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Seafood allergy: A comprehensive review of fish and shellfish allergens

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ABSTRACT

Seafood refers to several distinct groups of edible aquatic animals including fish, crustacean, and mollusc. The two invertebrate groups of crustacean and mollusc are, for culinary reasons, often combined as shellfish but belong to two very different phyla. The evolutionary and taxonomic diversity of the various consumed seafood species poses a challenge in the identification and characterisation of the major and minor allergens critical for reliable diagnostics and therapeutic treatments. Many allergenic proteins are very different between these groups; however, some pan-allergens, including parvalbumin, tropomyosin and arginine kinase, seem to induce immunological and clinical cross-reactivity.

This extensive review details the advances in the bio-molecular characterisation of 20 allergenic proteins within the three distinct seafood groups; fish, crustacean and molluscs. Furthermore, the structural and biochemical properties of the major allergens are described to highlight the immunological and subsequent clinical cross-reactivities. A comprehensive list of purified and recombinant allergens is provided, and the applications of component-resolved diagnostics and current therapeutic developments are discussed.

1. Classification of seafood

Seafood is comprised of the distinct taxa of fish (bony and cartilaginous fish), in the phylum of Chordata, and shellfish (crustacean and mollusc), in the phyla of Arthropoda and Mollusca, in the kingdom Animalia (Fig. 1). Aquatic animals of other phyla have not been investigated comprehensively regarding allergy due to limited consumption and hence are not discussed in this review. Other seafood, such as jellyfish (phylum Cnidaria), can trigger anaphylaxis upon ingestion (Imamura et al., 2013), but was reported to be safe for patients with allergy to the seafood groups mentioned above (Amaral et al., 2018).

1.1. Types of fish

Fish are divided into the superclasses of bony fish (Osteichthyes) and cartilaginous fish (Chondrichthyes). The third superclass of Vertebrata, the tetrapods (Tetrapoda), contains all the four-limbed vertebrates including amphibians, birds, mammals, and reptiles. The bony fish are the largest group of all vertebrates consisting of 45 orders and over 435 families. They can be further divided into the two subclasses ray-finned fish (Actinopterygii) and lobe-finned fish (Sarcopterygii). Actinopterygii is the largest subclass and includes all edible bony fish. Most Sarcopterygii species are extinct, with the coelacanths being the oldest discovered order - having a continuous presence for 100 million years. Bony fish have an endoskeleton made of stable cranial bones, reproduce mostly externally, and are found in fresh and marine water whereas, cartilaginous fish have an endoskeleton made of cartilage, reproduce internally, and are found primarily in marine water. They can be further divided into the subclasses; Elasmobranchii and Holocephali. Elasmobranchii consist of sharks (Selachii), rays, skates (Batoidea), and sawfish. In contrast, the subclass Holocephali (ghost sharks) has only one surviving order (Chimaeriformes), which consists of rat fish, rabbit fish, and elephant fish. The most

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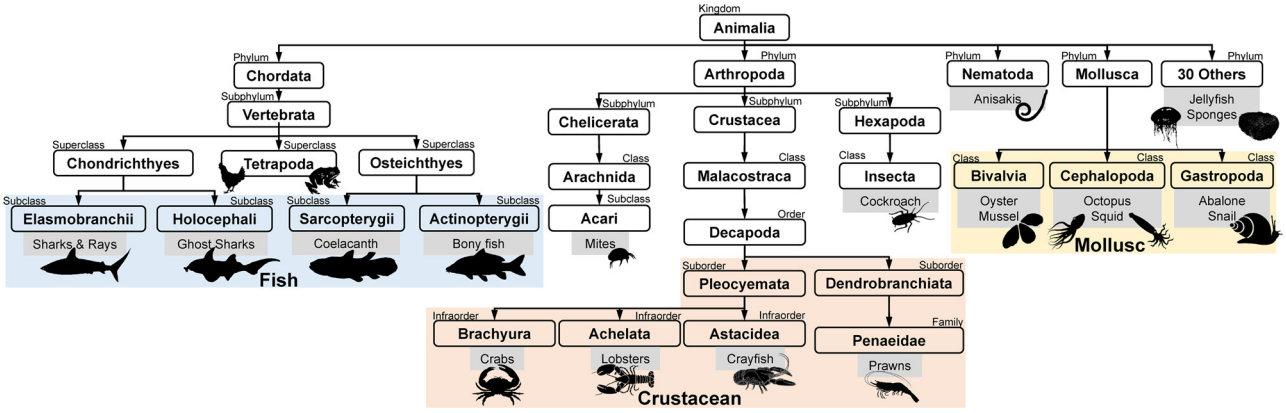

Fig. 1. Taxonomic tree of edible seafood species and related allergen sources. Classification and taxonomy of species are presented according to the NCBI (www.ncbi.nlm.nih.gov/taxonomy) and the Catalogue of Life (www.catalogueoflife.org/col/). Species in branches highlighted in blue, yellow, and red are considered as fish, mollusc, and crustacean, respectively. Allergic reactions to these and related species are discussed in this review (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

investigated species of ghost shark is the chimeric elephant fish, also known as the Australian Ghost Shark (*Callorhinchus milli*), as it is closely related to sharks, but also has distinct features like bony fish, such as gill covers. For consumption, and therefore allergy research, bony fish are the most relevant. Only in a few studies has the allergenicity of cartilaginous fish been investigated, and these suggest lower allergenicity compared to bony fish (Stephen et al., 2017).

