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PROCHONDRIX® CARTILAGE RESTORATION MATRIX CONTAINS GROWTH FACTORS NECESSARY FOR HYALINE CARTILAGE REGENERATION

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Introduction

The signaling environment of cartilage is notably complex and is comprised of many important growth factors that play an indispensable role in maintaining healthy cartilage tissues. It is clinically understood the loss of signaling due to injury or degeneration can lead to degradation of the healthy tissue environment and thus, a treatment option that maintains natural signaling factors is vital to the repair and regeneration of hyaline cartilage.[1] ProChondrix® is an intact, living cellular, fresh cartilage matrix processed from adult donors and designed to aid in the repair and regeneration of damaged cartilage tissues. ProChondrix is laser perforated to allow for the outgrowth of viable chondrocytes that aid in cartilage regeneration. The purpose of this study was to investigate the presence of growth factor proteins in ProChondrix and relate the signaling significance of these proteins as they pertain to cartilage defect repair.

Methods

A total of 15 ProChondrix samples from 11 deceased human donors were homogenized and lysed to extract proteins. Samples were also placed in explant, where the tissue was secured with fibrin glue into a 12-well plate and cultured in growth media. Cell supernatant was collected from the explanted grafts after seven days to show the excretion of certain growth factors from ProChondrix. Tissue homogenate and cell supernatant was then tested for the presence of various chondrogenic growth factors using enzyme-linked immunosorbent assays (ELISAs).

Results

ProChondrix expressed the following growth factors: bFGF (Basic Fibroblast Growth Factor), PRG4 (Superficial Zone Protein), TGF-β (Transforming Growth Factor Beta), IGF-1 (Insulin-Like Growth Factor 1), BMP-2 (Bone Morphogenic Protein 2), BMP-7 (Bone Morphogenic Protein 7) and PDGF (Platelet Derived Growth Factor). The significance of each of these growth factors and their role in cartilage healing is explained in (**Table 1**).

Growth Factor	Relative Levels of Growth Factors in ProChondrix®	Effects of Growth Factors in Cartilage Tissue
bFGF	+++	Respond to tissue injury, increase chondrocyte proliferation, collagen 2 deposition and prevents tissue hypertrophy.
PRG4	+++	Source of joint lubrication to protect against cartilage damage and inflammation.
TGF-β1	++	Maintains PRG4 levels allowing it to protect against cartilage damage and promotes cellular chondrogenesis.
IGF-1	- Graft + Explant	Remediates cartilage damage by generating hyaline cartilage.
BMP-2	+	Lowers chondrocyte proliferation while also increasing their deposition of hyaline cartilage.
BMP-7	- Graft + Explant	Promotes stem cell chondrogenesis and their production of PRG4 and hyaline cartilage.
PDGF	++	Increases chondrocyte proliferation and prevents cellular aging. Prevents cartilage hypertrophy and inflammation.
Key: +++ High Levels, ++ Medium levels, + Low Levels, - Not Present		

Table 1: Importance of Signaling and Functional Proteins in ProChondrix®
Where not indicated, symbols are representative of growth factor presence in the explant.

Discussion:

Growth factors control the differentiation and proliferation of chondrocytes, as well as the production of the matrix. Thus, ProChondrix provides control for growth factor production. Growth factors present in ProChondrix can promote Bone Marrow Derived Cell (BMDC) migration into the surgical site and encourage chondrogenesis after being liberated through microfracture. The combination of the live cell-signaling matrix and the presence of host BMDCs lead to incorporation, and helps to form healthy hyaline cartilage. Presence of PRG4 in ProChondrix allows for the immediate lubrication of the joint.[2] TGF-β works to maintain this lubricating superficial layer and remediate joint damage.[3,4] bFGF found in the matrix demonstrates that ProChondrix maintains an inherent ability to respond to mechanical tissue damage.[5,6] This directly correlates to the role of growth factors in the maintenance of glycosaminoglycans (GAGs) in cartilage which is the primary cushioning component of the extracellular matrix and is important for proper cartilage functioning. Growth factors such as TGFb are bound to the heparin sulfate portion of GAGs in cartilage. They remain bound to this portion of the GAG until they are released through mechanical or chemical stimulation where they will perform their signaling function. [7,8] BMP-2 promotes hyaline cartilage deposition.[9] PDGF allows chondrocytes to proliferate without undergoing the effects of cellular aging.[10,11] ProChondrix also expressed BMP-7 and IGF-1 in low levels as seen in healthy cartilage.[12,13] Moreover, when ProChondrix grafts were explanted, they displayed expression levels of BMP-7 and IGF-1, even at the maximum shelf life of 35 days. This indicates the chondrocytes in ProChondrix retain their signaling capability and are able to increase their production of signaling factors upon transplant. With this signaling capacity, when used in conjunction with microfracture, ProChondrix is able to signal the BMDCs of the host, promoting chondrogenesis and migration into the transplant site.[13]

The full interplay of ProChondrix, its growth factors and the recipient's tissue are shown in (**Fig. 1**).

