The Protective Effect of OP-1 on Articular Cartilage in the Development of Osteoarthritis

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Introduction: Osteoarthritis (OA) has many current treatments ranging from conservative options like NSAIDs and physical therapy to surgical procedures i.e., joint arthroplasty, but none of these available treatments protect articular cartilage. The purpose of this study was to determine whether Osteogenic Protein 1 (OP-1) would protect articular cartilage from degeneration during the development of osteoarthritis (OA) in the rabbit anterior cruciate ligament transection (ACL T) model. Previous studies have shown that OP-1 (BMP-7) is vital to cartilage matrix integrity and repair[1], stimulates synthesis of cartilage matrix components, proteoglycans and collagen[2], has a protective effect against catabolic mediators such as MMPs and IL-1[3,4].

Materials and Methods: The rabbit ACL T model was used in which the anterior cruciate ligament (ACL) was transected leading to osteoarthritis.[5] OP-1 was delivered to the joint surgically for approximately 6 weeks by implantation of an Alzet osmotic pump into the medial thigh with a catheter threaded from the pump into the knee joint. 40 rabbits (20 control, 20 experimental) had the ACL T surgery and implantation of the pump performed simultaneously. They were sacrificed 9 weeks after for analysis. The osteoarthritis was graded using the Outerbridge classification with India Ink staining. The criteria is: Grade 1 (intact surface), Grade 2 (minimal fibrillation), Grade 3 (overt fibrillation) and Grade 4 (erosion). Histological staining and histomorphometry with Hematoxylin & Eosin and Safranin O were performed to analyze OA progression and Semi-quantitative Polymerase Chain Reaction (PCR) was performed for anabolic genes, aggrecan and type II collagen, and catabolic genes, aggrecanase, MMP-3 and MMP-13.

Results: The experimental group showed less cartilage degradation than the control(Fig 1). The experimental group had an average Outerbridge score of 1.8 versus 2.5 for the controls (p<0.05)(Fig 2A). In the control group, 46% of the condyles were graded 3 or 4, indicating they had a high degree of cartilage fibrillation or loss. In the OP-1 treated group, only 12% of the condyles were graded either 3 or 4. Moreover, in the OP-1 treated group 28% of condyles did show Grade 1 or near normal cartilage compared to just 7% in the Control group(Fig 2B). Histomorphometry showed 10.9% surface deterioration or an average depression of 0.05mm versus 22.3% and 0.1mm for the controls (p<0.05)(Fig 3). Semi-quantitative PCR showed a significantly greater expression of aggrecan and collagen type II in the OP-1 treated cartilage when compared to controls and less expression of aggrecanase, a catabolic mediator.

Discussion: OP-1 may have a potential benefit in protecting articular cartilage during the development of OA.

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References:

Figure 1: Sample Gross Morphology

Figure 2: Gross Morphology Results

Figure 3: Histomorphometry Results