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REVIEW ARTICLE

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Newly defined allergens in the WHO/IUIS Allergen Nomenclature Database during 01/2019-03/2021

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Abstract

The WHO/IUIS Allergen Nomenclature Database (http://allergen.org) provides up-to-date expert-reviewed data on newly discovered allergens and their unambiguous nomenclature to allergen researchers worldwide. This review discusses the 106 allergens that were accepted by the Allergen Nomenclature Sub-Committee between 01/2019 and 03/2021. Information about protein family membership, patient cohorts, and assays used for allergen characterization is summarized. A first allergenic fungal triosephosphate isomerase, Asp t 36, was discovered in *Aspergillus terreus*. Plant allergens contained 1 contact, 38 respiratory, and 16 food allergens. Can s 4 from Indian hemp was identified as the first allergenic oxygen-evolving enhancer protein 2 and Cic a 1 from chickpeas as the first allergenic group 4 late embryogenesis abundant protein. Among the animal allergens were 19 respiratory, 28 food, and 3 venom allergens. Important discoveries include Rap v 2, an allergenic paramyosin in molluscs, and Sal s 4 and Pan h 4, allergenic fish tropomyosins. Paramyosins and tropomyosins were previously known mainly as arthropod allergens. Collagens from barramundi, Lat c 6, and salmon, Sal s 6, were the first members from the collagen superfamily added to the database. In summary, the addition of 106 new allergens to the previously listed 930 allergens reflects the continuous linear growth of the allergen database. In addition, 17 newly described allergen sources were included.

KEYWORDS
allergen discovery, allergen protein families, novel food allergens, novel respiratory allergens, WHO/IUIS Allergen Nomenclature Database

1 | INTRODUCTION

Every scientific discipline relies on unambiguously naming and describing the molecules, cells, and organisms that are the objects of their studies. These are the tasks of the nomenclature committees that enable effective communication among the various research areas. For example, the International Union of Pure and Applied Chemistry[1] is the universally recognized authority on chemical nomenclature. The complexity of the immune system requires worldwide efforts on nomenclature issues.[2] These include consensus nomenclatures

Abbreviations: ANDB, Allergen Nomenclature Database; ANSC, Allergen Nomenclature Sub-Committee; ATP, adenosine triphosphate; BAT, basophil activation test; cDNA, complementary deoxyribonucleic acid; DPLP, defensin-polyproline-linked protein; ELISA, enzyme-linked immunosorbent assay; GRP, gibberellin-regulated protein; GST, glutathione S-transferase; HDM, house dust mite; IgE, immunoglobulin E; IUIS, International Union of Immunological Societies; nsLTP, nonspecific lipid transfer protein; OEEP2, oxygen-evolving enhancer protein 2; PR, pathogenesis-related protein; SPT, skin prick test; SSP, seed storage protein; TIM, triosephosphate isomerase; WHO, World Health Organization.

for cytokines and chemokines, their receptors, and monoclonal antibodies for phenotyping immune cells.[3] The WHO/IUIS Nomenclature Committee[4] also includes the Allergen Nomenclature Sub-Committee (ANSC), an international body of experts, currently headed by Richard E. Goodman (http://allergen.org/committee.php), who review submissions of potential allergens, assign unambiguous allergen names and maintain the allergen nomenclature database (ANDB).[5,6] The WHO/IUIS ANSC assigns official allergen names to purified natural or recombinant proteins that are characterized by standard methods of biochemistry and molecular biology and that bind IgE of individuals who are allergic to the source of the protein. The application for a unique name from the ANSC prior to publication is a key step required by most journals to ensure unambiguous communications between researchers, clinicians, pharmaceutical companies, and regulatory authorities regarding specific allergens. All 106 allergens described in this article had to undergo the same reviewing process developed by the Sub-Committee.[7] So far, 58 of these 106 allergens have been published in peer-reviewed journals after having been assigned their official names.

As the process of identifying individual allergens in various allergen sources continues worldwide, there is a steady influx of allergen submissions to the ANSC. This review covers allergens added to the official list of allergens from January 2019 to March 2021 and highlights major milestone discoveries (summarized in Box 1). Many new allergens are described as members of already well-known protein families (Figure 1 and Table S1) such as nonspecific lipid transfer proteins (nsLTPs), profilins, or tropomyosins. Thus, gaps in previously identified allergen sources are filled. Newly designated allergens are first published in the ANDB and eventually in scientific journals.

2 | RESPIRATORY ALLERGENS

2.1 | Plant-derived

Respiratory plant allergens submitted to the ANDB in the reporting period are almost exclusively from pollen. It is noteworthy, that pollen-derived bioactive components co-delivered with the allergens often contribute to the allergic sensitization process (Table 1).[14]

The common mugwort (*Artemisia vulgaris*) is the best studied *Artemisia* species in regard to its pollen allergens with a sensitization prevalence of 10%–14% among Central European pollinosis patients.[15] The major *A. vulgaris* pollen allergen Art v 1 is a defensin-polyproline-linked protein, (DPLP), a protein type found only in Asteraceae pollen.[16] DPLPs are secreted proteins with a globular N-terminal cysteine-rich domain and a C-terminal proline-rich region. Using mugwort pollen-allergic Austrian patients' sera, novel Art v 1 homologues were identified from 6 additional *Artemisia* species with high sequence identities and equivalent IgE and T-cell cross-reactivities to Art v 1.[17] Using sera from pollen-allergic Chinese subjects,[5] allergenic DPLPs were identified from 5 further *Artemisia* species. A number of other *Artemisia* pollen allergens have been recently published in the ANDB. They belong to the nsLTP or the pathogenesis-related protein family 1 (PR-1).

Snakins/gibberellin-regulated proteins (GRPs), ubiquitous plant proteins, the expression of which is controlled by gibberellin plant hormones, play a crucial role in plant growth and development.[18] GRPs were recently described as a new allergen family playing a key role in a pollen food-associated syndrome involving Cupressaceae pollen and peach and/or citrus fruits.[19,20] The natural GRP, Cup s 7, from Mediterranean cypress (*Cupressus sempervirens*) pollen showed IgE-binding characteristics highly similar to the GRPs from peach, Pru p 7, and pomegranate, Pun g 7.[21] Pru p 7-homologous pollen allergens isolated from *Cryptomeria japonica* (Japanese cedar, Cry j 7) and *Juniperus ashei* (Ashe juniper, Jun a 7) will aid in the identification of Cupressaceae pollinosis patients at risk of developing fruit allergy with moderate and severe systemic symptoms.[22]

As profilins, ubiquitous cross-reactive plant proteins, are significantly associated with allergy to grass pollen and to Cucurbitaceae fruits,[23] the clinical impact of profilin sensitizations is being continuously updated and expanded.[24] Three new profilins received official designations, Pop n 2 from the black poplar (*Populus nigra*),[25] Amb t 8 from giant ragweed (*Ambrosia trifida*) pollen,[5] and Can s 2 from hemp (*Cannabis sativa*).[26] The profilin from sawtooth oak, Que ac 2, was also included in the ANDB.

