Household Arthropod Allergens in Korea

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Abstract: Arthropods are important in human health, which can transmit pathogens to humans, parasitize, or produce important allergens. Allergy prevalence becomes higher in Korea recently as well as other developed countries in contrast to a decrease of infectious diseases. Allergic diseases caused by household arthropods have increased dramatically during the last few decades since human beings spend more their time for indoor activities in modernized life style. Household arthropods are one of the most common causes of allergic diseases. Biological characterization of household arthropods and researches on their allergens will provide better understanding of the pathogenesis of allergic diseases and suggest new therapeutic ways. Therefore, studies on arthropods of allergenic importance can be considered one of the major research areas in medical arthropodology and parasitology. Here, the biology of several household arthropods, including house dust mites and cockroaches, the 2 most well known arthropods living indoor together with humans worldwide, and characteristics of their allergens, especially the research activities on these allergens performed in Korea, are summarized.

Key words: allergen, allergy, arthropod, cockroach, insect, mite

INTRODUCTION

More than million species of arthropods have been reported to be present in nature. These are very important in the ecosystem, and some species of which are closely related with human health. Arthropod-borne infectious diseases are of great importance, especially in developing countries. Important human parasitic diseases transmitted by arthropods include malaria, trypanosomiasis, leishmaniasis, and filariasis. They also transmit viral diseases, such as yellow fever, dengue fever, and Japanese encephalitis [1]. Arthropods are also associated with allergic diseases. They are easily found outdoors, however, a limited number of arthropod species co-exists with human beings in our homes. Household arthropods are one of the most common causes of allergic diseases. House dust mites (HDMs) and cockroaches are the most well-known household arthropods, which produce allergenic materials to humans. People are sensitized more with HDM-derived allergens than any others [2]. In addition to these, several other household arthropods of medical importance, especially in terms of producing allergens are also found in homes. Allergy prevalence is higher in developed countries in contrast to a decrease of infectious diseases. Allergic diseases caused by household arthropods have increased dra-

Usually IgE-reactive materials are considered allergens. Parasites, especially helminths, produce excretory or secretory materials, which induce IgE responses similar to allergens. A certain kind of parasite-derived materials are true allergens, such as an Anisakis simplex antigen, Ani s 1 [5]. However, we do not consider all these parasite-derived materials as allergens. Allergens should increase the IgE level, and should also induce allergic symptoms in atopic individuals. To date, several hundred allergens have been identified from various sources of our environment, including arthropods [6]. Even though the characteristics of allergens are not possible to be determined completely, allergens can be classified into several groups based on their molecular structures or biological functions. One of the most important groups of allergens is calycins which include lipid-binding proteins, fatty acid binding proteins, and lipocalins. More than 50% of major allergens are known to be calvoins. They are normally present in body fluids and secretions in arthropods, and some are known as pheromone-binding proteins [7,8]. The protease activity is considered important to be allergenic [9]. It is believed that protease allergens can directly damage the epithelium and increase the IgE production. They also have been shown to activate protease activated receptors and subsequently lead to pro-inflammatory responses. None of the known cockroach allergens, however, are active proteases [10,11]. But serine proteases in cockroach extract can influence allergic inflammation

matically during the last few decades since humans spend more their time for indoor activities in modernized life style [3,4].

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[12]. Chitinases are reported to be allergens in HDMs [13]. Actually, chitin is found in the exoskeletons of arthropods, and seems to contribute to the development of allergic diseases. Recently, mammalian chitinases are known to play an important role in mediating Th2 cell-driven inflammation in asthma [14]. Tropomyosin was found to be a major allergenic component accounting for the cross-reactivity between insects, mites, nematodes, and crustaceans, which is also an important heat-stable food allergen [15].

INDOOR ARTHROPOD ALLERGENS

Perennial allergy rather than seasonal type is more likely to be related with indoor arthropod allergy, since indoor arthropods are always found in homes only with some fluctuation of the population density.

