

## Basic fibroblast growth factor for stimulation of bone formation in osteoinductive or conductive implants

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Basic Fibroblast Growth Factor (bFGF) is one of the endogenous factors found in bone matrix. bFGF is a mitogen for many cell types, including osteoblasts and chondrocytes. It can stimulate angiogenesis and osteoblast gene expression. The purpose of this study was to investigate whether exogenous bFGF can stimulate the formation of bone in bone grafts and in a bone graft substitute. All experiments were performed in rats.

In a model using demineralized bone matrix implants for bone induction, a dose of 15 ng bFGF per implant increased the number of chondrocytes and the amount of bone, whereas 1900 ng greatly inhibited cartilage and bone formation. These results are consistent with previous studies with this model, showing that a lower dose of bFGF increased bone calcium content and a higher dose reduced it. Thus, exogenous bFGF can stimulate proliferation during early phases of bone induction.

A new device, the bone conduction chamber, was

developed for the application of bFGF to bone conductive materials. This model made it possible to demonstrate a difference between the conductive properties of bone grafts and porous hydroxyapatite. bFGF in a hyaluronate carrier increased bone ingrowth into bone graft inside the chamber and showed a biphasic doseresponse curve, so that 8–200 ng per implant ( $0.4\text{--}10\text{ ng/mm}^3$ ) increased bone ingrowth, but higher or lower doses had no effect. The same doses had the same effects in porous hydroxyapatite. In both bone grafts and porous hydroxyapatite, the highest dose still caused an increase in ingrowth of fibrous tissue. The effect on bone ingrowth was detected first 6 weeks after bFGF administration, regardless if this started at implantation or 2 weeks later, using an implanted minipump. Hyaluronate gel was effective as a slow-release carrier for bFGF.

In conclusion, bFGF stimulates bone formation in bone implants, depending on dose and method for administration.