PR-10 proteins are conserved ligand-binding plant proteins.[27] PR-10 allergens from birch and related trees of the families *Betulaceae* and *Fagaceae* are cross-reactive and a major cause of allergic rhinitis.[28] Although published earlier,[29] Que m 1, the PR-10 from the dominant Korean oak species *Quercus mongolica*, was only accepted in 2019 by the ANSC. Recombinant Que m 1 was able to inhibit IgE-binding to Bet v 1, indicating a strong cross-reactivity. Que i 1, the PR-10 from *Quercus ilex* pollen, was identified as the sensitizing allergen for pollen-food syndrome in Spanish patients not exposed to birch pollen.[30] Can s 5, a Bet v 1-homologue, was identified in cannabis-allergic subjects. The immunogenicity of the recombinant protein was evaluated by cytometric bead and mast cell activation assays.[26] Another sawtooth oak allergen, Que ac 1,[5] a PR-10 member, was identified in Korea by ELISA and Western blots.

Expansins are key endogenous regulators of plant cell enlargement which loosen the cell wall's network of polysaccharides.[31] Group 1 grass pollen allergens comprise a distinctive clade within the beta-expansin family and are needed for pollen separation and stigma penetration.[32] Group 2 and 3 grass pollen allergens are expansin-like proteins that contain only the expansin C-terminal region. Phl p 3 from timothy grass (*Phleum pratense*) is another example of an allergen that was published much earlier[33] but only entered into the ANDB in 2020. Zoy m 1, a group 1 allergen from the tropical and subtropical Manila grass (*Zoysia matrella*) is another recent addition to the ANDB.

Cobalamin-independent methionine synthases are zinc-binding methyltransferases that catalyze the *de novo* methionine biosynthesis in higher plants.[34] Mor a 2, the vitamin B12-independent enzyme, was identified as an allergen from white mulberry (*Morus alba*) pollen.[5]The oxygen-evolving enhancer protein 2 (OEEP2) is implicated in photosynthetic oxygen evolution, and it is associated with the

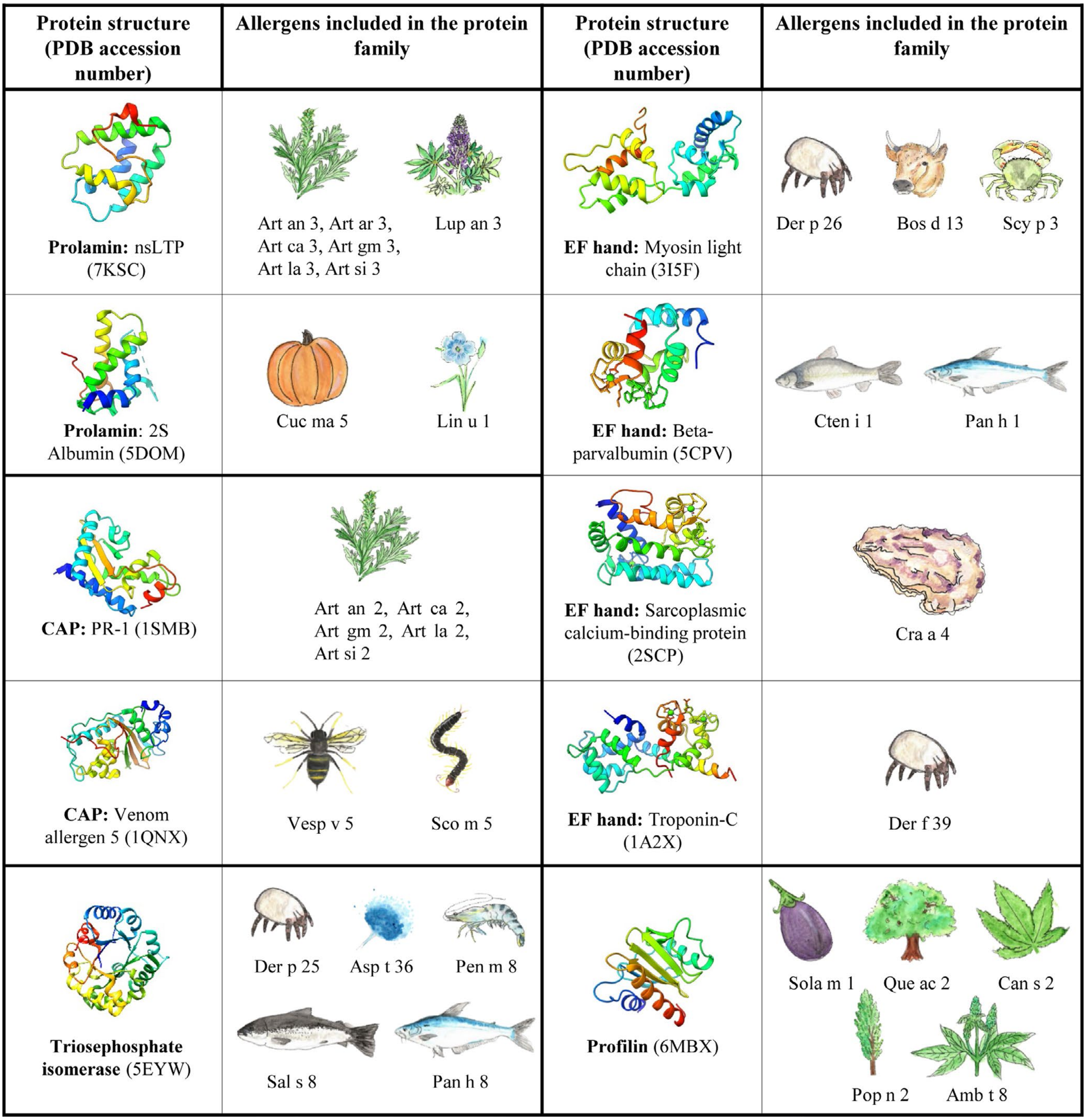

FIGURE 1 Protein superfamilies/families with the highest numbers of allergens defined from 01/2019 to 03/2021. Ribbon representations of available structures from homologues of the new allergens. Prolamin superfamily: nsLTP (PDB accession number: 7KSC, organism: *Punica granatum*), 2S albumin (5DOM, *Moringa oleifera*). CAP superfamily: PR-1 (1SMB, *Homo sapiens*), venom allergen 5 (1QNX, *Vespula vulgaris*). Triosephosphate isomerase family: triosephosphate isomerase from *Litopenaeus vannamei* (5EYW). EF-hand family: myosin light chain (3I5F, *Todarodes pacificus*), beta-parvalbumin (5CPV, *Cyprinus carpio*), sarcoplasmic calcium-binding protein (2SCP, *Hediste diversicolor*), troponin C (1A2X, *Oryctolagus cuniculus*). Profilin family: profilin from *Cucumis melo* (6MBX). Molecular graphics were done with UCSF ChimeraX, developed by the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco

photosystem II complex. Can s 4, the OEEP2 from *Cannabis sativa* leaves was expressed in *E. coli* and found to play a role, albeit a small one, in a Northwestern European study population of 113 cannabis-allergic individuals.[8] Functional tests indicated that both Can s 3 and Can s 4 may participate in eliciting clinical symptoms.

