TACSM Abstract

Beyond Sclerostin: Influence of Disuse and Recovery from Disuse on Mechanosensitive Osteocyte Proteins

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ABSTRACT

Osteocytes, mechanosensitive cells embedded in bone tissue, release proteins responsive to mechanical stimuli that signal osteoblasts and alter bone formation. Sclerostin (Scl), an inhibitor of the Wnt signaling pathway, is upregulated in disuse which inhibits bone formation. Osteocyte insulin-like growth factor-I (IGF-I) and interleukin-6 (IL-6) are both implicated to increase with mechanical or shear stress enhancing osteoblast function. **PURPOSE:** To determine osteocyte protein levels of sclerostin, IGF-I, and IL-6 in disuse and after recovery from disuse. **METHODS:** Male Sprague Dawley rats (6-mo old) were hindlimb unloaded (HU) to simulate disuse or allowed normal cage activity (CA) for 28 days (28d). Another group of HU and CA were allowed to recover for 2 months following 28 days HU (84d). **RESULTS:** Static histormorphometry of the proximal tibia metaphysis showed a 26% decline in cancellous bone volume at 28d ($p<0.05$), but no differences between CA and HU at 84d. Osteoclast surface increased 2-fold in HU at 28d ($p<0.05$), but was not different at 84d. Osteoid surface (a measure of bone formation) was nearly 3-fold lower in HU at 28d and 2.5-fold lower 84d ($p<0.05$). Immunohistochemical analyses for %positive cancellous osteocytes at the distal femur showed a 20% increase in %Scl+, a 29% decrease in %IGF-I+, and a 25% decrease in %IL-6+ at 28d ($p<0.05$). At 84d, %Scl+ and %IL-6+ were not statistically different between HU and CA, but %IGF-I+ in HU remained lower than CA ($p<0.05$). With combined 28d and 84d, regression analysis showed %IGF-I+ osteocytes predicted osteoid surface ($R^2=0.304$, $p<0.05$). **CONCLUSION:** After 28d, disuse from HU resulted in higher osteocyte Scl and lower IGF-I and IL-6 which corresponded with lower osteoid surface and bone volume. Following 2 months recovery, all HU values were similar to CA except for osteoid surface and osteocyte IGF-I which remained depressed. These data indicate that loss of mechanical stimuli from disuse affects not only osteocyte sclerostin, but osteocyte IL-6 and IGF-I as well. All three likely alter osteoblast signaling resulting in decrements in bone formation in disuse. Interestingly, in our study, osteocyte IGF-I remained low after recovery from disuse implicating a prolonged effect from disuse or other factors besides mechanical stimuli influencing osteocyte IGF-I.

TEXAS CHAPTER
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