

Cross-reactivity between cockroach allergens and arthropod, nematode and mammalian allergens

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SUMMARY

Cockroaches (CRs) are major indoor allergens that can pose a serious risk for respiratory allergies in sensitized subjects. Recent evidence suggests that CR allergens cross-react with allergens present in insect and other invertebrates. IgE antibodies of insect-allergic subjects were shown to react with silverfish, CR and chironomid extracts. Cross-reactivity between house dust mites, silverfish, CR and chironomids and between cockroach and the reduviid, German CR and chironomids, and CRs crustacea species was established by RAST inhibition. There is some evidence that CR cross-reacts with the nematodes *Anisakis* and *Ascaris*. No cross-reactivity has been demonstrated between CR and mammalian allergens. The protein implicated in the cross-reactivity of CR with invertebrate allergens is tropomyosin. Tropomyosin has been identified as a major allergen in shrimp and other crustacea, CR, dust mites, and squid; these tropomyosins show substantial amino acid homology as well as immunological cross-reactivity. Clinical relevance of these cross-reactivities is suggested.

KEY-WORDS: Cockroaches. – Cross-reactivity. – Arthropodes. – Nematodes. – Tropomyosin.

RÉSUMÉ

Réactivité croisée entre les allergènes des blattes et les allergènes des arthropodes, des nématodes et des mammifères. – Les blattes sont un allergène domestique majeur qui constitue un risque sérieux d'allergie respiratoire chez les sujets sensibilisés. On a récemment montré l'existence d'une réactivité croisée entre les allergènes des blattes et ceux des insectes et d'autres invertébrés. Les anticorps IgE des sujets allergiques aux insectes réagissent aux extraits de lépisme (poisson d'argent), de blattes et de chironomides. Par inhibition du RAST, a été démontrée une réactivité croisée entre l'acarien de la poussière de maison, de lépisme, la blatte et les chironomides, et entre la blatte et les reduviides, la blatte germanique et les chironomides, et la blatte et l'espèce des crustacés. Il semble aussi qu'existe une réactivité croisée entre les blattes et les nématodes *Anisakis* et *Ascaris*. Aucune réaction croisée n'a été démontrée entre les blattes et les allergènes des mammifères. La protéine impliquée dans la réactivité croisée des blattes avec les allergènes d'invertébrés est la tropomyosine. La tropomyosine a été identifiée comme l'allergène majeur de la crevette et d'autre crustacés, des blattes, des acariens de la poussière et du calmar; ces tropomyosines ont une forte homologie des amino-acides aussi bien qu'une réactivité croisée immunologique. Il est suggéré que ces réactivités croisées aient des implications cliniques.

MOTS-CLÉS: Blattes. – Réactivité croisée. – Arthropodes. – Nématodes. – Tropomyosine.

INTRODUCTION

As is evident from reports in the literature [1, 2] as well as presentations in this symposium, cockroaches (CRs) are major indoor allergens that can pose a serious risk for respiratory diseases such as allergic asthma in sensitized individuals.

Indeed, in some inner-city areas in the United States CR is the single most important environmental factor with regard to the induction of asthma. CRs belong to the Phylum *Arthropoda*, class *Insecta*, order *Blattaria*, family *Blattidae* or *Blattellidae*. There are at least eight different CR species thought to be important clinically as

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causes of respiratory allergies [2]. A number of allergens have been identified, particularly in the German CR, *Blattella germanica* (Bla g 1, Bla g 2, Bla g 4, Bla g 5) and the American CR, *Periplaneta americana* (Per a 1, Per a 3, Per a 7) as these are species that have been most thoroughly investigated. Allergen cross-reactivity among American and German CR proteins has been established [1, 2], and probably occurs in most CR species investigated. However, not all allergens present in one particular species are expressed in other species. Recent evidence that CR allergens may cross-react with allergens present in insects and other invertebrates adds additional importance to CR in the induction of allergic reactions.