2.2 | Animal-derived

The phylum Arthropoda which includes insects and mites among others contains more species than any other animal phylum. Hence, many allergens are derived from arthropods.[35]

BOX 1 Major milestone discoveries

- 106 allergens were added to the ANDB during 01/2019-03/2021, of which 58 were already published in scientific journals.
- 55 plant allergens (1 contact, 38 respiratory, and 16 food allergens), 50 animal allergens (19 respiratory, 28 food, and 3 venom allergens), and 1 fungal allergen were identified.
- First allergens identified from a specific protein group:
  - a. Oxygen-evolving enhancer protein 2 from Indian hemp (Can s 4)[8]
  - b. Filamin from mud crab (Scy p 9)[5]
  - c. Collagens alpha from barramundi (Lat c 6)[9] and Atlantic salmon (Sal s 6)[10]
  - d. Glucose-6-phosphate isomerase from striped catfish (Pan h 11)[10]
  - e. Group 4 late embryogenesis abundant protein from chickpea (Cic a 1)[11]
- Allergen families expanded to additional species:
  - a. Asp t 36,[12] first allergenic fungal triosephosphate isomerase (from *Aspergillus terreus*)
  - b. Rap v 2,[13] first allergenic paramyosin in molluscs (from *Rapana venosa*)
  - c. Sal s 4[10] and Pan h 4,[10] first allergenic tropomyosins in fish
  - d. Sal s 7[10] and Pan h 7,[10] first allergenic creatine kinases in fish

A study aiming to improve diagnostics of allergy to the mold mite *Tyrophagus putrescentiae* identified numerous allergens.[36] Tyr p 1 was identified as an allergenic cysteine protease. Tyr p 7 is a bactericidal permeability-increasing protein of the lipid-binding serum glycoprotein family. Tyr p 20 is an arginine kinase, a member of ATP:guanido phosphotransferases which reversibly catalyze the transfer of phosphate group between ATP and other phosphogens.[37] Although this study identified several novel allergens, their clinical relevance is yet to be investigated in detail.

The EF-hand family includes calcium-binding proteins whose functions include signal transduction of calcium as a second messenger.[38] This family contains allergens from pollens, fish, crustaceans, and cockroaches.[39] In a hybrid-assembled genome study of the European house dust mite (HDM), the authors identified various putative novel allergens, including the myosin light chain, Der p 26, shown to be IgE-reactive by skin prick test (SPT) and ELISA.[40] The Der f 39 allergen from American HDM, a troponin C, was another recent addition to the ANDB which was recognized by IgE from 7/76 subjects tested.

Der p 25,[40] the glycolytic enzyme triosephosphate isomerase (TIM), was a recent addition to the ANDB. Heat shock proteins are ubiquitous chaperones which assist in protein folding.[41] Allergens from various sources belong to these proteins including Mala s 10 and Der f 28 and the recently described Der p 28.[40] Cyclophilin is a peptidyl-prolyl *cis/trans* isomerase which catalyzes the *cis-trans* isomerization of the peptide bond preceding a proline residue.[42] Known allergens of this family derive from fungi and plants and now include Der p 29 from mites.[40] Der p 30 is an allergenic mite ferritin.[40] Ferritins are among the most important non-heme iron storage proteins.[43]

Cofilins, conserved proteins in all eukaryotic cells, play a role in the dynamic reorganization of the actin cytoskeleton.[44] Der f 31 was described as the first allergenic cofilin and as a minor allergen from HDM.[45] In a recent publication, another allergenic cofilin, Der p 31, was identified.[40] Similarly, a pyrophosphatase, Der f 32, was identified as a minor allergen[46] and more recently Der p 32 was described as an allergen.[40]

The tubulin/FtsZ family includes tubulin chains and bacterial FtsZ proteins. Tubulins are an integral part of the microtubules and play a role in cytoskeleton dynamics.[47] An allergenic tubulin, Der p 33, was identified in the European HDM.[40] In this study, the genome construction of the European HDM opened the possibility of the identification of numerous aeroallergens. The allergenicity of the identified allergens was tested using ELISA. However, the study lacks further immunological tests involving the patients, such as basophil activation test (BAT) or immunoblotting.

Glutathione S-transferases (GSTs), which catalyze the conjugation of reactive electrophilic compounds to glutathione,[48] contain allergens mainly from plants, fungi, mites, and cockroaches.[39] Tyr p 8, a GST, was previously identified as a storage mite allergen.[49] A study from Taiwan reported the high cross-reactivity of Tyr p 8 with the GSTs from American and European HDM.[5] Several other mites and cockroach aeroallergens were added to the ANDB in the past two years, which are yet to be published in scientific journals. These include the chitinase Bla g 12 from German cockroach, the low molecular weight IgE-binding protein Der f 5, the chitin-binding protein Der f 37, and the bacteriolytic enzymes Der f 38 and Der p 38.

Recently, Can f 8, an allergenic cystatin from dog was identified.[5] The cystatin superfamily includes proteins that are reversible inhibitors of cysteine proteases.[50]

2.3 | Fungal-derived

Fungi are well-known for containing a plethora of allergens.[51] Asp t 36 was reported as the first allergenic fungal TIM and was shown to be cross-reactive with TIMs from the cockroach *Blatella germanica* and the mite *Dermatophagoides farinae*, Der f 25.[12] Given the high conservation of TIM sequences, one might expect to see further examples of cross-reactivity between these fungal and arthropod allergens.

3 | FOOD ALLERGENS

3.1 | Plant-derived

Seed storage proteins (SSPs) are essential for seed development and defense.[52] SSPs are highly stable proteins in nuts, seeds, and legumes and are responsible for severe systemic reactions.[53] Cupin

TABLE 1 Overview of respiratory allergens included in the ANDB from 01/2019 to 03/2021

