

Dust Mite Allergens

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Introduction

Dust mite allergy has been shown to be an independent risk factor for the development of asthma (1–3). Because of this, dust mites have been the subject of intense study for more than two decades. A considerable body of data regarding mite ecology, allergy, and allergen chemistry has now been collected and a more complete understanding of the principal dust mite species and their allergens has emerged. The most important mite species in domestic dwellings belong to the family Pyroglyphidae, although mites belonging to the families Glycyphaginae, Acaridae, and Echymyopodidae also may also be important in specific geographical locations. In this article, the physicochemical and biochemical characteristics of allergens derived from these families are presented. In addition, the immunochemical characteristics of some of the most clinically important are described. In particular, the nature and potential use of defined epitopes or regions of individual allergens that may be of use in the development of novel immunotherapeutic treatments of mite-induced allergic disease are described.

Mites and Allergens

Our understanding of the allergens produced by the pyroglyphid mites such as *Dermatophagoides pteronyssinus*, *D. farinae*, *D. microceras*, and *Euroglyphus maynei* is relatively extensive (1–6). More recently, however, data on storage mites such as *Lepidoglyphus destructor*, and tropical mites such *Blomia tropicalis* have emerged (6–8). It is now clear that each of these mite species contains several allergens and that interspecies similarities, both with regard to physicochemical and biochemical properties, are present which account for the observed immu-

nological crossreactivity. However, the absence of immunological crossreactivity does not preclude the presence of a particular allergen in a mite species, since functionally equivalent proteins may exist (7).

The complete sequences of several representative mite allergens have been determined and the biochemical roles of some of these proteins in mites *per se* have been determined. At present, the allergens may be divided into those that possess enzymatic activity and those that do not or whose biochemical properties are unknown.

Enzymatic Mite Allergens

The enzymatically active allergens are found in mite fecal pellets, and the majority are hydrolases that correspond to those commonly associated with digestion in both vertebrates and invertebrates. It is, therefore, reasonable to assume that these allergenic mite enzymes play a similar role. In mites, digestion is both extracellular and intracellular, with the latter occurring in gut wall-derived epithelial cells. These are free floating and vacuolated, and ingest and digest food particles (7). As food and cells pass into the posterior midgut, they become enveloped in a peritrophic membrane and are subsequently excreted, after water reabsorption and aggregation, as fecal pellets containing a range of enzymes and other proteins. The enzymatically active allergens present include a cysteine protease (9), several serine proteases (10,11), a carbohydrase (12), and glutathione S-transferase (13) (*see* Table 1, pp. 138–139). Mite fecal extracts also contain other enzymes including amino- and carboxypeptidases, esterases, and glycosidases (14,15). However, the allergenicity of these hydrolytic enzymes, with the possible exception of the esterases (14), remains to be determined, although it is likely that they will be recognized by some mite-allergic individuals.

Nonenzymatic Mite Allergens

In addition to the enzymatically active allergens, several others have been described but the biochemical identities of most, with the exception of a heat-shock protein (16) and a high-density lipoprotein (17), have yet to be determined despite the availability of extensive amino acid sequence data. At present, it is not clear whether these proteins are associated with digestion since their presence in fecal pellets has not been established.

Allergens and Enzymes

In general, the spectrum of digestive enzymes detected in an organism will reflect trophic specialization and there are some data to suggest that this situation may occur in mites (18). Thus, it is possible

that the enzymes (and, therefore, allergens) detected in fecal extracts will reflect the diet of the mite (7). For pyroglyphid mites, this may include protein, lipid, and carbohydrate derived from sources such as human skin scales, bacteria, and fungi, whereas in storage mites such nutrients may be derived from seed protein as well as microorganisms. As such, it is possible that there will be quantitative and or qualitative differences in the spectrum of enzymes produced by mites occupying different ecological niches and, ultimately, recognized as allergenic in susceptible individuals.

For example, skin contains a number of coiled coil structural proteins usually resistant to conventional proteases found in the digestive tracts of both invertebrates and vertebrates. These include collagen and keratin and it is possible that the mite cysteine protease (*Der p 1*) has evolved to act in concert with a reducing environment (necessary for enzyme activation) in the mite gut to specifically degrade similar proteins prior to cohabitation with humans (7). Such proteins are unlikely to be present in grain, suggesting that a similar enzyme will not be prominent in the feces of storage mites. In this regard, a major group 1 allergen has yet to be described in such species.

