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Comparing BMP-9 with TGF-β1 for Tissue Engineering Stable Articular Cartilage

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Keywords

Cartilage, BMP-9, TGF-β, Progenitor

Abstract

Introduction

When damaged by acute injury or chronic degeneration, articular cartilage has limited ability to repair itself. Earlier studies indicated that articular cartilage progenitor (ACP) cells are good candidates for creating articular cartilage as they produce a matrix that more closely resembles the stable cartilage of the native tissue than that created by other stem/progenitor cell types, which produce hypertrophic cartilage. Previously, bone morphogenic protein 9 (BMP-9) was shown to increase matrix production in chondrocytes, but also increased hypertrophy. We aimed to determine the effects of BMP-9 on ACPs as part of ongoing efforts to develop optimal methods for tissue engineering stable articular cartilage.

Methods

We isolated and expanded multiple ACP clones from human cartilage of healthy donors and subjected them to the in vitro 3D chondrogenesis assay with either TGF-β1 (control) or BMP-9 (experimental) groups. We analyzed the effects of the growth factors at the gene and protein level after 14 days of differentiation.

Results

BMP-9 induced significantly greater sulfated glycosaminoglycan (sGAG) accumulation (a measure of proteoglycan production) and higher gene expression of SOX9 and PRG4 compared with TGF-β1 with no significant increase in COLXA1 gene expression or collagen X protein levels. However, total collagen production was lower with BMP-9 and matrix organization was less ordered.

Discussion

We found that BMP-9 increased proteoglycan accumulation in pellets without a significant shift towards hypertrophy. While there was a small increase in COLXA1, the collagen X

protein levels measured by ELISA were still far below the levels found in mesenchymal stromal cell (MSC) pellets, which are known to exhibit a hypertrophic phenotype. However, because BMP-9 induced less collagen production and a diminished matrix organization, it may not be a better alternative to TGF-β1 for generating biosimilar articular cartilage tissue.