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Review

Mineral homeostasis and regulation of mineralization processes in the skeletons of sharks, rays and relatives (Elasmobranchii)

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ABSTRACT

Sharks, rays and other elasmobranch fishes are characterized by a skeletal type that is unique among living vertebrates, comprised predominantly of an unmineralized cartilage, covered by a thin outer layer of sub-millimeter, mineralized tiles called tesserae. The mineralized portion of the skeleton appears to grow only by apposition, adding material at the edges of each tessera; maintenance of non-mineralized joints between tesserae is therefore vital, with precise control of mineral deposition and inhibition at the many thousands of growth fronts in the skeleton. Yet, we have only scattered evidence as to how the elasmobranchs mineralize and grow their skeletons. In this review, we take an "environment to skeleton" approach, drawing together research from a vast range of perspectives to track calcium and phosphate from the typical elasmobranch habitats into and through the body, to their deposition at tesseral growth fronts. In the process, we discuss the available evidence for skeletal resorption capability, mineral homeostasis hormones, and nucleation inhibition mechanisms. We also outline relevant theories in crystal nucleation and typical errors in measurements of serum calcium and phosphate in the study of vertebrate biology. We assemble research that suggests consensus in some concepts in elasmobranch skeletal development, but also highlight the very large gaps in our knowledge, particularly in regards to endocrine functional networks and biomineralization mechanisms. In this way, we lay out frameworks for future directions in the study of elasmobranch skeletal biology with stronger and more comparative links to research in other disciplines and into other taxa.

Contents

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1. Introduction

Although vertebrate animals represent only ~2–4% of living animal species, their ecological and body size diversity is truly impressive, with species occupying nearly every habitat on earth and exhibiting ~7 orders of magnitude variation in body mass [1]. A root of the functional and anatomical diversity of vertebrates is the mineralized skeleton, which provides body support and protection, muscular attachment, and ion storage [1,2]. These vital functions rely on apatite, a primarily calcium and phosphate mineral that pervades and reinforces the collagenous matrix of vertebrate skeletal tissues [1,2].

The development, evolution and diversification of vertebrate skeletons are therefore linked to how apatite minerals are constructed (and deconstructed, when and if the constituent ions are needed) [1–3]. Non-mammalian taxa are particularly poorly examined in these regards, but stand to tell us a great deal about the different strategies of vertebrate skeletal mineralization, their commonalities, and the degrees to which they are tied to ecology and phylogeny. The range of habitats and diets (with different ion availabilities), and of primary skeletal tissues and ultrastructures among vertebrate groups [1–3] suggests that there may be taxon-specific variation in how ions are moved from the environment to the skeleton, and that regulation can occur at a variety of levels in that process.

The Elasmobranchii (sharks, rays and relatives) are the only vertebrates with apatite-reinforced skeletons not made primarily of bone [e.g. 4–7]. Instead, the skeletons of all members of the class Chondrichthyes – which includes approximately ~1000 species of elasmobranch fishes and ~50 species of chimaera or Holocephalii, the sister group to the Elasmobranchii – are comprised primarily of a persistent, hyaline-like cartilage [8–10]. In living elasmobranch fishes, the skeletal cartilage is wrapped in an outer coat of apatitic tiles called tesserae, each <1 mm wide and deep, pressed together with very little space between them and forming a continuous surface over most of the skeleton [5,8–10] (Fig. 1). Tesserae are connected by non-mineralized collagen fibers and the whole skeleton wrapped in an outer, fibrous perichondrium layer [6,8,10–12]; some authors have reported an intervening layer of uncalcified cartilage between tesserae and perichondrium [e.g. 11–13], but it is unclear how pervasive this is. The resulting composite, “tessellated cartilage” is therefore comprised of relatively distinct layers of fibrous, mineralized and gel-like cartilaginous materials, with well-delineated boundaries between them (Fig. 1E).

The discrete nature of tesserae (i.e. the maintenance of non-mineralized joints between them) and the fact that they appear to grow in all directions simultaneously [7,8,10,14–16] indicates that the mineralization process must somehow be spatially regulated. Controlled placement of mineral is all the more vital, because elasmobranch skeletons have only a small amount of mineral in comparison with bone: by our approximations (Fig. 2 and Supplementary Information), less than 40% of skeletal dry mass and only 2% of a large shark’s body weight is skeletal mineral (in comparison with 60–70% and 15–20%, respectively, in humans [1]). Furthermore, since the tessellated skeleton appears incapable of remodeling ([17]; see Section 4.2), volumetric growth of the skeleton relies on tesserae remaining separate (i.e. providing intertesseral surfaces for mineral deposition) [7,9,10,18]. Clarification of the mechanisms of mineralization control is therefore important to understanding the development and mechanics of shark and ray skeletons.

This review is directed specifically toward understanding how the tesserae of modern (non-extinct) elasmobranchs are shaped and grown. We purposely limit our discussion of holocephalan (chimaera) skeletons and of areolar cartilage (the other primary, elasmobranch mineralized endoskeletal tissue), due to lack of data. Tessellated cartilage seems to have evolved once in stem chondrichthyans [18], but appears to have been secondarily lost in modern chimaeras. Instead, chimaera are thought to possess a form of non-tessellated “continuous calcified cartilage” [19]; however, the ultrastructure, distribution and mineralization of chimaera skeletal tissue has, to our knowledge, never been studied. Areolar mineralization is found only in the centra of the vertebral column of elasmobranchs and phylogenetically close fossil species [8,19,20], forming a reticulated, mineralized fibrocartilage around the center of the notochord [5,21,22]. The patterns formed by areolar mineralization of vertebral centra have traditionally been used in elasmobranchs for species classification [e.g. 5,21,23] or age estimation [e.g. 24,25]. The patterns and composition of areolar mineralization can also be related to size, activity and environment [e.g. 26–28]; however, the relationships with mineralization processes and the three-dimensional anatomy of areolar mineralized cartilage are still poorly known. Holocephalan cartilage and areolar mineralization are both largely unexamined: it is our hope that some of our discussions below (e.g. of elasmobranch ion balance and hormones) may also be generalizable to questions relating to these tissues.

In the following pages, we review the available evidence for how the elasmobranch fishes orchestrate the mineralization of tesserae. We focus in particular on calcium (Ca^{2+}) and phosphorous (as both inorganic and organic phosphate), tracking their acquisition from the environment (Section 2), their transport into and through the body (Sections 2 and 3), and their combination to form mineral in the right places and in the right arrangements to build the skeletal tissue that distinguishes this group (Section 4). In the process, we also highlight difficulties encountered while measuring free and total calcium (Section 2.1) and inorganic phosphate concentrations (Section 2.2) and physical chemistry, biochemistry, and nucleation theories (epitactic and secretory) relating to calcium phosphate mineral nucleation (Sections 2.3 and 4.1). Taken together, the topics provide a picture of the state of the knowledge of elasmobranch skeletal biomineralization; each section can be read as a standalone piece, referencing core literature the reader can turn to for more information. Despite excellent work covered in the next pages on elasmobranch ion balance, serum electrolyte composition, hormone function, and skeletal ultrastructure and development, these levels of investigation have not been integrated into a holistic understanding of elasmobranch skeletal biology (see, however, the studies of Urist: [4,29,30]). No elasmobranch fish is a