

Osteoclast Activity and Osteoporosis

김 홍 희

(교수, 조선대 치대)

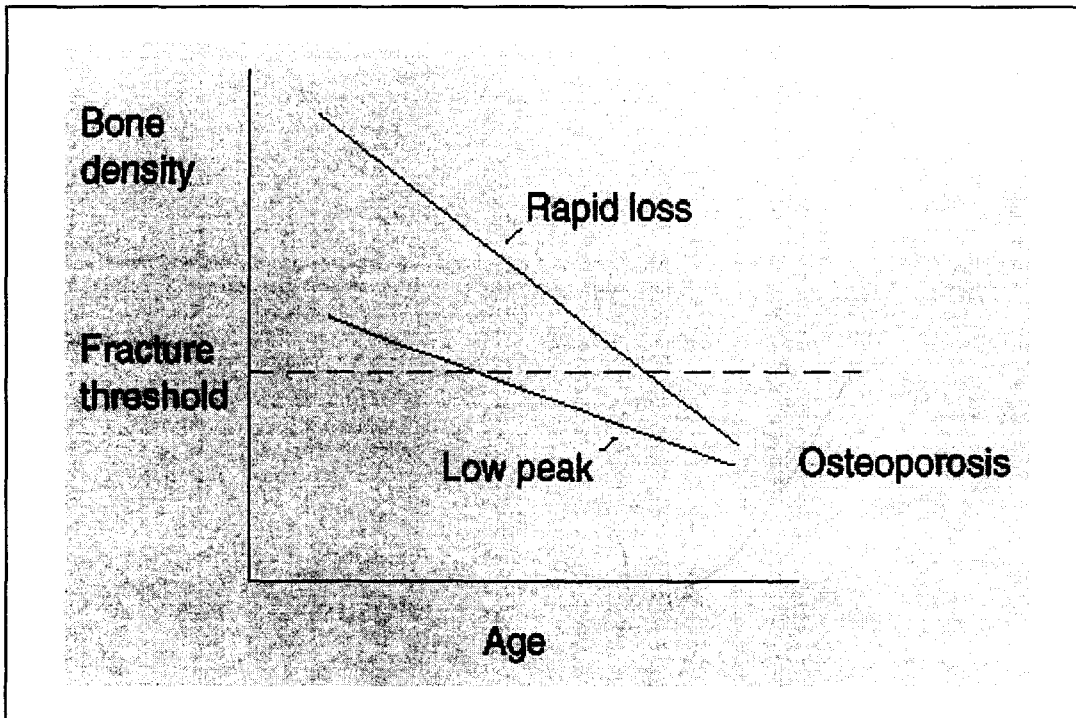
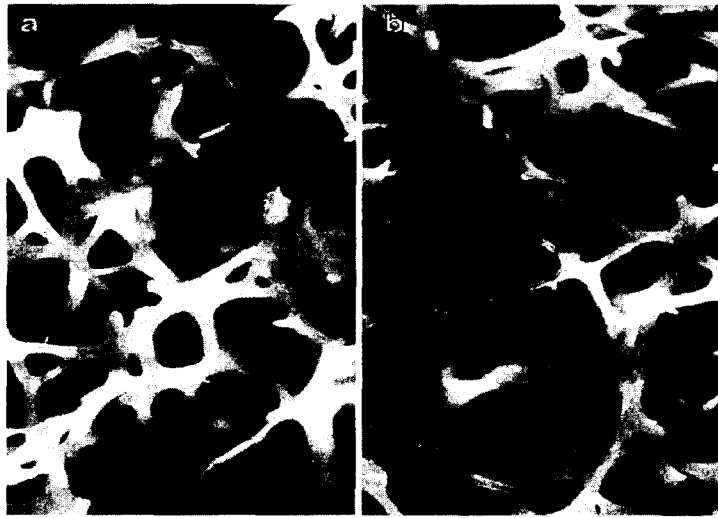
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Abstract

