Poster Session I:

1P-01 Novel chondro-protective mechanisms of hyaluronic acid: down-regulation of ADAMTS-7 and ADAMTS-12, and reduced COMP release from articular cartilage

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Keywords: COMP, ADAMTS, hyaluronic acid

Objective: Hyaluronic acid (HA) is known to down-regulate matrix metalloproteinases (MMPs) and a disintegrin and metalloproteinases with thrombospondin motifs (ADAMTSs) in both chondrocytes and synoviocytes, and widely used for both osteoarthritis and rheumatoid arthritis patients in the clinical settings. However, it is not well understood whether HA could protect articular cartilage from proteolytic degradation. Cartilage oligomeric matrix protein (COMP) is a noncollagenous extracellular matrix protein consisting articular cartilage, and released from matrix by proteolytic degradation in the presence of MMPs and ADAMTSs. In this study, we examined whether HA could inhibit the proteolytic release of COMP from articular cartilage.

Methods: Bovine articular cartilage was cut into small pieces and incubated with RPMI in the presence of IL-1 beta and synovium-derived SW982 cells, with or without HA. COMP levels were measured using ELISA. SW982 cells were also incubated with IL-1 beta in the presence of HA, then mRNA was extracted, and the expression levels of MMP-3, ADAMTS-4, -5, -7, and -12 were examined using real-time PCR.

Results: Proteolytic release of COMP from bovine cartilage samples was up-regulated about 2-fold over the control level when incubated with SW982 for 3 days. This up-regulation was significantly inhibited in the presence of HA. In SW982 cells, the expression levels of MMP-3, ADAMTS-7 and ADAMTS-12 were increased about 3- to 5-fold over the control levels when stimulated with IL-1 beta. HA also significantly inhibited these IL-1 beta-induced up-regulation of proteases.

Conclusions: Chondro-protective effects of HA were observed in this study. HA suppressed proteolytic release of COMP from articular cartilage stimulated by IL-1 beta and SW982 cells. This inhibitory effect is thought to be a result from down-regulation of MMP3.

1P-02 Ectopic bone formation after implantation of thermoreversible gelation polymer as a carrier of Bone morphogenetic protein-2

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Keywords: thermoreversible gelation polymer, carrier, Bone morphogenetic protein-2

Objective: Previous studies have reported that bone morphogenetic proteins (BMPs) induced ectopic bone formation after implanted with carrier materials in rats, and BMP-induced osteo-/chondrogenesis was highly dependent upon the carrier. Thermoreversible gelation polymer (TGP) is characterized by its temperature-dependent dynamic viscoelastic properties. The sol-gel transiting temperature (SgTT) of TGP is 20°C. The purpose of this study was to investigate the ectopic bone formation on implantation of rhBMP-2 using TGP as carrier in a rat subcutaneous assay model and disposal of residual rhBMP-2/TGP after ectopic bone formation.

Methods: Twenty 8-week-old Wistar rats were used in the experiment. Subcutaneous pockets were created on the back of rats. The pockets were implanted with rhBMP-2/TGP, TGP alone, rhBMP-2/collagen, collagen alone. The rats were sacrificed at 10days, 4 and 8weeks for histological evaluation.

Results: Both rhBMP-2/TGP group and rhBMP-2/collagen group at 4 and 8 weeks after implantation, ectopic bone formation was found. In rhBMP-2/TGP group, the bone formation was found on the surface of the implanted carriers. In the TGP alone group, ectopic bone formation was not observed and connective tissue was found on the surface of the implanted carrier. In each case, TGP became hydrogel under 22°C and could be removed easily out of the implanted samples.

Conclusion: This study suggests that rhBMP-2/TGP could induce ectopic bone formation around the implanted samples. TGP could maintain in the same size as implantation without absorption and its thermoresponsive behavior even after it was implanted in vivo.