

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

CD200: a new modulator of bone mass which promotes osteoclast fusion and differentiation

N°75 – April 2009

Multinucleate osteoclasts originate from the fusion of macrophages, and play a major role in the resorption of bone. Osteoclasts are essential for bone development and remodelling, and increases in the number and/or activity of osteoclasts lead to diseases associated with generalized bone loss, such as osteoporosis, and others associated with localized bone loss, such as rheumatoid arthritis and periodontal disease. Because fusion is a key step in the differentiation of osteoclasts, a detailed understanding of the molecular mechanism of macrophage fusion should help develop strategies to prevent bone loss.

CD200 is expressed in the bone, on mouse osteoblasts, but not on macrophages. By contrast, the receptor for CD200 (CD200R), is expressed predominantly at the surface of cells that belong to the myeloid lineage, including osteoclasts, and mediates downstream signaling, typically delivering an inhibitory signal. A recent study [1] shows that CD200 is de novo strongly expressed in macrophages at the onset of fusion, giving birth to osteoclasts. Osteoclasts from CD200^{-/-} mice differentiated at a reduced rate. Activation of the signaling pathways downstream of RANK, a receptor that plays a central role in the differentiation of osteoclasts, was depressed in these cells. A soluble recombinant protein that included the extracellular domain of CD200 rescued the fusion of CD200^{-/-} macrophages and their activation downstream of RANK. Conversely, inhibition of CD200R expression with molecular tools prevented fusion. Consistent with in vitro observations, CD200^{-/-} mice contained fewer osteoclasts and accumulated more bone than CD200^{+/+} mice.

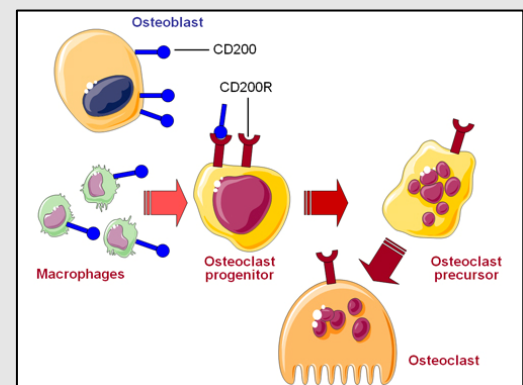
The CD200-CD200R axis is therefore a newly acknowledged putative regulator of bone mass, via the formation of osteoclasts.

1. Cui W et al. *Proc Natl Acad Sci USA*. 2007; 104: 14436-14441.

CD200 and its receptor, CD200R, modulate bone mass via the differentiation of osteoclasts

Mature osteoclasts result from the fusion of progenitors originating from a hematopoietic stem cell. Cells of this lineage express membrane receptors called CD200. The ligand of this receptor, called CD200, is synthesized by osteoblasts. At the onset of fusion of precursors, macrophages strongly express CD200. This expression plays a key role in the recruitment of osteoclasts.

In the absence of CD200, the number of osteoclasts decreases and bone mass is increased.



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