The inductive effect of BMP-4 protein on chondral-lineage differentiation and in-situ cartilage repair

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Objectives: Recent studies suggest that bone morphogenetic protein-4 (BMP-4) and BMP-7 are promising cartilage differentiation factors, so this study aimed to evaluate their efficacy for articular cartilage repair in vitro and in vivo.

Methods: Rabbit mesenchymal stromal cells (MSCs) and articular chondrocytes were treated with 10 ng/ml hrBMP-4 or hrBMP-7. The expression of cartilage-specific genes (Col II, Aggrecan, and Sox9) and FGF receptor genes were tested by real-time PCR in vitro. Also, full-thickness cartilage defects (diameter 4 mm, thickness 3 mm) were created in New Zealand white rabbits and treated with a bi-layer collagen scaffold (group II), BMP4 with scaffold (group III) or not treated (group I) (n=12/group). The repaired tissues were harvested for histology and mechanical testing at 6 or 12 weeks after operation.

Results: Cartilage differentiation of MSCs was more apparent after BMP-4 treatment as evidenced by the higher expression of type II collagen and aggrecan genes. Also, BMP-4 induced higher aggrecan and FGFr2 gene expression in chondrocytes, while BMP-7 had no effect. In the in vivo experiments, group III treated with BMP4 protein had the largest amounts of cartilage tissue, which restored a greater surface area of the defect and achieved higher International Cartilage Repair Society scores. Moreover, Young’s modulus, which indicates the mechanical properties of the repaired tissue, was markedly higher in group III than in groups I and II (p <0.05), but lower than in normal tissue.

Conclusion: BMP-4 is more potent than BMP-7 for cartilage differentiation. The delivery of BMP-4 protein in a bi-layer collagen scaffold stimulates the formation of cartilage tissue.