

## The Role of Extracellular Matrix and Matrix Molecular Fragments in Disc Degeneration.

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**INTRODUCTION:** The annulus fibrosus and nucleus pulposus have very different extracellular matrix organizations but have many matrix proteins in common. The remarkable lamellar organization of the type I and II collagen fibrils in the lamellae in the annulus provides an effective mechanism for controlling bending and twisting. While the fine type II collagen fibrillar network trapping abundant aggrecan helps maintain a fluid-like state, the nucleus pulposus with aging and degeneration matrix proteins are increased, lost, fragmented or covalently modified. Because it is postulated that there is a reciprocal feedback relationship between the matrix and the cell, these matrix modifications could accelerate degeneration.

**METHODS:** The thesis of matrix modification accelerating degeneration is explored in a review of the literature.

**RESULTS:** There is abundant evidence in the disc especially in the nucleus for the accumulation of many kinds of matrix molecular fragments. For example, aggrecan fragments accumulate after birth and increase in early degeneration. Fibronectin is an example of a protein that accumulates with age and degeneration. It is present at low levels in the low Thompson grade disc but the total fibronectin dramatically increases with grade and becomes a major non-collagenous protein during degeneration component of tissue<sup>1</sup>. In addition, multiple fibronectin fragments become dominant. It is well established that the fibronectin fragments produced in vitro with purified enzymes induce decreased anabolism and increases catabolism in many tissues. This may also happen in the disc *in vivo*.

The small leucine-rich proteoglycan biglycan increases in age and degeneration. Biglycan alters cell signalling via interactions with the EGF receptors<sup>2</sup>.

With age, the proteins that have long life, such as collagen, become increasingly glycosylated. Glycosylated molecules frequently alter normal signaling pathways or can initiate alternative signaling via receptors such as RAGE. (Ref)

**DISCUSSION & CONCLUSIONS:** In both the aging and especially the degenerated disc there is an accumulation of non-collagenous matrix molecules. However, fragmentation and covalent modification of matrix molecules are also observed. All of these can modify cellular responses and frequently promote matrix catabolism and decreased matrix synthesis. These matrix changes must be considered as mechanisms for promoting disc degeneration.

**REFERENCES:** <sup>1</sup>T.R. Oegema., L.B. Deloria, J.D. Sandy, et al (2002) Effect of Oral Glucosamine on Cartilage and Miniscus in Normal and Chymopapain-Injected Knees of Young Rabbits, *Arthr. & Rheum.* **46**:2495-2503. <sup>2</sup>G. Cs-Szabó, S Hussaini, K. Masuda, et al (2005): Levels of matrix proteins in human intervertebral disc change differently in response to aging and tissue degeneration. *Trans. ORS*, **30**: 1584.

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