

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

More about FSH and bone: TNF comes into the game

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Postmenopausal osteoporosis is traditionally attributed to declining estrogen levels. However, a recent study showed that follicle-stimulating hormone (FSH), the secretion of which is under estrogenic feedback, directly enhances osteoclast formation and function. The deletion of one of its subunits protects against bone loss despite severe hypogonadism. This finding suggests that elevated FSH contributes to the genesis of postmenopausal osteoporosis.

However, hypogonadal bone loss is accompanied by alterations in bone and bone marrow, notably enhanced bone formation, increased T lymphocyte production, and macrophage activation. The alterations in immune function have been attributed to an increase in TNF α production that is thought to arise from estrogen deficiency.

Ablation of the TNF α gene in mice abrogates gonadectomy-induced bone loss, osteoclast and osteoblast activation, and the accompanying immune cell alterations. TNF α may therefore be essential for, and downstream of, FSH action on bone. Moreover, there is direct evidence that FSH enhances TNF receptor and TNF α expression.

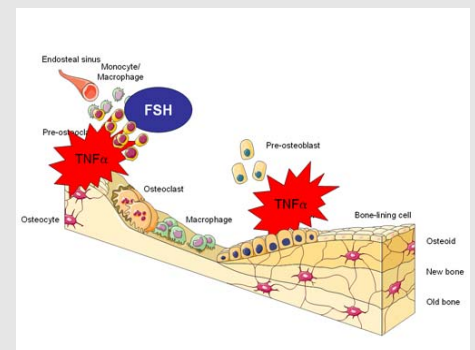
Iqbal et al. [1] explored whether FSH mediates the production of TNF α and whether the abrogation of bone loss in FSH-deficient mice arises in part from decreased TNF α production. They show that FSH-deficient mice have low circulating TNF α , that FSH directly stimulates TNF α production from bone marrow granulocytes and macrophages, and that TNF α stimulates osteoclast precursor expansion and osteoblast differentiation. They show that high-turnover bone loss is due to an expanded osteoclast precursor pool, together with enhanced osteoblast formation.

They propose that hypogonadal bone loss is caused, at least in part, by enhanced FSH secretion, which in turn increases TNF production by bone marrow macrophages and granulocytes to expand the number of bone marrow osteoclast precursors.

1. Iqbal J et al. *Proc Natl Acad Sci USA*. 2006;103:14925-14930.

TNF α mediates the bone effects of FSH

Increase in FSH secretion is involved in post-menopausal osteoporosis. FSH directly stimulates TNF α production from bone marrow granulocytes and macrophages. TNF α stimulates osteoclast precursor expansion and osteoblast differentiation. The overall effect of the FSH-TNF α tandem is an increase in bone resorption.



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