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Title: Investigation of Osteocyte Encoding of Differential Loading Parameters in Vivo

Karl Lewis PhD
Cornell University

ABSTRACT

The osteocyte is a critical cell type for the development and progression of osteoporosis, as it is the main source of factors that control bone resorption (e.g., RankL) and formation (e.g., Sost/Dkk1). Our lab uses intravital imaging approaches to interrogate osteocyte mechanobiology in vivo. We record real time molecular dynamics information using fluorescent reporters while maintaining intact paracrine, endocrine, and tissue crosstalk systems. Data from our group suggest the neurotransmitter acetylcholine has a potentiating role in bone mechanotransduction responses, offering a strong centrally regulated control mechanism which may contribute to modulating osteocyte responses to mechanical load. In the present pilot project, we propose investigations of a novel bone sensitivity control mechanism, consisting of local acetylcholine signaling nerve regulation of osteocyte responses to mechanical loading in vivo. Better understanding of this signaling phenomenon will provide important new insight into bone mechanotransduction and potentially offer a convenient, extracellular osteoporosis therapeutic target.

There are many redundant signaling pathways involved in osteocyte mechanotransduction and recently, evidence suggests cholinergic neuronal signaling as an important mediator of osteocyte mechanosensitivity via modulation of calcium signaling potential. The work proposed here will interrogate the impact of osteocyte cholinergic channels in osteocyte calcium signaling responses to mechanical loading in vivo using intravital imaging. We will use pharmacological perturbations to elucidate the role of cholinergic signaling in potentiating osteocyte responses acutely. These data will serve as preliminary results for a larger project aimed at fully outlining the details of cholinergic regulation of mechanotransduction.