

Special report

Allergen nomenclature*

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A. Introduction

Rapid advances have been made in the past few years in allergen characterization and sequence determination by chemical and molecular biological approaches. This is indicated by the list of allergens with known partial or complete amino acid sequences in Table 1. A number of other important allergens are known in addition to those in Table 1 but their sequences are as yet not known. A useful source for known allergens is the Allergen Database (ALBE) in which are compiled their known biochemical and immunological properties together with their sequence data if known (1).

To take into account these advances, a revision of the current allergen nomenclature system (2) is given below. As in the current nomenclature system, the proposed revisions are for allergens which induce IgE-mediated (atopic) allergy in humans. In addition to the expected thorough immunochemical characterization of any newly discovered allergen, investigators are urged to obtain partial, or preferably complete, sequence data before using the official nomenclature system. Also it is expected that investigators would screen a reasonable population size so as to establish the frequency of response in patients to the newly discovered allergens.**

Investigators frequently refer to allergens as major or minor ones. The generally accepted meaning of this terminology is that an allergen is designated as either major or minor depending on whether greater or less than 50% of patients tested have the corresponding allergen-specific IgEs (cf. 3-5).

The revised nomenclature for allergens is given

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** Investigators are invited to consult our committee members for assigning an allergen number before publication so as to avoid duplication.

below together with the proposed nomenclatures for (a) allergen genes, mRNAs and cDNAs and (b) recombinant and synthetic peptides of allergenic interest.

B. Revised allergen nomenclature

1. Allergens

Allergens are designated according to the accepted taxonomic name of their source as follows: the first three letters of the genus, space, the first letter of the species, space, and an Arabic number. The numbers are assigned to the allergens in the order of their identification, and the same number is generally used to designate homologous allergens of related species. As two examples, Lol p 1 refers to the first pollen allergen identified from *Lolium perenne*, ryegrass, and Cyn d 1 refers to the homologous pollen allergen from *Cynodon dactylon*, Bermuda grass.

In some instances, the above system of the first 3 letters of a genus and the first letter of a species has to be modified to include an additional letter for designation of the exact genus or species. For example, 4 of the many vespids which can cause insect allergy are *Vespula vulgaris*, *Vespula vidua*, *Vespula consobrina* and *Vespa crabo*. The homologous major venom allergens, antigen 5s, from *Vespula vulgaris* and *Vespula vidua* are both designated as Ves v 5 in the existing nomenclature, and those from *Vespula consobrina* and *Vespa crabo* are designated as Ves c 5. To avoid these ambiguities, antigen 5s from *Vespula vulgaris* and *Vespula vidua* will be designated as Ves v 5 and Ves vi 5 respectively, and those from *Vespula consobrina* and *Vespa crabo* as Ves c 5 and Vesp c 5. In the examples given, the modified nomenclature is used for the allergens from *Vespula vidua* and *Vespa crabo*, as the allergens from *Vespula vulgaris* were characterized prior to those for *Vespula vidua* and *Vespa crabo*.

Another example is for allergens from the domestic dog (*Canis domesticus*) and the mold *Candida albicans*. To avoid ambiguity, the modified system is used to designate Can d and Cand a allergens from these two sources respectively.

In the current nomenclature system (2) the letters are italicized and the numerals are Roman numerals. In the revised system, only letters of normal type and Arabic numbers are used. The proposed changes conform to the accepted nomenclature used in bacterial genetics (6) and the HLA system (7) in that italicized and normal characters are used to represent genotypes and phenotypes respectively.

2. Allergens and isoallergens

An allergen from a single species may consist of several closely similar molecules. These similar molecules are designated as isoallergens when they share the following common biochemical properties: a. similar molecular size; b. identical biological function, if known, e.g. enzymatic action; and c. 67% identity of amino acid sequences.

It is recognized that the recommended 67% sequence identity for 2 allergens to be assigned to the same group is only a guide. There are likely to be borderline cases. As an example, the ragweed allergens Amb a 1 and 2 share 65% amino acid sequence identity (8). These allergens were assigned to different groups because of their different immunochemical properties before their sequences were known.

