

Sclerostin antibodies increase bone mass in ovariectomized rats?

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Genetic studies in humans and mice have shown that the secreted protein sclerostin, synthesized by osteocytes, is a key negative regulator of bone formation, although the magnitude and extent of sclerostin's role in the control of bone formation in the aging skeleton is still unclear. To study this unexplored area of sclerostin biology and to assess the pharmacologic effects of sclerostin inhibition, the authors of a recent study [1] used a cell culture model of bone formation to identify a sclerostin neutralizing monoclonal antibody (Scl-AbII) for testing in an aged ovariectomized rat model of postmenopausal osteoporosis.

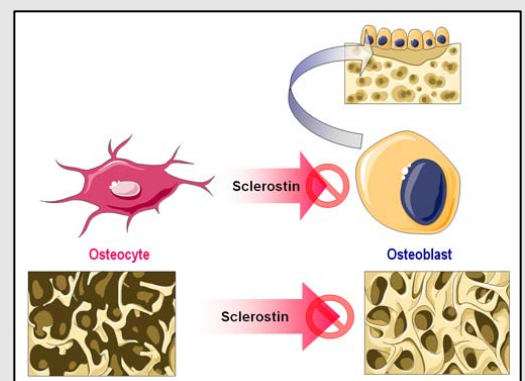
Six-month-old female rats were ovariectomized and left untreated for 1 y to allow for significant estrogen deficiency-induced bone loss, at which point Scl-AbII was administered for 5 wk. Scl-AbII treatment in these animals had robust anabolic effects, with marked increases in bone formation on trabecular, periosteal, endocortical, and intracortical surfaces. This not only resulted in complete reversal, at several skeletal sites, of the 1 y of estrogen deficiency-induced bone loss, but also further increased bone mass and bone strength to levels greater than those found in non-ovariectomized control rats.

Taken together, these preclinical results establish sclerostin's role as a pivotal negative regulator of bone formation in the aging skeleton and, furthermore, suggest that antibody-mediated inhibition of sclerostin might contribute to new approaches for the anabolic treatment of bone-related disorders, such as postmenopausal osteoporosis.

1. Li X et al. *J Bone Miner Res.* 2009; 24: 578–588.

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Sclerostin is a protein synthesized and released by osteocytes. Main targets of sclerostin in bone are osteoblasts which are inhibited by this protein in terms of differentiation. Inhibition of sclerostin effects by antibodies promotes osteoblast activity and increases bone formation. In ovariectomized rats, an animal model of postmenopausal osteoporosis, administration of sclerostin antibodies increased bone mass and reversed ovariectomy-induced bone loss, suggesting that this approach may implement the panel of interventions aimed to fight against bone loss.



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