Mite Allergens

Mite allergens have been divided into groups on the basis of immunological and physicochemical similarities, in a manner similar to that used to differentiate allergens from related species of grass pollen. They have been assigned specific names and seven groups have been delineated by the WHO/IUIS Allergen Nomenclature Subcommittee (19). However, other mite allergens have been identified and isolated but have yet to be assigned to specific groups (Table 1). These and the allergens comprising the designated groups are now described in more detail.

Group 1 Allergens

The group 1 allergens are 25 kDa acidic to neutral proteins recognized by most mite-allergic individuals (9). The allergen is found in both whole body and fecal extracts, and is synthesized by cells lining the gastrointestinal tract of the mite (20,21). The complete sequences of the group 1 allergens from *D. pteronyssinus* and *D. farinae*, and an almost complete sequence for the group 1 allergen from *E. maynei* have been reported (9,22,23). These data indicate that the group 1 allergens are synthesized as preproteins comprising a leader peptide (18 residues) and a propeptide (80 residues) together with the mature protein (222–223 residues) (22). Analyses of the available sequence data indicate that the group I allergens are very similar (81–84% identity), with

Table 1
Physicochemical and Biochemical Characteristics of Dust Mite Allergens

Allergen	Frequency of reactivity, %	Molecular weight/ ($\times 10^{-3}$)	Number of amino acid residues	Homology and/or biological activity
<i>D. pteronyssinus</i>				
<i>Der p 1</i>	>90	25	222	Cysteine protease; shows homology with mite group 1 allergens, papain, actinidin, cathepsins B and H
<i>Der p 2</i>	>90	14	129	Function unknown
<i>Der p 3</i>	51 to >90	25	?	Trypsin; shows homology with other mite serine proteases
<i>Der p 4</i>	25–46	56	?	Amylase
<i>Der p 5</i>	55	17	?	Function unknown
<i>Der p 6</i>	39	30	?	Chymotrypsin; shows homology with other mite serine proteases
<i>Der p 7</i>	53	22 (11–29)	198	Function unknown
<i>Der p 9</i>	>90	28	?	Serine protease; shows homology with other mite serine proteases
<i>Dpt 4</i>	?	244	?	Very high density lipoprotein
<i>Dpt 36</i>	?	14	?	Function unknown; shows homology with lytic enzyme from <i>Listeria</i> spp
26 kDa allergen	?	26	219	Shows homology with glutathione S-transferase
<i>D. farinae</i>				
<i>Der f 1</i>	>90	25	223	Cysteine protease; shows homology with mite group 1 allergens, papain, actinidin, cathepsins B and H
<i>Der f 2</i>	>90	14	129	Function unknown
<i>Der f 3</i>	16–42	30	?	Trypsin; shows homology with other mite serine proteases
<i>Der f 4</i>	?	56	?	Amylase
<i>Der f 6</i>	31	30	?	Chymotrypsin; shows homology with other mite serine proteases
<i>Der f 9</i>	?	28	?	Serine protease
39 kDa allergen	?	39	?	Function unknown
67 kDa allergen	>10	67	?	Shows homology with heat shock protein 70 family

Table 1 (continued)

Allergen	Frequency of reactivity, %	Molecular weight/ ($\times 10^{-3}$)	Number of amino acid residues	Homology and/or biological activity
<i>E. maynei</i> <i>Eur m 1</i>	?	25	?	Cysteine protease; shows homology with mite group 1 allergens, papain, actinidin, cathepsins B and H
<i>L. destructor</i> <i>Lep d 1</i>	87	16-18	?	Function unknown; shows homology with group 2 allergens
79/93 kDa allergen	?	79/93	?	Function unknown
<i>B. tropicalis</i> <i>Blo t 1</i>	>47	11-13	?	Function unknown
<i>Blo t 5</i>	70	14	?	Function unknown; shows homology with mite group 5 allergens

most of the differences occurring in the N-terminal region and C-terminal half of the molecule. A potential glycosylation site at amino acid residue position 52/53 has been detected in all three sequences, but the degree of glycosylation associated with these allergens is unclear at present. The sequence data also indicated the presence of polymorphisms (24) that may correlate with the observed heterogeneity in isoelectric and chromatofocusing studies (25,26).

