ORIGINAL ARTICLE

House dust mite sensitization shapes the clinical expression of shellfish allergy

Enrico Scala[1], Valeria Villella[1], Damiano Abeni[1], Mauro Giani[1], Emma Cristina Guerra[1], Maria Locanto[1], Giorgia Meneguzzi[1], Lia Pirrotta[1], Donato Quaratino[1], Alessandra Zaffiro[1], Elisabetta Caprini[1], Maria Barrale[2], Ignazio Brusca[2], Valerio Pravettoni[3], Lorenzo Cecchi[4], Danilo Villalta[5], Riccardo Asero[6]

[1]Fondazione Luigi Maria Monti, IDI-IRCCS, Rome, Italy

[2]U.O.C of Clinical Pathology, Buccheri La Ferla Hospital, Palermo, Italy

[3]Department of Internal Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

[4]Allergy and Clinical Immunology Unit, San Giovanni di Dio Hospital, Florence, Italy

[5]Immunology and Allergy Unit, S. Maria degli Angeli Hospital, Pordenone, Italy

[6]Allergology Unit, Clinica San Carlo, Paderno Dugnano, Milan, Italy

Corresponding author

Enrico Scala

Fondazione Luigi Maria Monti, IDI-IRCCS

Rome, Italy

via dei Monti di Creta 104

00167 Rome, Italy

ORCID: 0000-0002-9391-9168

E-mail: e.scala@idi.it

Summary

Background. Cross-reactivity among phylogenetically distant invertebrates—such as mites, crustaceans, and mollusks—is mainly driven by conserved panallergens including tropomyosin, arginine kinase, and troponin C. However, the clinical impact and molecular basis of these cross-reactivities remain incompletely defined. **Methods.** A multicenter observational study was conducted in 3,777 patients reactive to at least one arthropod or invertebrate allergen component. Serum IgE profiles were assessed using the ALEX^{2}® multiplex platform, including allergens from mites, crustaceans, mollusks, and related taxa. Clinical data were analyzed according to molecular sensitization patterns. **Results:** Mite sensitization was detected in nearly 80% of patients, 80% of whom showed co-sensitization to other invertebrates. Sensitization to mollusks and/or crustaceans occurred in 31.9% (n = 1,207), with a marked predominance of concomitant mite sensitization (79.1% for crustaceans, 60.3% for mollusks). Clinically relevant shellfish reactions were reported in > 95% of patients co-sensitized to mites and shellfish allergens but were uncommon among those mono-sensitized to decapod or mollusk components. Tropomyosin-specific IgE was detected in > 95% of symptomatic individuals and was significantly associated with moderate-to-severe reactions ($p < 0.001$). **Conclusions.** Mite–shellfish co-sensitization defines the major molecular and clinical phenotype of shellfish allergy, supporting a model in which mite-derived tropomyosin acts as the primary sensitizer enabling cross-reactivity to homologous invertebrate proteins. In contrast, isolated shellfish sensitization rarely results in symptoms. Component-resolved diagnostics are crucial to identify at-risk patients and to avoid unnecessary dietary restrictions.

Key words

Mite sensitization; shellfish allergy; cross-reactivity; tropomyosin; molecular diagnostics; component-resolved diagnosis.

Impact statement

This observational study reveals that mite-derived tropomyosin is the primary sensitizer driving shellfish cross-reactivity, establishing mite–shellfish co-sensitization as the dominant clinical phenotype and refining risk assessment through component-resolved diagnostics.

1 | Introduction

1.1 | Background and Rationale

Although arthropods (including Blattodea, Decapoda, Hymenoptera, other Insecta, Ixodida, and Sarcoptiformes), mollusks (Mollusca), and nematodes (Nematoda) belong to distinct taxonomic phyla, they share a set of highly conserved proteins that represent major allergenic molecules. These panallergens include tropomyosin (1), arginine kinase(2–4), troponin C(5), myosin light chain(6,7), and sarcoplasmic calcium-binding protein(3,8), all of which have been implicated in IgE cross-reactivity among phylogenetically distant invertebrates (1). Such immunological recognition of homologous proteins likely reflects convergent evolutionary constraints related to motility and muscle contraction (1,9).

