Skeletal Muscle – Bone Crosstalk Regulating Osteocyte Function

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Osteocytes are thought to be the primary cell in bone that responds to mechanical loading and the traditional view is that skeletal muscle's role relative to bone is in the application of those loads. We have hypothesized that muscle cells can exert influences on bone through the production of endocrine like factors that alter the behavior of bone cells. To test this hypothesis we have cultured MLO-Y4 osteocyte like cells in the presence of conditioned media (CM) from C2C12 differentiated muscle cell cultures, a myogenic cell line that closely represents adult mammalian skeletal muscle cells. We have observed that muscle cell CM causes increased dendrite lengthening and decreased cell body area similar to previously reported effects of fluid flow shear stress (FFSS) applied to the MLO-Y4 osteocytic cells. We next determined whether muscle cell CM could alter the regulation of early biochemical signaling pathways that are known to be activated by FFSS. The addition of 10% muscle cell CM during the application of FFSS for 2 hours resulted in a potentiation of Akt signaling activation by FFSS on MLO-Y4 osteocytic cells. Erk1/2 activation in response to FFSS is normally transient in MLO-Y4 cells reaching a peak at 15 minutes and declining by 2 hours; however, in the presence of 10% CM there was a sustained activation at 2 hours. These data are consistent with the production of a factor(s) by skeletal muscle cells that can modulate the function of the bone osteocytes and their response to loading. The identification of this factor could lead to the development of new paradigms or agents to treat diseases of low bone mass such as osteoporosis and muscle related diseases such as sarcopenia.

Key words: muscle, bone, loading, osteoporosis, cell signaling, sarcopenia