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Editorial: Crosstalk between bone and other cells

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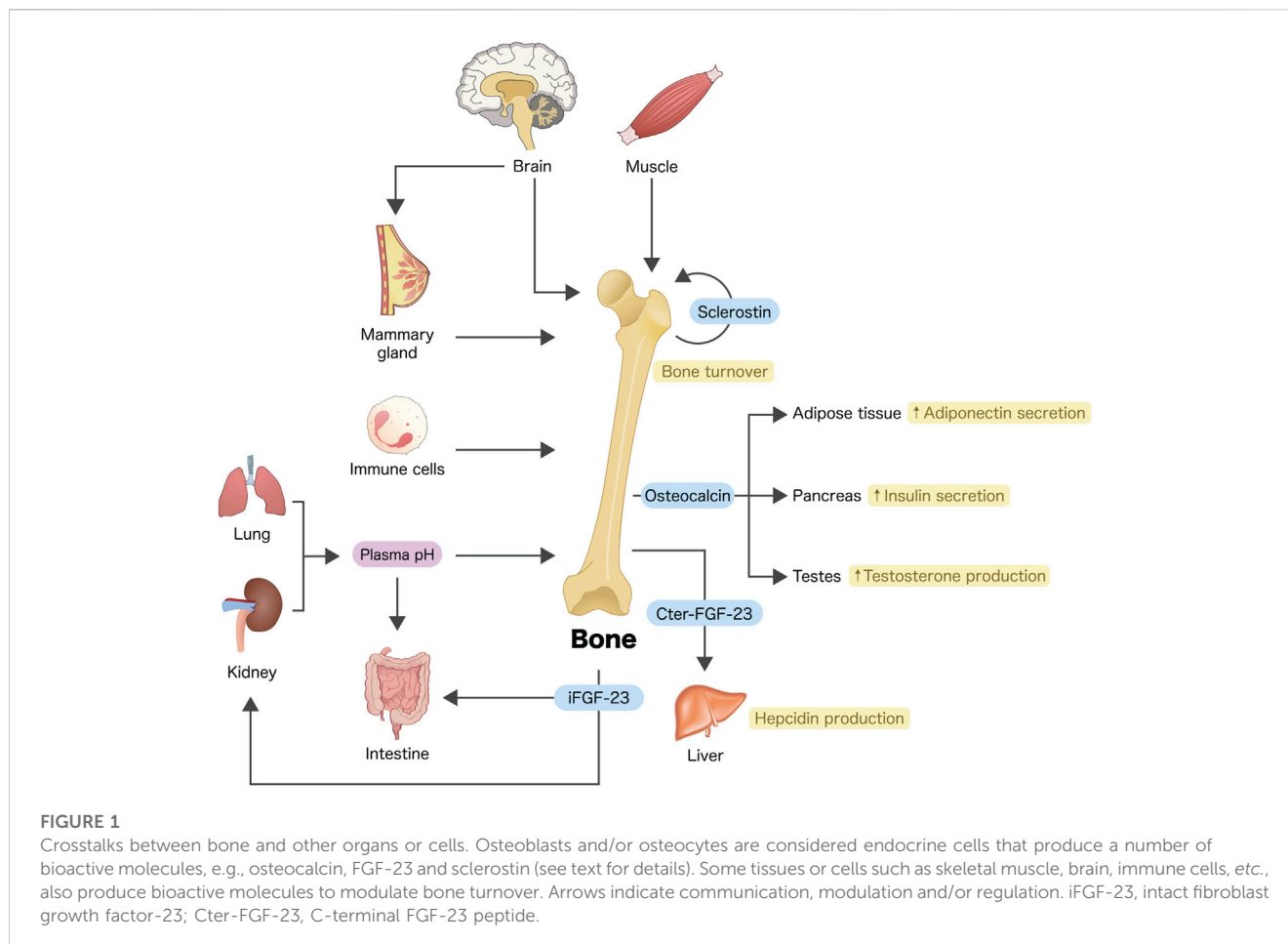
Editorial on the Research Topic

Crosstalk between bone and other cells

Communications between osseous tissues and other organs are very common and essential for physiology of overall body system. For example, osteoblasts and osteocytes—now as endocrine cells ([Figure 1](#))—are able to produce and release fibroblast growth factor (FGF)-23, which, in turn, regulates renal phosphate reabsorption ([Vervloet, 2019; Agoro and White, 2023](#)) and calcium transport across the intestinal epithelium ([Khuituan et al., 2012; Rodrat et al., 2018; Wongdee et al., 2018; Wongdee et al., 2021](#)). FGF-23 also downregulates the expression and activity of 25-hydroxyvitamin D 1 α -hydroxylase (CYP27B1) in the renal proximal tubular cells, thereby reducing the action of 1,25-dihydroxyvitamin D₃ ([Perwad et al., 2007](#)). During acute inflammation, osteocytes release certain mediators including C-terminal FGF-23 peptides to modulate hepatic hepcidin production and serum iron ([Courbon et al., 2023](#)). Moreover, osteocalcin or γ -carboxyglutamic acid-containing protein—as an osteoblast-derived endocrine factor—is capable of regulating pancreatic insulin production ([Lee et al., 2007](#)), adiponectin release from adipocytes ([Lee et al., 2007](#)) or testicular androgen biosynthesis ([Karsenty and Oury, 2014](#)).