Sensitization to arthropods(1), mollusks(10), and crustaceans may occur through multiple exposure routes, including inhalation, ingestion, or injection (11–13). Nevertheless, the predominant pathways and their contribution to inter-species cross-sensitization remain incompletely understood (14,15). A key unresolved question concerns the origin of IgE-mediated reactivity to shellfish allergens, particularly those from crustaceans and mollusks: whether it arises from primary sensitization through dietary exposure or from cross-reactivity following initial airborne sensitization to house dust mites (16,17).

1.2 | Objective of the Study

To address this issue, we investigated the molecular and clinical relationships between sensitization to house dust mite and IgE-mediated allergic reactivity to mollusks and decapods. We analyzed data from a large multicenter Italian cohort spanning three distinct geographical regions (North, Central, and South Italy). Participants were included based on evidence of molecular sensitization to one or more allergenic components from Blattodea, Decapoda, Hymenoptera, other Insecta, Ixodida, Mollusca, Nematoda, or Sarcoptiformes, as determined by component-resolved diagnostics.

2 | Methods

2.1 | Study Design and Population

This multicenter observational study was conducted between January 2020 and December 2024 in three specialized allergy referral centers located in Northern, Central, and Southern Italy. All participants underwent molecular allergy diagnostics using a standardized multiplex proteomic platform. Patient inclusion was strictly laboratory-based: individuals were enrolled if they exhibited molecular sensitization to at least one allergenic component or extract derived from arthropod or invertebrate taxa, including Blattodea (cockroaches), Decapoda (crustaceans), Hymenoptera (bees, wasps, ants), other Insecta, Ixodida (ticks), Mollusca (mollusks), Nematoda (nematodes), and Sarcoptiformes (house dust and storage mites). Clinical data were collected at the first visit by physicians who were blinded to the molecular results. No oral food challenges were performed in cases of uncertain clinical history. Patients aged between 1 and 95 years were eligible and included. Among those sensitized to Hymenoptera (n=784), venom allergy was systematically confirmed through in vivo testing (skin prick or intradermal testing) and/or in vitro assays (ImmunoCAP), and none of these patients were excluded from the study.

2.2 | Molecular Allergy Testing

Serum specific IgE profiles were assessed using a multiplex in vitro assay (Allergy Explorer-ALEX^{2}®, MacroArray Diagnostics, Vienna, Austria), which includes 300 allergenic molecules and extracts from both inhalant and food sources (18). Emphasis was placed on structural panallergens—tropomyosin, arginine kinase, troponin C, myosin light chain, and sarcoplasmic calcium-binding protein (19)—known to mediate cross-reactivity among phylogenetically distant invertebrates.

Sensitization was defined by specific IgE levels exceeding the manufacturer's cutoff (>0.3 kU/L) for each individual component.

2.3 | Clinical Data Collection

Clinical and laboratory data were integrated through the TD-Synergy® Laboratory Information System (Siemens Healthcare Diagnostics, Munich, Germany). A customized electronic database captured patients' baseline characteristics, suspected culprit foods or aeroallergens, and the nature and severity of allergic reactions.

Food-induced allergic reactions were classified by severity as follows:

(i) Mild – isolated oropharyngeal symptoms (e.g., oral allergy syndrome);

(ii) Moderate – cutaneous or respiratory manifestations (e.g., urticaria, angioedema, asthma) without systemic involvement;

(iii) Severe – systemic anaphylaxis with hypotension, multi-organ involvement, or loss of consciousness (20,21).

The study protocol received approval from the Ethics Committee of IDI-IRCCS (approval code 492/1), and written informed consent was obtained from all participants before enrollment.

2.4 | Statistical Analysis

Statistical analyses were performed using SPSS v29 (IBM SPSS, Chicago, IL, USA). Descriptive statistics summarized demographic, clinical, and molecular data. Categorical variables were compared using the χ^2 or Fisher's exact test, and continuous variables using Student's t-test or one-way ANOVA, as appropriate.

