

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

HIF α couples angiogenesis to osteogenesis during skeletal development

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Skeletal development and turnover occur in close spatial and temporal association with angiogenesis. Osteoblasts are ideally situated in bone to sense oxygen tension and respond to hypoxia by activating the hypoxia inducible factor α (HIF α) pathway. An elegant study [1] provides evidence that HIF α promotes angiogenesis and osteogenesis by elevating vascular endothelial growth factor (VEGF) levels in osteoblasts. Mice overexpressing HIF α in osteoblasts through selective deletion of the von Hippel–Lindau gene (*Vhl*), a factor which usually promotes degradation of HIF α , expressed high levels of *Vegf* and developed extremely dense, heavily vascularized long bones. By contrast, mice lacking *Hif1a* in osteoblasts had the reverse skeletal phenotype of that of the *Vhl* mutants: long bones were significantly thinner and less vascularized than those of controls. Loss of *Vhl* in osteoblasts increased endothelial sprouting from the embryonic metatarsals *in vitro* but had little effect on osteoblast function in the absence of blood vessels. Mice lacking both *Vhl* and *Hif1a* had a bone phenotype intermediate between those of the single mutants, suggesting overlapping functions of HIFs in bone.

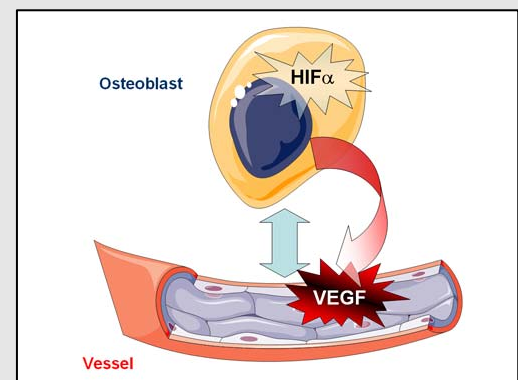
These studies suggest that activation of the HIF α pathway in developing bone increases bone modeling events through cell-nonautonomous mechanisms to coordinate the timing, direction, and degree of new blood vessel formation in bone.

1. Wang Y et al. *J Clin Invest*. 2007;117:1616-1626.

HIF α couples angiogenesis to osteogenesis during skeletal development

In response to hypoxia, osteoblasts express hypoxia-inducible factor (HIF) which promotes vascular endothelial growth factor (VEGF) synthesis by bone-forming cells.

VEGF acts on blood vessels and mediates angiogenesis. Activation of the HIF pathway in developing bone increases bone modeling events to coordinate the timing, direction, and degree of new blood vessel formation in bone.



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