Marine Glycoconjugates

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From 2012 to 2016 a special issue was edited in the journal Marine Drugs dedicated to marine glycoconjugates with the idea that from the end of the decade 1980-1990 increasing advances of analytical techniques boosted the field of glycobiology contributing to its growth with better recognition of structures and roles of complex molecules such as saccharides, glycoproteins, glycan, glycolipids, and proteoglycans (all defined as glycoconjugates). Tremendous impact in biomedical and biotechnological applications of glycoconjugates, like in terrestrial counterparts and the addition of more significance to the current –omic revolution toward a possible marine glycocode, generally based the hope of these studies.

Keywords: marine biotechnology ; marine glycomics ; oligosaccharides ; polysaccharides ; glycobiology

1. State of the Art

It is commonly accepted that in marine research studies on glycoconjugates have had just selective flourishing in a small number of classical processes (reproduction, chemical communications, bioadhesion). However in the decade 1980-1990 increasing advances of analytical techniques boosted the field of glycobiology contributing to its growth with better recognition of structures and roles of complex molecules such as saccharides, glycoproteins, glycan, glycolipids, and proteoglycans (all defined as glycoconjugates).

2. Content

Firstly two general points have to be remarked (i) the great molecular diversity, with fucose-containing molecular structures being the most prominent and important for biological activities and (ii) some important glycobiology related processes reviewed or discussed in this special issue. As for the first, the glycosides from marine sponge are reviewed in a very complete literature data analysis[1]. Monosaccharides characterizing these glycosides from marine sponges are more than two dozens types present in mono or oligoforms, free or more often as acylated derivatives. Thought to be membrane constituents, they have important biological activities connected with the biological role as defensive molecules. A quick search in Pubmed for articles dealing with these molecules shows that more than one hundred articles have been published since 2012, demonstrating the ongoing importance of these molecules.

However, the most prominent molecular types present are polysaccharides in nature possessing an important biological activity. Due to the complexity of molecular composition and variability of algae sulfated polysaccharides a first interesting article related to methodology is present in the collection. The article was focused on the development of a simple microplate assay for screening the quality of these molecules[2]. The same topic was later developed by this research group among other interests[3].

In a general analysis, the structure-activity relationships of algae polysaccharides were investigated using 33 different types prepared for this work investigating their action as anti-complement drug[4]. Influence of molecular weights, the presence of sulfate, branching, and type of monosaccharides present were all aspects analyzed.

In another article the interesting molecule apigalacturonan, that is a kind of apiose-rich pectin occurring in a small number of aquatic monocots[5] was the subject of investigation. After acidic or enzymatic depolymerization the authors reported about structures and anti-tumour activity of different fragments. No further articles were found on this polysaccharide from the publication of this article.

Hyaluronic acid is another important molecule from an economical point of view. As for this polysaccharide, known marine sources are poor in yields and it is currently massively produced by microbial synthesis. The article published explored the production by *Streptococcus* equi subsp. *zooepidemicus* in complex media constituted by peptones from *Scyliorhinus*

canicula viscera by-products[6]. The protein constituents from this fishing discards proved to be an appropriate alternative to replace commercial tryptone. The marine by-products valorization is a great topic in marine biotechnology and the same research group later investigated also the use of other economic alternatives from food industry[7].

Another important review present in this special issue is the one introducing the concept of glycomic with proposed subdivisions that are judged important in marine field. The focus is specially devoted to sulfated fucans and galactans with their respective fucanomics and galactonomics and to the importance of international recognition of these subclassifications within marine glycomics[8]. Indeed different other original articles are present that are focused on these concepts: (i) the evaluation of the anti-tumor activities of the oral administration of fucoidan extracted from the edible seaweed *Cladosiphon* okamuranus using a tumor (colon 26)-bearing mouse model[9], (ii) the antiproliferative activity of a nanogel constituted using the algal heterofucan from *Spatoglossum* schroederi[10], (iii) the preparation and evaluation of structure-activity relationship of the O-acylated derivative of fucosylated chondroitin sulfate from sea cucumber using the material with a low molecular weight fragment obtained from glycosaminoglycan of the *Thelenota ananas*[11], (iv) the purification and characterization of a fucoidanase from a marine bacterium *Sphingomonas paucimobilis*, a study in the frame of a the search for enzyme activities that efficiently degrade marine polysaccharides for structural analysis and for production of lower-molecular-weight bioactive oligosaccharides[12].

Another important contribution of the issue, in view of molecular diversity in this field, is the one reporting on the structure of an amino acid-decorated exopolysaccharide originated from a *Vibrio alginolyticus* strain[13]. The importance of the study resides both on the technical advantages of microbial production that can be easily controlled and is independent of seasonal variations, and on the possible use of these compounds in cosmetics.

Conopeptides constitutes conotoxins and are small peptides present in the venom of cone snails. These compounds contain a high frequency and variability of post-translational modifications such as O-glycosylation of high importance for biological activity. They can be used as specific neuropharmacological agents and chemical probes. A review on the currently existing knowledge of O-glycosylation of conotoxins is present[14].

Molecular diversity dedicated studies terminated with three additional articles focused on (i) three new ganglioside molecular species isolated from pyloric caeca of the starfish *Protoreaster nodosus* reporting the first case of invertebrate GM4-type ganglioside having a wide significance from chemical, biological, and biosynthetic points of view[15] and (ii) a structure-activity relationship study of the carbohydrate moiety of the ganglioside LLG-3 isolated from the starfish *Linchia laevigata* [16] and (iii) the structural investigation of the oligosaccharide portion of the lipooligosaccharide of psychrophilic organism *Psychrobacter arcticus* [17] which is important in the frame of studies related to the increase in the number of characterized LPS structures from psychrophiles to find a possible specific connection between the polysaccharide portion and membrane cold adaptation mechanism alternative to the higher content of unsaturated, polyunsaturated, and methyl-branched fatty acids.

Besides molecular diversity as the main subject of the published articles, few were devoted to bioprocesses and molecular mechanisms inherent to marine glycobiology. Namely, a general view of the state of art in the glycobiology of reproductive processes in marine animals[18] where authors focused on what known in the glycobiology from gametogenesis to fertilization and embryo development in marine animals picking up the concept of the species-specific chemical diversity of molecules involved. An interesting article investigating the skin mucus of eel for the induction of apoptosis and antitumor activity on human cells[19] is present in the special issue showing for the first time that eel skin mucus has anti-tumour activity in human cells. The microbial extracellular matrix contains exopolymeric substances (EPS) and proteins; the structural details of the first are not known but are of great importance in processes investigated in a marine isolated strain of *Bacillus pumilus* [20]. The last article present is focused on lectins that are glycan-binding proteins, namely on MytiLec that is an α-Gal-binding lectin isolated in 2012 from the mussel *Mytilus galloprovincialis*. Using a cell line with high globotriose expression this lectin has been studied for action on lymphoma cells [21].

3. Conclusion

Although the listed contributions are not numerous, after this analysis a conclusion can be drawn about the recognition of the importance of structural determination in glycobiology before the complex roles of all involved molecules can be defined. It is again confirmed too that in the marine field these studies are characterized by selective flourishing in a small number of classical processes. A search for marine glycobiology as keywords, conducted at the time of writing in Science Direct database, accounts for few articles but it is important to mention a modern book[22] as an important source of interesting information. Moreover is important to mention also a new special issue in Marine Drugs entitled Marine glycobiology, glycomics and lectins guest-edited by Prof. Yasuhiro Ozeki in 2018.

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