Multivariate logistic regression models were applied to evaluate the independent association between molecular sensitization patterns and clinical severity, adjusting for potential demographic confounding confounders such as age and sex. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). A two-sided p value < 0.05 was considered statistically significant.

Venn diagrams illustrating the overlap of sensitization profiles across allergen families were generated using the VennMaster 0.38 software package (22)

3 | Results

3.1 | Study Population and General Sensitization Patterns

A total of 3,777 patients exhibiting specific IgE reactivity to at least one molecular component or extract from arthropods, mollusks, or nematodes were included in the analysis. Sensitization to Sarcoptiformes (house dust and storage mites) was identified in 2,930 individuals (77.5%), whereas 847 (22.4%) tested negative for mite allergens. Among mite-sensitized patients, 1,110/2,930 (37.8%) showed co-sensitization to at least one of the allergenic components from arthropods, mollusks, or nematodes. Reactivity to Blattodea was significantly higher among Sarcoptiformes-sensitized participants (14.5% vs 5% in mite-negative individuals, $P < 0.01$), while sensitization to insects, mollusks, and Hymenoptera was more frequent in the mite-negative group ($P < 0.01$). Sensitization to Decapoda did not differ between the two patient groups. (Table 1).

3.2 | Sensitization to Mollusks and Decapods

Sensitization to mollusks and decapods was detected in approximately 16% and 20% of patients, respectively, with mollusk reactivity being more common among mite-negative individuals (Table 1). When examining participants reactive to Decapoda (crustaceans), Mollusca (mollusks), and/or Sarcoptiformes (house dust and storage mites), corresponding to 3,265 of the 3,777 individuals included, we found that 2,261 (69.2%) of those sensitized to Sarcoptiformes did not display co-sensitization to either mollusks or decapods (Figure 1). Among patients sensitized to decapods, 79.1% (530/670) also showed IgE reactivity to mites, and 60.3% (324/537) of those reactive to mollusks were likewise mite-sensitized (Table 1 and Figure 1), supporting the hypothesis that cross-reactivity is largely driven by shared molecular epitopes. Notably, 335 individuals (10.3% of the total cohort and 33.3% of those sensitized to mollusks and/or decapods) demonstrated monosensitization to these taxa in the absence of mite reactivity, suggesting the presence of alternative sensitizing sources or distinct primary exposure routes, such as ingestion.

3.3 | Mite Sensitization and Clinical Reactivity

Clinically relevant allergic reactions to shellfish were predominantly reported among mite-sensitized patients (Table 2). In contrast, allergic symptoms were infrequent in mite-negative individuals despite

detectable specific IgE, suggesting that mite exposure may act as a priming factor for the development of clinically relevant cross-reactivity.

Over 85% of patients dually sensitized to mites and mollusks and/or decapods showed IgE reactivity to multiple species-specific mite components (e.g., Der p 1, Der p 2, Der f 1, Der f 2, Der p 5, Der p 7, Der p 21, and Der p 23), reinforcing the hypothesis that house dust mites represent the dominant sensitizing source in this subgroup. Furthermore, sensitization to tropomyosin, arginine kinase, and troponin C was detected in more than 95% of mite-sensitized individuals with concomitant reactivity to crustaceans, mollusks, or cephalopods (Table 2). Among participants sensitized exclusively to mite-derived molecules, 17 (2.4%) were positive only for Der p 10, and 68 (2%) only for Der p 20. In the Der p 10–positive group, 30 patients exhibited severe or very severe reactions, primarily to crustaceans (crab, prawns, or shrimp), whereas isolated Der p 20 sensitization was associated with only six mild reactions to lobster, squid, mussel, or oyster (data not shown).

3.4 | Allergen Component Sensitization and Reaction Severity

Univariate analyses revealed a strong association between tropomyosin-specific IgE and moderate-to-severe allergic reactions to shellfish, while an inverse relationship was observed with mild reactions. In contrast, sensitization to arginine kinase was more frequently linked to mild or localized symptoms. Systemic reactions were predominantly observed in patients reactive to troponin C or sarcoplasmic calcium-binding protein (Table 3).

