

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

FSH directly regulates bone mass

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Postmenopausal osteoporosis is usually solely attributed to a drop in ovarian estrogen secretion. However, while estrogen is used in the therapy of osteoporosis, the primary mechanism of its action at the cellular level remains unclear.

A recent study challenges this dogma of the sole responsibility of estrogens [1]. Indeed, the decline in ovarian secretion of estrogens and inhibins relieves a negative feedback exerted by these hormones on the pituitary, and is accompanied by an overproduction of the pituitary-derived hormone FSH. Sun et al therefore hypothesized that FSH per se might affect bone remodeling. Several lines of evidence support such a hypothesis: first, plasma FSH concentrations are well correlated to markers of bone resorption in postmenopausal women; second, mice missing the estrogen receptor, but not estrogens, have only mild bone loss; third, the bone loss following an ovariectomy in the mouse occurs only if the pituitary is intact.

Mice deprived of FSH receptors, although suffering from severe hypogonadism, do not exhibit bone loss and have normal concentrations of remodeling markers. Invalidation of one of the subunits of FSH ligand leads to the same picture. Moreover, activation of osteoclasts by RANK ligand (RANKL) requires that FSH and its receptor are present in an experimental calvaria model.

How does FSH act on bone? FSH receptors have been evidenced on osteoclasts but not on osteoblasts. The FSH receptor density is increased by RANKL which, in turn, stimulates osteoclast activity more actively in the presence of FSH.

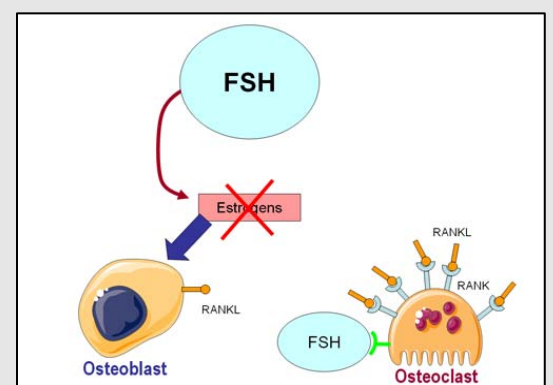
These data need now, of course, to be validated in women. If this is so, the fight against bone loss will have to be extended to the central nervous system.

1. Sun L et al. *Cell*. 2006;125:247-260.

Mode of action of FSH on bone cells

Before menopause, estrogen secretion exerts a negative feedback on FSH secretion. Estrogens inhibit bone resorption through inhibition of RANKL synthesis, and stimulate the activity of osteoblasts.

After menopause, the fall of estrogen secretion has two important consequences: the inhibitory effect on bone resorption is suppressed and FSH concentrations increase. FSH acts directly, through specific receptors, on osteoclasts which react more strongly to RANKL. Moreover, RANKL increases the number of FSH receptors. This results in increased bone resorption.



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