Annulus fibrosus repair

Intervertebral disc engineering strategies are increasingly focusing on the regeneration or repair of the AF in order to reduce the number of re-herniations, increase the potential of nucleus pulposus (NP) engineering strategies and to mechanically assist NP replacement therapies [1) 2)].

Currently, the only methods available for annulus fibrosus repair involve mechanical closure of defect, which does little to address biological healing in the damaged tissue. Collagen hydrogels are injectable and have been used to repair annulus defects in vivo. In this study, high-density collagen hydrogels at 5, 10, and 15 mg/mL were used to repair defects made to intact rat caudal intervertebral discs in vitro. A group of gels at 15 mg/mL were also cross-linked with riboflavin at 0.03 mM, 0.07 mM, or 0.10 mM. These cross-linked, high-density collagen gels maintained their presence in the defect under loading and contributed positively to the mechanical response of damaged discs. Discs exhibited increases to 95% of undamaged effective equilibrium and instantaneous moduli as well as up to fourfold decreases in effective hydraulic permeability from the damaged discs. These data suggest that high-density collagen gels may be effective at restoring mechanical function of injured discs as well as potential vehicles for the delivery of biological agents such as cells or growth factors that may aid in the repair of the annulus fibrosus [3)].

Annulus fibrosus repair techniques for the intervertebral disc (IVD) address the unsolved problem of reherniation after IVD herniation and might facilitate the development of nucleus pulposus replacement techniques for IVD diseases.

Annulus fibrosus cells (AFCs)from degenerated discs secreted factors which stimulated endothelial cells (ECs) production of factors known to induce matrix degradation, angiogenesis, and innervation. IL-8 and VEGF maybe the secreted factors from AFCs which mediate a pro-angiogenic stimulus often implicated in the development of disc degeneration [4)].

Healing capacity

Key and Ford studied the healing capacity of three different types of posterior annulus lesions in a dog model. The lesions included a square annular window, a transverse incision and puncture with a 20-gauge needle. At follow up, they found that the lesions were initially filled with extravasated blood, fibrin, bone and cartilage debris that was gradually replaced by a thin layer of fibrous tissue at later time points (up to 22 weeks). Some of the levels within the window and incision lesion group developed slowly progressive disc protrusion, which was most common in the transversely incised discs. The levels that underwent needle puncture revealed nothing abnormal and the site of puncture could not be identified after 22 weeks [5)].

1)
Andersson GB, An HS, Oegema TR, Jr, Setton LA. Directions for future research. J Bone Joint Surg Am. 2006;88(Suppl 2):110–114.
2)
Wilke HJ, Heuer F, Neidlinger-Wilke C, Claes L. Is a collagen scaffold for a tissue engineered nucleus replacement capable of restoring disc height and stability in an animal model? Eur Spine J. 2006;15(Suppl 3):S433–S438
3)

Borde B, Grunert P, Härtl R, Bonassar LJ. Injectable, high-density collagen gels for annulus fibrosus repair: An in vitro rat tail model. J Biomed Mater Res A. 2015 Aug;103(8):2571-81. doi: 10.1002/jbm.a.35388. Epub 2014 Dec 29. PubMed PMID: 25504661; PubMed Central PMCID: PMC4465422.

4)

Moon HJ, Yurube T, Lozito TP, Pohl P, Hartman RA, Sowa GA, Kang JD, Vo NV. Effects of secreted factors in culture medium of annulus fibrosus cells on microvascular endothelial cells: elucidating the possible pathomechanisms of matrix degradation and nerve in-growth in disc degeneration. Osteoarthritis Cartilage. 2014 Feb;22(2):344-54. doi: 10.1016/j.joca.2013.12.008. Epub 2013 Dec 18. PubMed PMID: 24361793.

5)

Key JA, Ford LT. Experimental intervertebral-disc lesions. J Bone Joint Surg Am. 1948;30A(3):621–630.