In multivariate analyses, the associations with tropomyosin, arginine kinase, and sarcoplasmic calcium-binding protein remained statistically significant, confirming their independent contribution to the clinical phenotype. However, the relationship between troponin C sensitization and moderate reactions did not persist after adjustment for potential confounders.

4 | Discussion

This large multicenter study, based on molecular allergy profiling in a real-world Italian population, reinforces the central role of house dust mite sensitization—particularly to Sarcoptiformes—as a key driver of IgE cross-reactivity with homologous allergens from mollusks and decapods (1,16,19,23). Nearly 90% of participants were sensitized to house dust or storage mites, and a substantial proportion exhibited co-sensitization to phylogenetically distant invertebrate taxa.

Strikingly, 60–80% of individuals reactive to mollusk or decapod allergens also demonstrated IgE reactivity to mites, strongly supporting the concept of immunological priming through mite exposure. Conversely, 20–40% of patients sensitized to mollusk or decapod components lacked mite co-sensitization, suggesting the existence of alternative primary sensitization routes—possibly through ingestion or direct environmental exposure (23). Nevertheless, the clinical relevance of these mite-independent sensitizations appeared limited: allergic symptoms upon shellfish ingestion were reported in over 95% of mite-sensitized individuals, but were rare among mite-negative patients, despite detectable specific IgE (Table 2) (24,25). This finding underscores the pivotal role of mite-derived allergens as primary sensitizers capable of triggering clinically meaningful cross-reactivity. Supporting this notion, most clinical reactors were sensitized to species-specific major mite allergens (Der p 1, Der p 2, Der f 1, Der f 2, Der p 5, Der p 7, Der p 21, Der p 23), reinforcing the hypothesis that shellfish sensitization often originates via the respiratory route.

Molecular profiling further substantiated this paradigm: over 95% of mite-sensitized individuals exhibited IgE recognition of cross-reactive panallergens such as tropomyosin, arginine kinase, and troponin C, irrespective of the invertebrate source (crustaceans, mollusks, or cephalopods). These conserved muscle proteins likely represent the key epitopes driving cross-reactive IgE binding across taxa.

Among the allergenic components investigated, tropomyosin emerged as the most robust molecular predictor of moderate-to-severe clinical manifestations (26). In contrast, arginine kinase (2–4) and sarcoplasmic calcium-binding protein (3,8,27), were more variably associated with milder or systemic reactions, respectively, suggesting distinct pathophysiological roles and hierarchical relevance along the clinical severity spectrum (3). Most associations remained significant after adjusting for demographic confounders (age and sex), confirming the specificity and stability of these molecular patterns. Overall,

our findings highlight the pivotal contribution of mite sensitization—and the molecular overlap it entails—to the clinical expression of shellfish allergy (16,23).

The present data emphasize the diagnostic and prognostic value of component-resolved diagnostics (CRD) in evaluating suspected shellfish allergy (16). Detection of IgE to mite-derived tropomyosin serves as a highly informative biomarker for identifying patients at increased risk of systemic reactions, enabling personalized dietary counseling and tailored risk mitigation strategies—including supervised oral food challenges where appropriate (1,26,28,29).

Conversely, isolated sensitization to mollusk or decapod allergens in the absence of mite-specific IgE was associated with a markedly lower probability of clinical reactivity. This observation supports a more individualized, risk-based approach to dietary restrictions, suggesting that such patients may often avoid unnecessary food avoidance. The capacity of CRD to distinguish between genuine primary sensitizations and clinically irrelevant cross-reactivities represents a major advance in precision allergy diagnostics, allowing refined risk stratification and improving patient quality of life (1,3,10,30).

Several limitations warrant consideration. First, clinical data were primarily based on self-reported symptoms rather than standardized oral food challenges, introducing the potential for recall bias and outcome misclassification. Second, the study population consisted of Italian patients referred to tertiary allergy centers, which may limit the generalizability of the findings to other populations or regions. Finally, while the ALEX^{2}® macroarray provides extensive molecular coverage, it may not include all clinically relevant allergens—particularly novel, region-specific, or uncharacterized components (31).

