

Enhancement of Periosteal Chondrogenesis *In Vitro*

Dose-Response for Transforming Growth Factor-Beta 1 (TGF- β 1)

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Transforming growth factor-beta 1 (TGF- β 1) has been shown to stimulate chondrogenesis in periosteal explants cultured in agarose suspension. In this study, the dose-response curve for such enhancement was measured. Periosteal explants and fascia lata were harvested from two-month-old rabbits, cultured for six weeks with 0, 0.1, 1, 5, 10, 50, or 100 ng/mL TGF- β 1 in agarose suspension, then analyzed by histomorphometry and quantitative collagen typing. Cartilage was produced by seven of 11 (64%) of the control periosteal explants cultured in agarose suspension without TGF- β 1. Transforming growth factor-beta 1 enhanced chondrogenesis in a dose-dependant manner in the range 0.1-100 ng/mL. It was most effective at 50 ng/mL. At very high doses (50 and 100 ng/mL) of TGF- β 1, even fascia lata control explants exhibited chondrogenesis. These data indicate that TGF- β 1 can induce differentiation toward cartilage production as well as enhance it once it has been initiated.

Biological resurfacing of damaged joints is an area of great interest and clinical promise because of the limited potential of damaged articular cartilage for healing.^{3,7,10,15,26,27} Periosteal transplantation has been used in an attempt to regenerate cartilage in experimental animals^{33,42,43,49} and clinically.^{13,23,32} To study the phenomenon of periosteal chondrogenesis *in vitro*, O'Driscoll *et al.*³⁴ have developed an organ culture model in which TGF- β was found to enhance periosteal chondrogenesis.³⁴

Transforming growth factor-beta (TGF- β) is a multifunctional protein that has the potential to influence cell differentiation, proliferation, and synthesis of extracellular matrix components, depending on the cell and tissue type being studied.³⁸ It is abundant in articular cartilage chondrocytes and osteocytes.^{8,9,28} It can be detected in other mesenchymal tissues, such as connective tissue and embryonic tissues, using immunohistochemical methods.^{8,12,25} These facts indicate that TGF- β is involved in connective tissue morphogenesis, including chondrogenesis. The effects of TGF- β on chondrogenesis or cartilage matrix production have generally been stimulatory.^{17,29,37,44} In developing a model for culturing whole periosteal explants *in vitro*, the authors found that TGF- β enhanced chondrogenesis in periosteal explants.³⁴ Only two concentrations (1 ng/mL and 10 ng/mL) were studied, and it appeared that the higher dose was more effective in stimulating chondrogenesis.

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