

Locally applied simvastatin promotes fracture healing in ovariectomized rat: A novel molecular mechanism

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Dear Editors,

My colleagues and I thank Dr. Namazi [1] for his interest in our article [2].

The RANKL/RANK/OPG system is recently thought to have a major role in bone metabolism. The balance between RANKL-RANK signaling and the levels of biologically active OPG regulate development and activation of osteoclasts and bone metabolism. All factors that inhibit or

increase bone resorption via osteoclasts act via regulation of RANKL-RANK and/or OPG-RANKL interactions.

In our recent study, we have found that ovariectomy can reduce the expression of OPG, and simvastatin can dramatically increase the expression of OPG (Fig. 1).

So we agree with Dr. Namazi that statins stimulate the OPG production by osteoblasts; however, we have reservations that the major mechanism of statins on bone is

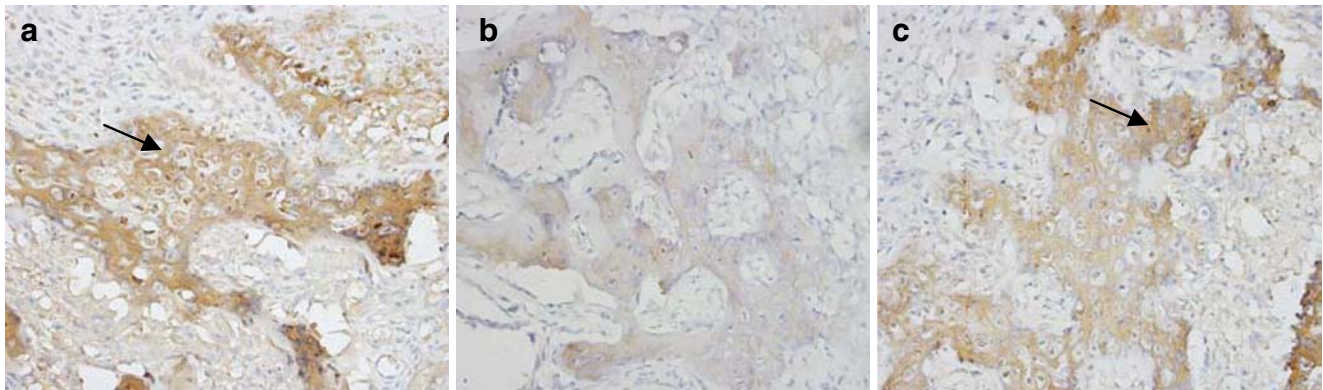


Fig. 1 OPG immunohistochemistry stain of callus at 2 weeks post fracture. Expression of OPG is lower in callus of the ovariectomy+vehicle group (**b**) than in callus of the sham+vehicle group (**a**), while

the expression of OPG is higher in callus of the ovariectomy+simvastatin group (**c**) than in callus of the ovariectomy+vehicle group (**b**) (black arrow: positive stain of OPG; $\times 400$)

mainly due to their stimulation of endogenous BMP-2 expression by osteoblast, not their effects on OPG.

A reply to this letter can be found at <http://dx.doi.org/10.1007/s00198-008-0621-3>

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