

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Central control of bone remodeling by neuromedin U

N°91 – August 2009

Bone remodeling, which is affected in osteoporosis, comprises two phases: bone formation by matrix-producing osteoblasts and bone resorption by osteoclasts. The demonstration that the anorexigenic hormone leptin inhibits bone formation through a hypothalamic relay suggests that other molecules that affect energy metabolism in the hypothalamus could also modulate bone mass. Neuromedin U is an anorexigenic neuropeptide that acts independently of leptin through poorly defined mechanisms.

A recent study [1] shows that neuromedin U-deficient mice have high bone mass owing to an increase in bone formation; this is more prominent in male mice than female mice. Physiological and cell-based assays indicate that neuromedin U acts in the central nervous system, rather than directly on bone cells, to regulate bone remodeling. Notably, leptin- or sympathetic nervous system-mediated inhibition of bone formation was abolished in neuromedin U-deficient mice, which show an altered bone expression of molecular clock genes such as *Per1* and *Per2* which are mediators of the inhibition of bone formation by leptin (see Osteoscoop issue N° 34 "Molecular bases of leptin control of bone formation"). Moreover, treatment of wild-type mice with a natural agonist for the neuromedin U receptor decreased bone mass.

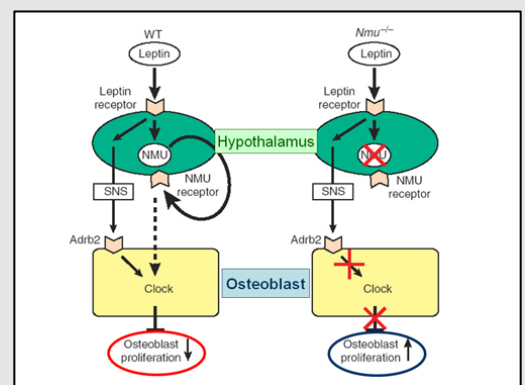
Collectively, these results suggest that neuromedin U may be the first central mediator of leptin-dependent regulation of bone mass identified to date. Given the existence of inhibitors and activators of neuromedin U action, these results may influence the treatment of diseases involving low bone mass, such as osteoporosis..

1. Sato S et al. *Nat Med.* 2007; 13:1234-1240.

Central control of bone remodeling by neuromedin U

Leptin, released from adipocytes, binds to its receptor located in the hypothalamus and promotes neuromedin U (NMU) synthesis. Neuromedin U activates a signaling pathway in osteoblasts. This pathway involves molecular clock genes which are also mediators of the inhibition of bone formation by leptin.

In neuromedin-deficient mice, this pathway is blocked and leptin is no longer active on osteoblasts to inhibit their proliferation. As a result, bone mass increases. Whether neuromedin inhibitors will be useful in the treatment of osteoporosis will have to be evaluated.



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