Allergens from different species of the same or different genus which share the above-mentioned common biochemical properties are considered to belong to the same group and the sequence identity requirement can be <67% as is the case for allergens of the same species. For example, Amb a 5 and Amb t 5 from short and giant ragweed pollens have about 45% sequence identity (9), and also have similar tertiary structures (10, 11). Another example is the minor pollen allergens Amb a 10, Poa p 10 and Lol p 10 from ragweed (12), Kentucky bluegrass (13) and ryegrass (14). Although their sequences are not known, they are assigned to the same allergen group as they clearly have the same biological function of cytochrome c.

3. Isoallergens and variants

cDNA cloning of allergens often shows nucleotide mutations which are either silent or which can lead to single or multiple amino acid substitutions. In the revised system, members of an allergen group which have $\geq 67\%$ amino acid sequence identity are designated as isoallergens. Each isoallergen may have multiple forms of closely similar sequences, which are designated as variants.

Isoallergens and their variants belonging to the

same allergen group are designated by suffixes of a period followed by four Arabic numerals. The first two numerals 01 to 99 refer to a particular isoallergen, and the two subsequent numerals 01 to 99 refer to a particular variant of a particular isoallergen designated by the preceding two numerals. In cases where there is only one known isoallergen but there are several variants, the system of a suffix of 4 numerals will still apply. These numerals will be chosen in the order of the identification of allergens and/or their cDNAs irrespective of the physicochemical properties of the allergens. In cases of silent mutations, there can be more than one suffix of 4 numerals designating the same allergen and in that case the suffix with the lowest number will be used to designate the allergen of interest.

The addition of suffixes of 4 numerals to designate isoallergens and their variants will permit their unambiguous designation. In many cases it is unnecessary to specify the isoallergen or variant and the corresponding suffixes may be deleted; e.g. Bet v 1 represents any Bet v 1 allergen and Bet v 1.0101 represents variant number 1 of isoallergen Bet v 1. Two other examples of this nomenclature system are given below.

On cDNA cloning, Amb a 1 showed multiple polymorphic forms which differ from each other by 12–24% in their sequences (8). Four such forms of Amb a 1 are known and they are designated as Amb a 1.01, 1.02, 1.03 and 1.04. Each isoallergen of the Amb a 1 group is found to have 1 to 3 variants with 97% of sequence identity. These variants of the Amb a 1.01 group will be designated as Amb a 1.0101, 1.0102, etc.

In contrast to Amb a 1, only two forms of Amb a 11 were found on cDNA cloning. These forms differ in two polymorphic sites and they have >99% amino acid sequence identity. They are designated as Amb a 2.0101 and 2.0102.

C. Nomenclature for allergen genes, mRNAs and cDNAs

At present the genomic structures of allergens are known in at least two cases; cat allergen Fel d 1 and mouse urinary allergen Mus m 1. Knowledge of the genomic structure can provide an understanding of how the different polymorphic forms are generated by differential splicing and/or exon usage. By adopting the revised nomenclature for allergens, we can reserve the italicized characters to designate an allergen gene. Normal characters are used for designation of mRNAs and cDNAs.

For example, Fel d 1 is a protein consisting of two polypeptide chains (15) which are encoded by two separate genes (16). The two allergen genes for chains 1 and 2 of Fel d 1 will be represented by *Fel*

d 1A and *Fel d 1B* respectively. Allelic forms of mRNAs and cDNAs of the *Fel d 1A* gene are designated as mRNA or cDNA *Fel d 1A.0101* where the numerals are to correspond to those of the polymorphic allergens.

D. Nomenclature for recombinant and synthetic peptides of allergenic interest

There is interest in the possible use of fragments of allergens as reagents to modulate allergen-specific immune responses. Such fragments may be prepared by recombinant technology or by chemical synthesis. Therefore it is useful to establish a generally accepted nomenclature for such peptides of allergenic interest.