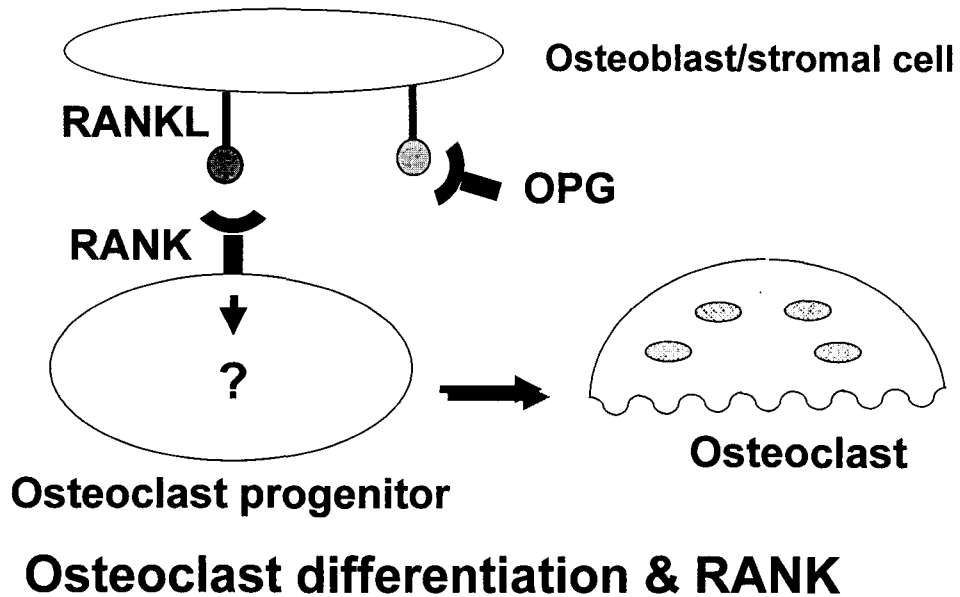
Bone homeostasis is maintained by a balance between activities of osteoblasts (bone forming cells) and osteoclasts (bone resorbing cells). The activities of these cells are closely regulated by multiple factors including hormones and cytokines. The cessation of estrogen at menopause disrupts the balanced regulation and is the main cause of osteoporosis in postmenopausal women. Recent molecular biological studies led to a discovery of tumor necrosis factor (TNF) and TNF receptor families genes that play critical roles in the regulation of osteoclast formation and function. RANKL (receptor activator of nuclear factor kappa B ligand; also called ODF, TRANCE, and OPGL) expressed on cells supporting osteoclast is essential for osteoclast differentiation, activation, and survival. RANK, the counter-receptor for RANKL, is expressed on progenitor and mature osteoclasts. The interaction between RANKL and RANK is regulated by a soluble decoy receptor OPG (osteoprotegerin). Gene knock out studies of these molecules showed profound effects on bone. These results prompted development of new strategies for treatment of bone diseases. Inhibition of osteoclast activity by blocking the RANKL-RANK interaction using OPG is being attempted. Research on the signaling pathways of RANK is also actively carried out. Screening natural products that inhibit the RANKL-RANK interaction or the activity of osteoclasts would be another effective means to a new drug target for bone resorbing diseases.

