Combination Cell-Morphogen Therapy for Treatment of Degenerative Disc Disease

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Introduction

The intervertebral disc is made up of two components: the nucleus pulposus and annulus fibrosis. Once injured, this structure has a limited repair capacity which is further compromised by ensuing inflammation and instability. Current surgical treatment options include disc arthroplasty, disc removal, spinal fusion and lumbar decompression. These modalities aim to relieve pain and neurological disability by artificially restoring spine kinematics via fusion or decompression. Our long term aim is to find a biological alternative capable of recreating a healthy, anatomical disc space and restoring native spine kinematics resulting in improved function, comfort, and avoids invasive surgery. This study explores a combination therapy for treating intervertebral disc disease using morphogens (BMP-2, GDF-5) and mesenchymal stem cells (MSC’s). The family of bone morphogenetic proteins (BMP’s) is known for stimulating joint formation and chondrogenesis and plays a crucial role in the developing musculoskeletal system. Mesenchymal stem cells are capable of differentiating into cartilage-like cells and functioning as nucleus pulposus. We hypothesize that morphogens together with MSC’s delivered into the degenerative intervertebral disc space will result in an improved biological repair in a model of degenerative disc disease.

Methods

20 adult male Sprague Dawley rats were enrolled for creation of the degenerative disc (IACUC# 2007-071) previously described by Rousseau et al. The rats were anesthetized with Isoflurane and a one inch incision was made 10mm distal to the sacroiliac joint exposing three coccygeal disc spaces (Co5-Co8). A #11 scalpel was inserted 1.5mm deep in order to iatrogenically injure the disc spaces and create a reproducible degenerative disc model. The skin was closed with 4.0 vicryl and pain medication was provided immediately post operatively with unrestricted activity for 3 weeks and then randomized to the following:

- Group I Control: the articul ar cartilage of both end -plates were fixed in formalin, decalcified and processed for paraffin sectioning. 5 um thick sagittal slices were cut and stained with hematoxylin and eosin and Mallory's trichrome. Analysis of the vertebral endplates, annulus fibrosis and nucleus pulposus was performed under light microscopy at 4X, 10X, and 100X.

Results

- Group I Control: The nucleus pulposus was observed to be hypocellular or completely reabsorbed, with joint space collapse. Needle tracks were typically observed in the annulus fibrosis. In general, the annulus always exhibited at least one side of complete collapse and herniation (Fig 1).

Discussion

This ongoing study allowed us to examine the repair process in a model of intervertebral disc degeneration. It was designed to mimic human disc injury stemming from arthritis, disc herniation, trauma and other disease processes. We were able to evaluate growth factors and mesenchymal stem cells alone or in combination, as agents of regeneration for the damaged disc. Overall, when grading the treatment groups with respect to cellularity and maintenance of disc height, order of worst to best regeneration is as follows: control>BMP-5>BMP-2>BMP-2 & MSC. The use of BMP-2 alone or with MSC caused increased chondrocytic growth and activity. It appears to have an additive effect with MSC’s. The effect of GDF-5 alone was more consistent than the GDF-5&MSC combination treatment, which did not act in an additive manner.

Figure 1. Light micrograph of Group I control showing degenerative process with collapse of annulus and loss of nucleus pulposus. A. Hematoxylin and Eosin stain (H&E) B. Mallory’s Trichrome stain (4X original magnification)

Figure 3. Light micrograph of Group III BMP-2 treated disc showing the two communicating chondrocytic pools in the endplate articular cartilage associated with parallel thicke ned nucleus pulposus basement membrane. A. H&E B. Mallory’s Trichrome (10X original magnification)

Figure 4. Light micrograph of Group V BMP-2 & MSC treated disc showing an isolated pool of small similar cells that is not in communication with the endplate on the lateral border of the annulus behaving as chondrocytes, staining for collagen and proteoglycan. A. H&E B. Mallory’s Trichrome (4X original magnification)

Reference