No.	Species	Allergen name	Type of protein	Allergy profile of the patients recruited	Allergenicity tests	Reference
1	*Ambrosia trifida* (Giant ragweed)	Amb t 8	Profilin	Ragweed PA (n=198)	POS ELISA in 85/198 subjects with rAmb t 8	ANDB[5]
2	*Artemisia absinthium* (Absinthe wormwood)	Art ab 1	DPLP	Mugwort PA (n=11) with IgE reactivity to Art v 1	POS SPT, ELISA, WB, RAST in 11/11 patients to natural Art ab 1 and POS BAT in 4/4 patients	Pablos et al.,[17]
3	*Artemisia annua* (Sweet wormwood)	Art an 1.0101	DPLP		POS ELISA, WB, RAST in 11/11 patients to natural Art an 1 and POS BAT in 4/4 patients	
4		Art an 1.0102	DPLP	PA (n=23)	POS ImmunoCAP in 16/23 subjects with purified Art an 1 and rArt an 1	ANDB[5]
5		Art an 2	PR-1	PA (n=29)	POS ImmunoCAP in 24/29 subjects with purified Art an 1 and rArt an 2	
6		Art an 3	nsLTP	PA (n=28)	POS ImmunoCAP in 14/28 subjects with rArt an 3	
7	*Artemisia argyi* (Silvery wormwood)	Art ar 1	DPLP	PA (n=18)	POS ELISA and ImmunoCAP in 14/18 individuals with purified Art ar 1 and rArt ar 1	
8		Art ar 3	nsLTP	PA (n=26)	POS ImmunoCAP in 15/26 subjects with Art ar 3	
9	*Artemisia californica* (California sagebrush)	Art c 1	DPLP	PA (n=11)	POS IgE-binding in 11/11 subjects with Art c 1, POS BAT in 4/4 subjects	
10	*Artemisia capillaris* (Capillary wormwood)	Art ca 1	DPLP	PA (n=25)	POS ImmunoCAP in 17/25 subjects with Art ca 1	
11		Art ca 2	PR-1	PA (n=21)	POS ImmunoCAP in 9/21 subjects with Art ca 2	
12		Art ca 3	nsLTP	PA (n=28)	POS ImmunoCAP in 14/28 subjects with Art ca 3	
13	*Artemisia frigida* (Silky wormwood)	Art f 1	DPLP	Mugwort PA (n=11) with IgE reactivity to Art v 1	POS ELISA, WB in 11/11 patients and POS BAT in 4/4 patients to natural Art f 1	Pablos et al.,[17]
14	*Artemisia gmelinii* (Russian wormwood)	Art gm 1	DPLP	PA (n=20)	POS ELISA in 13/20 subjects with natural Art gm 1	ANDB[5]
15		Art gm 2	PR-1	PA (n=29)	POS ImmunoCAP in 24/29 subjects with Art gm 2	
16		Art gm 3	nsLTP	PA (n=26)	POS ImmunoCAP in 15/26 subjects with Art gm 3	
17	*Artemisia ludoviciana* (White sagebrush)	Art l 1	DPLP	Mugwort PA (n=11) with IgE reactivity to Art v 1	POS ELISA, WB in 11/11 individuals with natural Art l 1 and POS BAT in 4/4 patients	Pablos et al.,[17]
18	*Artemisia lavandulifolia* (Lavender-leaved sagebrush)	Art la 1	DPLP	PA (n=20)	POS ELISA in 13/20 subjects with natural Art la 1	ANDB[5]
19		Art la 2	PR-1	PA (n=21)	POS ImmunoCAP in 8/21 subjects with Art la 2	
20		Art la 3	nsLTP	PA (n=27)	POS ImmunoCAP in 16/27 individuals with Art la 3	
21	*Artemisia sieversiana* (Sieversian wormwood)	Art si 1	DPLP	PA (n=18)	POS ELISA in 14/18 subjects with rArt si 1	
22		Art si 2	PR-1	PA (n=20)	POS ImmunoCAP in 14/20 patients with Art si 2	
23		Art si 3	nsLTP	PA (n=20)	POS ImmunoCAP in 14/20 patients with Art si 3	
24	*Artemisia tridentata* (Big sagebrush)	Art t 1	DPLP	Mugwort PA (n=11) with IgE reactivity to Art v 1	POS ELISA, WB in 11/11 individuals and POS BAT in 4/4 patients to natural Art t 1	Pablos et al.,[17]
25	*Aspergillus terreus* (Earth mold)	Asp t 36	TIM	Individuals with late summer conjunctivitis and rhinitis, and SPT POS to mugwort extract were recruited in the study.		Karmakar et al.,[12]

(Continues)

TABLE 1 (Continued)

No.	Species	Allergen name	Type of protein	Allergy profile of the patients recruited	Allergenicity tests	Reference
26	*Blattella germanica* (German cockroach)	Bla g 12	Chitinase	Patients sensitized to cockroach based on ImmunoCAP and SPT (n=23)	POS ImmunoCAP in 7/23 patients with rBla g 12	ANDB[5]
27	*Canis familiaris* (Domestic dog)	Can f 8	Cystatin	Dog-allergic patients (n=113)	POS ELISA in 15/113 patients with rCan f 8	
28	*Cannabis sativa* (Marijuana)	Can s 2	Profilin	Cannabis-allergic patients (n=45)	POS CBA in 5/45 patients and POS MAT with rCan s 2	Ebo et al.,[26]
29		Can s 4	Oxygen-evolving enhancer protein 2	Patients with immediate symptoms on cannabis exposure (n=113)	POS ImmunoCAP and BAT in 8/113 and 3/3 individuals respectively with the allergen	Decuyper et al.,[8]
30		Can s 5	PR-10 homologue	Cannabis-allergic patients (n=45)	POS CBA in 35/45 patients and POS MAT with rCan s 5	Ebo et al.26[4]
31	*Cryptomeria japonica* (Japanese cedar)	Cry j 7	GRP	Cypress pollen-sensitized subjects diagnosed with peach allergy (n=54), consecutive cypress pollinosis subjects unselected with respect to peach allergy (n=88) were recruited in study	POS ImmunoCAP in 16/16 individuals with Cry j 7	Ehrenberg et al.,[22]
32	*Cupressus sempervirens* (Mediterranean cypress)	Cup s 7	GRP	Cypress PA with POS IgE-binding to Pru p 7 and/or Pun g 7	POS FABER test in 16/31 subjects with Cup s 7	Tuppo et al.,[21]
33	*Dermatophagoides farinae* (American house dust mite)	Der f 37	Chitin binding protein	Asthmatic patients (n=192)	POS ELISA in 41/192 individuals and POS WB, DB in 4/10 subjects	ANDB[5]
34		Der f 38	Bacteriolytic enzyme	HDM-allergic patients (n=30)	POS SPT in 8/30 patients with rDer f 38	
35		Der f 39	Troponin C	Rhinitis or asthma patients (n=76)	POS ELISA in 7/76 subjects and POS WB, DB in 7/7 and 6/7 subjects respectively	
36		Der f 5	n.a.	Mite-allergic patients were recruited (n=192)		ANDB[5]
37	*Dermatophagoides pteronyssinus* (European house dust mite)	Der p 25	TIM	Perennial respiratory allergic and HDM-allergic individuals (n=26)	POS ELISA in 14/26 subjects with rDer p25	Liu et al.,[40]
38		Der p 26	Myosin light chain		POS ELISA in 16/26 subjects with rDer p26	
39		Der p 28	Heat shock protein 70		POS ELISA in 18/26 subjects with rDer p28	
40		Der p 29	Cyclophilin	Perennial respiratory allergic and HDM-allergic patients (n=26) recruited in the study		
41		Der p 30	Ferritin			
42		Der p 31	Cofilin			
43		Der p 32	Inorganic pyrophosphatase	Perennial respiratory allergic and HDM-allergic individuals (n=26)	POS ELISA in 12/26 subjects with rDer p32	
44		Der p 33	Alpha-tubulin		POS ELISA in 17/26 subjects with rDer p33	
45		Der p 38	Bacteriolytic enzyme	Patients (n=40)	POS SPT, IgE-binding in 18/40, 31/40 individuals with rDer p 38 and POS BAT in 3/3 individuals	ANDB[5]

