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Matrix metalloproteinase-9 (MMP-9) production is increased by recombinant human interleukin-6 and recombinant human tumor necrosis factor-α in immortalized human chondrocyte cell lines

The degradation of articular cartilage extracellular matrix proteins by matrix Metalloproteinases (MMPs) is a hallmark of rheumatoid arthritis (RA) and osteoarthritis (OA). We have shown that MMP-9 activity in OA synovial fluid was preserved by the formation of a complex between the enzyme and neutrophil gelatinase-associated lipocalin (NGAL) but dissolution of the MMP-9/NGAL complex resulted in the auto-degradation of MMP-9 and loss of MMP-9 activity. Interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) are 2 pro-inflammatory cytokines found in synovial fluid of RA and OA patients. In this study, human juvenile immortalized chondrocyte cell lines were employed to determine the extent to which recombinant human IL-6 (rhIL-6) and recombinant human TNF-α (rhTNF-α) increased MMP-9 production measured with an MMP-9 ELISA. We also determined if rhIL-6 blockade with Tocilizumab altered production of MMP-9 in response to rhIL-6. We used the pancreatic carcinoma cell line, PANC-1, which was previously shown to produce MMP-9 in response to phorbol myristate acetate (PMA), as the positive control for MMP-9 production. Thus, PMA (30.7 ng/ml) increased MMP-9 production after 24 hrs, from <100 pg/ml to >800 pg/ml. By comparison, after 24 hrs, rhTNF-α (20 ng/ml) increased chondrocyte MMP-9, from <50 pg/ml to 1200 pg/ml. In the presence of rhIL-6 (50 ng/ml), MMP-9 production increased from <50 pg/ml to 200 pg/ml. This was reduced by about 50% when Tocilizumab (200 ng/ml) was added together with rhIL-6. Of note, neither rhIL-6 nor rhTNF-α altered the production of MMP-9 by PANC-1 cells.

Biography

Charles J Malemud received the PhD from George Washington University in 1973 and completed Postdoctoral studies at the State University of New York at Stony Brook in 1977. He is Professor of Medicine & Anatomy in the Division of Rheumatic Diseases and Senior Investigator in the Arthritis Research Laboratory at Case Western Reserve University School of Medicine. He has published more than 200 papers and reviews primarily in the field of chondrocyte biology. He is on the editorial board of several rheumatology, immunology and musculoskeletal journals and is Editor-in-Chief of the Journal of Clinical and Cellular Immunology.

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