**92] Mesenchymal stromal cells rescue disc degeneration and function via suppression of fibrotic events**

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Chronic back pain and neuropathological conditions such as spondylomyelopathy and radiculopathy are associated with degeneration of the intervertebral discs in spinal column. Human and animal studies imply a role of fibrosis in the degeneration process. Mesenchymal stromal cells (MSCs) possess anti-fibrotic activities. We investigated if MSCs elicit disc regeneration through modulating fibrotic events. Skeletally mature rabbits with injury-induced lumbar disc degeneration were randomized to receive intradiscal engraftment of bone marrow-derived MSCs or control vehicle. Disc degeneration status was evaluated by MRI and radiographs. We showed that MSCs regenerated the disc along with a recovery of proteoglycan content, swelling pressure, and compressive strength in the disc core (nucleus pulposus). Motion segment stiffness was significantly attenuated, indicating MSCs recovered disc function. *In-situ* nano-characterization and expression study suggested MSCs significantly reduced collagen I deposition, prevented higher-order collagen assembly, and recovered fibril elastic modulus in the nucleus pulposus. MSC-conditioned media repressed expression of fibrosis-related genes encoding collagen I, collagen III, fibronectin, MMP12, and HSP47 in nucleus pulposus cells derived from idiopathic disc degeneration patients. Large-scale one-year follow up study indicated dosage and application time are critical modulators of MSC efficacy. Our findings suggest that MSCs can rescue disc degeneration and recover disc function by suppressing fibrotic events in nucleus pulposus via paracrine interactions. We propose a model in which MSCs reinforce the mechanical integrity of nucleus pulposus by normalizing the interplay between collagen meshwork and proteoglycan. Disc repair by augmenting the anti-fibrotic function of MSCs or use of other anti-fibrotic agents warrants further investigation.

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