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Primary Cilia Session

Primary cilia in bone

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While it has been known for decades that bone is a mechanosensitive organ, the responsible mechanism has been elusive. Primary cilia, once commonly thought to be vestigial organelles, are now being re-examined in development and in kidney tissue as a fluid sensing organelle. We have found primary cilia in both osteoblastic and osteocytic cell lines as well as in osteoblasts and osteocytes *in vivo*¹.

In kidney cells, primary cilia have been established as a necessary component of the cell's fluid flow-induced calcium response through stretch activated channels at the base of the primary cilia^{2,3}. Calcium mobilization also occurs following fluid shear stress in bone cells⁴. To determine whether primary cilia act as mechanosensors in bone, we examined two outcome variables, intracellular calcium release and prostaglandin E₂ release, which have been shown to be independently stimulated by fluid flow^{4,5}. We hypothesized that there would be a correlation between calcium mobilization and the presence of a primary cilium. Since gap junctional communication can transmit calcium signals from cell-to-cell, we also hypothesized that this correlation would increase if gap junctional communication was blocked.

Interestingly while the primary cilium was necessary for the flow-induced PGE₂ release, it did not play a role in the cell's mobilization of intracellular calcium. There was also no correlation between whether a cell had a primary cilium, and its likelihood of exhibiting a calcium response. This correlation was not strengthened with the inhibition of intercellular communication by blocking gap junctions. Our findings suggest that primary cilia are a component of the mechanotransduction pathway for PGE₂ release, but distinct from the kidney, do not play a role in intracellular calcium mobi-

lization. This independence of calcium and PGE₂ has been reported previously and suggests that there are multiple mechanisms by which bone cells sense their mechanical environment. These findings are currently in press in the Proceedings of the National Academy of Science.

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