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Editorial

Perspectives on steroid metabolism in marine organisms

Studies of steroid metabolism usually target the understanding of steroid function in humans and livestock, yet it is undeniable that these molecules also play significant physiological roles in most other multicellular organisms. From an evolutionary standpoint, steroid biology, as well as life itself, is thought to have arisen in the ocean; indeed, many major lineages of animals are restricted to marine environments. Although steroid metabolism and function have been less extensively studied in marine organisms, there is good reason to expect a diversity of signaling molecules and metabolic pathways.

In this special issue, we have gathered reviews and research papers on the diverse topics of the metabolism and physiological roles of steroids in marine organisms. The reviews touch on fields highly related to studies in mammals such as elucidation of aromatase function, the role of neurosteroids during gonadal development and the deactivation and catabolism of steroids. They also highlight our current understanding of the evolution of steroidogenesis by investigations of estrogen signaling in cephalochordates, the putative biosynthesis of vertebrate-like steroids in mollusks and the synthesis of ecdysteroids, a class of steroids absent in vertebrates, by the crustacean molting organ.

Teleost fish have colonized a staggering variety of marine and freshwater habitats and developed diverse body plans, adaptations and metabolic pathways. Two papers within this special issue examine sex steroid synthesis and function within ovarian and neural tissues in fish. First, Kazeto and colleagues [1] review their body of work on synthesis and function of sex steroids within the ovary of the Japanese eel, *Anguilla japonica*. Through this work, they have developed *A. japonica* as a powerful laboratory model for study of ovarian steroidogenesis and reproductive maturation. Next, Nagarajan et al. [2] characterize expression of steroidogenic enzymes and sex steroid receptors in the brain of a protandrous fish, the orange-spotted grouper *Epinephelus coioides*, during gonadal differentiation. They identified a developmental window for peak aromatase and estrogen receptor (ER) expression in the developing forebrain that precedes or coincides with high neural aromatase activity, estradiol concentrations and markers of cellular proliferation. This study contributes to a growing body of literature linking teleost brain development with gonadal differentiation (e.g., [3,4]). While the first two manuscripts focus on the synthesis and function of sex steroids in teleost fish, steroid concentrations within an organism reflect a balance of anabolic and catabolic processes. In this context, James [5] reviews the current state of knowledge regarding the degradation and excretion of sex steroids in marine and freshwater fish, which is mediated through a suite of enzymes and transporters, that can also be targets for endocrine disruption.

Vertebrate-type sex steroids, i.e. estrogens, have been detected in a variety of invertebrates, but the origins, metabolism and biological functions of these compounds have not been fully elucidated. Non-vertebrate chordates, such as the cephalochordate (amphioxus) *Branchiostoma floridae*, can provide important insight into the origins of steroid signaling pathways. Cephalochordates, for example, contain an estrogen receptor ortholog, can synthesize estrogens from androgen precursors, and are the only invertebrates in which a CYP19 aromatase ortholog has been identified. Callard et al. [6] review the literature regarding estrogen signaling in amphioxus and present analyses of ER and aromatase gene structure, characterization of ER function, and an *in silico* model of the *Branchiostoma* aromatase protein structure. Following this paper, Fernandes et al. [7] review pathways of steroid biosynthesis and metabolism in molluscs, with an emphasis on recent studies.

Ecdysteroids form a distinct family of invertebrate-specific steroids that act as hormones to regulate molting and other processes in arthropods. Ecdysteroid synthesis and signaling pathways have been extensively characterized in insects, and these studies have helped to guide investigation of corresponding processes in crustaceans and other arthropods. Mykles [8] presents a review of ecdysteroid synthesis within the crustacean molting gland with emphasis on the similarities and differences between insect and crustacean pathways. For example, while ecdysteroid synthetic pathways are similar between the insect and crustacean molting glands, the crustacean gland synthesizes and secretes a greater diversity of ecdysteroids.

Together these papers provide a snapshot of areas of current research on steroid metabolism in marine animals and they point clearly to directions for future research. Additional studies are needed to determine the physiological functions of the observed circulating steroids and metabolic pathways and to match observed enzymatic activities with the responsible genes. Supporting these goals, genomics and related technologies that have revolutionized our understanding of molecular regulation of steroid metabolism in humans, are increasingly applied to "non-model" organisms, including marine taxa. Furthermore, powerful phylogenetic methods allow us to identify genes and annotate their possible function based on studies conducted in other organisms; however direct functional characterization is needed for validation and to assess the gene's hypothetical physiological significance *in vivo*. Also, while characterization of steroid synthesizing enzymes in marine organisms progresses, a need remains for a greater understanding of how steroidogenesis is regulated. This issue is illustrated by Kazeto et al. [1], who discuss the role of CYPs in teleost gonadal steroidogenesis, but also point to a current lack of

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understanding of the roles of specific peptide hormones and hydroxysteroid dehydrogenases. Beyond characterizing steroid metabolism and function within whole organisms, it will be essential in coming years to move from the laboratory into wild populations. Marine environments continue to be impacted by a suite of other stressors, including for example climate change, endocrine disrupting compounds, and other pollutants. With a deeper and more synthetic understanding of the diverse metabolic and signaling pathways, it will be possible to also understand how steroidal signaling enables marine organisms to adapt and respond to their environments and how this capability may be impacted by environmental stressors.

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