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Editorial: Omics-based identification, characterization, and validation of marine bioactive peptides

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Editorial on the Research Topic
Omics-based identification, characterization, and validation of marine bioactive peptides

Marine organisms include diverse species living in the salt water of oceans and seas. By now, more than 242,000 marine species have been described, and an average of more than 2,300 new species are being documented per year (Bouchet et al., 2023). A key peculiarity of marine animals is their robust innate immune system, evolved over the period of several hundred million years in contacts with pathogens (Guryanova and Ovchinnikova, 2022). Marine organisms can produce numerous bioactive compounds, including toxins, antimicrobial or antihypertensive peptides, and so on. Onrush of omics-based technologies (such as genomics, transcriptomics, metagenomics, epigenomics, proteomics, and peptidomics) inspired researchers all round the world to apply them for characterization of genes and corresponding encoded proteins. Due to a high diversity of marine species, one of the most important aims of such a high-throughput analysis of nucleic acid and amino acid sequences is to identify novel bioactive peptides. By means of big data-based technologies important advances can be achieved in the search of marine peptides. Identification and characterization of novel peptides are a prime focus. Their validation with an eye on various biomedical purposes and design of powerful pharmaceuticals have recently come to the fore.

The phylum Cnidaria includes more than 12,000 species of aquatic animals, prevalently marine invertebrates (such as hydra, jelly fish, sea anemones, sea pens, and corals; World Register of Marine Species, 2023). Analysis of mitochondrial genes of cnidarians showed that they have emerged about 741 million years ago (Park et al., 2011). Cnidarians live in the water environment infested with disease-bearing bacteria and viruses. The genomes of cnidarians are of a great complexity including the repertoire of innate immunity genes, but

their immune system is still insufficiently studied. Along with other constituents of innate immunity, antimicrobial peptides (AMPs) are viewed as conserved molecular factors, having been identified in diverse plants and animals including marine organisms (Haney et al., 2017). Multifaceted features of marine AMPs enable them to combat exogenous pathogens through various mechanisms, including membrane disruption, cell penetration, and interference with intracellular molecular targets (Guryanova et al., 2023).

Defensins form one of the most abundant classes of cysteine-rich cationic AMPs (Dong et al., 2016). By now, only one AMP similar to defensins has been discovered in Cnidaria (Ovchinnikova et al., 2006). Aurelin has been isolated from the jellyfish *Aurelia aurita* and displayed activity against Gram-positive and Gram-negative bacteria (Ovchinnikova et al., 2006). To fill the gap in the present state of knowledge about the defensin family in Cnidaria, Leal et al. in this Research Topic reported the use of *in silico* strategies for characterization of cnidarian peptides with structural and functional characteristics of AMPs and their putative antimicrobial activities. The authors applied bioinformatic approaches to identify defensin-like AMPs in different cnidarian species. In particular, a search for sequences homologous to defensins was carried out in reported genomes of cnidarians. Homology-based molecular modelling, allowed to obtain 3D models of 12 AMPs derived from 11 cnidarian species, has exhibited structural similarity with reported defensins. Using machine learning approaches, functional characterization of these predicted defensins was carried out and their physicochemical peculiarities were investigated. Functional characterization showed a bactericidal potential of 20 peptides against multi-resistant strains of Gram-negative bacteria. Those peptides with antimicrobial potency were validated in 17 cnidarian species by homology with Aurelin from the jellyfish *Aurelia aurita* (Ovchinnikova et al., 2006) and Beta-defensin 7 (mBD-7) from the mouse *Mus musculus* (Bauer et al., 2001). Besides, a phylogenetic tree was constructed, which proved that many cnidarians belonging to different taxonomic groups produce defensins. Structural and functional characteristics of these peptides in Cnidaria are indicative of their antimicrobial potential as candidate scaffolds for design of novel antibiotic drugs (Leal et al.).

