Introduction: Whether facet joint osteoarthritis (OA) precedes intervertebral disc degeneration remains unresolved. However, significant facet joint cartilage changes can be found in young individuals under age 30 and the incidence of facet joint OA increases after 45 years of age [1]. Current conservative approaches to treat facet joint OA are limited to steroid injections or trigger point injections.

Osteogenic protein-1 (OP-1, or bone morphogenetic protein-7 (BMP-7)) has anabolic and anti-catabolic effects on the extracellular matrix (ECM) metabolism of articular chondrocytes [2]. The direct injection of growth factors into joints to treat cartilage degeneration holds some promise when it is used with collagen sponges or an infusion pump [2]. Recently, an attempt to restore the degeneration of the facet joint by an injection of BMP-2 has shown some success in the rat collagenase-induced facet degeneration model [3]. Based on the strong effects of OP-1 on the production of the ECM [1], we hypothesized that a direct injection of OP-1 may hold promise to restore degenerated facet joint cartilage.

The purpose of this study was to evaluate whether OP-1 is beneficial in stimulating proteoglycan (PG) synthesis and slowing down the degradation of PGs in degenerated human facet articular cartilages cultured in an organ culture system.

Materials and Methods: Nine human spines (male: 8; female: 1; mean age: 60.8 years-old) were obtained from a regional organ bank; the grades of degeneration of discs and facet joints were assessed by MRI and plain X-ray, respectively. A total of 41 facet joint were included in this study (Th12/L1: 6; L1/2: 10; L2/3: 10; L3/4: 10; L4/5: 5). The average Thompson grade (MRI) score for the discs was 3.0 (Grade 4: 11; Grade 3: 20; Grade 2: 10).

After removal of the paravertebral muscle and posterior component by sharp dissection of the facet joint capsule. After gross examination of the joint surface, normal or mildly degenerative cartilage was sharply dissected by surgical scalpels. Care was taken to avoid contamination by synovial tissues. Tissues from 8 or 10 facet joints from a single donor was pooled, cut into 5 mm x 5 mm pieces and cultured in medium (DMEM/F12 supplemented with 10% fetal bovine serum (FBS) and 25 μg/ml ascorbic acid) for 3 days with daily changes of media.

Treatments with OP-1: After a 3-day pre-culture period, the cartilage explants were cultured in DMEM/F12 with 10% FBS alone (control) or in the presence of 100 ng/ml or 200 ng/ml OP-1 (a gift from Stryker Biotech) for 2 days with daily changes of media.

PG content: At the end of the 2-day treatment period, after determining wet and dry weights (WW/DW, respectively), the cartilage explants were digested with papain and the PG contents were measured by the dimethylmethylen blue assay [4].

PG synthesis: PG synthesis, under the conditions described above, was assessed by radiolabeling the cartilage explant PGs with 35S-sulfate (20 μCi/ml) for the last 4 hours of culture. Cartilage explants were digested with papain and the total 35S-PGs in discs and media was quantified by a rapid filtration assay [5].

PG turnover (Pulse-Chase study): Cartilage explants were pre-labeled with 35S-PGs, washed and further cultured in DMEM/F12 with 10% FBS alone (control) or in the presence of OP-1 (200 ng/ml) up to 5 days [1]. The percentage of 35S-PGs remaining in the cartilage explants of the total 35S-PGs was measured to study the degree of PG degradation.

Statistical Analysis: The effects of treatments were statistically analyzed using the two-way ANOVA and the Fisher’s PLSD post hoc test.

Results: PG synthesis (Fig. 1-A): Treatments with OP-1 significantly affected PG synthesis expressed per dry weight (p<0.001) when the response to OP-1 was assessed using the cumulative data from 10 donors. Notably, a significantly increased PG synthesis was observed by treatment with 200 ng/ml OP-1 (+111% on day 2 after treatment, p<0.05, vs. control).

PG content (Fig. 1-B): Treatment with OP-1 for 2 days significantly affected the PG content of cartilage explants (p<0.05). The PG content expressed per dry weight in the 200 ng/ml OP-1-treated groups was significantly higher than that in the control group (+101% on day 2 after treatment, p<0.05, vs. control).

Discussion: In the study presented here, we have demonstrated, for the first time, that OP-1 can stimulate PG synthesis and inhibit the degradation of PGs during the organ culture of human facet joint cartilage. It was of interest that the treatment with OP-1 resulted in a change in the anabolic and catabolic cascade; this result and the inhibitory effects of cytokines [1, 6] suggest that OP-1 may also modulate pain generation through a cytokine pathway. Because the therapeutic approaches for facet joint osteoarthritis are limited, the application of OP-1 by direct injection into the joint space may be worthwhile to explore. However, close attention needs to be paid to ossification, osteophyte formation or fusion of joints.