Mechano-Active Cartilage Tissue Engineering: Effects of Biomechanical Conditioning

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Statement of Purpose: The compressive and shear forces are concerned in the development and maintenance of articular cartilage in the body[1]. It means the mechanical stimulation is a very important factor for formation of cartilage[2]. However, the excessive mechanical stimulation makes progress the cartilage ossification and fibrous tissue formation[3]. Therefore it is important to find out the proper mechanical stimulation for formation of tissue engineered articular cartilage. The purpose of this study is to evaluate the effect of dynamic compression for formation of tissue engineered cartilage and the effect of the duration of applying compressive stimulation for cartilaginous extracellular matrix secretion.

Methods: A highly elastic scaffold was fabricated from very elastic poly(L-lactide-co-ε-carprolactone)(5:5) with 85 % porosity and 300~500 μm pore size by a gel-pressing method. The scaffolds were seeded with chondrocytes and the continuous compressive deformation was applied to them with 0.1Hz for 10 days and 24 days respectively. Also, the chondrocytes-seeded constructs were implanted in nude mice subcutaneously to investigate their biocompatibility and cartilage formation. Cell-polymer constructs were characterized by SEM, MTS assay, Glycosaminoglycans (GAGs) and collagen quantitative analysis, and histological studies. For defining the gene expression for mechanical stimulation, reverse transcription-polymerase chain reaction was performed.

Results / Discussion: Mechano-active scaffolds having a complete rubber-like elasticity prepared by a gel-pressing method. They could be easily twisted and bended and showed almost complete (over 97%) recovery at strain applied of up to 500%. The accumulation of extracellular matrix of cell-polymer constructs which was increased through mechanical stimulation showed that chondrogenic differentiation was sustained and enhanced significantly. The GAG contents of implants stimulated by the dynamic compressive deformation were higher than them without stimulation and that of implants of stimulated on a compressive bioreactor before implantation for 10 days were higher than them for 24 days (Figure 1).

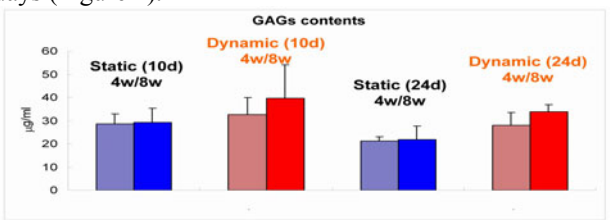

Figure 1. GAGs contents of engineered cartilage

Histological analysis showed that implants stimulated mechanically by compression for 10 days and for 24 days formed mature and well-developed cartilaginous tissue, as evidenced by chondrocytes within lacunae. Alcian blue staining indicated an abundant accumulation of sulfated GAGs, which are extracellular matrices produced by differentiated chondrocytes in the newly formed tissues. But in the implants stimulated mechanically by compression for 24 days, unhealthy lacunae shapes and hypertrophy forms were observed (Figure 2). These results would be due to continuous deformation for too long period under the bioreactor.

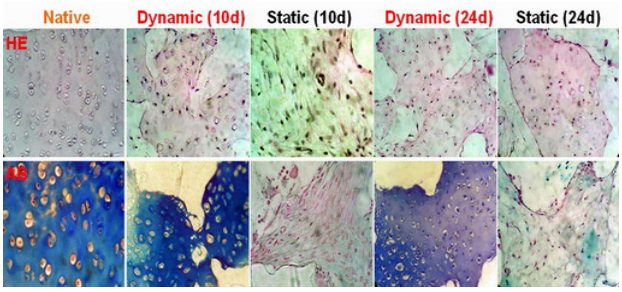

Figure 2. Histological studies of implants 8 weeks after implantation (HE: Hematoxylin and Eosin staining, AB: Alcian blue staining)

Conclusions: In this study**,** it was tested that the proper compressive deformation induces the phenotype of chondrocytes in engineered tissues in vitro to be similar to that of chondrocytes in native tissues in vivo. As a result, by the mechanical stimulation for 10 days, cell-polymer constructs formed mature and well-developed cartilaginous tissue, as evidenced by chondrocytes within lacunae and accumulated sulfated GAGs. In conclusion, the proper periodic application of dynamic compression can encourage chondrocytes to maintain their phenotypes and enhance GAGs production and consequently, improve the quality of cartilaginous tissue formed in vitro and in vivo.

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