House dust mites

More than 40 species of mites have been found in house dust. Of these, Dermatophagoides farinae and Dermatophagoides pteronyssinus belonging to the family Pyroglyphidae and class Arachnida are found most frequently. In a narrow sense dust mites are limited to mites belonging to Pyroglyphidae, but other mites found in house dust are also medically important since they can also elicit allergic symptoms with cross-reactive or their own specific molecules. It takes approximately a month from hatching of eggs to the adult stage. Adult mites have 4 pair of legs, but the larvae have 3 pairs. An adult Dermatophagoides can survive for a few weeks to several months. The HDM feeds on various protein sources, especially shed human skin scales. HDMs take water from their daily food or absorb it from the air. One g of dust may contain several hundred to thousand HDMs. They are found mostly in mattresses, blankets, pillows, and nearby environment in man-dwelling spaces. The most favorable conditions for HDMs are 80-90% relative humidity and a temperature of 23-30°C [1]. In Korea, D. farinae has been more frequently found than D. pteronyssinus with few exceptions [16, 17]. D. farinae is supposed to be found in the environment showing lower humidity, such as apartments in the city than D. pteronyssinus. The number of mites/g dust or the group 1 allergen concentration was the highest in August or in October according to different reports. There was no difference in the HDM inhabitation density among housing, such as a public housing (apartment) and a detached house. That also showed no difference between patients' houses and healthy control people's houses. Approximately one third to a half (31.2-56.9%) of house dust contained more than 2 μ g/g of dust of group 1 allergen, which was thought to be high enough to sensitize the people. Ten % of dust samples contained more than 10 μ g/g of dust of group 1 allergen, which was supposed to be very high enough to provoke allergy symptoms [18]. To remove HDMs, frequent washing, cleaning, and drying are recommended. Mechanical laundry is an effective tool for the environmental control of allergens, water temperature, and number of rinsing is a critical factor for the removal of HDMs [19].

More than 20 groups of dust mite allergenic proteins have been identified and characterized to date [20]. Dust mite allergens and their biological characteristics and functions are summarized in Table 1. Several studies performed using HDM crude extract were reported. Production of IL-5 and IL-10 in peripheral blood mononuclear cells was significantly higher in atopic asthmatics than those of non-atopic controls by stimulation of D. farinae antigen, but IFN- γ production was not [21]. It was also reported that D. pteronyssinus extract can increase expression of MCP-1, IL-6, and IL-8 in human monocytic THP-1 cells independent on protease activity [22]. The group 1 allergen is the most important one, which is a cysteine protease. The protease enzyme activity would be important to induce allergic inflammation [23]. The patterns of IL-4 and IFN- γ production after Der p 1 stimulation and the effect on the cytokine production from T cells were evaluated, and it was found that there was a significant difference on stimulation index of IFN- γ production as well as IL-4 after Der p 1 stimulation between atopic and non-atopic individuals [24]. The function of group 2 allergen has not been completely revealed, which was suspected to be related with a male reproductive organ. However, the group 2 allergen was localized in the intestinal epithelium and its content. It was revealed by immunofluorescent antibody technique using monoclonal antibodies [25-27]. The ELISA using monoclonal antibody was set up to measure the concentration of group 2 allergen in dust [28,29]. Isoallergens of Der p 2 showed different IgE immune responses. Quantification of Der p 2 with 2-site ELISA kits might be affected by the prevalence of the isoallergens in reservoir dust [30]. Recently, Der f 2 was described to induce phospholipase D1 activation and expression of IL-13 through activation of activating transcription factor-2 in human bronchial epithelial cells [31]. The group 3, 6, and 9 allergens have serine protease activities, respectively [20]. Positive association with human leukocyte antigen class II genes and specific IgE responses to Der p 1 and Der p 2 was described in Korean

