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Activation of the JAK/STAT pathway in the immortalized Human Juvenile Chondrocyte cell line, T/C-28a2

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The Janus Kinase/Signal Transducers and Activators of Transcription (JAK/STAT) pathway is activated by several of the pro-inflammatory and anti-inflammatory cytokines that are elevated in various types of arthritis. Phosphorylation of STAT proteins by activated JAKs transform cytosolic STAT proteins into potent transcription factors where they regulate STAT-responsive gene transcription, including the interleukin-6 (IL-6) gene. This study employed the T/C-28a2 immortalized human chondrocyte cell line which was previously shown to express the cartilage transcription factor, SOX9, to examine the extent to which the JAK/STAT pathway was activated in response to recombinant human IL-6 (rhIL-6), soluble IL-6 receptor (sIL-6R) and various combinations of rhIL-6 with small molecule inhibitors of JAK, sIL-6R and the IL-6R antagonist, Tocilizumab. T/C-28a2 was maintained in DME/F12 (1:1) supplemented with 0.1% fetal bovine serum for up to 60 min. Three STAT proteins, STAT1, STAT3 and STAT5, were localized on Western blots using antibodies specific for either the unphosphorylated (U-STAT) or phosphorylated (p-STAT) STAT proteins. As expected, the T/C-28a2 chondrocytes produced constitutive levels of U-STAT1, U-STAT3 and U-STAT5. However, unexpectedly, T/C-28a2 showed constitutive phosphorylation of STAT1 (p-STAT1), STAT3 (p-STAT3) and STAT5 (p-STAT5). In addition, none of the incubation conditions above resulted in STAT protein activation above constitutive levels. Presently, we are examining another immortalized chondrocyte cell line, C-28I/2, to determine if rhIL-6 activates the JAK/STAT pathway in this cell line. (Support provided by Genentech/Roche Group).

Biography

Charles J. Malemud received the Ph.D. from George Washington University in 1973 and completed postdoctoral studies at the State University of New York at Stony Brook in 1977. Since 1977, Malemud has been a member of the faculty at Case Western Reserve University School of Medicine where he is presently Professor of Medicine & Anatomy in the Division of Rheumatic Diseases and Senior Investigator in the Arthritis Research Laboratory. He has published more than 185 papers and reviews primarily in the field of chondrocyte biology. Professor Malemud 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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