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Invited Plenary Abstract

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Mesenchymal/haemopoietic interactions in osteoclastogenesis

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Osteoclasts, the multinucleated cells that resorb bone, originate from monocyte/macrophage lineage haemopoietic cells. Mesenchymal osteoblastic cells or bone marrow stromal cells are involved in osteoclast differentiation. Osteoclast precursors express RANK (a receptor of RANKL), recognize RANKL expressed by osteoblasts through cell-cell interaction and differentiate into osteoclasts in the presence of M-CSF. OPG, produced mainly by osteoblasts, is a soluble decoy receptor for RANKL. Deficiency of OPG in mice induces osteoporosis caused enhanced bone resorption. Elevated osteoblastic activity was suppressed by bisphosphonate administration in OPG-deficient mice. These results suggest that bone formation is accurately coupled with bone resorption. Collagen sponge disks containing BMP-2 were implanted into the dorsal muscle pouches in OPG-deficient mice. TRAP-positive osteoclasts and ALP-positive osteoblasts were observed in BMP-2-disks preceding the onset of calcification for one week. F4/80-positive osteoclast precursors were similarly distributed in both BMP-2- and control disks. OPG and soluble RANK inhibited BMP-2-induced osteoclast formation but not the appearance of ALP-positive cells in OPG-deficient mice. A small number of osteoclasts were observed in RANKL-containing disks in the absence of BMP-2 in the OPG-deficient mice. We then examined how osteoblasts are involved in osteoclastogenesis other than RANKL expression, using RANKL-deficient mice. RANKL-deficient mice showed severe osteopetrosis due to loss of osteoclasts. Injection of RANKL into RANKL-deficient mice induced many osteoclasts in bone but not soft tissues. Most of TRAP-positive osteoclasts localized in contact with ALP-positive cells in BMP-2-disks in RANKL-deficient mice injected with RANKL. These results suggest that mesenchymal osteoblasts determine the place of osteoclastogenesis from haemopoietic stem cells in bone.