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BMP2 is mandatory for fracture healing

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Bone repair is a key phenomenon to preserve skeleton stiffness and strength. It is not only important for fracture healing but also to repair bone microdamage resulting from mechanical constraints. The first step in this regenerative procedure is the resorption of injured bone by efficient osteoclasts, followed by synthesis of new bone by osteoblasts.

Bone morphogenetic protein 2 (BMP2), synthesized by osteoblasts, accumulates in the extracellular matrix and was acknowledged as a factor promoting fracture repair in adult bone [1]. In order to evaluate the role of BMP2 during growth, Tsuji et al. [2] generated transgenic mice in which *Bmp2* was inactivated in a limb-specific manner before the onset of skeletal development. These mice have few skeletal abnormalities at birth, suggesting that other BMPs present in the developing limb can compensate, at that stage, for the loss of BMP2.

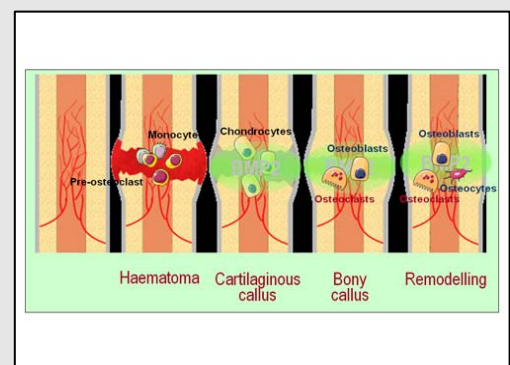
At 1 week of age, significant delays in formation of secondary ossification occurred along with a marked decrease in the production of the type II collagen-rich extracellular matrix at the articular surface of the cartilage. After weaning, when mice increase their weight-bearing movements, the absence of BMP2 had catastrophic effects on maintenance of bone function. By 13 weeks of age, 100% of the mice lacking skeletal BMP2 incurred forearm fractures, and by week 23, all of the mice show fractures bilaterally at sites that have a measurable deficit in bone mineral density compared with control littermates. There was no evidence of a healing response at any time point.

These results indicate that BMP2 is absolutely required for normal fracture healing. In the absence of BMP2, mesenchymal progenitors at the repair site do not differentiate, leading to a failed healing response. These data identify BMP2 as a necessary component of the inherent regenerative capacity of bone and provide the first molecular insight into the initiation of endogenous skeletal repair.

1. Seeherman H et al. *Cytokine Growth Factor Rev.* 2005;16: 329-345.
2. Tsuji K et al. *Nature Genet.* 2006;38:1424-1429.

BMP2 is mandatory to fracture repair

The occurrence of a fracture triggers sequential events starting with a haematoma and the arrival of circulating cells such as monocytes/macrophages, followed by the constitution of a callus made first of cartilage and then of bone. In the absence of BMP2, the cartilaginous callus does not develop because of a defective chondrogenesis. During development, the lack of BMP2 results in multiple spontaneous fractures which occur when weight-bearing movements begin. BMP2 is therefore a specific, crucial differentiation factor for mesenchymal progenitors involved in fracture and microdamage bone repair in both development and adult life.



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