J Musculoskel Neuron Interact 2002; 2(6):524

Perspective Article

Hylonome

Summary – Osteoarthritis Session: New ideas in cartilage biology

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Keywords: Cartilage, Matrix, Chondrocytes, Perlecan, IL-1, TNF

Interactions between chondrocytes and matrix molecules regulate processes important in synthesis as well as degradation of cartilage matrix and are important in developmental biology, normal matrix turnover and disease. An understanding of the role of molecules such as Perlecan may lead to greater understanding of processes involved in cartilage differentiation from mesenchymal precursors and thus have utility in cartilage tissue engineering applications. **Dr. D. D. Carson** (University of Delaware) reviewed his work on Perlecan, a large proteoglycan, and its expression in developing and mature cartilage. The importance of Perlecan in cartilage matrix development has been demonstrated in mouse model systems in which mutations in this gene result in severely abnormal cartilage phenotypes such as chondrodystrophies/mandibular hypoplasia. He also discussed data indicating that Perlecan cooperates with the key chondrogenic growth factor, BMP-2 to promote expression of hypertrophic chondrocyte markers. Perlecan expression is pronounced within cartilagenous tissues especially those undergoing endochondral ossification.

Processes involved in developmental biology were elegantly delineated by **Dr. L. Sandell** (Washington University School of Medicine) in a discussion of the vWFC domain of type II procollagen amino-propeptide and its functions as an antagonist of bone morphogenetic proteins (BMPs). The binding and regulation of BMPs by chordin in embryos was described as well as regulation of BMPs by matrix metalloproteinases. Dr. Sandell also described her work showing that Egr-1, an IL-1-induced transcription factor, interacts directly with the core COL2A1 promoter and reduces its constitutive activity. The basic message of her presentation emphasized the cellular and molecular mechanisms by which catabolic cytokines suppress the differentiated phenotype in chondrocytes.

Comments on IIA procollagen in disease and repair led to a description of molecular regulation of the chondrocyte phenotype by **Dr. M. B. Goldring** (Beth Israel Deaconess Medical Center). The central role of proinflammatory cytokines such as IL-1 and TNF-α in promoting cartilage degradation via induction of matrix metalloproteinases (MMP) have been identified as important in animal models of osteoarthritis described by **Dr. A. Bendele** through inhibition of cartilage degradation in animals treated with MMP inhibitors. The signal transduction pathways utilizing various kinases were described in detail. Effects of IL-1β on α1 (II) procollagen mRNA via inhibition of COL2A1 gene transcription were a major focus of the presentation.

Discussion following the talks centered on strategies for potential therapeutic intervention. The pros and cons of attempting modulation of osteoarthritis by anti-degenerative therapies vs. attempts at inducing cartilage regeneration and repair were debated.

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Accepted 10 August 2002