



House Dust Mite-Shrimp Allergen Interrelationships

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Abstract

Purpose of Review Focusing on the strict relationship between house dust mites and crustaceans from the allergenic point of view.

Recent Findings The well-known tropomyosin was considered for years as the cross-reacting allergen between shrimp and house dust mites. In the last few years, several allergens not only in shrimps but also in house dust mite have been identified and other molecules other than tropomyosin have been shown to cross-react between crustaceans and mites.

Summary The present review investigates the very complex allergen sources in shrimp and mites, giving a satisfactorily complete picture of the interrelationships between common allergens. Several minor HDM allergens are homologous to major and minor shrimp allergens; tropomyosin is not the only cross-reactive allergen between shrimp and mites.

Keywords House dust mite allergy · Shrimp allergy · Allergen interrelationship · Recombinant allergens · Anaphylaxis · Asthma

Introduction

House dust mites (HDM) are one of the most frequent causes of respiratory allergy worldwide, and the same can be said for crustaceans in the field of food allergy. Among Italian adults, shrimp allergy ranks second as a cause of type 1 food allergy and of food-induced anaphylaxis after the plant pan-allergen lipid transfer protein [1, 2]. The present review article will focus on the strict relationship between mites and crustaceans from the allergenic point of view.

Shrimp Allergens

Since the very beginning of the studies of shrimp allergy, it was noticed that the muscle protein tropomyosin (Pen m 1), the first allergen detected in crustaceans [3–5], showed such a widespread distribution and cross-reactive nature that led to it being defined as a pan-allergen of invertebrates [5–7]. In recent years, the allergenic profile of crustaceans has grown more and more in complexity in parallel with the advances in molecular biology, and this has led to the identification of a large spectrum of allergen proteins. Table 1 lists currently identified shrimp allergens. Of the many shrimp allergens detected so far, only four, namely arginine kinase (Pen m 2; 40 kDa) [8, 9], sarcoplasmic calcium-binding protein (Pen m 4; 20–22 kDa) [10, 11], troponin C (Cra c 6; 21 kDa), and myosin light chain (Lit v 3/Pen m 3; 20 kDa) [12], are currently available for in vitro diagnostics by using multiplex assays. Other shrimp allergens identified include hemocyanin (75 kDa) [13], triose phosphate isomerase (Cra c 8; 28 kDa), paramyosin (100 kDa) [14], myosin heavy chain (225 kDa), alpha-actin (31–42 kDa), smooth endoplasmic reticulum calcium ATPase (113 kDa), glyceraldehyde phosphate dehydrogenase (37 kDa) (reviewed in [15]), pyruvate kinase, thioredoxin, and enolase. However, this is a partial list, as the spectrum of crustacean allergens appears much wider, both in the low [16] and in the high molecular weight range [17•].

This article is part of the Topical Collection on *Allergens*

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Table 1. Currently identified shrimp allergens are reported in reverse order on the basis of the molecular weight (MW) in kDa. WHO/IUIS (www.allergen.org) registered crustacean allergens are reported, when available