(Continues)

TABLE 1 (Continued)

No.	Species	Allergen name	Type of protein	Allergy profile of the patients recruited	Allergenicity tests	Reference
46	*Juniperus ashei* (Ashe juniper)	Jun a 7	GRP	Cypress pollen-sensitized subjects diagnosed with peach allergy (n=54), consecutive cypress pollinosis subjects unselected with respect to peach allergy (n=88)	POS ImmunoCAP in 16/16 patients to the allergen	Ehrenberg et al.,[22]
47	*Morus alba* (White mulberry)	Mor a 2	Cobalamin-independent methionine synthase	Subjects that are SPT POS to mulberry extract and with inhalation allergy (n=11)	POS WB seen in 11/11 subjects with the allergen	ANDB[5]
48	*Phleum pratense* (Timothy)	Phl p 3	Expansin-like protein	Grass PA were recruited (n=70)		
49	*Populus nigra* (Black poplar)	Pop n 2	Profilin	Patients with symptoms of allergic rhinitis and SPT POS to *Populus nigra* pollen extract	POS IB in 13/20, 11/20 subjects to naturally purified Pop n 2 and rPop n 2 respectively	Shams et al.,[25]
50	*Quercus acutissima* (Sawtooth oak)	Que ac 1	PR-10	Pollen-allergic patients (n=24)	POS ELISA and WB in 22/24 individuals with rQue ac 1	ANDB[5]
51		Que ac 2	Profilin	Pollen allergic subjects (n=50)	POS RAST observed in 6/50 individuals with rQue ac 1	
52	*Quercus ilex* (Holly Oak)	Que i 1	PR-10	Patients that are SPT POS to Holly oak (n=38)	POS IB in 21/38 patients with rQue i 1	Pedrosa et al.,[30]
53	*Quercus mongolica* (Mongolian oak)	Que m 1	PR-10	Patients that are SPT POS to Mongolian oak extract (n=50)	POS ELISA and BAT in 46/50 and 3/35 subjects respectively with rTyr p 1	Lee et al.,[29]
54	*Tyrophagus putrescentiae* (Mould mite)	Tyr p 1	Cysteine protease	Patients with asthma, rhinitis, AD or eczema (206), 106/206 were sensitized to *T. putrescentiae*	POS ELISA in 65/106 patients with rTyr p 1	Yu et al.,[36]
56		Tyr p 7	Bactericidal permeability-increasing protein	Patients with asthma, rhinitis, AD or eczema (206), 106/206 were sensitized to *T. putrescentiae*	POS ELISA in 40/106 patients with rTyr p 7	
55		Tyr p 20	Arginine kinase	Patients with asthma, rhinitis, AD or eczema (206), 106/206 were sensitized to *T. putrescentiae*	POS ELISA in 51/106 patients with rTyr p 20	
57		Tyr p 8	GST	Storage mite-allergic patients were used in the study (n=10)		ANDB[5]
58	*Zoysia matrella* (Manilla grass)	Zoy m 1	Pollen expansin	Grass PA (n=57)	POS ELISA, WB in 14/57 patients to rZoy m 1	

Abbreviations: AD, atopic dermatitis; BAT, basophil activation test; CBA, cytometric bead array; DB, dot blot; ELISA, enzyme-linked immunosorbent assay; FABER®, friendly allergen nano-bead array; IB, immunoblot; MAT, mast cell activation test; PA, pollen-allergic patients; POS, positive; RAST, radioallergosorbent test; SPT, skin prick test; WB, Western blot.

SSPs include the 7S vicilin-type and the 11S legumin-type globulins.[54] Mac i 1 is a vicilin and Mac i 2 a legumin isolated from macadamia nuts.[5] Cuc ma 4 is a legumin from pumpkin seeds.[55] 2S albumin SSPs have diverse sequences but share a common disulfide-bonded core and similar physicochemical characteristics.[56] Two 2S albumins were recently added to the database, Cuc ma 5 from pumpkin seeds[55] and Lin u 1 from flaxseeds.[57] nsLTPs are major allergens in the Mediterranean area and play a less clarified role in Northern and Central Europe.[58] Lup an 3 is an nsLTP isolated from narrowleaf lupine seed flour (Table 2).[59]

Non-SSPs allergens of tree nuts and legumes include oil-body-associated proteins, enzymes, or proteins that protect against protein aggregation. Cor a 15[5] is one of three currently designated oleosins in hazelnuts, the others being Cor a 12 and Cor a 13. Oleosins stabilize lipid storage bodies, are highly hydrophobic and virtually lacking in diagnostic commercial products.[60] Ara h 18[5] from peanuts is a cyclophilin. Pru du 10[61] from almonds is a mandelonitrile lyase which catalyzes the cleavage of mandelonitrile to hydrogen cyanide and benzaldehyde. Cic a 1[11] from chickpea is a member of group 4 late embryogenesis abundant proteins which accumulate in response to water limitation.[62] An oleosin, Fag t 6, from Tartarian buckwheat was included in the ANDB.

Pru av 7[5] from sweet cherries was added to the growing family of GRPs and Sola m 1[63] from eggplant to the expanding family of profilins. Pun g 14, a chitinase III from pomegranate pulp, was shown to cross-react with kiwifruit chitinase IV in 35% of Pun g 14-sensitized patients.[64] Pru ar 5 is a Hev b 5-like acidic protein that was isolated from apricot.[5] Cari p 2 the cysteine protease from papaya,[65] known as an allergen for a long time, made its way into the ANDB.

3.2 | Animal-derived

Recently identified animal-derived food allergens are mainly from fish and shellfish. The EF-hand protein family contains several important allergen groups: parvalbumin, troponin C, sarcoplasmic calcium-binding protein, and myosin light chain. Among the parvalbumins, two new allergens were recently discovered. Cten i 1 is a beta-parvalbumin from grass carp and its IgE-binding was demonstrated by ELISA.[66] Two isoforms of the catfish parvalbumin, Pan h 1.0101 and Pan h 1.0201, had their IgE-binding demonstrated by immunoblotting.[10] The limitation of both studies is the lack of functional assays, such as SPT or BAT with purified allergens. In addition, sensitization to parvalbumin does not necessarily translate into clinical reactivity to specific fish as shown in food challenges.[67]

Another allergen from the EF-hand family, the myosin light chain Bos d 13 was identified from beef.[5] While the chicken myosin light chain, Gal d 7, was registered in 2015, a recent publication demonstrated that it is a major allergen for patients primarily sensitized to chicken meat and is cross-reactive with allergens from other poultry species.[68] Myosin light chains are a part of the myosin complex which consists of two heavy and two light chains, and several allergens from shellfish and mites belong to this group.[69] Scy p 3 was identified in mud crab.[70] Its immunogenicity was investigated with immunoblot and BAT. Another allergen from the EF-hand family is Cra a 4, a sarcoplasmic calcium-binding protein from the Pacific oyster.[71] The authors determined five epitope peptides of the allergen.

