

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Activation of renin-angiotensin system induces osteoporosis

N° 122 – March 2010

Hypertension and osteoporosis are two major age-related disorders; however, the underlying molecular mechanism for this comorbidity is not known. The renin-angiotensin system (RAS) plays a central role in the control of blood pressure and has been an important target of antihypertensive drugs. Using a chimeric RAS model of transgenic THM (Tsukuba hypertensive mouse) expressing both the human renin and human angiotensinogen genes, the authors of a recent study [1] showed that activation of RAS induces high turnover osteoporosis with accelerated bone resorption.

Transgenic mice that express only the human renin gene were normotensive and yet exhibited a low bone mass, suggesting that osteoporosis occurs independently of the development of hypertension per se. Ex vivo cultures showed that angiotensin II (AngII) acted on osteoblasts and not directly on osteoclast precursor cells and increased osteoclastogenesis-supporting cytokines, RANKL and vascular endothelial growth factor (VEGF), thereby stimulating the formation of osteoclasts. Knockdown of AT2 receptor inhibited the AngII activity, whereas silencing of the AT1 receptor paradoxically enhanced it, suggesting a functional interaction between the two AngII receptors on the osteoblastic cell surface. Treatment of THM mice with an ACE inhibitor, enalapril, improved osteoporosis and hypertension, whereas treatment with losartan, an angiotensin receptor blocker specific for AT1, resulted in exacerbation of bone loss.

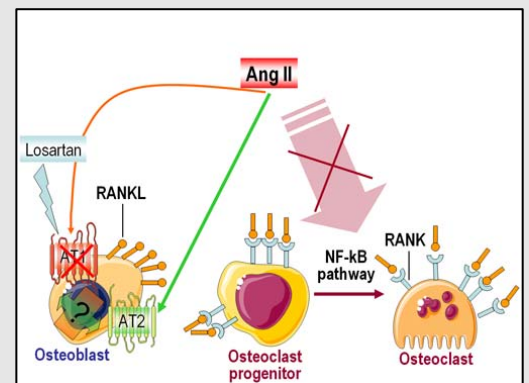
These results highlight the diverse roles of bone angiotensin receptors in the control of bone mass and turnover.

1. Asaba Y et al. *J Bone Miner Res.* 2009;24:241–250

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