Table 1. Characteristics of house dust mite allergens

Group	Biochemical identity	Molecular weight (kDa)	Allergen	Species
1	Cysteine protease	25	Der p 1	Dermatophagoides pteronyssinus
			Der f 1	Dermatophagoides farinae
			Blot 1	Blomia tropicalis
			Pso o 1	Psoroptes ovis
2	Niemann-Pick C2 homologue	14	Der p 2	D. pteronyssinus
	Ç		Der f 2	D. farinae
			Blot2	B. tropicalis
			Tyr p 2	Tyrophagus putrescentiae
			Lep d 2	Lepidoglyphus destructor
			Gly d 2	Glycyphagus domesticus
			Aca s 2	Acarus siro
			Sui m 2	Suidasia medanensis
			Pso o 2	P. ovis
3	Trypsin	25	Der p 3	D. pteronyssinus
	,		Der f 3	D. farinae
			Der s 3	Dermatophagoides siboney
			Blot3	B. tropicalis
			Tyr p 3	T. putrescentiae
			Eur m 3	Euroglyphus maynei
			Lep d 3	L. destructor
			Gly d 3	G. domesticus
			Sar s 3	Sarcoptes scabiei
1	Alpha-amylase	56	Der p 4	D. pteronyssinus
	, upria arrytado	00	Blot 4	B. tropicalis
5	Unknown	15	Der p 5	D. pteronyssinus
,	Officiowit	10	Blot5	B. tropicalis
			Lep d 5	L. destructor
			Gly d 5	G. domesticus
3	Chymotrypsin	25	Der p 6	D. pteronyssinus
	Griyirida yediri	20	Der f 6	D. farinae
7	Unknown	24	Der p 7	D. pteronyssinus
	Gridiewii		Der f 7	D. farinae
			Lep d 7	L. destructor
			Gly d 7	G. domesticus
3	Glutathione S-transferase	26	Der p 8	D. pteronyssinus
,	Glatati ilono o tranororado	20	Lep d 8	L. destructor
			Gly d 8	G. domesticus
)	Collagenolytic serine protease	29	Der p 9	D. pteronyssinus
)	Tropomyosin	35	Der p 10	D. pteronyssinus
•	Поролнуови	55	Der f 10	D. farinae
			Blo t 10	B. tropicalis
			Tyr p 10	T. putrescentiae
			Lep d 10	L. destructor
			Gly d 10	G. domesticus
			Cho a 10	Chortoglyphus arcuatus
			Pso o 10	P. ovis
	Paramyosin	100	Der p 11	D. pteronyssinus
11	ι αιαιτιγυσιιτ	100	Der f 11	D. farinae
			Blot 11	B. tropicalis
			Pso o 11	B. Iropicalis P. ovis
			Sar s 11	S. scabiei
)	Unknown	14	Blot 12	
2	OHNHOWIT	14		B. tropicalis
			Lep d 12	L. destructor

(Continued to the next page)

Table 1. (Continued from the previous page)

Group	Biochemical identity	Molecular weight (kDa)	Allergen	Species
13	Fatty acid binding protein	15	Blo t 13	B. tropicalis
			Tyr p 13	T. putrescentiae
			Lep d 13	L. destructor
			Gly d 13	G. domesticus
			Aca s 13	A. siro
14	Vitellogenin-apolipophorin like	177	Der p 14	D. pteronyssinus
			Der f 14	D. farinae
			Pso o 14	P. ovis
15	Chitinase	63	Der f 15	D. farinae
16	Gelsolin	55	Der f 16	D. farinae
17	Calcium binding EF protein	30	Der f 17	D. farinae
18	Chitinase-like	60	Der f 18	D. farinae
19	Antimicrobial peptide	7	Blot 19	B. tropicalis
20	Arginine kinase	20	Der p 20	D. pteronyssinus
21	Unknown		Der p 21	D. pteronyssinus
			Blo t 21	B. tropicalis
22	Unknown		Der p 22	D. pteronyssinus
23	Unknown	14	Der p 23	D. pteronyssinus
24	Troponin C	18	Tyr p 24	T. putrescentiae
	lpha-tubulin	51		L. destructor
				T. putrescentiae
	Heat shock protein 70	70		D. farinae
	·			B. tropicalis

adolescents [32].

Cross-reactivity between different organisms is believed to occur due to identical or similar IgE-binding epitopes. Tropomyosin derived from *D. farinae* was named Der f 10, and was described as a major allergen initially [33]. However, tropomyosin (Der p 10) from *D. pteronyssinus* was cloned thereafter, and the IgE binding frequency of Der p 10 was reported as low as 5.6% [34].

