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New Therapeutic Hope for Degenerative Disc Disease

Study Suggests Possible Role of Embryonic Cells from the Notochord of Dogs to Regenerate Disc Cartilage

Degenerative disc disease is one of today's most common and costly medical conditions. Marked by the gradual erosion of cartilage between the vertebrae, this destructive disease of the spine routinely provokes low back pain, the leading cause of disability in people under age 45 in the United States. This condition is also confounding: the factors that account for the vulnerability of the disc to degeneration and the limited capacity of the disc for repair remain largely unknown.

For some domestic mammals, including sheep, goats, and dogs, the occurrence of degenerative disc disease is extremely rare. Intrigued by this fact and how it might apply to humans, researchers in Toronto, Canada, decided to conduct a gene expression study on intervertebral discs from canines. Their results, presented in the December 2006 issue of *Arthritis & Rheumatism* (http://www.interscience.wiley.com/journal/arthritis), shed light on the regenerative potential of early embryonic cells within the disc nucleus.

The evolutionary precursor to the backbone, the notochord is a fine, flexible chord defining the body axis in the early embryos of all vertebrates. In certain breeds of dogs, notochord cells remain vibrant in the intervertebral disc into adulthood. Does the degree of biochemical protection notochord cells provide explain the difference in susceptibility to degenerative disc disease between canines and humans? For answers, the researchers examined samples of notochord cells from adult dogs, with attention to their effect on the regulation of important genes in chondrocytes, or cells found in cartilage.

What the researchers found was compelling: notochord cells secrete connective tissue growth factor (CTGF)—a recently characterized protein with multifunctional anabolic properties. CTGF gene expression was also found in cell cultures taken from the intervertebral discs of chondrodystrophic canines—dog breeds closer to humans in

musculoskeletal terms. But the population of notochord cells was much larger in nonchondrodystrophic dogs.

"Our results suggest that nonchondrodystrophic canines are protected against the development of degenerative disc disease because their discs contain an abundance of notochord cells that secrete a key anabolic factor, CTGF," states the study's senior author, Robert D. Inman, MD, Toronto Western Research Institute. "These findings provide insight into the biology of the intervertebral disc," he further notes, "and raise the possibility of future novel therapeutic options for this disabling condition."

But are there notochord cells within the mammalian adult spine? And if they do, what distinguishes them from spinal tissue? These are among the critical questions Juergen A. Mollenhauer, PhD, raises in his editorial on the notochord study. As he observes, the assumption that adult humans do not possess notochord cells may be biased by the lack of investigations on healthy human spinal discs. "Taken together, the currently known facts evoke hopes for a regenerative reservoir," Dr. Mollenhauer adds, with a firm emphasis on the need for more research. "Whether notochord cells can be preserved or reactivated remains to be resolved in the future."

Article: "Nucleus Pulposus Notochord Cells Secrete Connective Tissue Growth Factor and Up-Regulate Proteoglycan Expression by Intervertebral Disc Chondrocytes," W. Mark Erwin, Keith Ashman, Paul O'Donnel, and Robert D. Inman, *Arthritis & Rheumatism*, December 2006; (DOI: 10.1002/art.22258).

Editorial: "The Notochord in the Mammalian Adult: A Paradox," Juergen A. Mollenhauer, *Arthritis & Rheumatism*, December 2006; (DOI: 10.1002/art.22259).