Rated ★★★ Exceptional

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Classified as

New Finding | Good for Teaching

Coupling of bone formation to bone resorption is essential in the maintenance of bone homeostasis. A whole spectrum of molecules derived from the resorbed matrix, from osteoclasts and from osteogenic cells, are involved in the recruitment of osteoblasts to the resorption sites and in driving the transition from bone resorption to bone formation. In their study, Ikebuchi et al. demonstrate that RANK contained within small extracellular vesicles secreted by maturing osteoclasts binds to RANKL on the osteoblast membrane and promotes a reverse signaling that leads to bone formation. The authors also demonstrate that the proline-rich motif in the RANK cytoplasmic tail is required for this reverse signaling. The identification of this RANKL-dependent reverse signaling, which physiologically contributes to the maintenance of the coupling of bone formation to resorption, could represent a springboard for the development of drugs for treatment of osteoporosis, in which, the rate of resorption being greater than the rate of formation, uncoupling prevails. The work by Ikebuchi and colleagues may also have interesting implications for the understanding of the pathological changes in other human bone diseases characterized by abnormal osteogenesis and enhanced osteoclastogenesis (e.g. fibrous dysplasia) in which a dysregulated release of vesicles may contribute to the abnormal amount and quality of bone. The significance of the RANKL reverse signaling in these conditions deserves further studies.

Disclosures

None declared

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