In conclusion, this study provides compelling evidence that sensitization to house dust and storage mites constitutes a major risk factor for clinically relevant allergic reactions to mollusks, decapods, and related invertebrates. Tropomyosin-specific IgE emerged as the most reliable molecular predictor of reaction severity in cross-reactive individuals, underscoring its clinical value in risk assessment.

The integration of component-resolved diagnostics into routine allergy practice enhances diagnostic precision and supports personalized management strategies tailored to molecular sensitization profiles. Future prospective studies—including standardized oral food challenges, environmental exposure assessments, and longitudinal follow-up—are warranted to elucidate the immunologic mechanisms underpinning cross-reactivity and to refine individualized care pathways in invertebrate food allergy.

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Institutional Review Board Statement | The research was conducted in accordance with ethical standards outlined in the World Medical Association Declaration of Helsinki. The study protocol underwent review and approval by the IDI–IRCCS’s committee, with approval number IDI-IRCCS CE | 492/1.

Data Availability Statement | The data supporting the findings of this study are available upon request from the corresponding author. However, please note that the data are not publicly available due to privacy or ethical restrictions.

Author Contributions | E.S., V.V., and E.C. conducted the experiments and collected the data; E.S., D.V., and I.B. recruited the patients; E.S. and D.A. performed the statistical analysis; E.S. conceived the study and assisted in data interpretation and wrote the first draft of the manuscript; L.C., C.A., D.V. and R.A. assisted in data interpretation. All authors reviewed, edited, and approved the final manuscript. All authors consent to publication, confirm that this manuscript is original, has not been published previously, is not under consideration for publication elsewhere, and has not been submitted to a preprint server. All authors have read and agreed to the published version of the manuscript.

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Figure 1. Sensitization patterns to Sarcoptiformes, Mollusca, and Decapoda | The figure illustrates the distribution and overlap of specific IgE sensitization profiles to Sarcoptiformes (house dust and storage mites), Mollusca (mollusks), and Decapoda (crustaceans) in the subgroup of 3,265 patients exhibiting reactivity to at least one of these allergen groups. **Panel A** presents a crosstabulation summarizing the number and percentage of patients sensitized to each allergen group, providing a clear quantitative breakdown of isolated versus overlapping sensitization profiles. **Panel B** reports a detailed interaction table describing co-recognition patterns at the molecular level, indicating how many patients exhibit IgE reactivity to specific analytes within and across the three allergen groups. This table allows visualization of the molecular relationships driving cross-reactivity, as well as the proportion of subjects with strictly taxon-specific responses. **Panel C** shows the Venn diagram depicting the intersection of sensitization patterns across the three taxa, highlighting the proportion of patients with mono-sensitization and those with dual or triple co-sensitization.

A

N (%)	Sarcoptiformes	Decapoda	Mollusca
195 (6,0%)	(-)	(-)	(+)
122 (3,7%)	(-)	(+)	(-)
18 (0,6%)	(-)	(+)	(+)
2261 (69,2%)	(+)	(-)	(-)
139 (4,3%)	(+)	(-)	(+)
345 (10,6%)	(+)	(+)	(-)
185 (5,7%)	(+)	(+)	(+)

B

		Sarcoptiformes		Decapoda		Mollusca	
N= 3265		**(-)**	**(+)**	**(-)**	**(+)**	**(-)**	**(+)**
Sarcoptiformes	**(-)**	335 (10,3%)					
	(+)		**2930 (89,7%)**				
Decapoda	**(-)**	195 (6,0%)	2400 (73,5%)	2595 (79,5%)			
	(+)	140 (4,3%)	530 (16,2%)		**670 (20,5%)**		
Mollusca	**(-)**	122 (3,7%)	2606 (79,8%)	2261 (69,2%)	467 (14,3%)	2728 (83,6%)	
	(+)	213 (6,5%)	324 (9,9%)	334 (10,2%)	203 (6,2%)		**537 (16,4%)**