Homology searches indicate that the group 1 allergens belong to the cysteine group of proteolytic enzymes which include the mammalian enzymes cathepsin B and H, and the plant enzymes actinidin and papain. For example, the overall degree of homology between *Der p 1* and papain is about 31% (9,27), but increases significantly in those regions known to be involved in the catalytic site (Table 2). Recently, a structure for *Der p 1* has been modeled (27) which suggests that the structure of the allergen, with the exception of an extended N-terminus, will be very similar to that of papain and actinidin, namely, a globular protein comprising two domains held together by the N- and C-terminal ends of the peptide chain and separated by a cleft containing the catalytic site (28).

The native allergen has been shown to be proteolytically active after prior treatment with a suitable reducing reagent, such as dithiothreitol (10). Interestingly, it has been shown that concentrations of glutathione found in respiratory secretions are sufficient to activate the enzyme sug-

Table 2
Homology Among Papain, Actinidin, and *Der p 1*
in Residues Comprising the Catalytic Site

Enzyme	Sequence														
	19 ^a	22					26		64			69			133
Papain	Q	C	G	S	C	W		N	G	G	Y	P	W	V	
Actinidin	Q	C	G	S	C	W		D	G	G	Y	I	T	A	
<i>Der p 1</i>	Q	C	G	S	C	W		H	G	D	T	I	P	I	
	<i>c</i>					<i>c</i>			<i>d</i>	<i>d</i>	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>	
	157	160				175		177		205			207		
Papain	V	^e	D	H	A		N	S	W		S	S	F		
Actinidin	V	^e	D	H	A		N	S	W		M	P	S		
<i>Der p 1</i>	P	N	Y	H	A		N	S	W		Y	P	Y		
	<i>b</i>			<i>c</i>	<i>b</i>		<i>c</i>		<i>d</i>		<i>b</i>		<i>b</i>		

^aResidue numbering based on papain sequence.

^bNonpolar sidechain binding pocket.

^cResidues in catalytic site.

^dWalls of active site cleft.

^eDeleted residues.

Alignment based on refs. 9,24,27. One-letter code used for amino acids throughout.

gesting that the allergen may be proteolytically active when deposited on mucosal surfaces (29). The substrate specificity of the cysteine protease is unclear at present but the modelling studies suggest that the enzyme cleaves at basic residues, a suggestion consistent with the known specificities of other members of this family of proteins (27).

Group 2 Allergens

The group 2 allergens are 14-kDa nonglycosylated allergens recognized by the majority of mite-allergic individuals (11,30). They are neutral to basic proteins and are resistant to denaturation by heat and extremes of pH (31), and digestion by proteases (32). However, reduction and alkylation of the disulfide bonds significantly reduces the allergenicity of the protein (31). The complete amino acid sequences of the group 2 allergens from *D. pteronyssinus*, *D. farinae*, and the storage mite *L. destructor* have been obtained either by conventional means or from cDNA clones (33–36). The data obtained for *D. pteronyssinus* and *D. farinae* show that the cDNA code for preproteins with leader peptides of 11–17 residues and mature proteins of 129 residues. In contrast, the conventionally derived amino acid sequence of the mature group 2 allergen from *L. destructor* comprises 125 residues (36). The disulfide bond arrangement of the group 2 allergen has been determined and the three bonds comprise Cys8-Cys119, Cys21-Cys 27, and Cys73-78 (37) and are likely to be conserved in all three group 2 allergens.

Analyses of the three sequences indicates that the group 2 allergens from *D. pteronyssinus* and *D. farinae* are about 88% identical, whereas the degree of identity between the latter allergens and that from *L. destructor* is about 40%, although the degree of chemical similarity increases to about 85% if conservative amino acid substitutions are incorporated (36) (Table 3). In addition, the cDNA sequence studies indicate that the group 2 allergens demonstrate some polymorphism (33), the immunological significance of which has yet to be determined. Sequence homology searches have thus far failed to reveal the identity of the group 2 mite allergens, although the allergens share some overall properties with lysozyme, an enzyme associated either with defense against gram-positive bacteria or in food digestion. This suggestion is based on comparative biochemical and physicochemical data derived from studies performed on enzymes present in mite fecal and whole body extracts (38).

