

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

PTH does not need Lrp5 to stimulate bone formation in mice ?

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Low-density lipoprotein receptor-related protein 5 (Lrp5) is a membrane protein acting as a coreceptor in canonical Wnt signaling. Lrp5 increases osteoblast proliferation, differentiation, and function. The purpose of a recent study [1] was to use Lrp5-deficient mice to evaluate the potential role of this gene in mediating the bone anabolic effects of parathyroid hormone (PTH).

Cancellous and cortical bone mass were decreased with Lrp5 deficiency. Compared with wild type mice, cancellous bone volume in the distal femur and the lumbar vertebra in Lrp5 KO mice was 54% and 38% lower, respectively, whereas femoral cortical thickness was also significantly lower in the KO mice. The decrease in cancellous bone volume in the lumbar vertebrae was associated with a reduced osteoblast surface and a comparable decrease in bone formation rate. Osteoclast surface, an index of bone resorption, was 24% lower in Lrp5 KO compared with WT mice. Treatment of mice with PTH for 6 weeks resulted in a significant increase in osteoblast surface and in osteoclast surface in both genotypes, but did not augment cancellous bone volume in either genotype. Femur cortical thickness was higher in PTH-treated mice in comparison with vehicle-treated mice, regardless of genotype.

Whereas disruption of Lrp5 results in decreased bone mass because of decreased bone formation, Lrp5 does not seem to be essential for the stimulatory effects of PTH on cancellous and cortical bone formation. These findings are in favour of distinct signaling pathways involved in the effects of PTH and Lrp5 on bone formation.

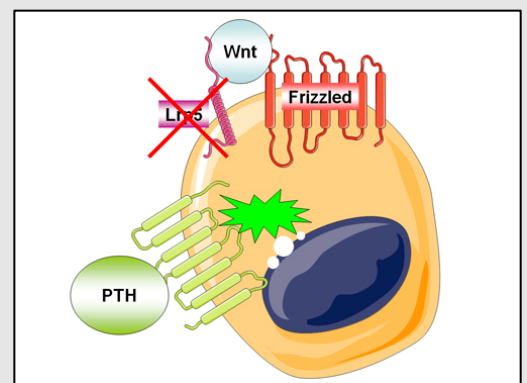
1. Iwaniec UT et al. *J Bone Miner Res.* 2007; 22: 394–402.

PTH stimulates bone formation in mice deficient in Lrp5

Low-density lipoprotein receptor-related protein 5 (Lrp5) is a membrane protein acting as a coreceptor in canonical Wnt signaling. Lrp5 increases osteoblast proliferation, differentiation, and function.

In the absence of Lrp5, bone mass is decreased and bone turnover is slower: bone formation and, to a lesser extent, resorption are lower than normally.

However, the anabolic effect of intermittent parathyroid hormone administration is preserved in the absence of Lrp5. These findings are in favor of distinct signaling pathways involved in the effects of PTH and Lrp5 on bone formation.



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