

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Neuronal regulation of bone mass by leptin

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The leptin regulation of bone remodeling, has been documented through studies of loss-of-function mutations of this hormone or of its receptor in mice and humans (see Osteoscoop Newsletter N°14, 15, 34, 37). However, unanswered questions remain. For instance, it has been assumed but not formally demonstrated that this regulation occurs through neuronal means. Likewise, it has not been possible until now to dissociate the influence leptin exerts on appetite and energy expenditure from this function.

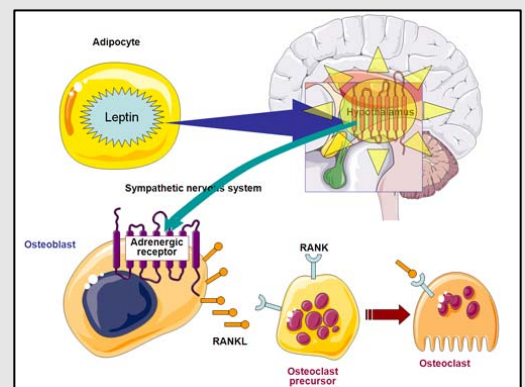
In a recent study [1], the authors show through mouse genetic studies that a deletion of the leptin receptor in neurons results in an increase in bone formation and bone resorption, resulting in a high bone mass as seen in leptin-deficient mice. In contrast, the same deletion in osteoblasts only does not influence bone remodeling. Furthermore, through the use of a mouse model of gain of function in leptin signaling harboring a mutation in the leptin receptor, they show that leptin signaling inhibits bone mass accrual by upregulating sympathetic activity independently of any change in appetite or energy expenditure.

This work establishes that in vivo leptin regulates bone mass accrual by acting through neuronal means and provides a direct demonstration that this function of leptin can occur independently of its regulation of energy metabolism.

1. Shia Y et al. *Proc Natl Acad Sci USA*. 2008;105:20529–20533.

Neuronal regulation of bone mass by leptin: direct evidence in vivo

It has been assumed but not formally demonstrated that regulation of bone mass by leptin occurs through neuronal means. A deletion of the leptin receptor in neurons results in an increase in bone formation and bone resorption, resulting in a high bone mass as seen in leptin-deficient mice. In contrast, the same deletion in osteoblasts only does not influence bone remodeling. Furthermore, in a model of gain of function in leptin signaling through a mutation in the leptin receptor, leptin signaling inhibits bone mass accrual by upregulating sympathetic activity independently of any change in appetite or energy expenditure.



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