Group 3 Allergens

The group 3 allergens are 30-kDa proteins that have been shown to be trypsin-like enzymes on the basis of substrate specificity and amino acid sequence homology studies (39–43). These enzymes cleave at the C-terminal side of the basic amino acids arginine and lysine. At present, the data suggest that the frequency of reactivity in mite-allergic populations varies from 16% with *Der f* 3, to 100% with *Der p* 3, although the reason for this wide variation is unclear (11,39,40). Chromatofocusing studies indicated that *Der p* 3 demonstrates marked charge heterogeneity with at least nine allergenic isoforms ranging in isoelectric points from 4 to >8 (39). In contrast, two major isoforms of trypsin with pI in the range 4–4.8 were found in *D. farinae* (11,39). In this regard, several N-terminal sequences of the group 3 allergens from both *D. pteronyssinus* and *D. farinae* have been determined (Table 4). Several polymorphisms were identified and it is possible that such differences contribute to the observed charge heterogeneity. It is also clear that the sequences of *Der f* 3 and *Der p* 3 are similar, with about 85% identity in this region (Table 4).

cDNA coding for the group 3 allergen from *D. pteronyssinus* has recently been cloned (43) and the deduced sequence shown to code for a preproprotein with a 232-residue mature protein of molecular mass 24,985 Da. These data also showed that the mite trypsin lacked the typical polyaspartyl-lysyl activation peptide, suggesting that the zymogen is activated by a mechanism other than enterokinase cleavage of the lysyl-isoleucyl bond (39). The allergen showed approx 40–50% identity with both vertebrate and invertebrate trypsins, with the most significant homology present in and around the catalytic site. Biochemical

Table 3
Amino Acid Sequences of the Known Mite Group 2 Allergens^a

	10	20	30	40	50
<i>Der p 2</i>	DQVDVKDCANHEIKKVLVPGCHGSEPCIIHRGKPFQLEAVFEANQNTKTAKIEI				
<i>Der f 2</i> (2)	N	M D	D	T	L D
<i>Der f 2</i> (11)	N	M D	D	T	L D
<i>Der f 2</i> (1)	N	M D	D	T	L D
<i>Der f 2</i>	N	M D	D	T	L D
<i>Lep d 2</i>	GKMTF	GHG VTELDIT	S - T V	EKM	K A D AKVT KV
<i>Der p 2</i>	60	70	80	90	100
<i>Der f 2</i> (2)	KASIDGLEVDVPGIDPNACHYMKCPLVKGQYDIKYTNWVPKIPKSENVVVTV				
<i>Der f 2</i> (11)	L I	T F			
<i>Der f 2</i> (1)	L I	T F		A	
<i>Der f 2</i>	L I	T FV			
<i>Lep d 2</i>	L I	T F		A	
<i>Der p 2</i>	110	120			
<i>Der f 2</i> (2)	L KVA TT Q	LE DG K I	VK EAL FI SGTI	A T	V-KAD A
<i>Der f 2</i> (11)	KVMGDDGVLACAIATHAKIRD				
<i>Der f 2</i> (1)	LI N	G			
<i>Der f 2</i>	LV N				
<i>Lep d 2</i>	E	H M G-TV	QVE		

^aSequences obtained from (30-33). Only those residues different from *Der p 2* are indicated. Disulfide bonds comprise C8-C119, C21-C27, and C73-78 (37).

Table 4
N-Terminal Sequences of Mite Serine Proteases from *D. pteronyssinus*
and *D. funnae* Obtained by cDNA Analysis and Conventional Sequencing^a

Protease	Sequence																			
Mite trypsin																				
	1																		20	
<i>Der f</i> 3	I	V	G	G	V	K	A	Q	A	G	D	X	P	Y	Q	I	S	L	Q	S
<i>Der f</i> 3								L				X			E				E	V
<i>Der f</i> 3								K				X			Q					
<i>Der p</i> 3	I	V	G	G	E	K	A	L	A	G	E	X	P	Y	Q	I	S	L	^b	
<i>Der p</i> 3												Q	X					L	Q	S
<i>Der p</i> 3 cDNA	I	V	G	G	E	K	A	L	A	G	E	C	P	Y	Q	I	S	L	Q	S
Mite chymotrypsin																				
<i>Der f</i> 6	(A)	(V)	G	G	Q	D	A	D	L	A	<u>E</u>	A	P	F	Q	I	S	L	L	K
<i>Der p</i> 6	(A)	I	G	X	Q	(P)	A	A	E	(A)	(E)	A	P	F	Q	I	(S)	L	M	K

^aX indicates that identity could not be determined. Spaces indicate homology. Letters in parentheses indicate uncertainty in residue identity. Group 6 sequences showing identity with any of the trypsin-like mite allergens are indicated by bold type, whereas those residues considered to be chemically similar (A,S,T; D,E; N,Q; I,L,M,V; F,Y,W; K,R) are underlined. Sequences were obtained from refs. 39-43.