A plenty of biologically active peptides are synthesized in the neuroendocrine, gut, and immune systems of mollusks (Tascedda and Ottaviani, 2016). Marine cone snails (*Conus* spp.) are venomous mollusks with beautiful shells. They are classified in the Conoidea superfamily of the Neogastropoda clade and form the most numerous genus in marine invertebrates (Modica and Holford, 2010; Bouchet et al., 2011). About 1,000 *Conus* species are known (World Register of Marine Species, 2023), and by now over 70,000 conotoxins have been estimated (Gao et al., 2017). Conotoxins and AMPs from *Conus* sp. are attractive resources for promising development of new drugs. In this Research Topic, high-throughput prediction of AMPs from the representative Chinese cone snail *Conus betulinus* was reported (Li et al.). The authors characterized AMPs along with AMP-encoded genes by integration of multi-omics datasets. A total of 466 putative AMP-encoded genes were identified in the *C. betulinus* genome and 77 AMP-derived genes were confirmed at the mRNA level. Moreover, 30 AMPs were validated by peptidomics data. Analysis *in silico* revealed 11 potential AMPs, and eight of them displayed an antifungal activity (Li et al.).

A transcriptome library of four different organs from the striated cone *Conus striatus* was sequenced with the use of both Illumina next-generation sequencing (NGS) and PacBio third-generation sequencing (TGS) technologies (Liao et al.). In this work, a total of 428 conotoxin precursors were reconstructed from the transcriptome data, and 413 of them were referred to 13 gene superfamilies, while 15 toxins were attributed to unclassified families. It should be noted that significant difference in the conotoxin diversity was observed by NGS and TGS technologies. For example, 82 and 366 conotoxins were identified from the NGS and TGS datasets correspondently. Interestingly, the authors revealed point mutations in signal peptides of several conotoxins with identical mature sequences. Thereby, the generally accepted view on the conserved conotoxin signal peptides and the variable mature sequences stated by NGS technology was disclaimed by TGS technology (Liao et al.). This discrepancy sheds light on the integrated strategy to mine diverse peptides from *Conus* species and to discover novel conotoxins.

High blood pressure or hypertension is a dangerous physiological condition, often increasing the prevalence of heart attack and cerebrovascular insult. Therefore, obstinate efforts are made to discover new hypotensive drugs and, in particular, to identify novel antihypertensive peptides (AHTPs). AHTPs may exhibit an antihypertensive activity via renin and/or angiotensin-converting enzyme (ACE) inhibitor pathways, but also may exert other ways (Majumder and Wu, 2014; Manzanares et al., 2015). Marine animals are an abundant resource of AHTPs. Abdelhedi and Nasri (2019) have analyzed and put together all identified AHTPs from more than 20 marine organisms.

Hippocampinae, also called seahorses, are small marine fishes. In this Research Topic, with the availability of whole genome (Lin et al., 2017), transcriptome (Lin et al., 2016), and proteome (Chen et al., 2020) sequences of the lined seahorse *Hippocampus erectus*, Huang et al. performed a high-throughput identification of AHTP structures. The authors revealed 14,695 AHTP-encoded genes, and most of them were validated by transcriptomic analysis, while only 495 AHTPs were detected by the proteome sequencing. Among the predicted AHTP-derived genes, titin and collagen sequences had the most hits with AHTP genes. These findings provided a fundamental basis for deeper insight into the role of various AHTPs in fish and open the door to development of antihypertensive drugs.

The green spotted puffer *Tetraodon nigroviridis* is a practical fish model for genomic studies (Roest Crollius et al., 2000; Bian et al., 2020). In this Research Topic, Jiang et al. have investigated the molecular mechanisms of *T. nigroviridis* resistance to *Vibrio parahaemolyticus* infection. *V. parahaemolyticus* is a widespread aquatic zoonotic bacterial pathogen that may lead to host death (Subramani and Vignesh, 2012). The authors employed multi-omics technologies to analyze the *T. nigroviridis* immune response to exogenous bacterial infection and to explore the molecular mechanisms of the host defense. The miRNA–mRNA–protein omics-based investigation revealed some differentially expressed genes of different immune system components. The

authors have showed that the complement component 3 (*C3*) gene and protein expression levels were up-regulated after *V. parahaemolyticus* infection, and miRNAs targeting *C3* were suppressed. At the same time, the gene and protein expression levels of complement 1 subunit qA (C1qA) were considerably lower, while mir-203 targeting *C1qA* was increased. As a result, four key genes (*C1qA, IG, C3*, and *C5*), participating in the complement system activation in the inflammatory response, were identified (Jiang et al.).

In summary, rapid development in multi-omics technologies has deepened our biological knowledge. In this Research Topic, all the authors have shown a high level of expertise in omics-based technologies and convincingly demonstrate that marine animals are abundant resources of valuable bioactive peptides, which may be developed as some promising pharmaceuticals with more validation practices and clinical investigations.

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Conflict of interest

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Publisher's note

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