In focus in HCB: Hard Tissue Biology

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Among the varieties of biological mineralization in nature, e.g., shell, coral, and bone, this special issue “Hard Tissue Biology” presented by Histochemistry and Cell Biology, focuses on the bone, cartilage, and teeth in mammals. Bone metabolism is not only strictly regulated by cellular events, local factors, mechanical stress, gender, age, and the hormonal/nervous system, but also orchestrated reciprocally with other organs, such as the kidney, muscle, and pancreas. We can, therefore, refer to this as an “osteo-network.” During the past decade, molecular and cellular mechanisms in the development/metabolism of bone, cartilage, and teeth has been expounded, and to that end, we believe a special issue of “Hard Tissue Biology” will provide up-to-date and invaluable information to the readers of this journal.

Mineralization—the occurrence of crystalline calcium phosphates in extracellular matrix, is an essential phenomenon in the hard tissue of humans. Mineralization induced by mesenchyme-derived cells, e.g., osteoblasts, chondrocytes, odontoblasts, is always initiated by matrix vesicles, which are small extracellular vesicles secreted by these cells. Recent studies have revealed that biological functions of several membrane transporters and enzymes (tissue nonspecific alkaline phosphatase, ENPP1, PHOSPHO1 and ANK, etc.) equipped in the matrix vesicles, as well as non-collagenous proteins, are coordinated to enable the spatiotemporal crystallization of calcium phosphate (hydroxyapatite).

In this special issue on “Hard Tissue Biology”, Hasegawa (2018) reviews the ultrastructure and cell biology of matrix vesicles-mediated mineralization, by introducing her own

and other researchers’ evidence. Among many osteotropic/calcitropic hormones, an active form, 1,25-dihydroxy vitamin D [1,25(OH)2D], plays a paramount role in mineral and skeletal homeostasis. Goltzman (2018) reviews biological functions of vitamin D in bone and cartilage, including the critical role of vitamin D in regulating mineral/skeletal homeostasis both indirectly and directly via the 1,25(OH)2D/VDR system.

Molecular cell biology on cell differentiation and tissue development of bone, cartilage, and teeth are important issues in hard tissue biology. The discovery of runt-related transcription factor 2 (Runx2), also known as Cbfa-1,—a key transcription factor associated with osteoblast differentiation and chondrocyte maturation, as well as receptor activator of nuclear factor- κ B ligand (RANKL)/RANK/osteoprotegerin system was epoch-making and highlighted in the research field of molecular cell biology in bone. In this issue, Komori (2018) describes the pivotal roles of Runx2 and related molecules, e.g., Ihh, Sp7 and canonical Wnt signaling Cbfb. Ono and Nakashima (2018) review osteoclasts biology, which is regulated by the signaling linked to RANK/RANKL and related molecules. Minqi Li’s research team (2018a) reports that IGF2 messenger RNA-binding proteins (IMPs)—a family of onco-fetal RNA-binding proteins that play an important role in cell migration, renewal and metabolism, is involved in bone remodeling by regulating the activity of osteoclasts and impairing their adhesion.

In addition to bone development, epiphyseal cartilage/growth plate cartilage is essential for endochondral ossification during skeletal growth. Nishimura et al. (2018) review the sequential steps of Sox9/Sox5/Sox6, Runx2/Runx3 and Osterix in cartilage development, as well as the pathological action of several transcription factors, including Runx2, C/EBP β and HIF-2 α in osteoarthritis. Ryuma Haraguchi and Sohei Kitazawa et al. (2018), using Gli1^{CreERT2} mice, demonstrate the fate of hedgehog-signal-responsive cells in cartilage; these progeny were then committed to the osteogenic lineage in subchondral bone. Based on established knowledge of cartilage development, Hoshi et al. (2018) introduce a method of tissue engineering of cartilage regeneration,

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focusing on autologous chondrocyte implantation method as well as biodegradable polymers such as poly-L-lactic acid. In tooth development research, neural crest-derived mesenchymal cells that differentiate into odontoblasts responsible for dentin formation of teeth is also presented. The research team of Ohshima (2018) examines how gene expression of nestin (known to be expressed in undifferentiated cells during neurogenesis and myogenesis) is regulated in odontoblasts, using nestin-EGFP (enhanced GFP) transgenic mice.

This issue also presents research on pathological bone response in inflammatory diseases, and osteoclastic function in osteolytic pathology. Minqi Li's team (2018b) reviews the pathological states of bone cells, immune cells and their inflammatory cytokines (TNF α , IFN γ , IL-1, IL-6, IL-17, IL-10, TGF β) in regulating the recruitment and cellular functions of mesenchymal stem cells and bone regeneration. Kitazawa and her team (2018) summarize osteolytic lesions typically observed in osteolytic metastases of malignancies, autoimmune arthritis, and giant cell tumors of bone.

Recent advances in optical imaging technology are also highlighted in this special issue. Multi-photon excitation microscopy has enabled visualization inside intact bone tissue in living animals, while the high resolution of focused ion beam scanning electron microscopy (FIB-SEM) is able to visualize three dimensional structures of bone cells. Using intra-vital multi-photon imaging of dynamic biological systems, Mizuno, Kikuta, and Ishii (2018) demonstrate the spatiotemporal nature of bone during remodeling, and bone cells' reaction to osteoporotic drugs. Hasegawa and Amizuka et al. (2018) show FIB-SEM images of three dimensional ultrastructure of osteocytes and their cytoplasmic processes. In clinical applications, Ikeda and Yokoyama et al. (2018) verify the biological function of the osteocytic network involved in bone turnover and the quality in the surrounding bone of dental implants.

In summary, this special issue "Hard Tissue Biology" offers a valuable resource for readers, by providing them with the most up-to-date information in the field of bone, cartilage and teeth.

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