

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Osteoblast-induced osteoclast differentiation: BMP2 helps a lot

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Bone morphogenetic proteins (BMPs) are members of the TGF β superfamily synthesized by bone cells and playing a major role in differentiation of the bone cell lineages. One of these proteins, BMP2, is synthesized by osteoblasts and accumulates in the extracellular matrix. It exerts paracrine effects at the vicinity of its sites of synthesis and its importance in bone development and repair has been acknowledged [1, 2].

Through the RANK/RANKL system, osteoblasts are involved in osteoclastogenesis and osteoclast activation. This pathway is finely tuned by osteoprotegerin (OPG), a decoy receptor of RANKL of osteoblast origin. Animals deprived from OPG have osteoporosis whereas animals missing RANKL exhibit osteopetrosis.

Using a combination of genetically modified animals in which RANKL or OPG was invalidated, and of a system involving BMP2-induced ectopic bone formation, Yamamoto and colleagues conducted a series of experiments with the purpose of defining the conditions of osteoclastogenesis [3]. They show that BMP2 promotes secretion of RANKL by osteoblasts, and that this mediator is crucial in osteoclast differentiation. In the absence of locally secreted RANKL, but when circulating RANKL is present, osteoclasts may differentiate provided that BMP2 is present at their vicinity.

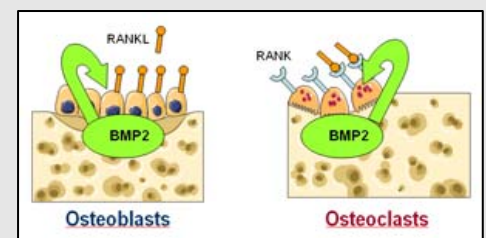
These data evidence that osteoblasts are crucial for osteoclast differentiation, not only because they secrete RANKL, but also by the suitable microenvironment they provide for the action of RANKL. BMP2, which accumulates in the extracellular matrix, appears now as essential for osteoclast differentiation at the right place.

1. Canalis E et al. *Endocrine Rev.* 2003;24:218-235.
2. Seeherman H et al. *Cytokine Growth Factor Rev.* 2005;16: 329-345.
3. Yamamoto Y et al. *Endocrinology.* 2006;147:3366-3374.

Effect of BMP2 on bone cells

BMP2 is secreted by osteoblasts, accumulates in the extracellular matrix, and exerts effects on both osteoblasts and osteoclasts. On osteoblasts, BMP2 stimulates the expression of RANKL which promotes osteoclast differentiation.

When BMP2 is present in the vicinity of osteoclasts, these cells differentiate even in the presence of low concentrations of RANKL.



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