1.2. Types of crustacean

Edible arthropods belong to the subphylum Crustacea and more specifically to the order Decapoda. This group includes prawns, shrimps, crabs, and lobsters (Fig. 1). Most crustaceans have five pairs of legs on the main thoracic body and five pairs of swimmerets on the abdomen or tail (Lee et al., 2012a). Crustaceans are closely related to arachnids (dust mites, spiders *etc.*) and insects such as cockroaches. Among the edible crustaceans, prawns constitute a major proportion of the consumed and farmed species. Decapods from the Penaeidae family are known as prawns, and those from the Caridae family, shrimps. Prawns and shrimps belong to two different taxonomical classifications with the main anatomical differences being the different overlapping pattern of the segments in the carapace and their brooding methods (Poore, 2004). Penaeids have a larger size compared to Caidae and are commercially important. Most of the species characterised for the existence and prevalence of allergens belong to this family. Shrimps are smaller in size and used mainly as additives or flavouring agents. Common examples of the caridean shrimps are the freshwater shrimp (*Macrobrachium rosenbergii*), and northern shrimp (*Crangon crangon*). However, the term “prawns” and “shrimps” are often used interchangeably in the commercial sector as well as in many research publications. The term prawn is used in the UK, Australia and other Commonwealth countries whereas the term shrimp is most commonly used in the USA and Europe. In addition, krill (*Euphausia superba*) are marine crustaceans that belong to the Euphausiidae family and are widely used in processed food products and the production of krill oil.

1.3. Types of molluscs

The mollusca are the second largest phylum of the kingdom Animalia with 104 edible species recorded by the Food and Agriculture Organization of the United Nations (FAO). This phylum consists of 9–10 taxonomic classes, with only three, Cephalopoda, Bivalvia, and Gastropoda, being commonly consumed by humans. In 2011 molluscs contributed around 12% of global fishery production; nearly 75% were farmed (Campbell and Pauly, 2013). Bivalvia is the most important class commercially, with oysters, mussels, scallops, clams, and cockles constituting a significant part of total production. Bivalves have a shell consisting of two hinged parts, while cephalopod either have an internal calcareous cuttlebone (cuttlefish), an internal chitinous pen (squid), or no shell at all (octopus). About 80% of all mollusc species belong to the class of Gastropoda including abalone, snails, and slugs with very diverse anatomic features. Molluscs mainly inhabit aquatic environments. The only edible terrestrial molluscs are the land snails of the genus *Helix*.

2. Adverse reactions to seafood including IgE-mediated allergy

The clinical presentation of seafood allergy is similar to other food allergies. Single or multiple symptoms usually appear immediately or within two hours following exposure; however, late phase reactions of up to eight hours after ingestion have been reported (Lopata et al., 1997). Respiratory reactions along with oral allergy syndrome are reported more frequently than in other food allergies, and seafoods are one of the most common triggers of life-threatening anaphylactic reactions (Matricardi et al., 2016). Sensitisation and subsequent reactions occur most frequently upon ingestion; however, they can also occur due to skin contact or inhalation of aerosolised proteins generated during cooking or processing. Unlike most other food allergies, seafood allergy persists for life in up to 90% of patients, a trend also observed with peanut allergy.

Adverse reactions to seafood can be classified into three categories, based on underlying mechanisms: 1) Immunological reactions, including allergic reaction and Food Protein-Induced Enterocolitis Syndrome (FPIES), 2) Toxic reactions, including marine biotoxins and 3) Food intolerance. Adverse reactions due to toxins and/or food intolerance often resemble clinical symptoms of seafood allergy. A good patient workup and sensitive diagnostic analysis of IgE antibody reactivity can distinguish between a true seafood allergy and other adverse reactions.

This review focuses on IgE-mediated allergic reactions to seafood and the allergenic proteins involved. In contrast, adverse clinical reactions to seafood often involve non-immunological toxic reactions as detailed below (Fig. 2).

2.1. Adverse reactions to ingested seafood

In the USA, seafood is responsible for at least 1 in 6 food poisoning outbreaks and the proportion is even higher in Japan (Trevino, 1998). Diagnosis and treatment are generally similar to those for any other food poisoning. Seafood toxins are very stable, and their toxicity is not reduced by preparation procedures (*e.g.* cooking, pickling).