Alginate/Hyaluronate Hybrid Hydrogels for Cartilage Regeneration

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Introduction

Injectable cell delivery using hydrogels has been attractive in many tissue engineering applications. Alginate and hyaluronate have been widely used in biomedical applications due to their biocompatibility. We previously reported that RGD-modified alginate can form cell-cross-linked gel structures with fibroblasts [1] and chondrocytes [2]. In this study, we hypothesized that an addition of hyaluronate to the system could enhance interactions with primary chondrocytes and promote cartilage regeneration in vivo. We measured various characteristics of alginate/hyaluronate hybrid hydrogels in the presence of chondrocytes and tested their tissue forming capability in mice.

Materials and Methods

Sodium alginate was dissolved in MES buffer (pH 6.5) and G4RGDSP peptide was added to the solution in the presence of water soluble carbodiimide. Primary chondrocytes were isolated from articular cartilage of New Zealand white rabbits. The cartilage fragments were digested with collagenase type II. Isolated cells were cultured in DMEM/F-12 media. NIH3T3 mouse fibroblasts were cultured in DMEM. Viscoelastic properties of cell/polymer mixtures were measured using a rotational rheometer. Chondrocytes and polymer mixtures were subcutaneously injected into the dorsum of the nude mice. Retrieved tissues were stained with H&E and Safranin-O. GAGs contents were determined with assay kits (Biocolor) and gene expression of chondrogenic markers including collagen type I/II, aggrecan, SOX-9 was investigated by PCR.

Results

When chondrocytes ([cell] = 1.25×10^7 cells/ml) were added to the mixture of 2% RGD-alginate and 0.5% hyaluronate solutions, the storage modulus (G') of the mixture was higher than the loss modulus (G''), indicating the gel formation. However, fibroblasts did not form the gel structures (Fig. 1). Alginate/hyaluronate was able to form the cell-cross-linked structures with primary chondrocytes at this experimental condition, due to enhanced interactions between cells and polymers.

Discussion and Conclusions

We demonstrated that RGD-alginate/hyaluronate was useful to form cell-cross-linked gels with primary chondrocytes due to enhanced specific interactions between cells and polymers. These gels were injectable into animals and showed potential in cartilage regeneration.

References


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Disclosures

Authors have nothing to disclose.