C

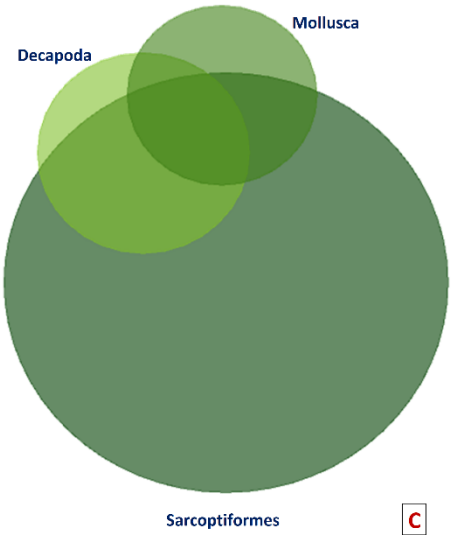

Table 1 | Demographic characteristics of the study population stratified by IgE reactivity to Sarcoptiformes. Includes age, sex distribution, and total IgE levels among mite-sensitized and non-sensitized individuals.

			Patients No (%)	Age mean±STD	Gender Male | Female		Total IgE (median)
Sarcoptiformes	Negative (847, 22.4%)	**Overall**		41±20	315 (20.5%)	532 (23.7%)	106
		Blattodea	42 (5.0%)	44±24	14 (4.4%)	28 (5.3%)	84.5
		Decapoda	140 (16.5%)	45±17	54 (17.1%)	86 (16.2%)	125
		Hymenoptera	367 (43.3%)	44±19	173 (54.9%)	194 (36.5%)	143.5
		Insect	194 (22.9%)	40±18	57 (18.1%)	137 (25.8%)	144
		Ixodida	3 (0.4%)	29±26	1 (0.3%)	2 (0.4%)	113
		Mollusca	213 (25.1%)	35±22	65 (20.6%)	148 (27.8%)	67
		Nematoda	27 (3.2%)	49±19	13 (4.4%)	14 (2.8%)	117.5
	Reactive (2930, 77.5%)	**Overall**		29±73	1220 (79.5%)	1710 (76.3%)	155
		Blattodea	425 (14.5%)	31±18	213 (17.5%)	212 (12.4%)	359
		Decapoda	530 (18.1%)	33±19	257 (21.1%)	273 (16.0%)	417
		Hymenoptera	416 (14.2%)	31±20	220 (18.0%)	196 (11.5%)	371
		Insect	481 (16.4%)	28±54	236 (19.3%)	245 (14.3%)	359
		Ixodida	14 (0.5%)	22±13	7 (0.6%)	7 (0.4%)	1182
		Mollusca	324 (11.1%)	30±17	152 (12.5%)	172 (10.1%)	303
		Nematoda	155 (5.3%)	30±21	79 (6.8%)	76 (4.7%)	471

Table 2 | Prevalence of food allergy to crustaceans and mollusks, and IgE reactivity to allergenic molecules in the overall population and in mite-sensitized versus non-sensitized individuals. Binary stratification based on IgE reactivity to Sarcoptiformes.

		House dust mite reactivity							
		Overall		Present		Absent			
Variable	**Level**	**N**	**%**	**N**	**%**	**N**	**%**	**OR (95% C.I.)**	**P**
DECAPODA (Crustaceans)		670	100%	530	79%	140	21%		
Food Allergy Symptoms	*NO*	449	67%	317	71%	132	29%	1	
	YES	221	33%	213	96%	8	4%	11.1 (5.3-23.1)	<.0001
Pen m 1 (Tropomyosin)	*Absent*	483	72%	346	72%	137	28%	1	
	Present	187	28%	184	98%	3	2%	24.3 (7.6-77.3)	<.0001
Pen m 2 (Arginine kinase)	*Absent*	478	71%	346	72%	132	28%	1	
	Present	192	29%	184	96%	8	4%	8.8 (4.2-18.3)	<.0001
Pen m 3 (Myosin light chain)	*Absent*	623	93%	496	80%	127	20%	1	
	Present	47	7%	34	72%	13	28%	0.7 (0.3-1.3)	.237
Pen m 4 (Sarcoplasmic CBP)	*Absent*	647	97%	511	79%	136	21%	1	
	Present	23	3%	19	83%	4	17%	1.3 (0.4-3.8)	.674
Cra c 6 (Troponin C)	*Absent*	592	88%	455	77%	137	23%	1	
	Present	78	12%	75	96%	3	4%	7.5 (2.3-24.2)	<.0001
MOLLUSCA (Mollusk)		537	100%	324	60%	213	40%		
Food Allergy Symptoms	*NO*	444	83%	236	53%	208	47%	1	
	YES	93	17%	88	95%	5	5%	15.5 (6.2-38.9)	<.0001
Pen m 1 (Tropomyosin)	*Absent*	421	78%	209	50%	212	50%	1	
	Present	116	22%	115	99%	1	1%	116.7 (16.1-842.9)	<.0001
Pen m 2 (Arginine kinase)	*Absent*	470	88%	259	55%	211	45%	1	
	Present	67	12%	65	97%	2	3%	26.5 (6.4-109.4)	<.0001
Pen m 3 (Myosin light chain)	*Absent*	523	97%	312	60%	211	40%	1	
	Present	14	3%	12	86%	2	14%	4.1 (0.9-18.3)	.049