The nomenclature for recombinant and synthetic peptides of allergenic interest is to be based on the nomenclature for naturally occurring allergens since it is well accepted by the scientific and the clinical communities. An allergen which is prepared by recombinant (r) or chemical synthetic (s) means is to be differentiated from a natural (n) allergen by the addition of the prefix r or s followed by a suffix of the amino acid residue positions which are given in parenthesis. For example, a recombinant hornet venom allergen Dol m 5.0201 which contains the entire sequence of 204 residues will be designated as rDol m 5.0201, and a recombinant or synthetic peptide of residue 151–165 of Dol m 5.0201 will be designated as r or sDol m 5.0201 (151–165) respectively.

Natural allergens may contain post-translational modifications as many proteins do. These modifications include glycosylation, acylation, methylation, etc. Recombinant or synthetic allergen, designated by the prefix r or s, is taken to indicate that it does not contain the post-translational modification of the natural allergen. If the recombinant or synthetic allergen does contain the exact same modification as that of the natural allergen, it will be designated by a prefix of rn or sn. For example, the honeybee venom allergen phospholipase A₂, Api m 1, is a glycoprotein with an oligosaccharide attached at the asparagine residue number 13 (17, 18). A synthetic peptide of residues 1–20 of Api m 1 without the oligosaccharide at residue 13 will be designated as sApi m 1

(1–20), and a synthetic peptide of residues 1–20 with the exact same oligosaccharide of the natural allergen will be designated as snApi m 1 (1–20).

For recombinant or synthetic fragments which are derivatives of sequences contained within the native allergen structure, an additional suffix enclosed in square brackets will be used to indicate that the peptide referred to is an analog. Substitutions or modifications of amino acid residues are given with the standard one-letter code and superscript numbers indicate the residue positions at which modifications occur. The one-letter codes for L-amino acids are given in upper-case letters and those for D-amino acids are in lower-case letters. The modifications, which can be substitution, insertion or deletion, are specified in parenthesis within the brackets. Obviously when there are many changes, it will not be practical to follow this nomenclature but to give the fully modified sequences. Examples of these analogs of sDol m 5.0201 (151–165) are given below:

Unmodified: sDol m 5.0201 (151–165)

Substitution: sDol m 5.0201 (151–165) [K¹⁵³]

– L-lysine residue at position 153 of sDol m 5.0201 (151–165) is substituted with D-lysine

Insertion: sDol m 5.0201 (151–165) [+K¹⁵³]

– one residue of L-lysine is inserted between positions 153–154

Deletion: sDol m 5.0201 (151–165) [–K¹⁵³]

– L-lysine residue at position 153 is deleted

N-terminal modification: sDol m 5.0201 (151–165) [N-Ac]

– N-terminal amino group is acetylated

C-terminal modification: sDol m 5.0201 (151–165) [C-NH₂]

– C-terminal carboxyl group is in the form of carboxamide

The nomenclature proposed above is very similar to that used for synthetic peptides representative of immunoglobulin sequences (19).

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Table 1 Some allergens with known sequences

