

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Selective inhibition of RANK blocks osteoclast maturation

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Regulation of the formation and function of bone-resorbing osteoclasts is a key to understanding the pathogenesis of skeletal disorders. Gene-targeting studies have shown that the RANK signaling pathway plays a critical role in osteoclast differentiation and function. Although pharmaceutical blockade of RANK may be a viable strategy for preventing bone destruction, RANK is implicated in multiple biological processes. Recently, a cytoplasmic motif of RANK was identified that may be specifically involved in osteoclast differentiation. In a recent study [1], the authors developed a cell-permeable inhibitor termed the RANK receptor inhibitor (RRI), which targets this motif.

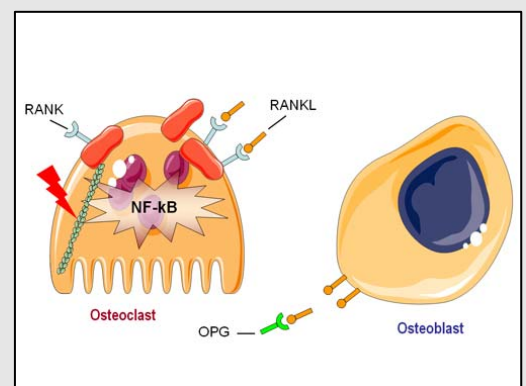
The RRI peptide blocked RANKL-induced OC formation from murine bone marrow-derived macrophages. Furthermore, RRI inhibited the resorptive function of OCs and induced OC apoptosis. Treatment with the peptide impaired downstream signaling of RANK and resulted in disruptions of the actin cytoskeleton in differentiated osteoclasts. In addition, RRI blocked inflammation-induced bone destruction and protected against ovariectomy-induced bone loss in mice.

These data may be useful in the development of selective therapeutic agents for the treatment of osteoporosis and other bone diseases.

1. Kim H et al. *J Clin Invest.* 2009;119:813–825.

Selective inhibition of RANK blocks osteoclast maturation

In osteoclasts, activation of NF- κ B by RANKL/RANK promotes bone resorption. In order to inhibit RANK signaling, a peptidic inhibitor was elaborated to block a specific motif involved in RANK signaling. This inhibitor is cell permeable so that it can enter the cell through the plasma membrane. In the cell, the inhibitor induces disruption of actin cytoskeleton and osteoclast apoptosis.



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