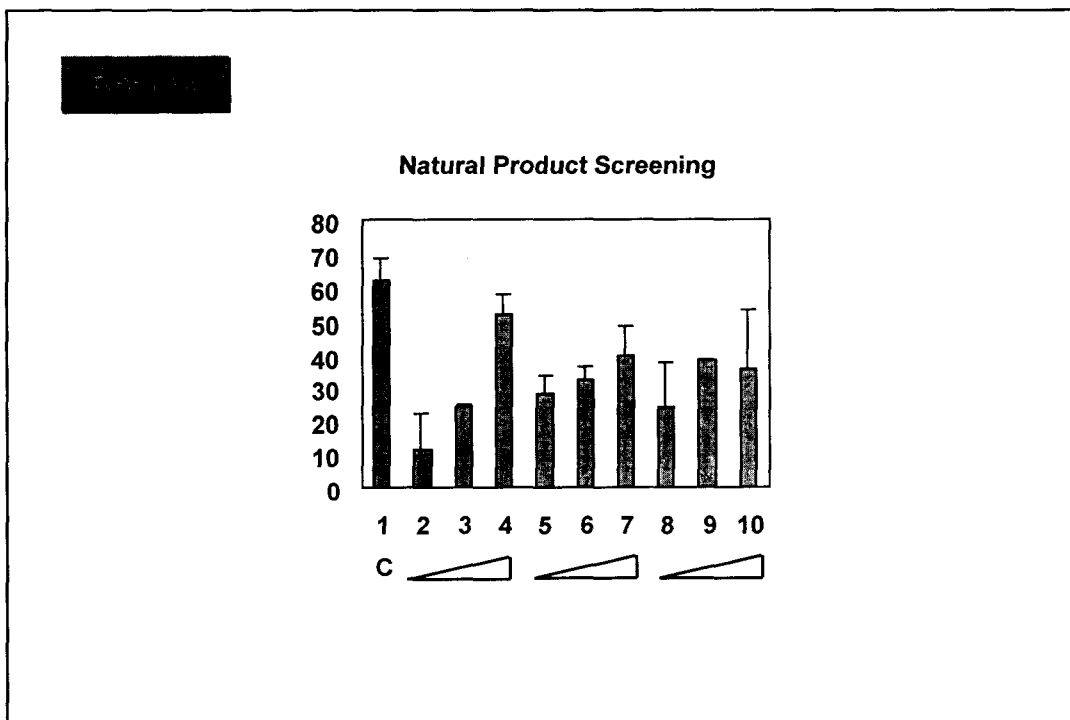
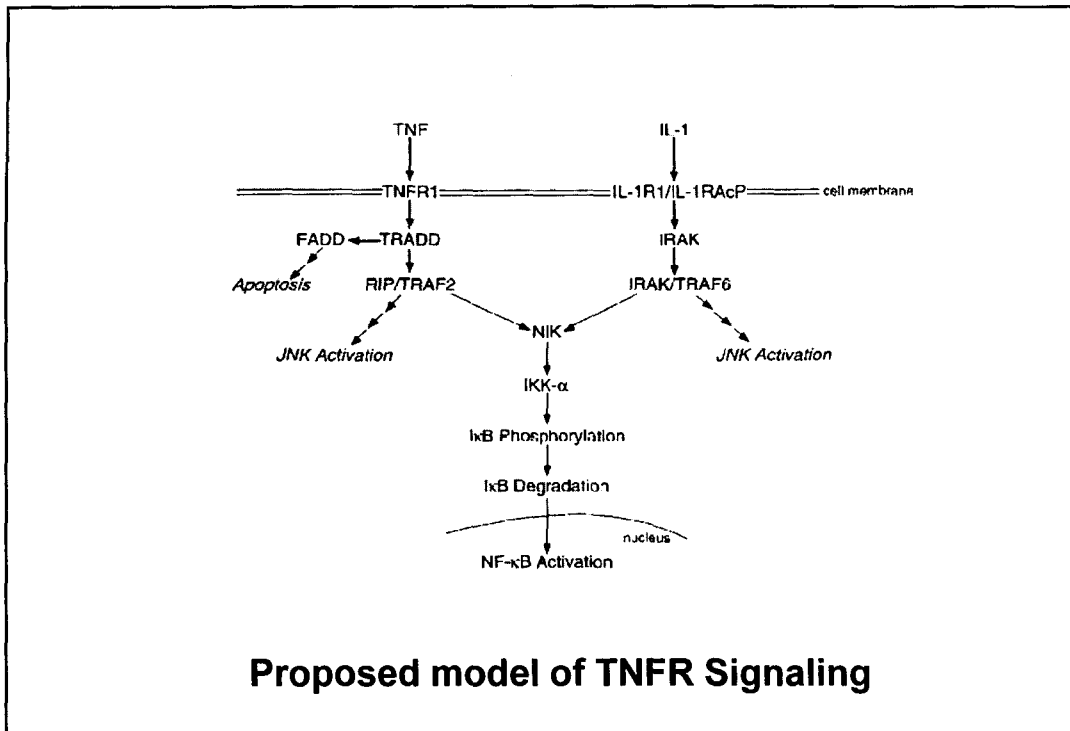
Figure 10