Storage mites

Storage mites are found in our foods, such as flours, nuts, cakes or rice, and feed on plants and microorganisms. Occupational allergic diseases caused by storage mites have been reported [35]. Allergic symptoms can be also induced by ingestion of the food contaminated with storage mites. There are a number of reports that storage mite allergens are cross-reactive with HDM allergens [36]. However, storage mites are recognized as specific inhalant allergens recently [37]. A bronchial asthma case due to sensitization with *Tyrophagus putrescentiae* was reported in Korea [38]. *Blomia* spp., especially *Blomia tropicalis*, is the most commonly distributed in homes in tropical and subtropical regions, such as Southeast Asia [39,40]. The 2 most abundant species of storage mites in Europe are *Lepidoglyphus destructor* and *Euroglyphus maynei* [41,42]. Recently, *L. destructor* and *T. putrescentiae* were described as the leading causes of allergic sensitization in a gen-

eral population from warm and humid climates [37]. T. putrescentiae and Acarus siro occur worldwide and also could contribute to significant allergen levels in house dust [43]. There are many other kinds of storage mites reported worldwide which could cause an allergy [44,45]. In Korea, T. putrescentiae is the third most common species of dust mites and the most commonly found species of storage mites in home. They are found especially in the kitchen area nearby the areas where the rice is stored, which is a main food for Koreans [17]. Although the storage mite specific allergy patient has been reported rarely in Korea, sensitization to storage mites was commonly found [46]. The sensitization rate to *T. putrescentiae* was investigated to be 30.8% of 196 inhabitants in Daejeon as similar as those to D. farinae (31.2%) and *D. pteronyssinus* (29.9%). Of these, 2.6% of patients with perennial asthma showed sensitization to T. putrescentiae only. Mass rearing technique on T. putrescentiae was established for the research purpose [47]. T. putrescentiae extract showed strong cross-reactivity with D. pteronyssinus extract [48]. T. putrescentiae specific allergens have been investigated. Expressed sequence tags analysis was performed to identify possible new storage mite allergens, and the cDNA sequence encoding a protein homologous to fatty acid binding protein, a mite group 13 allergen, was identified and named Tyr p 13 [49]. Cloning and expression of α -tubulin, which sequence was also obtained from T.

putrescentiae expressed sequence tags, was performed. The deduced amino acid sequence of the α -tubulin from the storage mite showed as much as 97.3% identity to the α -tubulin sequences from other organisms. The highly conserved amino acid sequences of α -tubulins across different species of mites may indicate that cross-reactivity for this potential allergen exists [50]. A cDNA encoding troponin C, homologous to cockroach allergen Bla g 6, was also identified and named Tyr p 24 from T. putrescentiae expressed sequence tags. It shares 62.7 to 85.5% sequence identity with troponin C from various arthropods. Interestingly, the intensity of IgE binding to troponin C was increased approximately 2-fold by the addition of 10 mM CaCl₂ [51]. However, Tyr p 24 and Bla g 6 was not shown to be cross-reactive significantly. A partial cDNA sequence encoding tropomyosin was isolated from the cDNA library by immunoscreening using antimouse IgG1 sera raised against T. putrescentiae whole body extract. Full-length information of T. putrescentiae tropomyosin was obtained by reverse transcriptase-PCR (RT-PCR). The deduced amino acid sequence shares 64-94% identity with previously known allergenic tropomyosins. Recombinant Tyr p 10 showed 12.5% (5/40) IgE-binding reactivity [52]. Biological characteristics of storage mite allergens are summarized in Table 1.

Cockroaches

Cockroaches are frequently found in homes worldwide. They had been cave-dwellers with our ancestors, nowadays which are also well adapted to modern human residential areas. Over 3,500 cockroach species exist worldwide. Most of the species live outdoors, but about 50 species live in or around human houses. Reproduction occurs year-round, but do not proliferate fast compared with other insects, such as flies and midges. Their flattened body shape is rather efficient to hide in a narrow space so they can survive easily in our homes. Cockroaches feed on various plants and animal products, including human food, sewage, and garbage. Cockroaches live in kitchens, bathrooms, and other sites close to water sources, since they consume water frequently [53]. Excreta, regurgitated food, excreted body fluid, dead body, and castovers contain allergenic molecules and elicit strong allergic symptoms in genetically predisposed individuals. Major IgEbinding components of cockroach were found to be concentrated in the feces [54]. Cockroach-induced asthma is a severe form which would need intensive attention and investigation [55]. It has been reported that a cockroach allergy is an important risk factor for asthma-related emergency room visits and hospitalization [56].