Allergen source	Allergens; systematic and original names	MW (kDa)	Sequence data	References ¹	
A. Weed pollens					
<i>Asterales</i>					
<i>Ambrosia artemisiifolia</i> (short ragweed)	Amb a 1; antigen E	38	C	8, 20	
	Amb a 2; antigen K	38	C	8, 21	
	Amb a 3; Ra3	11	C	22	
	Amb a 5; Ra5	5	C	11, 23	
	Amb a 6; Ra6	10	C	24, 25	
	Amb a 7; Ra7	12	P	26	
	Amb a?	11	C	27	
<i>Ambrosia trifida</i> (giant ragweed)	Amb t 5; Ra5G	4.4	C	9, 10, 28	
<i>Artemisia vulgaris</i> (mugwort)	Art v 2	35	P	29	
B. Grass pollens²					
<i>Poales</i>					
<i>Cynodon dactylon</i> (Bermuda grass)	Cyn d 1	32	C	30, 31	
	<i>Dactylis glomerata</i> (orchard grass)	Dac g 1; AgDg1	32	P	32
		Dac g 2	11	C	33
<i>Lolium perenne</i> (ryegrass)	Dac g 5	31	P	34	
	Lol p 1; group I	27	C	35, 36	
<i>Phleum pratense</i> (timothy)	Lol p 2; group II	11	C	37	
	Lol p 3; group III	11	C	38	
	Lol p 5	31	P	34	
	Lol p 9; Lol p 1b	31, 35	C	39	
<i>Poa pratensis</i> (Kentucky bluegrass)	Phi p 1	27	C	40, 41	
	Phi p 5; Ag25	32	C	42, 43, 44, 45	
<i>Sorghum halepense</i> (Johnson grass)	Poa p 1; group I	33	P	46	
	Poa p 5	31	P	34	
	Poa p 9	32, 34	C	47	
<i>Sorghum halepense</i> (Johnson grass)	Sor h 1		C	48	
	C. Tree pollens				
<i>Fagales</i>					
<i>Alnus glutinosa</i> (alder)	Aln g 1	17	C	49	
	<i>Betula verrucosa</i> (birch)	Bet v 1	17	C	50
Bet v 2; profitin		15	C	51	
<i>Corylus avellana</i> (hazelnut)	Car b 1	17	C	52	
<i>Corylus avellana</i> (hazel)	Cor a 1	17	C	53	
<i>Quercus alba</i> (white oak)	Que a 1	17	P	54	
<i>Pinales</i>					
<i>Crypthomena japonica</i> (sugi)	Cry j 1	41–45	C	55, 56	
	Cry j 2		C	57, 58	

Table 1. Continued.

Allergen source	Allergens; systematic and original names	MW (kDa)	Sequence data	References ¹
<i>Juniper sabinoides</i> (mountain cedar)	Jun s 1	50	C	58
<i>Juniper virginiana</i> (eastern red cedar)	Jun v 1	45–50	C	58
Oleales				
<i>Olea europaea</i> (olive)	Ole e 1	16	C	59–60
D. Mites				
<i>Dermatophagoides pteronyssinus</i> (mite)	Der p 1; antigen P ₁ Der p 2 Der p 3; trypsin Der p 4; amylase Der p 5 Der p 6; chymotrypsin Der p 7	25 14 28–30 60 14 25 22–28	C C P P C P C	61 62 63 64 65 66 67
<i>Dermatophagoides microceras</i> (mite)	Der m 1	25	P	68
<i>Dermatophagoides farinae</i> (mite)	Der f 1 Der f 2 Der f 3	25 14 30	C C P	69 70, 71 72
<i>Lepidoglyphus destructor</i> (storage mite)	Lep d 1	15	P	73
E. Mammals				
<i>Canis domesticus</i> ³	Can d 1 Can d 2	25 27	C C	74, 75 74, 75
<i>Felis domesticus</i> (cat saliva)	Fel d 1; cat-1	38	C	15
<i>Mus musculus</i> (mouse urine)	Mus m 1; MUP	19	C	76, 77
<i>Rattus norvegicus</i> (rat urine)	Rat n 1	17	C	78, 79
F. Fungi				
<i>Aspergillus fumigatus</i>	Asp f 1 Asp f? ² Asp f? ²	18 90 55	C P P	80 81 82
<i>Candida albicans</i>	Cand a? ²	40	C	83
<i>Alternaria alternata</i>	Alt a 1	28	P	84–86
<i>Trichophyton tonsurans</i>	Tri t 1	30	P	87
G. Insects				
<i>Apis mellifera</i> (honeybee)	Api m 1; phospholipase A ₂ Api m 2; hyaluronidase Api m 4; melittin	16 44 3	C C C	88 89 90

Table 1 Continued.

