

38th International Sun Valley Workshop
August 3-6, 2008
Translational Research in OA-
From Molecules to Animals to Humans Session

Metabolism of chondrocytes in osteoarthritis: Why all this activity?

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Keywords: Chondrocytes, Osteoarthritis, Cartilage, IL-1 β

Normal chondrocytes maintain a functional extracellular matrix that replaces itself very slowly and provides a shock absorber for bones - for life. In osteoarthritis, the cells become metabolically hyperactive, synthesizing both anabolic components (signaling and matrix molecules) and catabolic components (nitric oxide, and matrix metallo-proteinases). Recent studies have investigated this metabolic response in more detail and a few important observations have been made. First, the chondrocytes synthesize both degradative enzymes and matrix-building macromolecules implying that the cells are taking on the task of repair as well as degeneration. One of the molecular mechanisms for this dual effect can be found in the response to the pro-inflammatory cytokines IL-1 β and TNF- α : both catabolic enzymes and the growth factor BMP-2 are increased indicating that the chondrocytes are attempting to repair their matrix after (or while) degrading it. Secondly, the contribution of inflammatory molecules may be more significant than was originally thought, and a specific pattern of chemokines may provide a molecular "fingerprint" to identify cells in the initial stages of response. Lastly, the cells through the depth of the cartilage (from superficial to deep cells) do not display the same pattern of gene expression, indicating that there may be more than one mechanism responsible for increased gene expression. The cells in the superficial zone "dedifferentiate" making large amounts of type III collagen and fibronectin while the cells in the middle and deep zones make predominantly

cartilaginous extracellular matrix molecules. This difference in gene expression will yield a different kind of matrix and, potentially, the superficial cells may become more susceptible to erosion. These and other new concepts regarding the metabolic life of the chondrocyte will be presented.

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The author has no conflict of interest.

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Accepted 11 August 2008