Four cockroach species, the German (Blattella germanica) (36.2%), the American (Periplaneta americana) (33.3%), the Japanese (Periplaneta japonica) (1.1%), and the dusky brown (Periplaneta fuliginosa) (1.7%) cockroach, have been found to infest homes in Seoul, Korea [57]. The German cockroach, B. germanica, is the most commonly encountered species in our homes [58]. The detached house showed higher trapping rates than the apartment. At the same time sensitization rate was investigated so that the positive skin test rates were 46.2% in the healthy control group and 43.8% in the allergy patients. The positive rate of specific IgE to crude German cockroach extract in children with atopic asthma was 18.7%. Of those children, the elevated specific IgE levels both to Bla g 1 and Bla g 2 were 58.3%, respectively [59]. Very recently, the sensitization rate to cockroach allergens would have decreased in city dwellers since the garbage disposal system is improved and insecticides are supposed to be more commonly used in homes in Korea (personal communication).

The allergenicity of cockroach extract has been demonstrated in human subjects by means of skin tests, bronchial provocation tests, and RASTs [59]. Immunoblot analysis identified several allergenic components in German cockroach extract with molecular weights of 12.5 to 110 kDa [60,61]. It is generally accepted that the major German cockroach allergens are Bla g 1 and Bla g 2. Subsequently, several additional allergens, such as Bla g 4 (lipocalin or calycin), Bla g 5 (glutathione S-transferase), and Bla g 6 (troponin c) have been cloned, and their allergenicities were studied [62-65]. Compared with HDM allergens, cockroach allergens have not been studied in details relatively. Cockroach allergens and their characteristics are summarized in Table 2. German cockroach extract contains effector molecules to various human cells, which induces activation of human eosinophils to release cytotoxic inflammatory mediators, such as superoxide and granular proteins [66]. That also has a direct effect on human airway epithelial cells, in particular generating [Ca⁺⁺] oscillations through Ca⁺⁺ release from thapsigargin-sensitive Ca⁺⁺ stores through activation of PAR-2 [67]. German cockroach extract with protease activity-induced IL-8 expression is regulated by transcriptional activation of NF-κB and NF-IL6 coordinating with the ERK pathway in human airway epithelial cells [68].

Bla g 1 gene is exclusively expressed by midgut cells, up to 7 amino acid repeats were identified by dotplot matrix analysis [69]. It shows 37% sequence identity with midgut villi membrane protein from Tenebrio molitor [70], but the biological function of cockroach group 1 allergen still remains to be elucidat-

Table 2. Characteristics of cockroach allergens

Group	Biochemical identity	Molecular weight (MW)	Allergen	Species
1	Midgut microvilli protein homologue	25-90	Bla g 1	Blattella germanica
			Per a 1	Periplaneta americana
2	Aspartic protease homologue (inactive)	36	Bla g 2	B. germanica
			Per a 2	P. americana
3	Arylphorin/hemocyanin	46-79	Per a 3	P. americana
4	Lipocalin	21	Bla g 4	B. germanica
			Per a 4	P. americana
5	Glutathione S-transferase (Sigma class)	23	Bla g 5	B. germanica
6	Troponin C	17	Bla g 6	B. germanica
			Per a 6	P. americana
7	Tropomyosin	33	Bla g 7	B. germanica
			Per a 7	P. americana
			Per f 7	Periplaneta fuliginosa
8	Myosin light chain		Bla g 8	B. germanica
9	Arginine kinase	40	Per a 9	P. americana
10	Serine protease	28	Per a 10	P. americana
	Trypsin	28		B. germanica
	Glutathione S-transferase (Delta class)	25.7		B. germanica