The tropomyosin protein family contains major allergens from crustaceans, whose homologues are present across invertebrates such as mites, cockroaches, and Anisakis.[72] Using fish-allergic patients' sera, the catfish tropomyosin Pan h 4 and the salmon tropomyosin Sal s 4 were identified.[10] These are the first fish tropomyosins registered as allergens. Considering a high tropomyosin conservation, the cross-reactivity between fish and shellfish tropomyosins remains to be elucidated. Scy p 1, a tropomyosin from mud crab, was another new addition to the ANDB. Its conformational and linear epitopes were determined with the aim to generate a hypoallergenic variant.[73]

The allergenicity of fish collagen, abundant in muscle and skin, was not obvious due to its particular biochemical characteristics resulting in a low abundance in common allergy tests.[74] In 2020, collagen alpha chains from salmon and barramundi were identified as IgE-reactive proteins in fish-allergic individuals, some of who were not sensitized to parvalbumin.[9] Besides IgE-binding, extracted collagen induced IgE cross-linking in rat basophil leukemia assays. The allergenicity of tuna collagen was also shown in this study; however, this protein has not yet been registered with the ANDB.

Myosin heavy chains (paramyosin) were previously identified as IgE-binding proteins from mites and herring worm.[75] Yu et al. identified Rap v 2, a paramyosin from veined rapa whelk, a sea snail, as an allergen and reduction in its IgE-binding was demonstrated upon heating. Although being the first to describe an allergenic paramyosin in molluscs, this study included a small number of subjects and did not use any functional test to confirm this allergen's clinical relevance.[13]

Several allergens with enzymatic activity were recently discovered from animal food sources. Fructose-bisphosphate aldolase class I (aldolase A) and beta-enolases are known fish allergen.[76] Pan h 3, catfish aldolase, and Pan h 2, a catfish beta-enolase, have been recently added to the ANDB.[10] Additionally, carp beta-enolase, Cyp c 2, has also been registered as an allergen.[5]

Creatine kinase was previously described as a potential allergen from pork meat and fish.[77,78] For the first time, two allergenic creatine kinases from fish were registered in the ANDB, Sal s 7 from salmon and Pan h 7 from catfish.[10] However, the capability of these proteins to induce IgE cross-linking remains to be studied.

TIM, a known allergen from crustaceans and mites, is now also recognized as relevant in fish allergy. Using raw fish extracts, Ruethers et al. demonstrated IgE-binding to salmon TIM, Sal s 8, and catfish TIM, Pan h 8.[10] A TIM from black tiger shrimp, Pen m 8, was shown to bind IgE from shrimp allergic subjects in ELISA, but in BAT, only two patients were positive.[5]

Four additional catfish allergens, all involved in the catalysis of various steps of glycolysis, were identified as pyruvate kinase (Pan h 9), L-lactate dehydrogenase (Pan h 10), glucose 6-phosphate isomerase (Pan h 11), and glyceraldehyde-3-phosphate dehydrogenase (Pan h 13). These proteins bound IgE from 6% to 13% of the

TABLE 2 Overview of food allergens included in the ANDB from 01/2019 to 03/2021

No.	Species	Allergen name	Type of protein	Allergy profile of the patients recruited	Allergenicity tests	Reference
1	*Arachis hypogaea* (Peanut)	Ara h 18	Cyclophilin - peptidyl-prolyl cis-trans isomerase	Peanut-sensitized subjects (n=15)	POS IgE-binding in 13/15 subjects for rArah18	ANDB[5]
2	*Ascaris lumbricoides* (Giant roundworm)	Asc l 5	Divalent cation binding protein	Children from the "Risk Factors for Asthma and Allergy in the Tropics" (FRAAT) cohort (n=254) and all-age subjects from Santa Catalina (SC) cohort (n=298)	POS IgE-binding in 81/254 subjects in FRAAT cohort and 155/298 subjects in SC cohort with the allergen	Ahumada et al.,[81]
3	*Bos domesticus* (Domestic cattle)	Bos d 13	Myosin light chain	Beef-allergic patients (n=30)	POS ELISA in 8/30 patients to rBos d 13	ANDB[5]
4	*Callinectes bellicosus* (Warrior swimming crab)	Cal b 2	Arginine kinase	Crab-allergic patients (n=12)	POS WB in 8/12 subjects to Cal b 2	
5	*Carica papaya* (Papaya)	Cari p 2	Cysteine protease	Papaya-allergic patients (n=10)	POS SPT in 3/3 patients, POS RBL in 6 patients with rCari p 2	
6	*Cicer arietinum* (Chickpea)	Cic a 1	Group 4 late embryogenesis abundant protein	Subjects with clinical reactions following chickpea ingestion (n=38)	POS IB in 7/36 patients with rCic a 1	Wangorsch et al.,[11]
7	*Corylus avellana* (Hazelnut)	Cor a 15	Oleosin	Food-allergic patients (n=26)	POS SPT in 30/30 subjects and POS IgE-binding in 17/26 with natural Cra a 4 and rCra a 4	ANDB[5]
8	*Crassostrea angulate* (Pacific oyster)	Cra a 4	Sarcoplasmic calcium-binding protein	Oyster-sensitized subjects (n=10)	POS WB and DB in 10/10 patients with the allergen	Han et al.,[71]
9	*Ctenopharyngodon idella* (Grass carp)	Cten i 1	Beta-parvalbumin	IgE-mediated allergy against grass carp (n=69), confirmed grass carp allergy by food challenge (n=16)	POS ELISA in 69/69 patients to native Cten i 1	Leung et al.,[66]
10	*Cucurbita maxima* (Giant pumpkin)	Cuc ma 4	11S globulin	Subjects allergic to pumpkin seeds (n=4)	POS WB in 4/4 subjects	Bueno-Díaz et al.,[55]
11		Cuc ma 5	2S albumin	Subjects allergic to pumpkin seeds (n=4)	POS WB in 2/4 subjects	
12	*Cyprinus carpio* (Common carp)	Cyp c 2	Beta-enolase	Fish-allergic patients (n=29)	POS SPT in 24/29 patients with extract and ELISA/DB POS in 5/29 patients with rCyp c 2	ANDB[5]
13	*Fagopyrum tataricum* (Tartarian buckwheat)	Fag t 6	Oleosin	Buckwheat-allergic patients (n=20)	POS ELISA,WB and DB in 12/20 subjects with Fag t 6	
14	*Lates calcarifer* (Barramundi)	Lat c 6	Collagen alpha	Fish-allergic patients (n=101)	POS ELISA in 21/101 patients with purified collagen	Kalic et al.,[9]
15	*Linum usitatissimum* (Flax)	Lin u 1	2S albumin	Patients that experienced previous anaphylaxis due to flax seed ingestion (n=2)	POS SPT, IB in 2/2 patients with Lin u 1	Basagaña Torrentó et al.,[57]
16	*Lupinus angustifolius* (Narrow-leaved blue lupin)	Lup an 3	nsLTP	Study group of individuals with different allergy profiles (n=31)	Lupine sensitization detected by ImmunoCAP and SPT	Jappe et al.,[59]