Pen m 4 (Sarcoplasmic CBP)	*Absent*	529	99%	316	60%	213	40%	1	
	Present	8	1%	8	100%	0	0%	1.0 (1.0-1.0)	.021
Cra c 6 (Troponin C)	*Absent*	507	94%	295	58%	212	42%	1	
	Present	30	6%	29	97%	1	3%	20.8 (2.8-154.2)	<.0001

Table 3 | Univariate and multivariate analysis of clinical symptoms associated with IgE sensitization patterns. Association of allergic reactions with sensitization to tropomyosin and other invertebrate allergens, using Pearson's χ^2 or Fisher's exact test, and multivariate logistic regression adjusted for age, sex, and total IgE.

	Univariate					
	Mild Reaction		**Moderate Reaction**		**Severe Reaction**	
Allergen	**OR (95% C.I.)**	**P**	**OR (95% C.I.)**	**P**	**OR (95% C.I.)**	**P**
Pen m 1 (Tropomyosin)	.6 (.4-.9)	**.007**	3.4 (2.7-4.3)	***<.0001***	2.0 (1.5-2.8)	**<.0001**
Pen m 2 (Arginine Kinase)	6.1 (4.7-7.8)	**<.0001**	1.1 (.8-1.4)	*.652*	*1.1 (.7-1.6)*	.707
Cra c 6 (Troponin C)	.9 (.4-1.8)	*.751*	2.1 (1.3-3.5)	***.002***	*1.5 (.7-3.1)*	.300
Pen m 3 (Myosin light chain)	.5 (.2-1.5)	*.213*	1.6 (.9-3.0)	*.112*	*1.6 (.7-3.8)*	.295
Pen m 4 (Sarcoplasmic CBP)	.8 (.2-2.8)	*.768*	1.2 (.5-2.9)	*.681*	11.9 (5.2-27.2)	**<.0001**

	Multivariate					
	Mild Reaction		**Moderate Reaction**		**Severe Reaction**	
Allergen	**OR (95% C.I.)**	**P**	**OR (95% C.I.)**	**P**	**OR (95% C.I.)**	**P**
Pen m 1 (Tropomyosin)	0.4 (0.2-0.5)	**<.0001**	3.5 (2.8-4.5)	**<.0001**	1.9 (1.4-2.7)	**<.0001**
Pen m 2 (Arginine Kinase)	8.3 (6.2-11.0)	**<.0001**	0.7 (0.6-1.0)	*.057*	0.8 (0.5-1.3)	*.412*
Cra c 6 (Troponin C)	0.6 (0.3-1.4)	*.258*	1.3 (0.8-2.3)	*.296*	0.9 (0.4-2.1)	*.833*
Pen m 3 (Myosin light chain)	0.5 (0.2-1.4)	*.176*	1.2 (0.6-2.3)	*.548*	1.1 (0.5-2.9)	*.774*
Pen m 4 (Sarcoplasmic CBP)	0.7 (0.2-2.5)	*.552*	0.8 (0.3-2.1)	*.671*	10.5 (4.5-24.6)	**<.0001**