

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Lrp5 controls bone formation by inhibiting serotonin synthesis in the duodenum

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Loss- and gain-of-function mutations in the broadly expressed gene LDL receptor-related protein 5 (Lrp5) affect bone formation, causing osteoporosis and high bone mass, respectively. Although Lrp5 is viewed as a Wnt coreceptor, osteoblast-specific disruption of β -catenin does not affect bone formation.

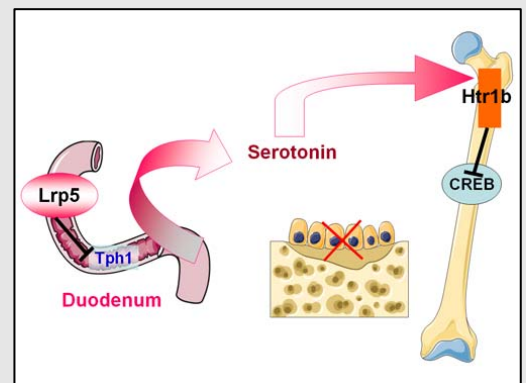
Instead, the authors of this study [1] show here that Lrp5 inhibits expression of tryptophan hydroxylase 1 (Tph1), the rate-limiting biosynthetic enzyme for serotonin in enterochromaffin cells of the duodenum. Accordingly, decreasing serotonin blood levels normalizes bone formation and bone mass in Lrp5-deficient mice, and gut- but not osteoblast-specific Lrp5 inactivation decreases bone formation in a β -catenin-independent manner. Moreover, gut-specific activation of Lrp5, or inactivation of Tph1, increases bone mass and prevents ovariectomy-induced bone loss. Serotonin acts on osteoblasts through the Htr1b receptor and CREB to inhibit their proliferation.

By identifying duodenum-derived serotonin as a hormone inhibiting bone formation in an Lrp5-dependent manner, this study broadens our understanding of bone remodeling, and suggests alternative avenues to increase bone mass.

1. Yadav VK et al. *Cell*. 2008;135: 825–837.

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Lrp5 favors bone formation and bone mass accrual by inhibiting Tph1 expression and serotonin synthesis in duodenal enterochromaffin cells. Following its binding to Htr1b, serotonin inhibits CREB expression and function, which results in a decrease in osteoblast proliferation.



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