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Title: A potential mechanism for meniscus involvement in degenerative joint disease

Summary: Meniscus injury is a known predisposing factor for osteoarthritis (OA), but the mechanisms by which meniscus injury leads to OA are unknown. Matrix metalloproteinases (MMPs) are enzymes involved in joint tissue destruction in OA. This study sought to identify the expression pattern of MMPs produced by aged and degenerative menisci.

Methods: The effects of aging were studied using menisci from six healthy young and old vervet monkeys due to difficulty obtaining normal young adult human menisci. Human meniscal cells and chondrocytes were isolated from patients undergoing total knee arthroplasty for end-stage OA. Vervet meniscal explants were used to measure cytokine and MMP production by protein arrays and immunoblotting. Primary human cell cultures were stimulated with inflammatory interleukins (IL) and MMP expression measured by protein array, immunoblot and gene expression analysis.

Results: Older and degenerative monkey menisci secreted increased amounts of MMP-1, -3, and -8 and the cytokines IL-6 and IL-7 when compared to younger and non-degenerative menisci. Human OA meniscus cultures secreted MMP-1,-3 and -8 but not MMP-13, while OA chondrocytes secreted primarily MMP-3 and -13. Meniscal cells were more responsive to IL-6 which stimulated MMP-1 and -8 production, while chondrocytes were more responsive to IL-1 which stimulated MMP-13 production.

Conclusion: Aged and degenerative menisci produce both matrix-degrading enzymes and inflammatory cytokines known to stimulate cartilage degradation, which is consistent with a biologic role of the meniscus in OA. Human OA menisci and chondrocytes respond to cytokines with unique patterns of increased MMP production. Different matrix composition in meniscus and cartilage likely accounts for the differences in MMP production. Further investigation into the factors released by aging and degenerative menisci should provide new targets to improve meniscus repairs and to prevent joint tissue destruction in OA.