NILS SEMINAR

“NIK’ing the bone: How alternative NF-κB encourages the osteoclast”

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NF-κB is a critical signal for osteoclast (OC) differentiation downstream of RANKL, and its disruption blocks bone loss in a variety of disease models in mice. Differently from other TNF family members, RANKL activates both the classical NF-κB pathway, activating p65 and cRel, and the alternative pathway, inducing expression and activation of RelB. Our studies on the role of individual NF-κB subunits have demonstrated that p65 is important for OC precursor survival during a critical period of differentiation, but is not necessary for transcription of the OC differentiation program. In contrast, RelB is required for OC differentiation *in vitro*, and for pathological bone loss in vivo. Both deletion and activation of NIK, the upstream kinase regulating RelB activation, significantly modulates osteoclastogenesis, especially in models of inflammatory arthritis. Constitutive NIK activation also increases the resorptive capacity of individual osteoclasts, associated with an increase in the size of the actin ring, indicating that NIK controls OC function in addition to differentiation. Thus, the alternative NF-κB pathway represents an interesting potential target for the control of bone loss in diseases such as rheumatoid arthritis.

平成23年5月19日（木曜日）午後4時～5時
第2研究棟2F会議室

運動器疾患研究部　竹下（5047 or 5514）