

# OSTEOSCOOP

News on current events in osteoporosis and rheumatology

## Blockade of TNF- $\alpha$ and Interleukin-1 action on bone reduces resorption in early postmenopausal women

N°46 – September 2008

The increase in bone resorption caused by estrogen deficiency is the major cause of postmenopausal bone loss and osteoporosis. This increase in bone resorption is thought to be mediated largely by changes in cytokine levels in the bone microenvironment. Based mainly on studies in ovariectomized rodents, proinflammatory cytokines, including TNF- $\alpha$  and interleukin (IL)-1 $\beta$  have been suggested as mediators. However, their roles are unclear in humans, whose immune system differs markedly from that of rodents.

This issue was recently addressed in a clinical study [1] including 42 early postmenopausal women. Subjects were randomly assigned to intervention groups receiving 3 weeks of injections with 0.9% saline, anakinra (a human IL-1 receptor antagonist), or etanercept (a soluble recombinant TNF- $\alpha$  receptor fusion protein). Bone turnover was assessed by measuring serum carboxyl-terminal telopeptide of type 1 collagen (CTX) and amino-terminal telopeptide of type 1 collagen (NTX), markers for bone resorption, and serum amino-terminal propeptide of type 1 collagen (P1NP), a marker for bone formation.

Bone formation, reflected by serum P1NP, was not affected by either treatment. The increase in the resorption markers NTX and CTX observed in the control group was blunted significantly by etanercept. Anakinra treatment was less efficient on resorption markers.

These data are consistent with a role for TNF- $\alpha$ , and possibly for IL-1, in mediating increased bone resorption during estrogen deficiency in women. Although either cytokine blocker reduced serum CTX by about one half, the effect of combined blockade could not be tested because of concerns about toxicity. The data do not exclude, however, direct or indirect contributory roles for RANKL or for other cytokines.

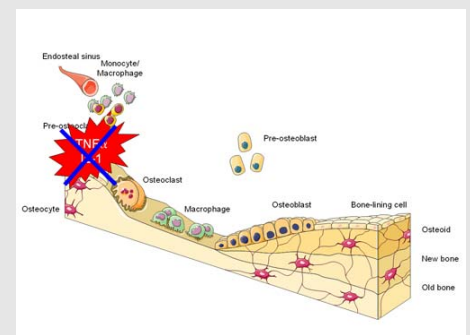
1. Charatcharoenwithaya N et al. *J Bone Miner Res.* 2007;22:724–729.

### Blockade of TNF- $\alpha$ and IL-1 action on bone reduces resorption

Postmenopausal bone loss secondary to estrogen deficiency involves locally produced cytokines such as TNF alpha and interleukin1.

TNF- $\alpha$  and IL-1 production by bone marrow macrophages and granulocytes expands the number of bone marrow osteoclast precursors and mature osteoclasts.

Blockade of the effect of TNF- $\alpha$  and IL-1 through interaction with their receptors decrease bone resorption.



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