INTRODUCTION. There are several reports on experimental animal models of disc degeneration, which have been used to assess biomechanical behavior, biochemical composition and biological changes in the intervertebral discs. Although it is difficult to distinguish normal age-related alterations in the intervertebral disc from pathological degeneration, it is well known that the nucleus pulposus (NP) originally derived from notochord undergoes phenotypical changes with aging and becomes fibrocartilaginous tissue containing chondrocyte or fibroblasts-like cells. Correlation between morphological and biochemical changes of the NP has been documented in these experimental models. However, little is known if a direct injection of growth factors into degenerative discs could delay or reverse degenerative processes via inhibition of the catabolic events and/or stimulation of the anabolic, regenerative processes. The long-term focus of our laboratory is Osteogenic Protein-1 (OP-1), which is expressed in cartilage (3) and is able to induce the synthesis of the extracellular matrix in cartilage and normal intervertebral discs [4]. It has been also shown that the injection of OP-1 following chondroitinase ABC could induce chemonucleolysis resulted in the recovery of the rabbit disc height [4]. Based on previously published methods we developed an experimental animal model of disc degeneration, in which an Ilizarov-type apparatus was used to immobilize and chronically compress the intervertebral discs in rats [5]. The objectives of this study were to investigate the effect of the injection of human recombinant OP-1 on the catabolic processes induced in the degenerative intervertebral discs by the application of this experimental model.

MATERIALS AND METHODS. We used 10 male Sprague-Dawley rats weighting about 250g each, which were divided into five experimental groups (each group; n=2). In the sham group, two 0.8 mm diameter Kirschner’s wires were inserted percutaneously through the third and fifth caudal vertebra. Each wire was fixed separately to a specially designed aluminum ring, consisting of two 30-mm diameter external rings. In the compressed NP group, the two rings were linked with four rods to immobilize and chronically apply compression on the Kirschner’s wires until the tail exhibited maximum angular deformity. Four weeks after surgery, those animals were divided into three subgroups: saline and OP-1 groups, where 1 μl of physiological saline and 0.5 μg/g OP-1 were injected into the nucleus pulposus of the instrumented vertebrae, respectively. OP-1 treated animals were divided into two subgroups. In the COP-1 group, compression was continuously applied to the tail after OP-1 treatment. In the ROP-1 group, compression was released at the time of the treatment. Tails in all four groups were amputated eight weeks after primary treatment. Two rats with no treatment were used as the control group. To investigate anabolic and catabolic effects of OP-1, experimental groups were supplemented in the NP with collagen putty induced the synthesis of autocrine OP-1 synthesis. Enhanced intracellular staining for both forms of OP-1 and colocalization of these stains in the OP-1 treated groups suggests a new synthesis of endogenous OP-1 in all disc compartments rather than incorporation of OP-1 after the injection into the intervertebral discs. Similar response to the treatment with OP-1 was observed by us previously in goat osteochondral defect studies, where OP-1 was detected on collagen putty induction of OP-1 in both articular cartilage and bone. Important finding of this study is also an anti-catabolic effect of rhOP-1, which was identified in the discs where compression was released at the time of OP-1 injection. Under these conditions OP-1 reduced or blocked aggrecanase, MMP-13, substance P and TNF-α confirming an anti-catabolic activity of this BMP shown previously in our numerous studies with human articular cartilage, in which OP-1 down-regulated MMP-13, MMP-13, and counteracted the effect of interleukin-1 and fibroconnectin fragments via the inhibition of NF-κB. Since substance P is an indicative of pain, reduction in this protein confirms previously reported results on the effect of OP-1 on pain-related behavior (6). The data obtained in this study provide critical evidences for the OP-1 therapy in the treatment of disc degeneration and suggest molecular mechanisms responsible for OP-1 effects. The long-term focus of our laboratory is Osteogenic Protein-1 (OP-1), which is expressed in cartilage (3) and is able to induce the synthesis of the extracellular matrix in cartilage and normal intervertebral discs [4]. It has been also shown that the injection of OP-1 following chondroitinase ABC could induce chemonucleolysis resulted in the recovery of the rabbit disc height [4]. Based on previously published methods we developed an experimental animal model of disc degeneration, in which an Ilizarov-type apparatus was used to immobilize and chronically compress the intervertebral discs in rats [5]. The objectives of this study were to investigate the effect of the injection of human recombinant OP-1 on the catabolic processes induced in the degenerative intervertebral discs by the application of this experimental model.

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