CROSS-REACTIVITY OF COCKROACHES WITH OTHER ARTHROPODS

The arthropods that have been most frequently investigated for cross-reactivity with CRs include members of classes *Insecta* and *Arachnida* such as caddis fly, may fly, moth and butterflies, non-biting midges (*Chironomidae*), the reduviid *Triatoma infestans* and housedust and storage mites [2, 3]. Attempts to define allergenic relationships between arthropod allergens, CRs in particular and mites have yielded contradictory results [2]. The problem with many of these studies is that cross-reactivity was neither directly determined nor allergens identified. Witteman *et al.* [4] demonstrated that IgE antibodies of insect allergic subjects react with silverfish, CR and/or chironomid extracts. RAST inhibition confirmed cross-reactivity between housedust mites and silverfish, CR and chironomid extracts. Alonso *et al.* [3] demonstrated cross-reactivity between the CR (*Periplaneta americana*) and the reduviid (*Triatoma infestans*) by RAST and RAST inhibition. Additional studies by Pascual and coworkers using CAP-inhibition and immunoblot inhibition analysis demonstrated several common IgE binding components between German CR and chironomids [5]. Another member of the *Arthropoda* phylum, although less closely related to CRs than members of the *Insecta* and *Arachnida* class, is the crustacea family. The crustacea are composed of many edible sea creatures most notably shrimp, crab, lobster, and crawfish; these crustaceans are of particular interest since they are major food allergens. IgE binding components present in boiled Atlantic shrimp and German CR were shown to cross-react [6]; similar studies [7] demonstrated that CR antigens cross-react with several crustacea species. Although CR allergens were not investigated, a related study by Eriksson

et al. [8] reported cross-reactivity between the larvae of chironomids (non-biting midges) and shrimp.

CROSS-REACTIVITY OF COCKROACHES WITH OTHER INVERTEBRATES

Pascual *et al.* [5] tested a serum pool of 18 pediatric patients with specific IgE to *Anisakis simplex* and sera from 21 German CR sensitive pediatric patients for IgE reactivity by immunoblot and immunoblot inhibition to determine whether the observed association of sensitization to nematodes and arthropods was due to immunological cross-reactivity or multiple sensitization. Immunoblot of *Anisakis* was partially inhibited with Chironomids and German CR extracts. A related study [9], investigated IgE antibody reactivity to a variety of arthropod insect inhalant allergens and the nematodes *A. simplex* and *Ascaris suis*. Anti-chicken tropomyosin demonstrated tropomyosin was the IgE binding component in arthropod and nematode extracts suggesting that this cross-reacting allergen was present in a variety of extracts from insects, mites, crustaceans, mollusks and parasites.

There is no evidence that CR and mammalian allergens cross-react even though Bla g 4 and important animal allergens such as murine urinary proteins, beta-lactoglobulin (milk), and dog, cow and horse allergens are members of the ligand-binding protein family known as lipocalins or calycins [1]. Although the sequence homology among these molecules is only about 20%, their three-dimensional structure is conserved. However, no immunological cross-reactivity or common allergenic epitopes between CR and these mammalian allergens have been demonstrated.

NATURE OF THE CROSS-REACTING ALLERGEN: TROPOMYOSIN

Tropomyosin molecule is associated with the thin filament of muscle and microfilaments in many non-muscle cells and plays a regulatory role in muscle contraction. The function of tropomyosin in non-muscle cells is not well understood, but it is generally believed to participate in the regulation of cell morphology and motility. In muscle, two parallel alpha-helical tropomyosin molecules are wound around each other forming a coiled-coil structure. Coiled-coil proteins are characterized by hapted repeats with hydrophobic amino acids spaced every four and then three residues apart.

1	10	20	30	40	50	60	70	80	90	100	110	120
MDAIKKMQAMKLEKNDAMDCEQQAARDANLRAEKAEEARSLOKKIQQJENDLDQJMEQLMQVNAKLDEKDKALQNAESEAALNRRRIQLLEEDLERSEERLATATAKLAESQAV												
Met e 1												
Pen a 1												
Pen i 1												
Hom a 1												
Pan s 1												
Tod p 1												
Der p 10												
121	130	140	150	160	170	180	190	200	210	220	230	240
DESERARKILSKGLADEERMDALENQLKEARFMAEADKKYDEVARKLAMVEADLERAEAEESKIVLEELRVVGNLKSLEVSEEEKANIREEEYKQKIKTLITRIKEAEARAE												
Met e 1												
Pen a 1												
Pen i 1												
Hom a 1												
Pan s 1												
Tod p 1												
Der p 10												
241	250	260	270	280	284							
FAERSVQKLQKEVDRLDELVHEKEKYKFCDDLDMTFTTELACY												
Met e 1												
Pen a 1												
Pen i 1												
Hom a 1												
Pan s 1												
Tod p 1												
Der p 10												

Fig. 1. — Amino acid sequences of allergenic Tropomyosins: American cockroach *Periplaneta americana* (Per a 7) [16], greasy-back shrimp *Metapenaeus ensis* (Met e 1) [12], brown shrimp *Penaeus aztecus* (Pen a 1) [14], Indian shrimp *P. indicus* (Pen i 1) [11], spiny lobster *Paralichthys stimpsoni* (Pan s 1), American lobster *Homarus americanus* (Hom a 1) [13], Pacific flying squid *Todarodes pacificus* (Tod p 1) and house dust mite *Dermatophagoides pteronyssinus* (Der p 10) [17].