ed. Bla g 1 shows high IgE-binding frequency but weak intensity among Korean cockroach-sensitized subjects [71]. Measurement of Bla g 1 levels has been used to estimate the exposure to cockroach allergens and exposure above 2 U/g dust is thought to be a strong risk factor for sensitization [72]. Bla g 2 was found to be the most important cockroach allergen, showing the highest prevalence of sensitization (54 to 71%) [73]. It shows primary sequence homology to aspartic proteinases. However, amino acid substitutions in the catalytic triads of the molecule suggested that Bla g 2 is inactive. High concentrations of Bla g 2 were found to be expressed in digestive organs (esophagus, gut, and proventriculus) and feces [74]. Cockroach allergens appeared to be particularly effective at sensitizing atopic individuals, considering the finding that the proposed threshold value of Bla g 2 for sensitizing is 0.08 μ g/g dust (2 U/g), whereas those of mite group 1 and cat allergens are 2 μ g/g dust and 8 μ g/g dust, respectively [75]. Bla g 4 is one of the most important German cockroach allergens, and a major IgE epitope of Bla g 4 was revealed to be located at amino acid sequences 118-152 of C-terminal. Bla g 4 has a sequence diversity [76]. A study was undertaken to compare the IgE reactivity of German cockroach GSTs, Bla g 5 (sigma class) and delta class GST (BgGSTD1). A certain serum sample with highest IgE reactivity showed a limited cross-reactivity. IgE-binding frequency to the cockroach GSTs was low, but the titer of IgE reactivity was strong in some sera [64]. Tropomyosin was cloned from the American cockroach (P. americana), Per a 7, and the purified tropomyosin could recognize 41% (12/29) of IgE-reacting sera [77,78]. A cDNA sequence encoding for the German cockroach tropomyosin, Bla g 7, was obtained, and its recombinant protein was produced [79]. Its recombinant or native protein showed 16-18% IgE reactivity to the sera tested to be a minor allergen. German cockroach tropomyosin has only minor sequence variations that did not seem to affect its allergenicity significantly [80]. Recombinant German cockroach tropomyosin expressed in Pichia pastoris showed higher allergenicity than that expressed in Escherichia coli [81]. Other factors in addition to the structural differences of native and recombinant proteins may also influence the IgE reactivity of tropomyosin. To investigate the cross-reactive allergenic components of the dusky brown cockroach, P. fuliginosa, enzymelinked immunosorbent assay inhibition and immunoblot analyses for the dusky brown cockroach were performed with B. germanica and D. farinae allergic sera. P. fuliginosa appears to possess allergens that are highly cross-reactive with allergens of B. germanica and D. farinae [82]. Tropomyosin was found to be a major allergenic component accounting for the cross-reactivity between cockroaches and dust mites [83]. Trypsin from German cockroach was found to be a putative allergen [84], and a serine protease from American cockroach was identified as a major allergen [85].

Miscellaneous indoor arthropods

Silverfish live in houses, and feed on the starch in human possessions, such as books, clothes, or beddings. Specific IgE reactivity was reported [86,87]. There are silverfish in Korean home, but no study has been performed so far. Mosquito bites



Fig. 1. Booklouse (Lipocelis sp.) isolated from a dust bag of a house-hold vacuum cleaner.

can elicit allergic reactions; IgE-mediated immediate type responses and delayed type local skin responses [88]. Rarely systemic anaphylactic reactions may occur [89], but so far no report has been available in Korea. Various species of non-biting midges, i.e. chironomids cause allergic diseases. Hemoglobin of chironomid larvae has been identified as the most important allergen found in midge-asthmatic patients [90]. Recently, analysis of adult midge Chironomus kiiensis has identified tropomyosin (Chi k 10) as an important allergen in Korea [91,92]. Cross-reactivity of allergens is an important issue. Tropomyosin from various arthropods is the most well characterized example [82]. Paramyosin, arginine kinase, and glutathione S-transferase are also considered pan-allergens [93,94]. The mayfly, caddisfly, housefly, and fruit fly were reported to be the source of allergens [95, 96]. However, no report is available in Korea. It is also well known that fire ants (Pachycondyla chinensis) contain potent allergens in their venom [97-99]. The fire ant stings and injects venomous components similar to those of wasps, which can cause systemic allergic reactions. Major allergens from P. chinensis belonging to the antigen 5 family were characterized [100]. The Pharaoh ant, Monomorium pharaonis, often infests homes and can cause respiratory allergy, which was initially reported in Korea [101]. Various kinds of arthropods, such as lady bugs, beetles, rice weevils, bedbugs, crickets, spiders, booklice (Fig. 1), pill bugs, earwigs, and flour beetles in our homes may cause allergies, but little is known about their respective allergens [102,103].

CONCLUSIONS

Human beings live together with small creatures, especially several kinds of arthropods, in homes with or without recognition. These arthropods rarely transmit infectious organisms to

humans, but they produce excreta, secretions, and leave dead bodies containing allergenic molecules. Allergic diseases have increased worldwide recently and information on household arthropod allergens also has been accumulated. Household arthropods and their allergenic products, however, need more investigation in Korea and worldwide. Studies on the characteristics, biological functions, and molecular structures of allergens, and their interactions with host cells can provide us with valuable scientific information to understand the basic mechanism for development of allergic diseases, and facilitate practical development of new therapeutic drugs in the future.

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