BRIEF EXPOSURE TO HIGH-DOSE TRANSFORMING GROWTH FACTOR-β1 ENHANCES PERIOSTEAL CHONDROGENESIS IN VITRO

A PRELIMINARY REPORT

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Background: Articular cartilage has limited potential for repair. There have been various attempts aimed at improving the repair process in articular cartilage. Transforming growth factor-β1 (TGF-β1) has a stimulatory effect on chondrogenesis in periosteal explants. The purpose of the present study was to determine the effect of brief exposures (i.e., thirty and sixty minutes) of high concentrations of TGF-β1 on periosteal chondrogenesis.

Methods: Five hundred and seventy-three periosteal explants were harvested from forty-six two-month-old male New Zealand White rabbits. Explants were exposed to 50 or 100 ng/mL of TGF-β1 for thirty or sixty minutes. The amount of cartilage formed was then determined with use of a standardized six-week agarose culture assay.

Results: There was a significant increase in the amount of cartilage formation ($p < 0.01$), Type-II collagen content ($p < 0.05$), and sulfate incorporation ($p < 0.0001$) in explants treated with TGF-β1. Maximal stimulation occurred following exposure to 100 ng/mL of TGF-β1 for thirty minutes. There was also an increase in chondrocyte proliferation as measured by [^{3}H-] thymidine incorporation on day 5 of culture ($p < 0.049$).

Conclusions: The findings of this study indicate that exposure to TGF-β1 has a stimulatory effect on periosteal chondrogenesis. This stimulatory effect is observed even with a very brief exposure time of thirty minutes.

Clinical Relevance: A possible clinical application of these findings is exposure of periosteal grafts that are currently utilized clinically to resurface articular defects to TGF-β1 during the short time between graft procurement and implantation into the joint. This may obviate the need for intra-articular administration of TGF-β1 and may enhance the ultimate graft incorporation and quality of cartilage repair.

Periosteal grafts have been used experimentally and clinically[1-3] to repair articular cartilage. Periosteum lends itself to tissue-engineering applications, as it contains undifferentiated mesenchymal stem cells in a scaffold. These cells are responsive to growth-factor stimulation. We previously reported that exposure of periosteal explants to transforming growth factor-β1 (TGF-β1) for two weeks stimulated cartilage formation in a dose-dependent fashion[4,5]. Additional work in our laboratory revealed that chondrogenesis by periosteal explants could be stimulated just as effectively by shorter durations (two days) of exposure to TGF-β1[6]. As a possible way to obviate the need to culture periosteum before implanting it back into the patient, we conceived of the idea of stimulating the periosteum with growth factors intraoperatively. There is a short period of time between procurement and implantation of a periosteal graft during which the articular defect is being prepared for the implantation of the graft. Conceptually, tissue-engineering techniques, such as exposure to growth factors and/or mechanical stimulation, could be applied to the graft in the operating room during this period. The purpose of this study was to test the hypothesis that, with use of high doses of TGF-β1, periosteal chondrogenesis can be stimulated by very brief exposures (thirty to sixty minutes) that could be achieved during the course of an operation. Such a technique could be used to enhance graft incorporation and cartilage repair.

Materials and Methods

Explant Harvest

The protocol for explant harvest used in our laboratory has been described previously[5]. In the present study, 573 explants were harvested from the anteromedial side of the proximal part of the tibiae of forty-six two-month-old male New Zealand White rabbits. The rabbits were killed by injection of