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BONE

Osteocyte-specific activation of the canonical Wnt–β catenin pathway stimulates bone formation

Activation of canonical Wnt–β catenin signalling exclusively in osteocytes leads to bone gain, shows a new study in mice. This finding highlights the key role of osteocytes in regulating bone anabolism.

Bone homeostasis relies on the balance between bone formation by osteoblasts and bone resorption by osteoclasts. "Osteocytes, the most abundant type of bone cells, live inside the mineralized bone matrix and coordinate the function of bone surface cells—osteoclasts and osteoblasts," explains Teresita Bellido, senior author of the study. However, the mechanisms underlying the regulation of osteoblasts and osteoclasts by osteocytes are still poorly understood.

"We focused on the study of canonical Wnt–β catenin signalling because hormonal and mechanical stimuli that increase bone formation activate this pathway and human mutations of components of the pathway underscore its essential role in bone accrual," explains Bellido.

The researchers used a mouse model in which the canonical Wnt–β catenin signalling pathway was activated specifically in osteocytes. These mice had high numbers of osteoclasts and osteoblasts, and increased levels of bone formation and bone resorption markers. The net effect of stimulation of canonical Wnt–β catenin signalling in osteocytes was increased BMD and bone volume. Activation of the Notch pathway was also observed in these mice. "These findings contrast with previous evidence in the literature that canonical Wnt–β catenin signalling in osteoblasts decreases resorption and induces perinatal death from leukaemia," comments Bellido.

By separating the effects of stimulation of canonical Wnt–β catenin signalling into bone accrual by osteocytes and inhibition of bone resorption and development of leukaemia by osteoblasts, the new findings might advance the therapy of bone diseases such as osteoporosis. Osteoblasts are short-lived and scarce, whereas osteocytes are

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long-lived and abundant, which makes them "more logical and effective target cells to induce bone anabolism," says Bellido.

"Future studies are needed to fully understand the downstream mechanisms and molecular mediators of osteocyte-driven regulation of osteoblasts and osteoclasts," concludes Bellido.

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Original article Tu, X. *et al.* Osteocytes mediate the anabolic actions of canonical Wnt/β-catenin signaling in bone. *Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.1409857112