

# OSTEOSCOOP

News on current events in osteoporosis and rheumatology

## Osteocytes are crucial actors in mechanotransduction

N° 40 – July 2008

The role of osteocytes in bone is still an enigma. It was thought that osteocytes are passive cells or “placeholders” in bone or, conversely, that osteocytes could potentially be mechanosensors and transducers of mechanical load. A new study [1] now sheds light on the role of osteocytes in maintaining skeletal homeostasis and regulating skeletal responses to mechanical loading. Loading, as occurs with exercise, increases bone mass. Conversely, unloading, as occurs with space flight or immobilization, results in bone loss. The complex lacunocanalicular network connecting all of the osteocytes within bone and cells on the bone surface supports the idea that these cells can sense loading on the skeleton or its absence and then translate those signals to biochemical signals of resorption or formation. The authors used an ingenious approach to determine the role of osteocytes by loss-of-function studies. Using mice carrying a diphtheria toxin (DT) receptor specifically expressed in osteocytes, the authors were able to kill off osteocytes using single injections of DT.

Two days after DT injection, transgenic mice showed an increase in mRNA for an activator of osteoclasts (RANKL) and no change in markers of osteoblasts (Runx2, alkaline phosphatase/ALP, and OPG) but significant reduction in a marker of late osteoblasts (osteocalcin) and markers of osteocytes (DMP1, E11/gp38, MEPE, Phex, and SOST). Eight days after DT injection, a dramatic increase in empty lacunae was observed, as well as an increase in osteoclast number and activity. A reduction in bone formation rate was observed. Therefore, viable osteocytes prevent osteoclast activation and dying or apoptotic osteocytes may send signals to recruit osteoclasts. If DT was injected 1 day before unloading by tail suspension, no loss of bone occurred, which confirms that osteocytes could send signals of bone resorption with unloading. In normal mice, bone loss with unloading can be recovered with normal ambulation. After 7 days of unloading, the transgenic animals responded with bone loss as expected, but if given a DT injection between unloading and reloading, bone recovery was normal. This suggests that bone recovery by reloading does not depend on osteocytes.

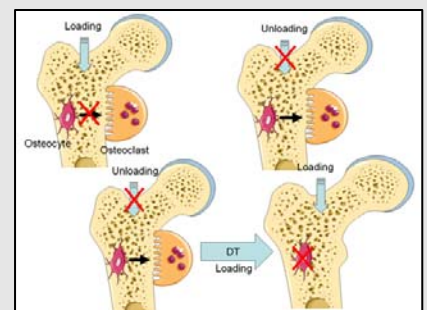
These results indicate that the mechanisms responsible for maintaining bone mass with normal load are not the same as those for recovering bone mass after unloading. They also show that the role of osteocytes is underscored.

1. Yoshiko Y et al. *Mol Cell Biol.* 2007;27:4465-4474.

### Osteocytes are crucial actors in mechano-transduction

During normal loading or ambulation, osteocytes send inhibitory signals (red X) to osteoclasts to maintain bone mass, while viable osteocytes are necessary to send signals activating osteoclasts in response to unloading. Osteocytes do not play a role in bone restoration in response to reloading after loss due to unloading. In the absence of load, the osteocyte sends signals to the osteoclast to resorb bone. But if the osteocytes are killed by diphtheria toxin (DT) injection and then reloaded, bone is nonetheless regenerated.

These results indicate that the mechanisms responsible for maintaining bone mass with normal load are not the same as those for recovering bone mass after unloading.



**PROTELOS**<sup>®</sup>  
Treatment of postmenopausal osteoporosis to reduce the risk of hip and vertebral fractures

