

Osteocytes are dynamic, not passive cells in their response to strain and remodeling of their microenvironment

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The matrix producing osteoblast is highly metabolically active compared to the osteocyte. This is probably due to the fact that osteoblasts exist as matrix producing cells for only days or a few weeks and must generate several times their volume in matrix while the encapsulated osteocyte is viable for years or decades. However, the osteocyte is not an inactive cell, especially in response to mechanical strain. While fairly well accepted and documented that the osteocyte can send biochemical signals in response to mechanical strain, studies addressing osteocyte modification of its lacunae have been controversial. New studies suggest that the osteocyte is a dynamic, active cell that can modify its microenvironment. Holmbeck and colleagues have found that osteocytes in mice lacking MT-1 MMP, a matrix metalloproteinase that cleaves collagen, fail to form canaliculi (*J. Cell Sci.* 2005). Our preliminary data, like that of Holmbeck and co-workers, shows that the number and branching of dendrites increases with age. Data showing increased expression of a molecule thought to play a role in dendrite formation, E11, in osteocytes with loading also supports this hypothesis. Recent experiments show that osteocyte lacunae in mice treated with the Glucocorticoid (prednisolone) are enlarged and the surrounding matrix is hypomineralized. Lacunae around osteocytes in mice subjected to loading label with fluorochrome dyes. These data suggest that the osteocyte is a dynamic cell that can generate processes even when embedded in mineralized tissue and can also alter its microenvironment (eg enlarge or reduce the size of its surrounding lacunae).

These studies have implications with regards to type and magnitude of fluid flow shear stress moving through the lacunae and canaliculi of osteocytes. It could be inferred that if the osteocyte can modify the size of its lacunae, it can modify the diameter of its canaliculi. Generation of additional canaliculi with their internal dendritic processes and removal of matrix from lacunae and canaliculi would dramatically modify bone fluid flow. For the same rate of bone fluid flow within a canaliculi, a narrower canal diameter would increase shear stress, while widening the canal would decrease shear stress. Widening of canals and lacunae in addition to increasing numbers and branching of canaliculi would lead to reduced shear stress. This may explain why the aging skeleton is less responsive to strain. Osteocytic response in diseased physiological states could play a role in pathological changes in bone.