

# OSTEOSCOOP

News on current events in osteoporosis and rheumatology

## Anti-aging lamin A/C is crucial for bone formation

N°116 – January 2010

**A**ge-related osteoporosis is characterized by low bone mass, poor bone quality, and impaired osteoblastogenesis. Recently, the Hutchinson-Gilford progeria syndrome (HGPS), a disease of accelerated aging and premature osteoporosis, has been linked to mutations in the gene encoding for the nuclear lamina protein lamin A/C. Here [1], the authors tested the hypothesis that inhibition of lamin A/C in osteoblastic lineage cells impairs osteoblastogenesis and accelerates osteoclastogenesis. Lamin A/C was knocked down with small interfering (si)RNA molecules in human bone marrow stromal cells (BMSCs) differentiating toward osteoblasts.

Lamin A/C knockdown led to an inhibition of osteoblast proliferation by 26% and impaired osteoblast differentiation by 48% based on the formation of mineralized matrix. In mature osteoblasts, mRNA levels of two osteoblast markers, *runx2* and osteocalcin, were decreased by lamin A/C knockdown by 44% and 78%, respectively. Furthermore, protein analysis showed that osteoblasts with diminished levels of lamin A/C also secreted less osteocalcin and expressed a lower alkaline phosphatase activity (-50%). Lamin A/C inhibition increased RANKL mRNA and protein levels, whereas osteoprotegerin (OPG) expression was decreased, resulting in an increased RANKL/OPG ratio and an enhanced ability to support osteoclastogenesis, as reflected by a 34% increase of TRACP+ multinucleated cells.

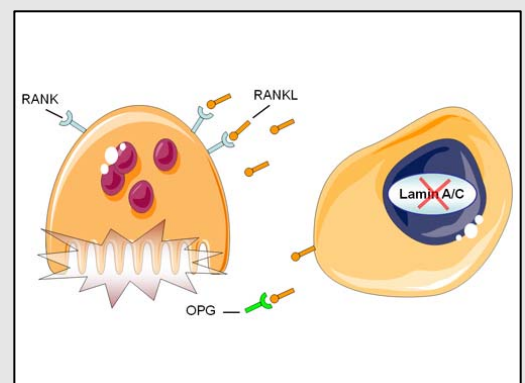
These data indicate that lamin A/C is essential for proper osteoblastogenesis. Moreover, lack of lamin A/C favors an osteoclastogenic milieu and contributes to enhanced osteoclastogenesis.

1. Rauner M et al. *J Bone Miner Res.* 2009;24:78-86.

### Anti-aging lamin A/C is crucial for bone formation

Lamin A/C is a nuclear protein which mutations are responsible for the progeria syndrome with accelerated aging. Lamin A/C knockdown in the osteoblast lineage results in impaired osteoblast differentiation. Expression of osteoblast markers is decreased, RANK ligand expression was increased and Osteoprotegerin expression was decreased. These changes resulted in osteoclast activation.

These data indicate that lamin A/C is essential for proper osteoblastogenesis. Moreover, lack of lamin A/C favors an osteoclastogenic milieu and contributes to enhanced osteoclastogenesis.



**PROTELOS®**

Treatment of postmenopausal osteoporosis to reduce the risk of hip and vertebral fractures

