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Intracellular Calcium Signaling In Osteocytes: A Mechano-Transduction-Mechano Paradigm

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ABSTRACT

The position and the ability to communicate with other bone cells make the 3-dimensional (3D) osteocyte network ideal mechanosensors in bone. The role of osteocyte network and intercellular communication between osteocytes in response to mechanical stimulation may clarify the mechanisms behind normal bone adaptation to mechanical loading. We have been using intracellular calcium ($[Ca^{2+}]_i$) as a ubiquitous real-time signaling indicator for studying mechanotransduction in osteocytic network and individual osteocytes, and recently discovered that 2D osteocytic networks are much more sensitive than osteoblasts in terms of $[Ca^{2+}]_i$ responses. In addition, we used a novel mouse tibia loading model for the real-time measurement of $[Ca^{2+}]_i$ signaling in osteocytes *in situ* when the intact long bone was under dynamic loading. We confirmed that *in situ* osteocytes, but not bone surface cells, displayed repetitive $[Ca^{2+}]_i$ spikes in response to dynamic loading, with spike frequency and magnitude dependent on the loading magnitude, bone tissue strain, fluid flow speed, and fluid shear stress in the lacunar-canalicular system. However, positing a biological reason for this robust $[Ca^{2+}]_i$ behavior in osteocytes has been difficult. Using a novel quasi-3D microscopy technique, we were able to simultaneously measure both $[Ca^{2+}]_i$ and actin network deformation. We demonstrate phasic contractility in MLO-Y4 osteocytes synchronized with $[Ca^{2+}]_i$ spikes, possibly mediated through smooth muscle myosin. Similar to myocytes, a tight coupling between $[Ca^{2+}]_i$ oscillations and reversible actomyosin contractions is observed. The implications of having smooth muscle myosin ATPase in osteocytes ushered a new mechano-transduction-mechano paradigm in mechanobiology of bone cells.

BIOGRAPHY

Dr. X. Edward Guo is a Professor of Biomedical Engineering at Columbia. He received his B.S. in Applied Mechanics/Biomechanics from Peking University in 1984 and his M.S. (1990) and Ph.D. (1994) in Medical Engineering and Medical Physics from Harvard-MIT Division of Health Science and Technology. After postdoctoral training in Orthopaedic Bioengineering from the University of Michigan, he joined the faculty at Columbia University in 1996. His research interests are in bone mechanics, image analysis of bone microstructure, mechanobiology of bone, and bone cell mechanics. He received a New Investigator Recognition Award from Orthopaedic Research Society, a National Research Service Award from NIH, an NSF CAREER award, and Funds for Talented Professionals from Chinese National Natural Science Foundation.

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