

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Thyroid-stimulating hormone prevents ovariectomy-induced bone loss

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Clinical data evidence the strong correlation between fracture risk and serum thyroid-stimulating hormone (TSH). Recent evidence that TSH receptor polymorphisms are associated with low bone mass, and evidence that bone loss occurs in patients with subclinical hyperthyroidism with normal and low TSH levels all support a role for low TSH in the pathogenesis of hyperthyroid osteoporosis, hitherto attributed solely to high circulating levels of thyroid hormones. In mice, TSH receptor deficiency induces a high-turnover osteoporosis, with elevated bone formation and resorption. In cell cultures continually exposed to TSH, both osteoblastic bone formation and osteoclastic bone resorption were suppressed. Recent studies on both mice and human subjects provide compelling evidence that thyroid hormones and TSH have the opposite effects on the skeleton.

In a recent study [1], the authors show that TSH, when injected intermittently into rodents, even at intervals of 2 weeks, displays a powerful antiresorptive action in vivo. By virtue of this action, together with the possible anabolic effects shown earlier, TSH both prevents bone loss and restores the lost bone after ovariectomy. Importantly, the osteoclast inhibitory action of TSH persists ex vivo even after therapy is stopped for 4 weeks. This profound and lasting antiresorptive action of TSH is mimicked in cells that genetically overexpress the constitutively active ligand-independent TSH receptor (TSHR). In contrast, loss of function of a mutant TSHR in congenital hypothyroid mice activates osteoclast differentiation, confirming once again the premise that TSHRs have a critical role in regulating bone remodeling.

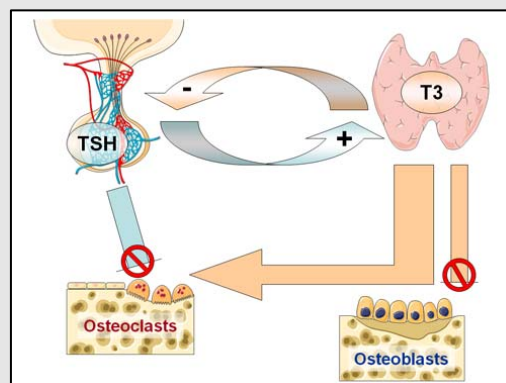
1. Sun L et al. *Proc Natl Acad Sci USA*. 2008; 105:4289–4294.

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Thyroid hormone T3 is known to inhibit bone formation by osteoblasts and to promote bone resorption by osteoclasts. Thyroid hormone synthesis is under the control of pituitary thyroid-stimulating hormone TSH.

TSH was recently demonstrated to exert a direct, inhibitory effect on osteoclasts and to reduce bone resorption. Moreover, TSH was shown to prevent ovariectomy-induced bone loss.

TSH is therefore a newly acknowledged modulator of bone resorption with potential impact on post-menopausal osteoporosis



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