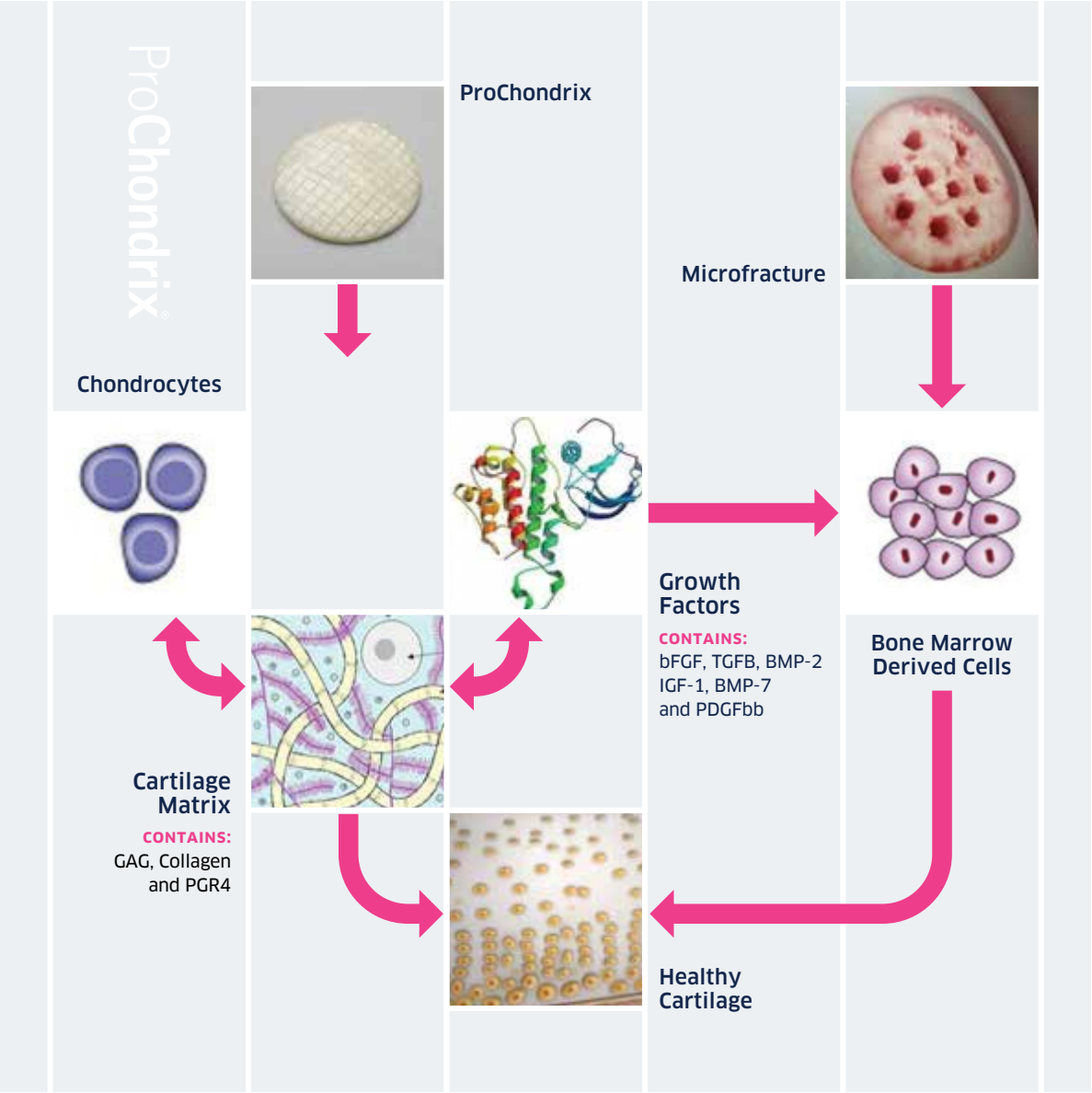

Figure 1: Role of ProChondrix in Cartilage Repair

Significance:

Independently, marrow stimulation procedures do not promote the excretion of growth factors or extracellular matrix proteins necessary for repair and regeneration of healthy hyaline cartilage, making it a short-term solution. As shown in this study, ProChondrix expressed levels of growth factor proteins and can augment the reformation potential of a healthy articular surface. ProChondrix, a fresh, living cellular allograft, supplies the necessary growth factors and maintains an intact matrix that helps promote the regeneration of hyaline cartilage; further supporting the healing of chondral defects and providing the potential for long-term clinical success.

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Notes:

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