Osteoporosis

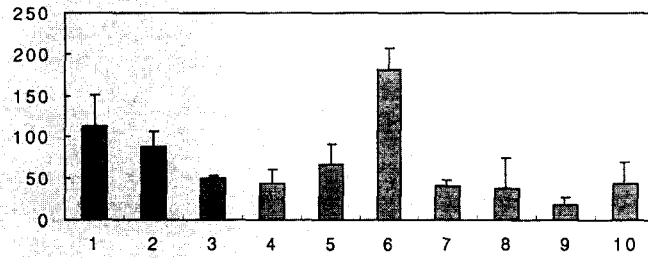
- > 28 million Americans at risk
15% men
- 2.3 million fractures/yr
\$15 billion
- osteoporosis-related fracture :
1/2 women, 1/8 men over 50
- FOSAMAX^R (bisphosphonate) :
> \$500 million (1997)



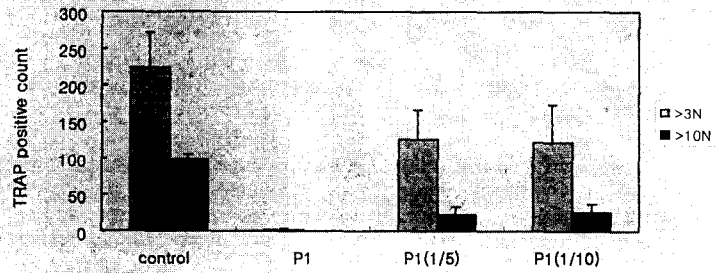


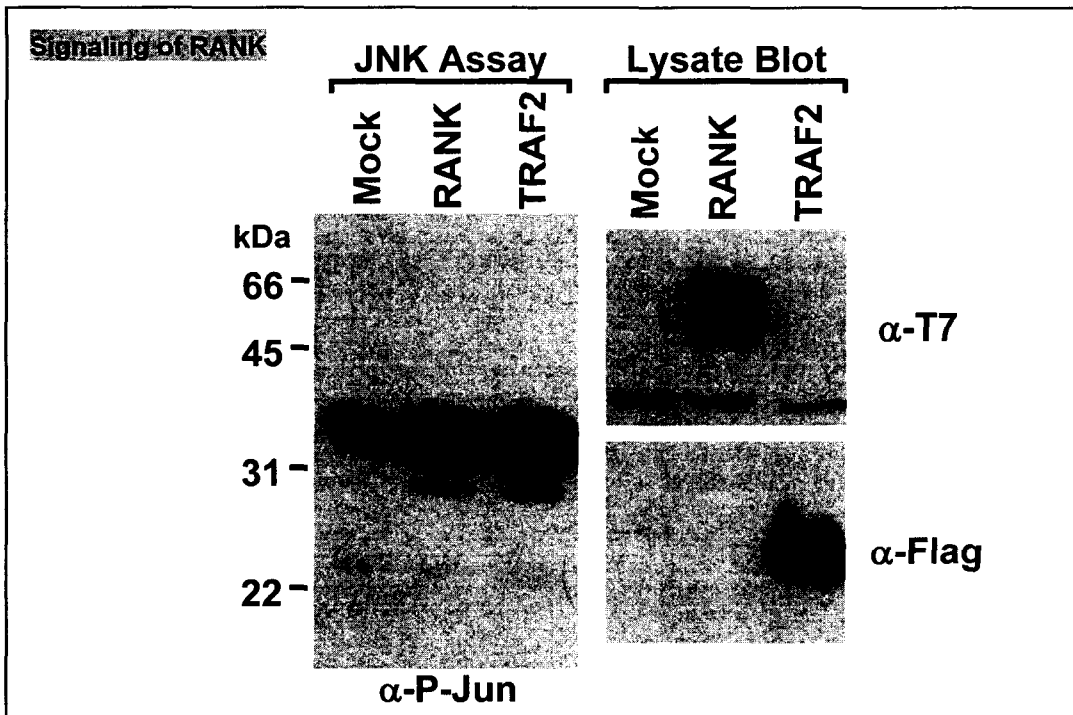
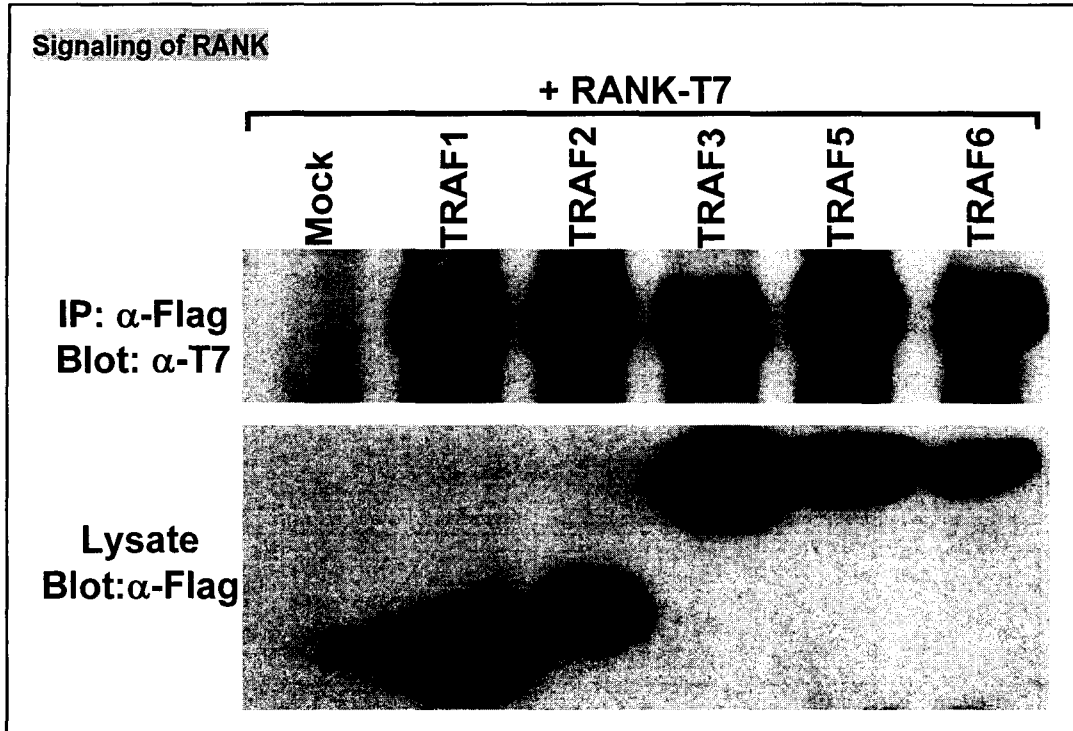
Natural Product Screening

(Silica gel column chromatography)