Allergen source	Allergens; systematic and original names	MW (kDa)	Sequence data	References ¹
<i>Bombus pennsylvanicus</i> (bumblebee)	Bom p 1; phospholipase	16	P	91
	Bom p 4; protease		P	91
<i>Blattella germanica</i> (cockroach)	Bla g 2	20	C	92
<i>Chironomus thummi thummi</i> (midge)	Chi t 1; hemoglobin	16	C	93
<i>Dolichovespula maculata</i> (white-face hornet)	Dol m 1; phospholipase A ₁	35	C	94
	Dol m 2; hyaluronidase	44	C	95
	Dol m 5; antigen 5	23	C	96, 97
<i>Dolichovespula arenaria</i> (yellow hornet)	Dol a 5; antigen 5	23	C	98
<i>Polistes annularis</i> (wasp)	Pol a 1; phospholipase A ₁	35	P	99
	Pol a 2; hyaluronidase	44	P	99
	Pol a 5; antigen 5	23	C	98
<i>Polistes exclamans</i> (wasp)	Pol e 1; phospholipase A ₁	34	P	101
	Pol e 5; antigen 5	23	C	98
<i>Polistes fuscatus</i> (wasp)	Pol f 5; antigen 5	23	C	100
<i>Polistes metricus</i> (wasp)	Pol m 5; antigen 5	23	P	100
<i>Vespula flavopilosa</i> (yellow jacket)	Ves f 5; antigen 5	23	C	100
<i>Vespula germanica</i> (yellow jacket)	Ves g 5; antigen 5	23	C	100
<i>Vespula maculithrons</i> (yellow jacket)	Ves m 1; phospholipase A ₁	33.5	C	102
	Ves m 2; hyaluronidase	44	P	103
	Ves m 5; antigen 5	23	C	98
<i>Vespula pennsylvanica</i> (yellow jacket)	Ves p 5; antigen 5	23	C	100
<i>Vespula squamosa</i> (yellow jacket)	Ves s 5; antigen 5	23	C	100
<i>Vespula vidua</i> (wasp)	Ves vi 5	23	C	100
<i>Vespula vulgaris</i> (yellow jacket)	Ves v 1; phospholipase A ₁	35	C	99
	Ves v 2; hyaluronidase	44	P	99
	Ves v 5; antigen 5	23	C	98
<i>Vespa crabo</i> (European hornet)	Vesp c 1; phospholipase	34	P	101
	Vesp c 5.0101; antigen 5	23	C	100
	Vesp c 5.0102; antigen 5	23	C	100
<i>Solenopsis invicta</i> (fire ant)	Sol i 2	13	C	104, 105
	Sol i 3	24	C	104
	Sol i 4	13	C	104
H. Foods				
<i>Gadus callarias</i> (cod)	Gad c 1; allergen M	12	C	106

Table 1. Continued.

Allergen source	Allergens; systematic and original names	MW (kDa)	Sequence data	References
<i>Gallus domesticus</i> (chicken)	Gal d 1; ovomucoid	28	C	107, 108
	Gal d 2; ovalbumin	44	C	107, 108
	Gal d 3; conalbumin (Ag22)	78	C	107, 108
	Gal d 4; lysozyme	14	C	107, 108
<i>Penaeus aztecus</i> (brown shrimp)	Pen a 1	36	P	109
	Pen a 2; tropomyosin	34	P	110
<i>Brassica juncea</i> (oriental mustard)	Bra j 1; 2S albumin	14	C	111
<i>Hordeum vulgare</i> (barley)	Hor v 1; BMAI-1	15	C	112
<i>Sinapis alba</i> (yellow mustard)	Sin a 1; 2S albumin	14	C	113
I. Others				
<i>Ascaris suum</i> (worm)	Asc s 1	10	P	114
<i>Hevea brasiliensis</i> (rubber)	Hev b 1; elongation factor	58	P	115

¹ References refer to those where partial (P) or complete (C) sequence data are available. The original references describing the initial characterization studies are not given because of limited space. Also we apologize to our colleagues whose allergen sequence data we may have overlooked for inclusion in this table.

² Sequence data for groups 5 and 9 allergens from several grass pollens indicate that they are highly homologous proteins. Comparison of complete sequence data of groups 5 and 9 allergens from a single grass species will clarify whether these two groups are the same protein.

³ *Canis domesticus* is also designated as *Canis familiaris*.

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