(Continues)

TABLE 2 (Continued)

No.	Species	Allergen name	Type of protein	Allergy profile of the patients recruited	Allergenicity tests	Reference
17	*Macadamia integrifolia* (Macadamia)	Mac i 1	Vicilin	Macadamia nut-allergic patients (n=8)	POS ELISA in 4/8 patients with Mac i 1	ANDB[5]
18		Mac i 2	Legumin	Macadamia nut-allergic patients (n=8)	POS ELISA in 6/8 with Mac i 2	
19	*Pangasianodon hypophthalmus* (Striped catfish)	Pan h 1	Beta-parvalbumin	IgE-mediated allergy symptoms after fish ingestion in children, SPT POS to commercial salmon and in-house catfish preparations (n=77)	IgE-binding to heat labile and heat stable salmon and catfish proteins was analyzed in the patients	Ruethers et al.,[10]
20		Pan h 10	L-lactate dehydrogenase			
21		Pan h 11	Glucose-6-phosphate isomerase			
22		Pan h 13	Glyceraldehyde-3-phosphate dehydrogenase			
23		Pan h 2	Beta-enolase			
24		Pan h 3	Aldolase A			
25		Pan h 4	Tropomyosin alpha			
26		Pan h 7	Creatin kinase			
27		Pan h 8	TIM			
28		Pan h 9	Pyruvate kinase PKM-like			
29		Pen m 13	Fatty acid binding protein	Patients with history of allergy to *Penaeus monodon* (n=30)	POS ELISA in 20/30 subjects and POS BAT in 7/12 subjects with rPen m 13	ANDB[5]
30		Pen m 8	TIM	Patients with history of allergy to *Penaeus monodon* (n=30)	POS ELISA in 12/30 subjects with rPen m 8and POS BAT in 2/12 subjects	
31	*Prunus armeniaca* (Apricot)	Pru ar 5	Acidic protein Hev b 5-like	Patients with Hev b 5 allergy and apricot allergy (n=5)	POS FABER test in all 5 subjects	
32	*Prunus avium* (Sweet cherry)	Pru av 7	GRP	Sweet cherry-allergic patients (n=25)	POS BAT and IgE-binding in 11/25 patients with Pru av 7	
33	*Prunus dulcis* (Almond)	Pru du 10	Mandelonitrile lyase 2	Patients with allergic reactions following almond ingestion (n=18)	POS sensitization in 12/18 patients with Pru du 10	Kabasser et al.,[61]
34	*Punica granatum* (Pomegranate)	Pun g 14	Chitinase III	Subjects with history of allergic reactions to pomegranate fruit and/or POS SPT (n=10)	POS DB in 5/10 subjects and POS IB in 8/10 patients with Pun g 14	Tuppo et al.,[64]
35	*Rapana venosa* (Veined rapa whelk)	Rap v 2	Paramyosin	Snail-allergic subjects (n=5) and controls (n=3)	POS WB, DB in 5/8 subjects	C. Yu et al.,[13]
36	*Salmo salar* (Atlantic salmon)	Sal s 4	Tropomyosin	IgE-mediated allergy symptoms after fish ingestion in children, SPT POS to commercial salmon and in-house catfish preparations (n=77)	IgE-binding to heat labile and heat stable salmon and catfish proteins was analyzed in the patients	Ruethers et al.,[10]
37		Sal s 6	Collagen alpha			
38		Sal s 7	Creatine kinase			
39		Sal s 8	TIM			
40		Sal s 9	n.a.	n.a.	n.a.	ANDB[5]

(Continues)

TABLE 2 (Continued)

No.	Species	Allergen name	Type of protein	Allergy profile of the patients recruited	Allergenicity tests	Reference
41	*Scylla paramamosain* (Mud crab)	Scy p 1	Tropomyosin	Crab-allergic subjects (n=10)	POS ELISA with Scy p 1, rScy p 1, and mutant Scy p 1	G. Y. Liu et al.,[73]
42		Scy p 3	Myosin light chain	Crab-sensitized subjects(n=10)	Immunogenicity analyzed by DB, BAT with rScy p 3	M. S. Li et al.,[70]
43		Scy p 9	Filamin C	Crustacean-allergic patients (n=100)	POS ELISA, WB, DB in 30/100 subjects with Scy p 9 and rScy p 9	ANDB[5]
44	*Solanum melongena* (Eggplant)	Sola m 1	Profilin	Eggplant-allergic patients confirmed with SPT and ImmunoCAP (n=36)	POS IB in 36/36 subjects with rSola m 1 and POS BAT in 6/6 subjects	Maity et al.,[63]

Abbreviations: BAT, basophil activation test; CBA, cytometric bead array; DB, dot blot; ELISA, enzyme-linked immunosorbent assay; FABER®, friendly allergen nano-bead array; IB, immunoblot; n.a., not available; POS, positive; SPT, skin prick test; WB, Western blot.

77 fish-allergic patients included in the study.[10] In contrast to raw extracts, these allergenic enzymes lost their ability to bind IgE when the extract was heated.

Among other recently identified allergens from animal, foods were filamin C (Scy p 9) from mud crab and arginine kinase (Cal b 2) from warrior swimming crab.[5] Moreover, an allergenic fatty acid-binding protein, Pen m 13, from black tiger shrimp showed IgE reactivity in ELISA and BAT.[5] Previously, allergens from this protein group were identified in mites but not in foods.[79,80]

An allergen from common roundworm, Asc l 5, was discovered by immunoscreening of an *Ascaris lumbricoides* cDNA library. Infection by these roundworms happens by eating food contaminated with their eggs. Asc l 5 belongs to the SXP/RAL-2 protein family, which also contains three *Anisakis simplex* allergens. In Ascaris-sensitized individuals, Asc l 5 bound IgE with high frequencies of 44% and 58% in two large patient cohorts.[81] In addition, its ability to induce basophil activation and histamine release was shown. In regions with frequent *Ascaris* infections, understanding the allergen repertoire of these worms may help understand the relationship between helminth infection and allergy. Human IgE against helminths is a normal component of the whole protective response elicited during infestation, when specific IgE to a great number of antigens is produced. However, few of these IgE-binding components are actual allergens that belong to a small group of helminthic proteins for which an allergenic activity, that is, the ability to induce IgE-mediated inflammation, has been clinical or experimentally demonstrated. *Ascaris lumbricoides* infestation (ascariasis) exerts a dual effect on allergic diseases such as asthma, it can increase prevalence and symptoms or diminish the allergic inflammation through immunomodulating molecules.[82]

4 | OTHER ALLERGENS

A DPLP, Aes h 1, from horse chestnut was identified as cross-reactive with Art v 1 in subjects allergic to Art v 1 with pollinosis or contact reactions to horse chestnut seeds.[5] Centipede bites can cause excruciating pain and clinical manifestations like erythema, blisters, necrosis,[83] and rarely anaphylaxis.[84,85] A recently discovered centipede allergen is Sco m 5, a venom allergen 5 of the CAP superfamily. The complete coding sequences of the Asian hornet venom allergens Vesp v 1 and Vesp v 5 were determined[86] and added to the ANDB. Vesp v 1 is a glycosylated phospholipase A1, while Vesp v 5 belongs to the CAP superfamily. The authors suggest that the purified components could be of advantage when measuring the IgE levels of patients with anaphylactic shocks following the hornet sting, but further clinical data are yet to be obtained.

