Skeletal Plasticity and Bone Regeneration in Fish: Mechanisms, Influences, and Applications

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ABSTRACT

Fish have exceptional skeletal flexibility and bone regeneration ability, allowing them to adapt to environmental changes and recover from traumas. Fish, unlike mammals, can continuously remodel and regenerate their skeletal structures. This article explores the structure of fish skeletons, skeletal plasticity mechanisms, and the cellular and molecular basis of bone regeneration, including the roles of osteoblasts and osteoclasts, as well as pathways such as Wnt and Bone morphogenetic protein (BMP). It also looks into the effects of genetic, dietary, and environmental factors on bone health. Comparative studies with mammals demonstrate fish's superior regenerating ability, which has implications for regenerative medicine and aquaculture. Understanding these mechanisms can help to enhance fish health in farming and conservation, as well as further biomedical research.

INTRODUCTION

Fish have unique skeletal plasticity and bone regeneration capabilities, which allow them to adapt to changing environmental conditions and heal from skeletal injuries. In contrast to mammals, which predominantly rely on endochondral

ossification for bone formation and have limited regeneration potential, many fish species may remodel and regenerate skeletal structures throughout their lives (Witten & Huysseune, 2009). These processes play a crucial role in growth, biomechanical adaptation, and survival in fluctuating aquatic habitats. The term "skeletal plasticity" describes fish's capacity to modify bone density and structure in response to physiological and environmental stimuli. This flexibility is especially important for species that are subject to varying water conditions, dietary shifts, and mechanical stress alterations. Conversely, bone regeneration enables fish to replace and repair damaged skeletal structures. Furthermore, studying skeletal plasticity in fish helps us better understand how environmental stresses like climate change and pollution affect vertebrate skeletal health (Afonso *et al*., 2022). The study of these processes not only improves our understanding of fish biology, but it also has larger implications in domains like bioengineering, evolutionary biology, and environmental research.

1. Structure and Function of the Fish Skeletal System

Fish have an internal skeletal system that supports the body, enables movement, and protects vital organs. In cartilaginous fish like sharks and rays, the skeleton is made entirely of cartilage, which is lightweight and flexible. In contrast, bony fish (Osteichthyes) have a calcified skeleton that includes a vertebral column for structural support and muscle attachment, a skull to protect the brain, and rib bones to shield internal organs. Their fin rays (lepidotrichia) are segmented and flexible, allowing for precise movement. The skeletal system is divided into cranial bones (skull), the axial skeleton (spine), and the appendicular skeleton (fins and girdles). Overall, fish bones provide shape, aid in locomotion, and guard critical organs. Zebrafish, a common model organism, show typical vertebrate skeletal development from cartilage to bone (Javidan & Schilling, 2004).

2. Mechanisms for Skeletal Plasticity

Skeletal plasticity is the ability of the skeletal system to adapt and remodel in response to different internal and external stimuli. This dynamic process keeps bones structurally intact, strong, and functioning in the face of changing environmental and physiological factors. The mechanisms that underpin skeletal plasticity are complicated, involving adaptations to environmental stimuli, mechanical stress, and biochemical signalling pathways.

2.1 Adaptations to Environmental Conditions

The ability of the skeletal system to adjust to external factors including temperature, salinity, and pressure is astounding. For example, the calcium carbonate skeletons of marine animals like corals and molluscs form are extremely resilient to variations in pressure and salinity (Cohen & Holcomb, 2009). Environmental elements like nutrition and solar exposure can have a immense impact on bone health in terrestrial vertebrates. Calcium absorption and bone mineralization depend heavily on vitamin D, which is produced in the skin by exposure to ultraviolet (UV) light (Holick, 2007). Reduced cutaneous synthesis of vitamin D in populations residing in low-sunlight regions is associated with decreased bone mineral density, highlighting the critical role of environmental factors in skeletal adaptation.

2.2 Influence of Mechanical Stress and Load-Bearing Activity

Mechanical stress is a key driver of skeletal plasticity. Wolff's Law asserts that bone tissue

remodels in response to mechanical loads. Individuals who participate in regular weight-bearing exercises, such as jogging or resistance training, have higher bone density and strength than inactive people (Turner & Robling, 2003). Reduced mechanical loading, such as during prolonged bed rest or in microgravity conditions, can result in considerable bone loss. According to studies, astronauts lose 1-2% of their bone mass per month when in space due to a lack of gravitational loading (Vico *et al*., 2000). This demonstrates the importance of mechanical stress in sustaining bone health.

