

Introduction

Chondrogenic growth factors and ECM proteins are integral parts of the optimal microenvironment to support articular cartilage repair.¹ Factors that regulate chondrocyte activity in healthy cartilage are multifunctional. Following injury, these factors can recruit host mesenchymal stem cells (MSCs) to the injury site and promote chondrogenesis and matrix synthesis by MSCs. Cartiform is a cryopreserved viable osteochondral allograft that is designed to treat articular cartilage defects. The goal of this study was to determine if the articular cartilage-specific chondrogenic growth factors and ECM proteins are preserved in Cartiform. Additionally, the ability of Cartiform to release these factors over time was investigated.

Methods

Cartiform was thawed, minced into small pieces and lysed to create tissue extracts that were used to evaluate the growth factor and ECM contents in Cartiform. In order to evaluate the release of these factors from the tissue, Cartiform was cultured in basal media and supernatants were collected at 7, 14 and 21 days. Chondrogenic growth factors and ECM proteins in Cartiform tissue extracts and supernatants were detected by enzyme-linked immunosorbent assays (ELISAs).

Results

The Cartiform tissue extracts and supernatants contained chondrogenic growth factors, including TGF-β1, TGF-β3, BMP-2, BMP-4, BMP-7, bFGF and IGF. The ECM proteins aggrecan, hyaluronan and type II collagen were also detected in the tissue extracts. Chondrogenic growth factors were continuously released by Cartiform, leading to accumulation of growth factors in the culture supernatants. Accumulation of TGF-β1 over a three week period is shown in **Figure 1**.

Discussion

Cartiform contains a variety of proteins necessary for cartilage repair, including chondrogenic growth factors and ECM proteins. The growth factors are known to have a wide range of biological activities including the promotion of chondrogenesis, stimulation of chondrocyte proliferation, and regulation of ECM synthesis **Table 1**.^{1,2} The ECM proteins serve as a scaffold for cell attachment, mediate cell-cell and cell-matrix interactions, and act as a reservoir for growth factors.² Due to the presence of viable chondrocytes and a dense extracellular matrix, Cartiform provides a sustained release of growth factors and ECM proteins over time that creates a favorable microenvironment for the formation of hyaline cartilage.

Significance

Cartiform, a cryopreserved viable osteochondral allograft, contains and releases chondrogenic growth factors and ECM proteins known to support articular cartilage repair. By providing a growth factor and ECM-rich microenvironment throughout the entire lesion, Cartiform’s ability to support the formation of hyaline cartilage is not limited by lesion size, unlike that observed with marrow stimulation alone.³

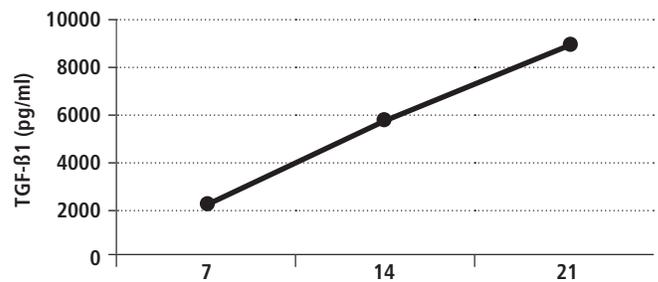


Figure 1. Sustained release of TGF-β1 from Cartiform into the media leads to accumulation over three weeks.

Chondrogenic Factors	Function
TGF-β1, 3	Promotes chondrogenic differentiation and regulates type II collagen expression
BMP-2, 4, 7	Induces chondrogenesis of MSCs and stimulates ECM production by chondrocytes
bFGF	Stimulates proliferation of chondrocytes
IGF-1	Induces ECM synthesis

Table 1. Chondrogenic factors present in Cartiform and their roles in articular cartilage repair.

References

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