

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Role of the phosphate transporter PiT1 in bone mineralization by osteoblasts

N°39 – July 2008

Osteoblasts develop, synthesize, and deposit extracellular (osteoid) matrix comprising collagen and noncollagenous proteins, and participate in osteoid mineralization. The control of systemic inorganic phosphate (Pi) levels is known to be indispensable for bone formation, especially for osteoid mineralization processes, but the parathyroid hormone (PTH) (decreasing serum Pi levels)-vitamin D (increasing serum Pi levels) axis does not fully explain systemic Pi homeostasis. Attention has been paid to the role of local Pi handling by osteoblasts in bone mineralization. Two related sodium-Pi cotransporters, named Pit1 and Pit2, have been found in osteoblastic cell lines. Molecular inhibition of PiT1 abrogates differentiation and matrix mineralization in osteoblastic cells. In contrast, PiT1 overexpression in smooth muscle cells switches their phenotype from a contractile to an osteogenic one.

To test the hypothesis that osteoblast-mediated Pi handling is crucial for mineralization, the authors of a recent study [1] exploited models in vivo and in vitro to assess local Pi effects on mineralization separately from effects on osteoblast proliferation and differentiation. They show that stringent regulation of Pi handling by osteoblasts through the sodium-Pi cotransporter Pit1 is indispensable for bone mineralization. Fosfarnet, an inhibitor of sodium-Pi transport, blocked mineralization of osteoid formation in osteoblast cultures and local mineralization after injection over the calvariae of newborn rats. Mineralization was also down- and upregulated, respectively, with under- and overexpression of Pit1 in osteoblast cultures. Among molecules expressed in osteoblasts and known to be related to Pi handling, stanniocalcin 1 was identified as an early response gene after fosfarnet treatment; it was also regulated by extracellular Pi, and itself increased Pit1 accumulation in both osteoblast cultures and in vivo.

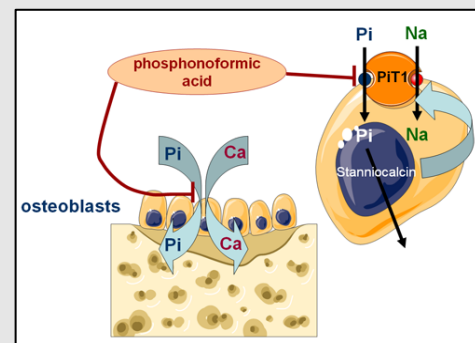
These results provide new insights into the functional role of osteoblast autonomous Pi handling in normal bone mineralization and the abnormalities seen in skeletal tissue in hypophosphatemic disorders.

1. Yoshiko Y et al. *Mol Cell Biol.* 2007;27:4465-4474.

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Osteoblasts develop, synthesize, and deposit extracellular (osteoid) matrix comprising collagen and non collagenous proteins and participate in osteoid mineralization. The sodium-phosphate cotransporter PiT1 is expressed in osteoblasts and is believed to play an important role in matrix mineralization.

Inhibition of PiT1 activity by phosphonoformic acid (fosfarnet) blocked mineralization of osteoid formation in osteoblast cultures and local mineralization after injection over the calvariae of newborn rats. Stanniocalcin was identified as an early response gene after fosfarnet treatment; it was also regulated by extracellular Pi, and itself increased Pit1 accumulation in both osteoblast cultures and in vivo. These results emphasize the role of PiT1 in bone mineralization.



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