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PHYSIOLOGICAL COLLAGEN ARCHITECTURE IN ENGINEERED TISSUE CARTILAGE THROUGH A COMBINED APPROACH OF MECHANICAL STIMULUS AND ANISOTROPIC FIBROUS SAFFOLDS

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ABSTRACT

This work consists on improvement of the functionality of tissue engineered cartilage through a combined approach of mechanical stimulus with anisotropic fibrous scaffolds provided on a bioreactor culture environment, in order to bring the structural organization of engineered cartilage close to the native tissue, reducing the risk of failure of this promising method for osteoarthritis treatment.

Keywords: biomechanics, mechanical stimulus, anisotropic fibrous scaffolds

INTRODUCTION

The major challenge associated with tissue engineered cartilage is the difficulty to approximate the mechanical properties of the engineered tissues to the native ones (Johnstone et al 2013). Various experimental studies in bioreactors had concluded that the mechanical properties of engineered cartilage can be improved by appropriate mechanical stimulation (Kock et al 2012). These indications are promising, but the properties of these engineered cartilages remain inferior to native. The major shortcoming of tissue-engineered cartilage is believed to be the lack of collagen content and consequently its poor tensile properties. Collagen reaches only 15-35% of the native content after 5–12 weeks (Kock et al, 2012). Another shortcoming is that tissue-engineered cartilage does not possess native zonal variations. The importance of the arcade-like collagen structure for the load-bearing properties of native cartilage is well emphasized in literature (Danisovic et al, 2012). However, despite extensive cartilage tissue engineering research, few studies have assessed the importance of collagen fibril depth-orientation on the mechanical properties of engineered cartilage. Culture conditions that have impact on collagen synthesis and fibril organization in-vitro include scaffold properties (McCullen et al, 2012) and mechanical stimulation (Bandeiras et al, 2014; Bandeiras et al, 2015). Future research should particularly focus on approaches to increase collagen content and fibril organization. For tissue engineered cartilage to be mechanically functional, some investigators, believe that depth arcade-like collagen architecture should be reproduced to some extent in engineered cartilage. But how can this be best achieved? Some investigators hypothesize that applying depth-varying mechanical cues would stimulate extracellular matrix synthesis/organization depth dependently (Kock et al 2012). Others, suggested the use of anisotropic fibrous scaffolds, in order to provide a template to organize the newly deposited matrix (McCullen et 2012).

RESULTS AND CONCLUSIONS

This work plan search exploring different process parameters, related with electrospun scaffolds like fiber size, spacing and orientation is possible produces scaffolds with different depth-dependent structural organizations through a nanofiber Electrospinning machine (McCullen et al, 2012). By varying the fiber size, the resultant pore size and mechanical strength can be varied over a wide range. Fiber orientation can be varied by modifying collector geometry or rotating collector speed, yielding fibrous scaffolds that vary from randomly oriented scaffolds to highly aligned networks with concomitant variations in tensile strength (McCullen et al, 2012). A technique to incorporate multiple electrospun layers with distinct fiber sizes and orientations is that of sequential electrospinning onto the same collector under varying operating conditions. Additionally, exploring the mechanical stimulus parameters like load type (compression, traction, shear, hydrostatic pressure or combined), load magnitude, applied frequency and loading period during the culture phase, in an active bioreactor previously developed, is possible generate different strain distribution along scaffold depth which may enhances collagen content and a depth-varying collagen orientation (Bandeiras et al, 2014). A promise loading regime involving sliding of the indenter with lateral compression may stimulate the formation an arcade-like collagen architecture.

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