^bEnd of sequence.

studies have indicated that extracts of *E. maynei* and storage mites also contain trypsin, although the allergenicities of these enzymes have yet to be determined (18,44).

Group 4 Allergens

The group 4 allergens are 60-kDa proteins that appear to be intermediate or minor allergens (Table 1). Physicochemical studies have shown that these allergens are amylases (12) that in other species hydrolyze 1,4 glucosidic linkages to yield maltose. Group 4 equivalents have been demonstrated in most mite species examined so far including *D. pteronyssinus*, *D. farinae*, *E. maynei*, and storage mites (18,44). However, the allergenicities of the enzyme from mites other than *D. pteronyssinus* have yet to be determined. Studies indicate that the allergenicity of the group 4 allergen from *D. pteronyssinus* is dependent on the integrity of the disulfide bonds (12). The N-terminus of the group 4 amylase has been determined and the sequence obtained shows some homology to the amylases from certain insects, such as *Bombix mori*, but not to vertebrate or fungal enzymes. However, the mite enzyme is enzymatically similar to most amylases in that the enzyme contains a free sulfhydryl group (12).

Group 5 Allergens

The group 5 allergens are approx 14-kDa proteins that are recognized by about 50% of mite-allergic individuals (45). A cDNA clone for the allergen from *D. pteronyssinus* has been isolated and shown to code for a protein of 148 amino acid residues with a molecular weight slightly larger than that of the native allergen. The N-terminus of the native protein has yet to be sequenced and it is, therefore, not possible to determine whether the higher molecular weight of the deduced sequence reflects the presence of residues associated with a leader- or pro-sequence. The biochemical identity of the this protein is unknown. However, cDNA coding for an homologous protein from the tropical mite *B. tropicalis* has recently been reported (46). The *Blo t 5* allergen showed 41% homology with *Der p 5* and the allergen was recognized by 70% of a *B. tropicalis* allergic population.

Group 6 Allergens

The group 6 allergens are 25-kDa proteins that are recognized by about 40% of mite-allergic individuals (40). They have been shown to be serine proteases with specificities similar to vertebrate and invertebrate chymotrypsins, namely, a preference for substrates containing C-terminal phenylalanine and tyrosine. N-terminal sequences of both the group 6 allergens from *D. pteronyssinus* and *D. farinae* have been determined (Table 4). The data show that the two enzymes are similar to each other and, to a limited extent, the group 3 trypsins.

Group 7 Allergens

The group 7 allergens are 22-kDa proteins recognized by just over 50% of mite-allergic individuals as judged by skin test. cDNA coding for the group 7 allergen from *D. pteronyssinus* has been cloned and shown to code for a 198 mature protein with a predicted molecular mass of 22,177 Da (47). At present, the biochemical identity of this allergen is unknown despite the availability of the complete sequence. The deduced sequence indicated the presence of a potential glycosylation site and it is feasible that the allergen is glycosylated and may explain why the allergen appears in different molecular weight forms.

Heat-Shock Protein

Recently, a clone coding for an IgE binding protein from a *D. farinae* cDNA library was isolated and sequenced (16). The partial deduced amino acid sequence obtained (145 residues) showed marked sequence homology (66%) with the C-terminal region of the heat-shock cognate protein *Hcs 71* from the heat shock protein 70 family. This protein is highly conserved and can be found in bacteria, insects, plants, and

mammals. The native protein was determined to be about 67 kDa and the frequency of reactivity in a mite-allergic population was about 10%. However, this may be an underestimate given that the recombinant material used represented only a small portion of the native protein.

Glutathione S-Transferase

A cDNA clone coding for glutathione S-transferase has been cloned from a *D. pteronyssinus* library, and the expressed protein shown to be allergenic (13). These homodimeric enzymes are ubiquitous and catalyze the conjugation of reduced glutathione with a number of electrophiles. They are thought to play a major role in detoxification. The deduced sequence indicated that the mite enzyme comprises 219 amino acid residues with a molecular mass of 25,589 Da.

Other Mite Allergens

Mite allergens other than those described have been reported. For example, a 39-kDa protein has been isolated from *D. farinae* (48) and preliminary studies from our laboratory indicate that *D. pteronyssinus* contains at least three other allergens. They include a serine protease (tentatively designated group 9), which is biochemically distinct from the group 3 and 6 enzymes (49); glucoamylase; and an allergen designated *Dpt* 36 (50). The N-terminal sequence of the latter allergen has been determined and it shows some homology with a bacteriolytic enzyme from *Listeria monocytogenes*.