On the other hand, several tissues, such as muscle and brain, also send signals to modulate bone remodeling ([Rousseaud et al., 2016; Gomasasca et al., 2020](#)). For instance, myokines (e.g., interleukin-6 and irisin) have been reported to positively regulate bone formation ([Gomasasca et al., 2020](#)), whereas central sympathetic outflow probably enhances bone resorption through β_2 -adrenergic receptor ([Bonnet et al., 2008; Huang et al., 2009](#)). Certain organs such as lung and kidney are principal regulators of plasma pH, a disturbance of which (e.g., metabolic acidosis) profoundly affects intestinal calcium absorption ([Charoenphandhu et al., 2007](#)) and osteoblast-mediated bone formation ([Bushinsky and Krieger, 2022](#)).

In the present Research Topic, there are publications that clearly point out the crosstalk between bone and some other tissues and cells, including the respiratory tissues, adipose tissue, mammary tissue, brain, and immune cells (e.g., monocytes, T-cells, *etc.*). Specifically, in an original article by [Ivanova et al.](#), the results corroborated that a disruption of Wnt-sclerostin pathway contributed to osteopathy (i.e., osteopenia and osteoporosis) in patients



with Gaucher's disease, a common lysosomal storage disease caused by acid β -glucocerebrosidase gene mutation with cellular accumulation of glucocerebroside. Another original article by Kurgan et al. demonstrated the effects of treadmill exercise on serum sclerostin levels in male mice. Sclerostin has been recognized as a secretory glycoprotein that strongly negates bone formation (Delgado-Calle et al., 2017; Liao et al., 2022), especially during mechanical unloading (Lin et al., 2009). It is predominantly expressed by osteocytes in order to suppress osteogenesis by regulating proliferation, differentiation, mineralization and apoptosis of osteoblasts (Winkler et al., 2003; van Bezooijen et al., 2004; Liao et al., 2022). Sclerostin is also expressed in some other tissues, e.g., cartilage, heart, kidney, and liver as well (Brunkow et al., 2001; Weivoda et al., 2017). Since Kurgan and others (Kurgan et al.) assessed serum sclerostin in exercising male mice and found a decrease in serum sclerostin in exercising group, mechanical loading during exercise is probably an efficient way to restrict sclerostin secretion from both osteocytes and adipose tissue (Kurgan et al.; Oniszczuk et al., 2022).

Generally, Wnt/ β -catenin signaling plays a critical role in bone homeostasis by promoting osteoblastogenesis and bone formation. On the other hand, sclerostin—known as a Wnt signaling antagonist—binds to Wnt co-receptors, i.e., low-density lipoprotein receptor-related proteins 5 and 6 (LRP5 and LRP6),

thereby preventing Wnt from binding to these co-receptor proteins. As a consequence, sclerostin blocks the Wnt downstream signaling pathway and downregulates the expression of genes involved in osteoblast commitment, such as *RUNX2* (Delgado-Calle et al., 2017). Several factors have been reported to suppress the expression of sclerostin including parathyroid hormone, estrogen as well as mechanical loading (Drake and Khosla, 2017). These factors thus act in concert with the Wnt/ β -catenin signaling pathway to modulate bone homeostasis.

This Research Topic also contains review and mini-review articles that elaborate the crosstalk between bone and other tissues. Specifically, Ma and others (Ma et al.) explained how pulmonary tuberculosis, lung cancers, pollutant exposure [including particulate matter 2.5 ($PM_{2.5}$)], asthma and chronic obstructive pulmonary disease are able to cause or aggravate osteoporosis. In a mini-review by He and Jiang, the interdependent interactions between immune cells (e.g., T cells, macrophages, NK cells, and dendritic cells) and cancer cells in bone microenvironment are well delineated. Lastly, Athonvarangkul and Wysolmerski discussed the physiological significances of the brain–breast–bone axis and maternal skeletal changes. A maternal pathological condition known as pregnancy/lactation-associated osteoporosis was also mentioned. Maternal central nervous system—particularly hypothalamus—controls bone

metabolism by altering a number of humoral factors, e.g., prolactin, oxytocin and gonadotropin-releasing hormone, the latter of which is the salient regulator of circulating gonadotropins and estrogen. Prolactin not only enhances the intestinal calcium absorption (Charoenphandhu et al., 2009) but also modulates the expression of osteoblast-derived osteoclastogenic factors (Wongdee et al., 2011) and sclerostin production (Athonvarangkul and Wysolmerski).

Therefore, the present Research Topic is certainly able to shed some light on the crosstalks between bone and other distant cells, especially in lung and adipose tissue as well as cells in the brain–breast–bone axis (Figure 1). Indeed, interactions between bone cells and neighboring hematopoietic cells or stem cells within marrow tissue microenvironment are not uncommon and their detailed signaling networks are worth exploring.

Author contributions

All authors listed have made a substantial, direct, and contribution to the work and approved it for publication.

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