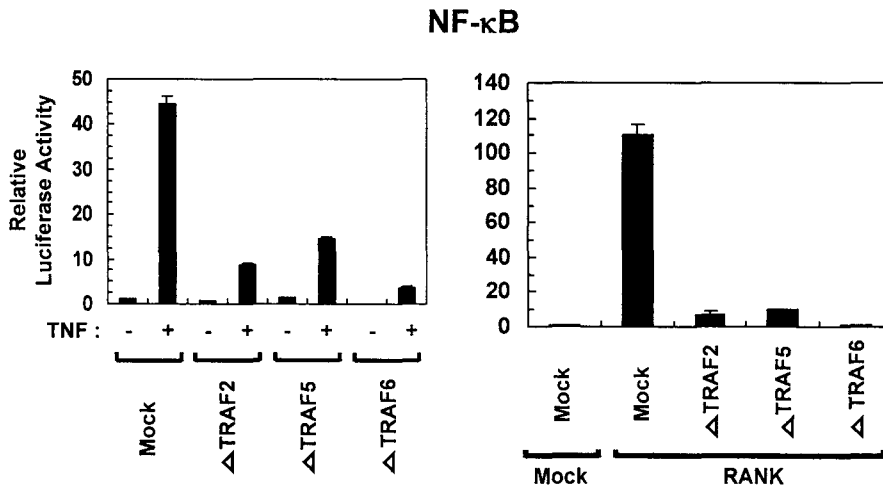


Peptide Screening

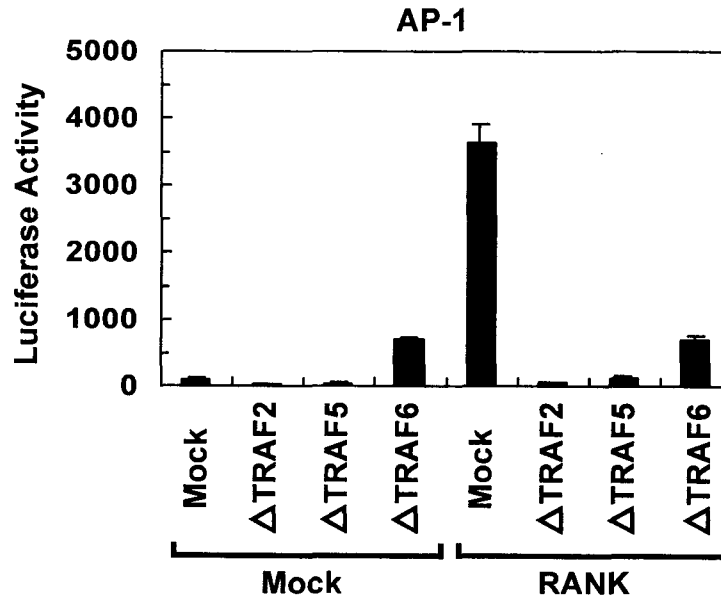




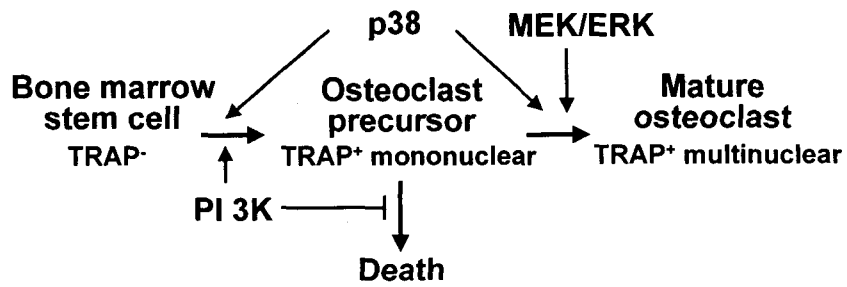
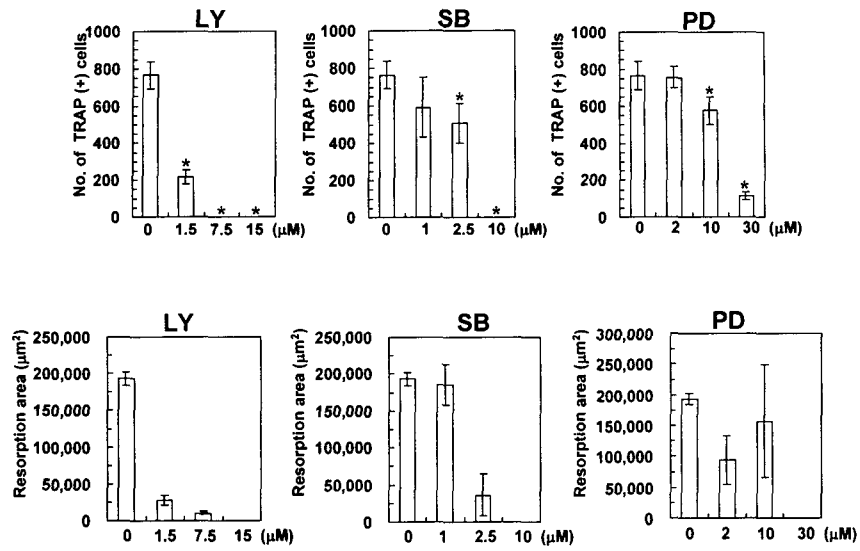
Signaling of RANK