2.3 Role of Endocrine and Paracrine Signaling in Skeletal Adaptation

Endocrine and paracrine signaling pathways play a pivotal role in regulating skeletal adaptation. Hormones such as parathyroid hormone (PTH), calcitonin, and estrogen are key regulators of bone metabolism. PTH, for example, stimulates bone resorption by activating osteoclasts, while calcitonin inhibits osteoclast activity, promoting bone formation (Karsenty & Ferron, 2012). Estrogen is particularly important in maintaining bone density, as its decline during menopause often leads to osteoporosis (Riggs *et al*., 2002). Additionally, paracrine signaling molecules such as insulin-like growth factor 1 (IGF-1) and bone morphogenetic proteins (BMPs) are critical for local bone remodelling. IGF-1 promotes osteoblast proliferation and differentiation, while BMPs regulate bone formation and repair (Yoon & Lyons, 2004).

3. Bone regeneration in fish: cellular and molecular mechanisms

Bone regeneration is a complex biological process that requires the coordinated activity of multiple cell types, signalling pathways, and molecular mechanisms. This process is especially notable in fish, which have extraordinary regenerating capacities that frequently outperform those of mammals. This investigates the cellular basis of bone regeneration in fish, with an emphasis on osteoblasts, osteoclasts, and osteocytes, as well as the involvement of progenitor cells and dedifferentiation. It also goes into the molecular pathways that control this process, including Wnt, BMP, and Hedgehog signalling.

3.1 Cellular Basis of Regeneration: Osteoblasts, Osteoclasts, and Osteocytes.

Bone regeneration in fish is dependent on the dynamic interaction of three main cell types: osteoblasts, osteoclasts, and osteocytes. Osteoblasts secrete the extracellular matrix, which is mineralized to generate new bone tissue (Witten & Huysseune, 2009). Osteoclasts, on the other hand, are multinucleated cells that reabsorb bone and play an important part in bone remodelling. The balance of osteoblast and osteoclast activity is critical for bone integrity and regeneration (To *et al*., 2012). Osteocytes, which are produced from osteoblasts, are embedded in the bone matrix and operate as mechanosensors, controlling bone remodelling in response to mechanical stress (Franz-Odendaal *et al*., 2006).

3.2 The role of progenitor cells and dedifferentiation

Fish regenerative capacity relies heavily on progenitor cells and dedifferentiation. Progenitor cells, which are undifferentiated cells with the ability to develop into osteoblasts, are stimulated during bone regeneration (Knopf *et al*., 2011). In addition, dedifferentiation—the process by which mature cells revert to a less specialized state—is critical for fish bone repair. For example, dedifferentiated cells can proliferate and redifferentiate into osteoblasts, helping to generate new bone tissue (Poss *et al*., 2003). This ability to dedifferentiate and

redifferentiate is a critical feature that distinguishes fish from mammals in terms of regeneration capacity.

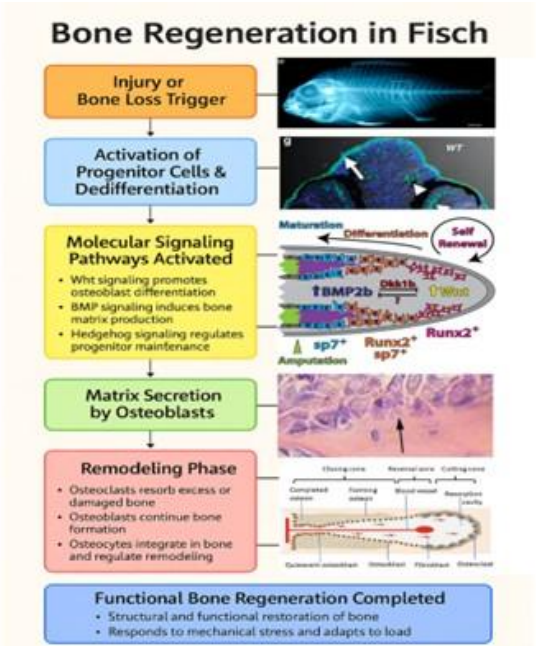

Fig. 1: Bone regeneration in fish

(Image sources- 1. https://www.mdpi.com/2076-2615/13/4/557, 2. https://www.nature.com/articles/oncsis201410, 3. https://www.sciencedirect.com/science/article/pii/S2211124714000114, 4. https://images.app.goo.gl/hGqxM61p9nXiYV7R6, 5. https://images.app.goo.gl/bfo27wkdC9uhqBrG8)