Epitope Mapping Studies

The availability of complete sequence data for several major mite allergens has stimulated studies to identify amino acid sequences reacting with either B- or T-cells, particularly CD4+ T-cells since the latter play a central role allergic disease. These cells recognize epitopes or fragments that have been bound by major histocompatibility complex (MHC) Class II molecules on professional antigen presenting cells. Once recognized, they become activated in the presence of other stimulatory molecules and initiate the induction and regulation of IgE mediated inflammation. Thus, any modulation of the individual components of the trimolecular complex, either epitope, T-cell, or Class II molecule, may have clinical application (51–53). For example, a variety of animal model studies indicate that T-cell unresponsiveness can be induced using immunodominant (i.e., those most readily and frequently recognized) epitopes in the absence of concomitant inflammatory signals (53). In addition to modulating T-cells, attention has also been directed to determining the epitopes recognized by antibody (B-cell epitopes).

Such an approach is based on the possibility of tolerizing allergen-specific IgE-producing B-cells, generating immunomodulatory anti-idiotypic antibodies or inducing antibodies with the capacity to sequester allergen from sensitized mast cells. With regard to mite allergens, epitopes on the group 1 and 2 allergens have been studied in some detail.

Group 1 Epitopes

Specific human T- and B-cell epitopes have been identified using both peptides and recombinant fragments representing different portions of the molecule. In this regard, data from immunochemical studies showed that the major IgE binding regions of the allergen comprised residues 15–33, 60–80, 81–94, 101–111, and 101–154 (54). On the basis of the observed structural similarity between the allergen and the plant cysteine proteases, the latter regions correspond to the peptide linking of the two domains of the molecule (27,52). Similar results have been obtained by other workers using biological assays (55). They showed that peptides corresponding to residues 52–71 and 117–133 were both potent stimulators of histamine release from sensitized human basophils, and activators of sensitized platelets. The location of *Der p* 1 T-cell epitopes has also been studied and several regions shown to stimulate either T-cell clones or peripheral blood lymphocytes (PBL). These studies indicated that residues 45–67, 117–143, and 94–104 (56), and 101–143 (57) were recognized using clones. In contrast, fragment 1–56 was the most commonly recognized region using PBL (58).

Group 2 Epitopes

Der p 2 B-cell epitopes have been located, but the degree of reactivity as expressed as the number of epitopes detected is relatively low and binding is weak. For example, studies showed that, in contrast to the whole recombinant *Der p* 2 allergen where binding was easily demonstrable, only certain sera (<10 and <40% in adult and children, respectively) recognized the two recombinant peptides representing the two halves of the molecule (59,60). These data suggest that the group 2 allergenic epitopes were conformational, a finding supported by the demonstration that disulfide bond integrity is important. Similar findings have been obtained using synthetic peptides where only two regions, namely, residues 1–15 and 65–78 weakly bound IgE (61). More recently, an epitope mapping study of native *Der p* 2 was undertaken using fragments obtained by enzymatic digestion or chemical cleavage (32). These studies indicated that the N-terminal half of the protein contained the majority of the IgG- and IgE-binding properties of this allergen, with residues 15–39 being most important.

Der p 2 T-cell epitopes have also been described in both mice and humans using T-cell clones and PBL (62–64). These studies showed that the major T cell epitopes in humans and mice mapped to residues 11–31, 22–40, 61–86, 78–104, and 105–129, with the human immunodominant regions comprising residues 11–50 and 61–104.

Epitopes on Other Allergens

At present, information on epitopes from other allergens are lacking, but two IgE binding epitopes from the 39 kDa *D. farinae* allergen have been described. They comprise residues 56–70 and 104–115, respectively (65). In addition, IgE-binding low molecular weight fragments from specific allergens, such as *Der p 3*, have been demonstrated (39). However, little is known regarding their chemical structure.

Conclusions

In this article, the physicochemical, biochemical, and immunochemical properties of the major and minor mite allergens from the clinically important mite species have been described. The data indicate that a significant number of the allergens are associated with the fecal pellet, which is consistent with the notion that these particles are the principal means by which susceptible individuals become exposed. The allergens are varied both with regard to apparent molecular weight and biochemical properties. The study of mite allergens *per se* has proved central to the development of reagents suitable for monitoring allergen in the environment and, in addition, their study may be of major significance in the therapy of allergic disease.

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