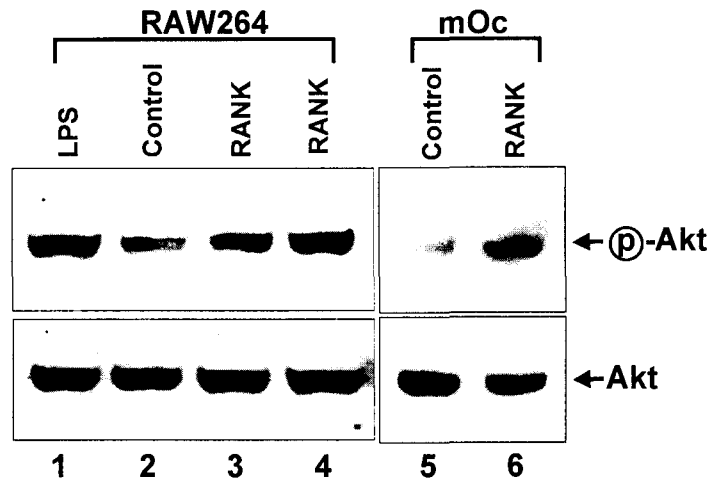
Signaling of RANK



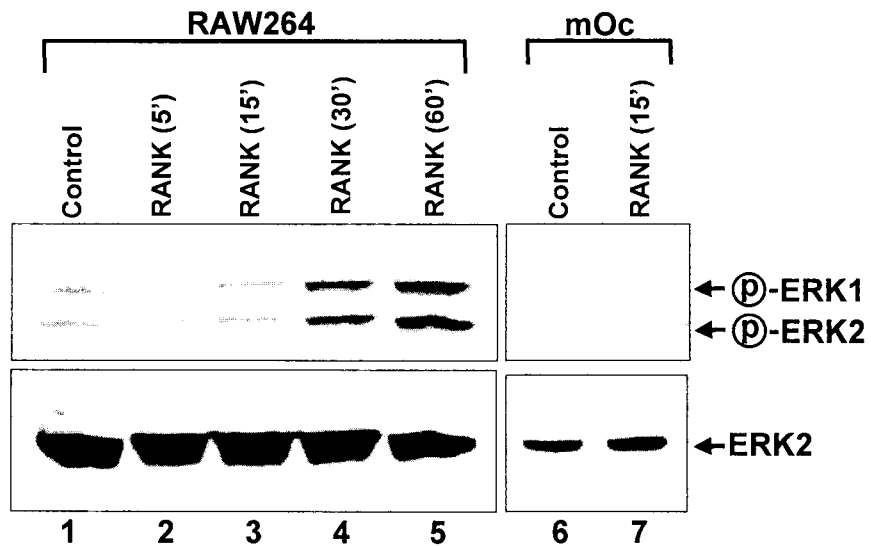
Signaling of RANK




Signaling of RANK



Signaling of RANK



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