3.3 Molecular Routes: Hedgehog, BMP, and Wnt Signalling

Among the most researched molecular mechanisms that control bone regeneration in fish are Wnt, BMP (Bone Morphogenetic Protein), and Hedgehog signalling. The Wnt signalling pathway is essential for bone formation because it influences osteoblast differentiation and proliferation. On the other hand, BMP signalling is necessary for controlling the synthesis of bone matrix and inducing osteoblast development (Wagner & Aspenberg, 2011) and Hedgehog signalling has a role in bone development regulation and progenitor cell maintenance (Quint *et al*., 2002). To guarantee efficient bone regeneration, these pathways work together in a highly coordinated fashion.

4. Factors Influencing Skeletal Plasticity and Regeneration

Fish exhibit remarkable skeletal plasticity and regenerative abilities, allowing them to adapt to environmental and physiological challenges. These processes are governed by genetic and epigenetic mechanisms, nutritional status, and environmental factors. Key developmental pathways such as Wnt/β-catenin and Bone morphogenetic protein (BMP) are vital for bone formation and remodelling, and any disruption in these can lead to deformities (Zhang *et al*., 2021). Epigenetic factors like DNA methylation and non-coding RNAs regulate bone gene expression in response to environmental changes, influencing osteogenesis and regeneration (Witten & Hall, 2015). Nutrition also plays a critical role—minerals such as calcium and phosphorus are essential for bone matrix formation, while deficiencies can lead to poor mineralization and deformities (Boglione *et al*., 2013). Vitamin D helps regulate calcium balance, and omega-3 fatty acids like Ecosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) support bone health by reducing inflammation (Witten & Huysseune, 2021). Environmental pollutants, including heavy metals (Hg, Cd, Pb), endocrine-disrupting chemicals like Bisphenol A (BPA) and Polychlorinated Biphenyls (PCBs), and as well as other factors including hypoxia and acidification, can impair skeletal development by disrupting hormonal regulation, calcium metabolism, and enzymatic activities essential for bone formation (Witten & Hall, 2015; Zhang *et al*., 2021). These factors collectively influence skeletal health, with significant implications for both wild and farmed fish.

5. Applications in Aquaculture and Conservation

Fish skeletal plasticity and regenerative capacity have significant implications for aquaculture and conservation. Fish possess remarkable bone remodelling abilities that enable them to adapt to diverse environmental conditions and recover from skeletal injuries, making them valuable models for advancing aquaculture practices and species protection (Witten & Huysseune, 2009). In aquaculture, skeletal deformities negatively affect fish growth, survival, and market value. By understanding the genetic and environmental factors influencing bone health, selective breeding programs can be developed to enhance skeletal traits. Studies on zebrafish have identified genetic markers linked to bone density and strength, which can be applied to produce robust farmed fish (Witten *et al*., 2017). Environmental factors, including nutrition, stocking density, and water quality, also significantly affect bone development. For example, supplementing salmonid diets with calcium and phosphorus has been shown to improve bone mineralization. Maintaining bone health in captive populations requires a multifaceted approach. Proper nutritional management, particularly ensuring adequate intake of calcium and phosphorus, is essential to prevent deformities, such as those observed in rainbow trout. Environmental enrichment, such as tank design and water flow that encourages natural swimming behaviour, supports skeletal strength. Regular monitoring of bone health allows early detection and correction of issues through dietary or husbandry adjustments. Beyond aquaculture, skeletal plasticity also plays a crucial role in conservation. Understanding bone regeneration aids in rehabilitating injured fish, improving their chances of survival and reintroduction. Additionally, recognizing environmental factors affecting bone development supports habitat restoration efforts by ensuring the restored environments promote healthy skeletal growth and long-term population sustainability.

CONCLUSION

Fish have amazing skeletal plasticity and regeneration, which is facilitated by various cellular and molecular pathways. These processes, regulated by genetic, dietary, and environmental factors, allow fish to adapt and recover from injuries faster than mammals. Insights from fish bone regeneration have major implications for regenerative medicine, notably in the treatment of human skeletal ailments. This understanding can be applied in aquaculture to eliminate bone abnormalities and increase fish health. Future study using modern technologies such as CRISPR-Cas9 will elucidate the genetic and molecular underpinnings of these processes, aiding both biomedical science and fish conservation. The study of fish skeletal biology can connects evolutionary adaptation to practical applications in medicine and aquaculture.

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