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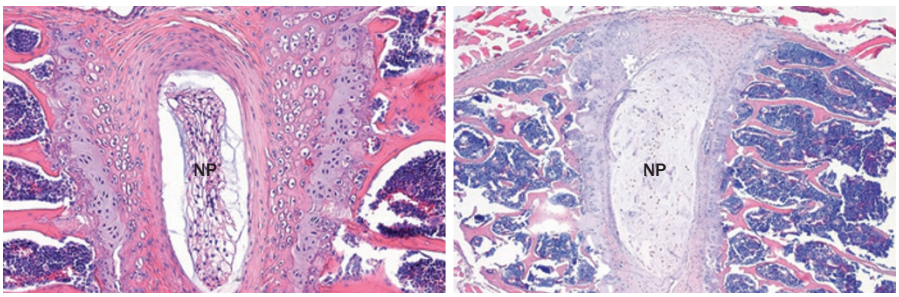
DEGENERATIVE DISC DISEASE

Altered Wnt signalling in intervertebral disc degeneration

Back pain is often caused by intervertebral disc degeneration. Cellular changes occur early during the degenerative process —chondroid metaplasia of the nucleus pulposis (NP), in which notochordal cells become chondrocyte-like cells, reduces the regenerative potential of the disc. Investigators from The Netherlands have used a canine model of intervertebral disc degeneration to examine the biochemical changes associated with chondroid metaplasia, and have found a downreguation of Wnt signalling and caveolin-1 expression.

Chondrodystophic dogs (e.g. Beagles) have disproportionately short limbs relative to their spines, and show signs of intervertebral disc degeneration by the time they reach 1 year of age. Microarray analysis of discs in different stages of degeneration from chondrodystrophic and nonchondrodystrophic dogs revealed a downregulation of genes involved in Wnt signalling throughout the degenerative process. The investigators hypothesized that the increased levels of Wnt signalling observed in chondrodystrophic dogs could be an ineffective attempt to preserve the notochordal phenotype of NP cells.



H&E-stained intervertebral disc sections from wild-type mice (left) and mice lacking expression of caveolin-1 (right). From Smolders, L. A. *et al. Arthritis Res. Ther.* doi:10.1186/ar4157 which is published under the terms of the Creative Commons Attribution License.

Caveolin-1 regulates Wnt signalling through multiple proposed mechanisms. Decreased caveolin-1 expression in canine discs with chondrocyte-like cells prompted the investigators to examine intervertebral discs from mice lacking expression of caveolin-1. NP tissue from these mice showed abnormal structure, with dying cells and a large amount of chondroid-like matrix. "The local changes in biomolecular signalling may also, and probably primarily, affect the niches of stem cells and their cross-talk with the resident cells within the intervertebral disc," says author Mariana Tryfonidou. She plans to investigate the effects of caveolin-1 on the different cell types found in intervertebral discs.

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Original article Smolders, L. A. *et al.* Gene expression profiling of early intervertebral disc degeneration reveals a down-regulation of canonical Wnt signaling and caveolin-1 expression: implications for development of regenerative strategies. *Arthritis Res. Ther.* doi:10.1186/ar4157