The Effect of Cyclic Mechanical Compression on Articular Cartilage Tissue Engineering

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Introduction: Mechanical stimulation has been suggested as one of the critical factors for articular cartilage tissue engineering [1]. It has been shown that mechanical compression effects chondrocyte behavior in the cartilage explants and chondrocyte-hydrogel complex. However, few reports have been published regarding the influence of mechanical compression on chondrocytes seeded in scaffolds. The purpose of this study is to investigate chondrocytes' responses to cyclic mechanical compression when cells are seeded in elastic scaffolds.

Materials/Methods: Elastic scaffolds composed of chitosan and gelatin were fabricated by a freeze-gelation method [2]. The porosity of chitosan/gelatin scaffolds whose pore size was 25-50 μm was approximately 95%. Chondrocytes were harvested from articular cartilage of one-week-old New Zealand white rabbits. Passage-2 chondrocytes were seeded in the scaffolds at a density of $8x10^5$ cells/scaffold. After 3 days of culture, the complex were under a dynamic compression at 40% in amplitude and at a frequency of 0.1 Hz for 3, 6, or 9 hrs, and then gene expression of type I and II collagen (COL I & II) and aggrecan (AGG) was analyzed by RT-PCR. The effects of long-term compression (3 weeks, 6 hrs/day) on chondrocytes were also studied. DNA contents of the constructs were determined by Hochest 33258; GAGs contents were determined by DMMB assay; collagen contents were determined by Chloramine T assay.

Results/Discussion: Expression of all COL I, COL II, and AGG genes was stimulated after 3-hr compression (25%, 20% and 49%, respectively, Fig. 1). The expression of COL I and AGG genes continued to increase until 6-hr compression, while COL II gene was not further enhanced after 3-hr compression. Therefore, for long-term culture, the cell/scaffold constructs were compressed for 6 hrs/day. After 3-week compression, the cell number and the GAG content in the compressed constructs was significantly higher than those in the control group, uncompressed constructs (36.4% and 25.8% increase, respectively, Fig. 2a and b). However, we did not find any differences in collagen contents between the compressed and control samples. We show that mechanical compression affects the behavior of chondrocytes which are attached to a porous scaffold. The increase in cell number and GAG content after long-term compression suggests the promise of applying mechanical compression to articular cartilage tissue engineering.

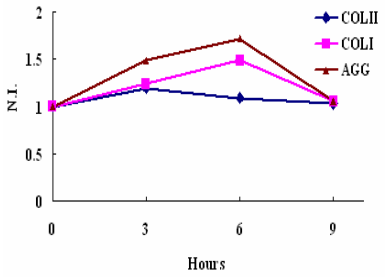
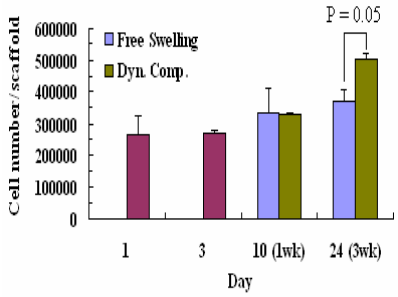


Fig. 1. Gene expression. Normalized intensity (N.I.) = loading/unloading construct.

(a)



(b)

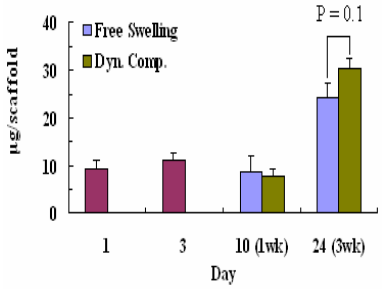


Fig. 2. (a) Cell proliferation and (b) GAGs content after 3-week compression (6 hrs/day).

Conclusion: Mechanical compression enhances proliferation of chondrocytes and synthesis of ECM matrix. Combining with elastic scaffolds, physical compression may benefit articular cartilage tissue engineering.

References:

1.Grodzinsky AJ. Annual Review of Biomedical Engineering. 2000;**2**(1):691-713.

2.Ho MH. Biomaterials. 2004;**25**(1):129-138.