

Intradiscal Growth Factor Therapies for Intervertebral Disc Degeneration

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INTRODUCTION: Although the precise etiology of disc degeneration remains unknown, it may be surmised that the degenerative cascade can be slowed or halted by altering the homeostatic balance in favor of increased anabolic activity by intradiscal growth factor therapy. Moreover, growth factors may influence the inflammatory pathway, thereby having a direct effect on the pain associated with disc degeneration.

INTRADISCAL INJECTION OF GROWTH FACTORS PROMOTES REGENERATION:

Thompson *et al.* first proposed to stimulate IVD repair by exogenous growth factors¹. A number of studies have since shown that intradiscal injection of growth factors can be used to stimulate regenerative activity within the IVD. Walsh *et al.* compared the effects of single vs. multiple injections of growth and differentiation factor-5 (GDF-5), transforming growth factor- β (TGF- β), insulin-like growth factor-1 (IGF-1) and basic fibroblast growth factor (bFGF) in a mouse-tail model of disc degeneration and demonstrated that intradiscal injection of either GDF-5 or TGF- β stimulated cell proliferation and extracellular matrix protein synthesis². Subsequent studies in both juvenile³⁻⁵ and adult⁶ rabbits have shown that intradiscal injections of recombinant human osteogenic protein-1 (rhOP-1) or rhGDF-5 (Fig. 1) can stimulate regenerative changes in injury^{3,4,6} and chemical⁵ models of disc degeneration. *In vitro* studies have shown that in addition to anabolic stimulation, OP-1 can also down-regulate expression of matrix-degrading enzymes, such as ADAMTs-4⁷ further tipping the homeostatic balance away from additional degeneration.

ANTI-INFLAMMATORY EFFECT OF GROWTH FACTORS:

In addition to the effects of growth factors in controlling the balance of anabolic and catabolic activity, recent studies have shown that OP-1 can influence the levels of cytokines such as IL-1 β , IL-6, and TNF- α both *in vitro*⁷ and *in vivo*⁸. Moreover, *in vivo* pain assessment in rats has demonstrated that OP-1 reduced hyperalgesia in both disc degeneration⁹ and herniation¹⁰ models.

DISCUSSION: Since growth factor therapy requires cells with biosynthetic activity and a nutritional pathway adequate for supporting

increased metabolic activity, it is expected that intradiscal growth factor therapy will only be effective for relatively early stage disc degeneration. Nonetheless, the promise of a minimally-invasive therapy for the treatment of degenerative disc disease is encouraging.

REFERENCES: ¹JP Thompson *et al.* (1991)

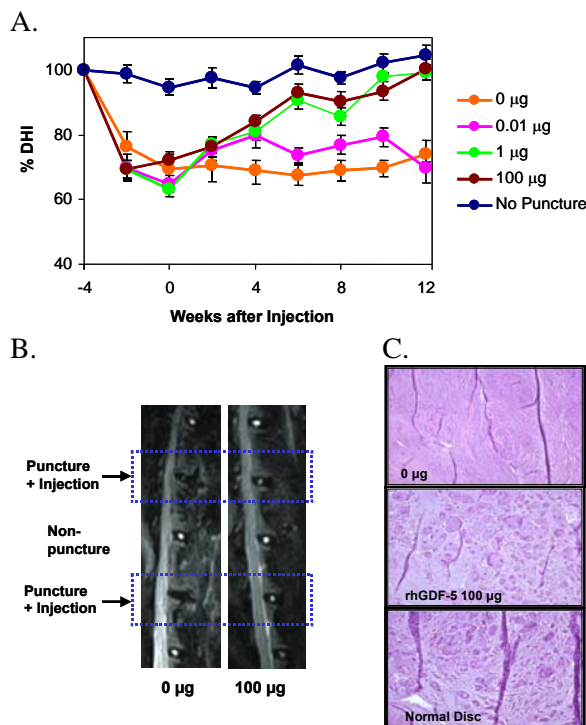


Fig 1. Effects of rhGDF-5 in the rabbit annulus puncture model⁴. (A) Disc height recovery following rhGDF-5 injection at $t=0$. (B) T2-weighted MRI images 12 wks after rhGDF-5 injection. (C) H&E histology of rabbit nucleus pulposus 12 wks after rhGDF-5 injection.

Spine 16:253-60. ²AJL Walsh *et al.* (2004) Spine 29:156-63. ³K Masuda *et al.* (2006) Spine 31:742-754. ⁴T Chujo *et al.* (2006) Spine 31:2909-17. ⁵I Cowgill *et al.* (2006) Trans ORS #1185. ⁶T Chujo *et al.* (2007) Trans ORS #267. ⁷R Pichika *et al.* (2007) Trans ORS #243. ⁸K Masuda (2008) Trans WFSR #81. ⁹M Kawakami *et al.* (2007) Trans ORS #1202. ¹⁰M Kawakami *et al.* (2007) Trans WFSR #38.