

(1) Most Significant Contributions

(1) *Matyas JR, M.G. Anton, N.G. Shrive, and C.B. Frank: Stress governs tissue phenotype at the femoral insertion of the rabbit MCL. J. Biomech., 28:147-157, 1995.* This study—the first of its kind—explores the spatial relationship of cell phenotype and mechanical stress *in situ*. The femoral insertion of the medial collateral ligament is a model system in which there is a gradient in cell phenotype ranging from cigar-shaped, type I collagen-producing fibrocytes in the ligament midsubstance to rounded, type II collagen-producing fibrochondrocytes near the soft tissue-hard tissue interface. Ligament elongation induces a gradient in mechanical stress state ranging from almost pure tension in the midsubstance, to high internal compression near the soft tissue-hard tissue interface. In this model, cell phenotype and mechanical stress state are highly predictive of one another, suggesting that mechanical stress state governs cell phenotype *in vivo*. That the metabolism of mature chondrocytes *in situ* can be modulated by the mechanical stress in the tissue has far-reaching implications. If, as this study suggests, chondrocytes respond to mechanical stress, then it may be possible to develop rational and optimal physical therapies for treating cartilage diseases such as osteoarthritis.

(2) *Matyas, J.R., Adams, M.E., Huang D.Q., and Sandell, L.J.: Discoordinate gene expression of aggrecan and type II collagen in experimental osteoarthritis. Arthr. Rheumat. 38:420-425, 1995.* This study describes the novel observation that the genes of two major macromolecules of articular cartilage are expressed discoordinately in the early “hypertrophic” phase of post-traumatic osteoarthritis. We found that the message for type II collagen is elevated eight-fold compared to a two-fold increase in the message of aggrecan core protein. These findings suggest that the stimulus for type II collagen and aggrecan transcription are different or that these genes have different mechanisms for controlling their transcription. The importance of detecting early changes in matrix molecule metabolism cannot be overemphasized since treatments and therapies aimed at altering the pathogenesis of osteoarthritis are likely going to be most effective during the early stages of this disease.

(3) *Matyas, J.R., Ehlers, P.F., Huang, D., and Adams, M.E.: The early molecular natural history of experimental osteoarthritis: I. Progressive discoordinate expression of aggrecan and type II procollagen mRNA in the articular cartilage of adult animals. Arthritis and Rheumatism. 42:993-1002, 1999.* This study describes changes in aggrecan and type II collagen gene expression in articular cartilage during the pathogenesis of experimental osteoarthritis. Aggrecan and type II collagen mRNA levels increase progressively at three and eight months. While both aggrecan and type II collagen gene expression increased progressively, their relative expression became increasingly disproportionate over eight months. These findings suggest that the stimuli for aggrecan and type II collagen transcription in articular cartilage exists early after joint injury and are sustained throughout the early phases of this experimental osteoarthritis. These findings also confirm and extend our previous observations that discoordinate gene expression of aggrecan and type II collagen is a hallmark feature of articular chondrocytes in experimental osteoarthritis that may serve as a useful predictor of stage of disease in this model.

(4) *Matyas JR, Ionescu M, Eyre D, Poole AR: Analysis of cartilage biomarkers in the early phases of canine experimental osteoarthritis. Arthritis & Rheumatism 50:543–552, 2004.* Significant elevations in several cartilage-specific biomarkers were detected by sensitive immunoassay in serum, urine, and joint fluid. This study assessed biomarker levels prior to joint injury (surgery) and at specific times thereafter. We discovered substantial individual variation in baseline biomarker levels (not available in

humans) and showed significant changes in all three body fluids by using repeated measures statistical design.

(4). McDougall JJ, Andruski B, Schuelert N, Hallgrimsson B, Matyas JR: *Unravelling the Relationship Between Age, Pain Sensation and Joint Destruction in Naturally Occurring Osteoarthritis of Dunkin Hartley Guinea Pigs*. *Pain*. 141:222-232, 2009. This paper offers an explanation for the widely recognized, but poorly understood discrepancy between the severity of joint pathology and the intensity of pain in an animal model of osteoarthritis. Moreover, using a sophisticated multivariate approach, extensive measures were made of joint pathology and nociceptive nerve activity in response to mechanical loading (torque) of the knee. Not surprisingly, nociceptive activity increased as a function of mechanical torque in both young (normal) and aged (osteoarthritic) knee joints. Surprisingly, tonic nociceptive discharge was a feature of osteoarthritic joints before torque was applied. As animal activity appeared unrelated to nociceptive activation, it appears that modulation of chronic pain of the knee is located centrally, i.e., in the brain. The identity of sites where pain is evoked and where it is processed is crucially important for understanding how to develop rational treatments and therapies for joint pain.

(2) Activities and Contributions

Reviewer: J Orthop Res, J Biomed Eng, J Histochem Cytochem, Arch Biochem Biophys
J Biomech, Arthritis Rheumatism, Conn Tissue Res, Scand J Rheumatol, APMIS, J App Physiol, J Pathology

Grant Reviewer: CIHR (Bioeng; Clinical), Whitaker Foundation, NIH (Ortho Study Section), The Arthritis Society, Physician Services Incorporated, Saskatchewan Health Research Foundation, Canadian Arthritis Network

Scientific Advisory Committee (Chair), The Arthritis Society

(3) Interruptions/delays

None.

(4) Patents and intellectual property rights

Patents Issued:

J.R. Matyas, J.B. Rattner: Method of Tissue Transfer and Retrieval. U.S. Patent Office, US Patent Number 5,858,781, Issued January 22, 1999.

J.R. Matyas, J.B. Rattner: The Method of Tissue Transfer. U.S. Patent Office, US Patent Number 5,866,417, Issued February 2, 1999.

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Contributions PIN: 037521

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