General Introduction

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As guest editor, I am happy to introduce to you the latest special issue of Clinical Reviews in Bone and Mineral Metabolism, focusing on *Osteocyte Communication*. This subject was inspired by new scientific discoveries that once again highlight the importance of osteocytes for bone homeostasis. Most notably, osteocytes have recently been found to be the major source of receptor activator of nuclear factor κ B ligand (RANKL), thereby determining bone mass in adults.

Previous special editions of Clinical Reviews in Bone and Mineral Metabolism include a special issue on “The response of the skeleton to mechanical load” as well as an issue on “Mechanosensing in Bone.” Osteocytes played a central role in both of these special issues, since these cells are most suitably located within the bone to sense mechanical signals. In addition, osteocytes are equipped with a multitude of molecular features that allow mechanosensing, making them the bone mechanosensors par sang. Yet, osteocytes are more than “just” highly specialized mechanosensing cells. Several signaling molecules are more or less exclusively produced by osteocytes, and awareness is rising that osteocytes hold a tight reign over osteoclast formation. One of the signaling molecules produced by osteocytes, i.e., sclerostin, may inhibit bone mass accrual by osteoblasts, and sclerostin antibodies are currently being investigated as a potential osteoporosis therapy. Osteocytes also play a role in phosphate homeostasis, by communicating with the kidney, making bone a truly

endocrine organ. This underscores the possibility that factors produced by osteocytes reach remote organs, where they may modulate cell behavior. Therefore, the focus of this issue will be signaling from and toward osteocytes. A better understanding of the biochemical signals received by osteocytes, and produced by osteocytes, may allow a more targeted manipulation of the balance between bone formation and resorption, and mineral deposition and dissolution.

The first chapter, by Dr. van Oers and colleagues, describes how osteocytes play a central coordinating role in driving osteoblast and osteoclast recruitment and activity within a bone multicellular unit, through production of signaling factors.

The second chapter, by Dr. Bakker and Dr. Everts, further explores the lines of communication between osteocytes and osteoclasts. Several signaling molecules produced by osteocytes and affecting osteoclasts are discussed in detail. In addition, molecular pathways that may allow communication from osteoclasts toward osteocytes are discussed.

In the third chapter, Drs. Jaspers and Bravenboer explore which pathways may allow communication between muscle and bone, including pathways emanating from the osteocytes.

In the fourth chapter, Dr. Ito et al. focus on one factor produced by osteocytes, fibroblast growth factor 23 (FGF23), and the involvement of this key phosphate-regulating hormone in human disease.

These articles bring together the latest thoughts about communication between osteocytes and their target cells, which sometimes are located in remote organs. Hopefully, this special issue will encourage a fresh view on bone, as an endocrine organ, by both basic scientists and clinicians.

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