

In vivo effects of recombinant human growth and differentiation factor 5 on the intervertebral disc

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INTRODUCTION: Growth and differentiation factor-5 (GDF-5) is a member of the bone morphogenetic protein family. Although GDF-5 has been studied using the mouse tail compression model [1], there has been no quantitative data on the capacity of GDF-5 to repair the degenerative intervertebral disc (IVD). The purpose of this study is to determine the reparative capacity of recombinant human GDF-5 (rhGDF-5) in an *in vivo* setting using the rabbit annular needle puncture model [2].

METHODS: Twelve adolescent New Zealand white rabbits received an annulus puncture (18G) in two non-contiguous discs to induce disc degeneration. Four weeks later, PBS (10 μ l) or GDF-5 (1 and 100 μ g, in 10 μ l) were injected into the center of the NP of previously punctured discs.

Radiological assessments: Disc height was radiographically monitored biweekly from the day of needle puncture injury to 12 weeks post-injection. IVD height was expressed as the disc height index (DHI)[3]. Percent DHI (%DHI = (postoperative DHI/preoperative DHI) x100) was subsequently calculated.

Histological Analysis: The experimental IVDs were excised from each vertebral body-disc-vertebral body unit, and each IVD were fixed in 10% formalin, decalcified, embedded in paraffin, sectioned and assessed by histology. Sagittal sections (5-8 mm) of each IVD were stained with hematoxylin and eosin, as well as Safranin-O.

RESULTS:

Changes in DHI: The intradiscal injection of GDF-5 significantly altered the time course of changes in disc height in degenerated IVDs ($p < 0.001$). At 4 weeks after injection, the %DHI in the GDF-5 group (both 1 μ g and 100 μ g) began to increase and return towards that of the non-punctured disc, whereas the PBS groups did not show any recovery of disc height during the 12

weeks after injection. At the 16-week time point, the DHI of GDF-5 injected discs remained significantly higher than that of the PBS-injected discs (PBS vs GDF-5: 1 μ g and 100 μ g, $p < 0.001$).

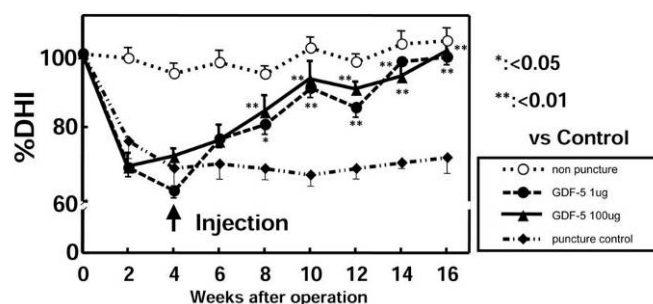


Fig. 1. Change of percent DHI

Histological Analysis: rhGDF-5 treated discs showed a greater percentage of proliferating cells compared to PBS controls. However, the 100 μ g rhGDF-5 group demonstrated more cellularity over the 1 μ g group.

DISCUSSION & CONCLUSIONS: The preliminary results of this study showed that rhGDF-5 enhanced cell proliferation as well as matrix synthesis and accumulation in the rabbit IVD. The study provided encouraging preliminary evidence that a single injection of GDF-5 induced recovery of disc height in the IVDs of rabbits with degenerative changes previously induced by annular needle puncture. Stimulation of the anabolic cascade by rhGDF-5 could therefore prove useful as a therapeutic approach to delay the progression of disc degeneration or to promote the repair of the degenerating human IVD.

REFERENCES: ¹ A. Walsh et al (2004) Spine 29: 156-163. ² K. Masuda et al (2004) Spine 29: 1-9. ³ D. Lu et al (1997) Spine 22: 1828-34