Biochemical name	MW	Species	Common name	Allergen
Myosin heavy chain (MHC)	200	<i>Fenneropenaeus merguensis</i>	Banana shrimp	
Smooth endoplasmic reticulum Ca ⁺⁺ ATPase (SERCA)	100			
Paramyosin (PM)	98			
Hemocyanin (HC)	75			
Pyruvate kinase (PK)	63	<i>Litopenaeus vannamei</i>	White shrimp	
Enolase (EA)	43			
Glyceraldehyde 3-phosphate dehydrogenase (GAPDH)	38			
Arginine kinase (AK)	38	<i>Crangon crangon</i>	North Sea shrimp	Cra c 2
		<i>Litopenaeus vannamei</i>	White shrimp	Lit v 2
		<i>Penaeus monodon</i>	Black tiger shrimp	Pen m 2
		<i>Procambarus clarkii</i>	Red swamp crayfish	Pro c 2
		<i>Scylla paramamosain</i>	Mud crab	Scy p 2
Tropomyosin (TM)	35	<i>Charybdis feriatus</i>	Crab	Cha f 1
		<i>Crangon crangon</i>	North Sea shrimp	Cra c 1
		<i>Homarus americanus</i>	American lobster	Hom a 1
		<i>Litopenaeus vannamei</i>	White shrimp	Lit v 1
		<i>Macrobrachium rosenbergii</i>	Giant freshwater prawn	Mac r 1
		<i>Meliceratus latisulcatus</i>	King prawn	Mel l 1
		<i>Metapenaeus ensis</i>	Shrimp	Met e 1
		<i>Pandalus borealis</i>	Northern shrimp	Pan b 1
		<i>Panulirus stimpsoni</i>	Spiny lobster	Pan s 1
		<i>Penaeus aztecus</i>	Brown shrimp	Pen a 1
		<i>Penaeus indicus</i>	Shrimp	Pen i 1
		<i>Penaeus monodon</i>	Black tiger shrimp	Pen m 1
		<i>Portunus pelagicus</i>	Blue swimmer crab	Por p 1
		<i>Procambarus clarkii</i>	Red swamp crayfish	Pro c 1
Troponin I (TnI)	30	<i>Pontastacus leptodactylus</i>	Narrow-clawed crayfish	Pon l 7
Ovary development-related protein	28	<i>Eriocheir sinensis</i>	Chinese mitten crab	Eri s 2
Triose phosphate isomerase (TIM)	27	<i>Archaeopotamobius sibiriensis</i>	Crustacean species decapod	Arc s 8
		<i>Crangon crangon</i>	North Sea shrimp	Cra c 8
		<i>Procambarus clarkii</i>	Red Swamp Crayfish	Pro c 8
		<i>Scylla paramamosain</i>	Mud Crab	Scy p 8
Troponin C (TnC)	24	<i>Crangon crangon</i>	North Sea shrimp	Cra c 6
		<i>Homarus americanus</i>	American lobster	Hom a 6
		<i>Penaeus monodon</i>	Black tiger shrimp	Pen m 6
Myosin light chain (MLC)	18	<i>Crangon crangon</i>	North Sea shrimp	Cra c 5
		<i>Crangon crangon</i>	American lobster	Hom a 3
		<i>Litopenaeus vannamei</i>	White shrimp	Lit v 3
		<i>Penaeus monodon</i>	Black tiger shrimp	Pen m 3
		<i>Procambarus clarkii</i>	Red swamp crayfish	Pro c 5
Sarcoplasmic Ca ⁺⁺ -binding protein (SCP)	18	<i>Crangon crangon</i>	North Sea shrimp	Cra c 4
		<i>Litopenaeus vannamei</i>	White shrimp	Lit v 4
		<i>Penaeus monodon</i>	Black tiger shrimp	Pen m 4
		<i>Pontastacus leptodactylus</i>	Narrow-clawed crayfish	Pon l 4
		<i>Scylla paramamosain</i>	Mud crab	Scy p 4

House Dust Mite Allergens

House dust mites (HDM) show also a very complex allergenic profile including up to 40 distinct allergens (Table 2). The presence of circulating IgE specific for four of these, namely Der p 1, Der p 2, Der p 10 (the pan-allergen tropomyosin), and Der p 23 from *Dermatophagoides pteronyssinus*, is currently detectable by in vitro singleplex assays, whereas IgE specific for Der p 5, Der p 7, Der p 11, Der p 20, and Der p 21 are detectable by a recently available multiplex assay. Der p 1, Der p 2, and Der p 23 are major allergens, and recent studies

demonstrated the strict correlation between Der p 23 hypersensitivity and the occurrence of HDM-induced asthma [17•].

Shrimp-HDM Interrelationship

The interrelationship between shrimp and HDM allergens has been recently addressed by an Italian multicenter study [18•], where shrimp-allergic patients not sensitized to the major allergen tropomyosin (Pen a 1) underwent SPT with a commercial extract of HDM; interestingly 43/62 (69%) showed clear

Table 2 House dust mite allergen list as reported in the WHO/IUIS (www.allergen.org) database

	Allergen	Biochemical name	MW	Allergen	
<i>Dermatophagoides farinae</i>	Der f 1	Cysteine protease	27	Der p 1	<i>Dermatophagoides pteronyssinus</i>
	Der f 2	NPC2 family	15	Der p 2	
	Der f 3	Trypsin	29	Der p 3	
	Der f 4	Alpha-amylase	58	Der p 4	
				Der p 5	
	Der p 6	Chymotrypsin	25	Der p 6	
	Der p 7	Bactericidal/permeability-increasing-like protein	30	Der p 7	
	Der p 8		32	Der p 8	
			29	Der p 9	
	Der p 10		37	Der p 10	
	Der p 11	Glutathione S-transferase	98	Der p 11	
	Der p 13	Fatty acid-binding protein		Der p 13	
	Der p 14	Apolipoprotein	177	Der p 14	
	Der p 15	Chitinase	98	Der p 15	
	Der p 16	Gelsolin/villin	53	Der p 16	
	Der p 17	Calcium-binding protein	53	Der p 17	
	Der p 18	Chitin-binding protein	60	Der p 18	
	Der p 20	Arginine kinase	40	Der p 20	
	Der p 21		41	Der p 21	
	Der p 22				
	Der p 23	Peritrophin-like protein	19	Der p 23	
	Der p 24	Ubiquinol-cytochrome c reductase binding protein homologue	13	Der p 24	
	Der p 25	Triosephosphate isomerase	34		
	Der p 26	Myosin alkali light chain	18		
	Der p 27	Serpin	48		
	Der p 28	Heat shock protein	70		
	Der p 29	Peptidyl-prolyl cis-trans isomerase (cyclophilin)	16		
	Der p 30	Ferritin	16		
	Der p 31	Cofilin	15		
	Der p 32	Secreted inorganic pyrophosphatase	35		
	Der p 33	Alpha-tubulin	52		
	Der p 34	Enamine/imine deaminase14	16		
	Der p 35				
	Der p 36			Der p 36	
		Petrotrophic-like protein domain	30	Der p 37	

