13	14.8	Fatty acid binding	10

*Additional allergens Blo t 1, 3, 4, 6 and 19 have recently been entered in the IUIS data base but no information has been published (www.allergen.org). **All IgE-binding data obtained with recombinant proteins so values could be underestimates.

molecular weight bands with high IgE-binding has been repeatedly recognized, the study of high molecular allergens has been neglected. The fragmentary information which exists however, indicates that the 98 kDa paramyosin, the 177 kDa vitellogenin/apolipoprotein-like allergen [16, 17] and the 98 kDa chitinase [18], could be as important as the group 1 and 2 allergens. These allergens which are designated group 11, 14 and 15, respectively, are difficult to study because of instability in extracts, and in the case of the group 14 and 15 allergens because the proteins undergo secondary modifications. The highly allergenic peptide described here for paramyosin is likely to expedite research into this allergen and it is possible that it may have application as a diagnostic. Similar constructs may also be useful for Der f 11 and Der p 11.

As the knowledge of mite allergens broadens, the question of the importance of biochemical function should be revisited. The group 15 allergens are interesting in this regard. As well as binding IgE in over 70% of mite-allergic sera, Der f 15 is the major allergen recognized by IgE from mite-allergic dogs and is far more allergenic than the group 1 cysteine protease allergen [18]. The fact that dogs preferentially respond to a chitinase and not to the group 1 suggests that the concept that proteolytic activity is a key adjuvant for sensitization is not straightforward. The lack of documentation of group 1 allergen for *B. tropicalis* and *L. destructor* also argues against a central

role for the importance of biochemical function in allergenicity. Either the proteins are not allergenic or they are present in low concentration, which would not be compatible with an adjuvant function. *B. tropicalis* is certainly a potent allergen which causes the same degree of allergic disease as the *Dermatophagoides* mites [2, 3, 6, 7] so the differences in the allergen profile do not appear to compromise the allergenicity. It will be of considerable interest to identify the *B. tropicalis* homologues of the group 1 and 2 allergens and to determine their immunobiology, their abundance in the environment and their aerobiological properties.

The diagnosis of allergy to *B. tropicalis* will be an increasing problem because it typically coexists with *D. pteronyssinus*. For the most part the allergens of *B. tropicalis* and *Dermatophagoides* mites are not cross-reactive but some allergens share IgE-binding specificities. Tropomyosin, with its highly conserved sequence, is an important cross-reactive specificity, both between mites and between other disparate species. The tropomyosin Blo t 10 has 96% amino acid identity to Der p 10 and Der f 10 and thus would share extensive IgE-binding activity. Studies with the recombinant Blo t 10 have shown that it induces IgE antibody in 30% of subjects but this is probably higher because the expression of mite tropomyosin has not been optimized. Paramyosin has often been proposed as a cross-reactive allergen because the paramyosin is a protective antigen in the tegument of a number of helminthic parasites. The paramyosin sequence identity between mites and helminths is however, only 50% and there is no evidence of cross-reactivity. In contrast, the sequence is highly conserved between mites. The amino acid sequence of Blo t 11 and Der f 11 has 90% identity so it is likely to be a cross-reactive allergen. Another source of cross-reactivity for *B. tropicalis* is with the closely related *L. destructor* storage mites [10]. These have mostly been associated with farming activities and hence the allergy has been readily distinguished from sensitization by the domestic exposure to *B. tropicalis*. It is possible however, that as allergic sensitization increases cosensitization to these species will increase. Reagents to distinguish the cross-reactivity within the *Glycyphagoides* will also be required.

A system of component-resolved diagnosis could have an important application for determining cross-reactivity in the diagnosis of allergy [19]. The IgE-binding to an array of the major allergens of *B. tropicalis* and *Dermatophagoides* would reveal the different reactivities. It has been shown that purified Der p 5 and Blo t 5 have little if any cross-reactivity and inclusion of the group 10 and 11 allergens would show the cross-reaction due to tropomyosin and paramyosin. The epitope analysis by Ramos et al. [1] will lead to the production of both the highly reactive allergens for the arrays and constructs which lack cross-reactivity to distinguish the mite species. Array technologies are now highly advanced and can be used for many types of clinical applications. Once established, allergen arrays can be easier to use than the multiple allergy tests currently employed and, because of the miniaturization of the technology, less reagents are required. It is anticipated that some logistical problems in the establishment of arrays with allergens from different sources and propriety interests will need to be resolved.

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W. R. THOMAS, B. J. HALES and W. SMITH
 Centre for Child Health Research
 University of Western Australia
 TVW Telethon Institute for Child Health Research
 PO Box 855, West Perth 6872, Western
 Australia
 E-mail: wayne@icmr.uwa.edu.au