

# **Expression of matrix metalloproteinase-9 (gelatinase B) in gouty arthritis and stimulation of MMP-9 by urate crystals in macrophages.**

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## **Abstract**

To investigate the relevance of gelatinase-B (matrix metalloproteinase 9, MMP-9) in gouty arthritis (GA), we tested the occurrence of MMP-9 in GA patients and cell culture system. Gelatinolytic activity in the synovial fluid (SF) of patients with different kinds of arthritis was assessed by gelatin zymography. A predominant 92-kDa MMP-9 gelatinolytic activity was evident in rheumatoid arthritis (RA) and GA samples, but no activity was observed in osteoarthritis (OA) samples. Among the 53 SF samples (9 RA, 24 GA, and 20 OA) analyzed for MMP-9 and tissue inhibitor of metalloproteinase (TIMP-1) antigen levels by ELISA, MMP-9 antigen levels were elevated tenfold in GA SF compared with OA SF. In addition, GA synovial tissue extracts revealed elevated levels of MMP-9 expression as compared to OA tissue extracts by Western blot and RT-PCR analysis. Immunohistochemical studies demonstrated that MMP-9 immunoreactivity was more intense in GA than in OA synovial tissues. Furthermore, macrophages activation by gouty crystals in vitro was examined. Crystals stimulated MMP-9 gene expression in macrophage cell line and such stimulation was suppressed by PD98059. These findings suggest that the abnormal production of MMP-9 by macrophages is a reflection of the pathological conditions in joints of patients with GA, and that the activation of MMP-9 in the joint is known to play an important role in joint disease.