Table 3 American and German cockroach allergen list as reported in the WHO/IUIS (www.allergen.org) database

	Allergen	Biochemical name	MV	Allergen	
American cockroach (<i>Periplaneta americana</i>)	Per a 1	Nitrile specifier-like protein	27	Bla g 1	German cockroach (<i>Blattella germanica</i>)
	Per a 2	Aspartic protease like	15	Bla g 2	
	Per a 3	Hemocyanin	29	Bla g 3	
		Calycin	58	Bla g 4	
	Per a 5	Glutathione S-transferase		Bla g 5	
	Per a 6	Troponin C	25	Bla g 6	
	Per a 7	Tropomyosin	30	Bla g 7	
		Myosin, light chain	32	Bla g 8	
	Per a 9	Arginine kinase	29	Bla g 9	
	Per a 10	Serine protease	37		
	Per a 11	Alpha-amylase	98	Bla g 11	
	Per a 12	Chitinase			
	Per a 13	Glyceraldehyde-3-phosphate dehydrogenase	177		

signs of house dust mite hypersensitivity. This proportion largely exceeded that of a control population of allergic patients sensitized to plant-derived foods, suggesting a strong allergenic similarity between invertebrates. Since the three major HDM allergens—group 1 (e.g., Der p 1), group 2 (e.g., Der p 2), and group 23 (e.g., Der p 23)—do not seem to be involved in cross-reactivity phenomena, one has to conclude that the similarities between crustaceans/molluscs and HDM are based on the homology of several minor HDM allergens characterized by conserved three-dimensional structures [19]. Conversely, 9% of house dust mite-allergic patients included in a recent Italian multicenter study vs 0% of controls (atopic patients with pollen allergy) showed shrimp allergy ($p < 0.001$), a relevant proportion if one considers that cross-reactivity does not involve the three major HDM allergens. Interestingly, shrimp allergy occurs mainly in HDM-allergic subjects who are not co-sensitized to other airborne allergens (either pollens, molds, or animal dander) [20•].

In a study by Pastorello et al. [21], patients with true shrimp allergy (i.e., a positive double-blind placebo-controlled food challenge or a documented anaphylaxis) positive to Pen a 1, that is to say to Der p 10, with positivity to Der p 1–2 had more frequent mite-induced asthma than patients positive to Der p 1–2–10 without shrimp allergy. Thus, shrimp allergy is a triggering factor for HDM asthma.

Several allergens other than tropomyosin have been found to show a cross-reactive nature (Table 3). One is arginine kinase (Der p 20) whose cross-reactive nature has been known for almost 20 years [22]. Subsequently, the cross-reactivity between shrimp myosin light chain and a house dust mite allergen was observed [16]. More recently, inhibition studies showed that shrimps and mites may share also high molecular weight allergens [18•], two of which being hemocyanin [13] and paramyosin [17•, 18•]. It is likely that the list of homologous allergens will increase in the next years.

Primary Sensitization

It is still unclear whether shrimp sensitization occurs via the respiratory or the gastrointestinal tract, or, in other words, whether it is a secondary phenomenon that follows HDM sensitization or a true primary allergy. Since virtually all shrimp-allergic patients are hypersensitive to HDM, the only way to respond to this question is to assess hypersensitivity to Der p 1, Der p 2, and Der p 23 by in vitro component-resolved diagnosis. If the patient shows IgE to one of the three major HDM allergens, primary sensitization from the respiratory tract via HDM is quite probable, a possibility, however, that remains theoretically viable also in the absence of hypersensitivity to the three mentioned allergens.

Conclusions

Since both crustaceans and HDM are very complex allergen sources, much work remains to be done before we get a satisfactorily complete picture of their interrelationships. Nonetheless, it is already clear that several minor HDM allergens are homologous to major and minor shrimp allergens and that shrimp allergy may represent in the end one further example of food allergy that originates from the airways.

Compliance with Ethics Guidelines

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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