5 | CLINICAL EVALUATION OF THE NEW ALLERGEN SOURCES

Seventeen new allergen sources were described during the reporting period (Table S2). They comprise six new food allergens, 10 inhalant allergens, and 3 toxins. The clinical relevance of the newly described food allergens is obvious for the grass carp beta-parvalbumin (Cten i 1). Sixty-nine patients from Hong Kong who developed clinical symptoms after the consumption of this fish species also had a positive ImmunoCAP result for the grass carp parvalbumin.[66] For two molluscs, the sea snail *Rapana venosa* (veined or Asian rapa whelk) and the Portuguese oyster (*Crassostrea angulata*), allergenic proteins were described for the first time. Sera of 10 out of 10 oyster-allergic patients and sera of 8 out of 8 sea snail-allergic patients exhibited IgE reactivity against Cra a 4 and Rap v 2, respectively.[13,71]

The clinical relevance of the first allergen described in eggplant, a member of the profilin family, is a striking example for the widely observed cross-reactivity of profilins. Thirty-six highly atopic patients with markedly elevated total IgE and a clinical history of eggplant allergy had a positive SPT to a raw eggplant extract and all patients' sera reacted to the recombinant Sola m 1.[63] No data were presented on the IgE reactivity to a boiled eggplant extract. No publications are currently available for Cuc ma 4 and Cuc ma 5, the 11S globulin and the 2S albumin in *Cucurbita maxima* seeds. The clinical relevance of these new allergens remains to be determined.

While many *Artemisia* species occur worldwide, allergy research so far has only focused on *Artemisia vulgaris*. Six novel Art v 1 homologues from several additional *Artemisia* species with high sequence identities and equivalent IgE reactivities were identified and designated as Art ab 1, Art an 1, Art c 1, Art f 1, Art l 1, and Art t 1.[17] These data demonstrate that DPLPs in various *Artemisia* species have high allergenic potentials and related *Artemisia* species have to be considered to be allergen elicitors, especially due to their potential geographic expansion due to climate changes.

Asp t 36, a major allergen from the mold *Aspergillus terreus*, has been described for the first time.[12] Fifteen *Aspergillus terreus* allergic patients' sera reacted with this allergen, defining its importance for characterizing mold allergy.

The pollen food allergy syndrome related to PR-10 homologues from vegetables is common in northern Europe. However, there are pollen-allergic patients reactive to Bet v 1 in birch-free regions. *Quercus ilex* pollen has been shown to be the main sensitizing pollen source for this clinical entity in central Spain and its major allergen, Que i 1, elicited high sensitization rates in patients reporting a pollen food allergy syndrome.[30] The major allergen Que m 1 from Mongolian oak (*Quercus mongolica*), a dominant species in Korea, was cloned and its recombinant protein produced.[29] Specific IgE to recombinant Que m 1was detected in 92.0% of 50 serum samples from Korean pollen food allergy syndrome patients, showing the regional importance of oak pollen as a main sensitizing pollen source in Korea.

The Asian hornet venom allergen, Vesp v 5, and a centipede (*Scolopendra mutilans*) allergen, Sco m 5, are new additions to the venom allergen 5 group of the CAP family. Given the importance of this protein family in insect bite allergy they can be regarded as major allergens for these allergen sources, but data for their clinical relevance are scarce.[86] In addition, a hyaluronidase from the venom of the Asian hornet, Vesp v 1 has been characterized.

The clinical relevance for all newly described respiratory allergens is summarized in Table 1, and for the newly described food allergens in Table 2.

6 | OUTLOOK

The WHO/IUIS Allergen Database continues to play an essential role in keeping track of newly discovered allergens and ensuring their unambiguous designations. This will remain of importance for clinicians, researchers, regulatory authorities, and companies providing allergen products. Targeted research on the link between physicochemical and immunological characteristics of allergens will enable improvements in prevention, diagnosis, and treatment of allergic diseases. The addition of 106 new allergens in the reporting period reflects a slight increase in the continuous linear growth of the allergen database. New additions averaged 33 allergens annually from 2008 to 2018 and increased to an average of 47 new allergens per year in 2019–2020 (Figure S1). While the numbers of allergens from plant and animal sources keep increasing, the number of fungal allergens remains almost stagnant except in 2009 when 23 new fungal allergens were added to the database (Figure S2). In the reporting period, 17 new allergen sources were added including 11 plants, 5 animals, and 1 fungal species (Table S2) thereby increasing the number of individual species included in the database from 295 to 311 (Table S3).

All 106 allergens were tested for their ability to bind IgE by various *in vitro* assays including ELISA, immunoblots, bead arrays, or dot blots (Tables 1 and 2). While BAT data are available for 14/106 allergens and MAT data for 2/106, SPT data are available only for 8/106 allergens (Tables 1 and 2), no allergen challenges were performed using any of these allergens. This clearly indicates a future need to define the clinical significance of these allergens (Box 2).

Among the first allergenic members identified in a particular protein family (Box 1), fish collagens represent a class of allergens that are expected to improve the diagnosis of fish allergy. Allergen families that were first described in additional species include paramyosins in

BOX 2 Future research perspectives

- Raise awareness of importance of including newly discovered allergens in the Allergen Nomenclature Database.
- Determine complete cDNA and amino acid sequences of allergens already deposited in the database.
- Perform detailed physicochemical characterization of food allergens to understand their sensitizing capacity.
- Complete the repertoire of homologous allergens from related sources.
- Determine the clinical relevance of the identified allergens and their importance in molecular allergy diagnosis.

molluscs and tropomyosins in fish (Box 1). These types of allergens were so far mainly known as arthropod allergens. These discoveries might indicate cross-reactivities that were unknown before. In addition, gibberellin-regulated proteins, only recently described as a new allergen family, seem to play a key role in pollen food-associated syndromes involving Cupressaceae pollen and peach and/or citrus fruits.[19,20] About 5% of the 106 allergens added to the database in the reporting period belong to protein families not previously known to contain allergens. More discoveries of novel allergens can be expected as allergen sources specific for certain countries are being analyzed.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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