

A10 Proteolysis of collagen in osteoarthritis

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Osteoarthritis (OA) is characterized by the progressive degeneration of articular cartilage over a period of 15-30 years. The extracellular matrix of cartilage contains a network of collagen fibrils which endow it with its tensile strength. This is primarily composed of type II collagen. Excessive cleavage of the triple helix of this molecule by collagenases results in a loss of tensile properties. It also involves upregulation of expression of the collagenases MMP-1 and MMP-13. Both appear to be involved in this proteolysis. Their expression by chondrocytes is regulated by the cytokines interleukin-1 (IL-1) and/or tumor necrosis factor α (TNF α) which are expressed by chondrocytes.

Upregulation of expression and activities of the cytokines and collagenases can be selectively triggered by a specific peptide of type II collagen which can be generated by proteolysis. This involves chondrocyte differentiation (hypertrophy) a common feature of OA.

Thus a chronic cyclic pathway involving proteolysis of collagen and a positive feedback leading to stimulation of further chondrocyte-mediated collagenolysis may represent a key component of the pathology of osteoarthritis.

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