

# 6<sup>th</sup> International Conference and Expo on Immunology

October 24-26, 2016 Chicago, USA



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### **STAT3 isoforms produced by the C-28/I2 human immortalized chondrocyte cell line**

Interleukin-6 (IL-6) is a potent pro-inflammatory cytokine which is elevated in patients with the diagnosis of rheumatoid arthritis. We have previously shown that recombinant human (rh) IL-6 stimulated the production of matrix metalloproteinase-9 (MMP-9) in the T/C28a2 and C-28/I2 lines of immortalized juvenile human chondrocytes. IL-6 is known to activate the Janus Kinase/Signal Transducers and Activators of Transcription (JAK/STAT) signaling pathway through the interaction of IL-6 with the IL-6 receptor- $\alpha$  (IL-6R $\alpha$ )/gp130 complex, with membrane-bound IL-6R or with soluble IL-6R. STAT3 is a major STAT protein activated by IL-6. Importantly, the production of MMP-9 by C-28/I2 chondrocytes was inhibited by tocilizumab (TCZ), a fully humanized monoclonal antibody which neutralizes IL-6-mediated JAK/STAT signaling. To begin a systematic analysis of rhIL-6-mediated STAT3 protein activation by human chondrocytes, C-28/I2 chondrocytes were employed to determine the repertoire of STAT3 proteins produced by these cells. Western blot analysis showed that C-28/I2 chondrocytes produced 2 STAT3 isoforms; one STAT3 isoform migrated on 10% SDS-PAGE at a position similar to STAT3 $\alpha$  (~75kDa) reported in other cell types. A second STAT3 isoform migrated somewhat faster than STAT3 $\alpha$  which we presume to be a truncated isoform of STAT3 and thus may be STAT3 $\beta$ . The 2 STAT3 isoforms were detected in C-28/I2 chondrocytes without any additions or after incubation with rhIL-6 or with rhIL-6 plus TCZ for up to 60 min. Of note, a protein extract produced from HeLa cells which were supplied by the manufacturer of the anti-STAT3 antibody used in this study showed that HeLa produced only STAT3 $\alpha$ . Thus, it will be of interest to determine whether or not both STAT3 isoforms produced by C-28/I2 chondrocytes are differentially phosphorylated by rhIL-6 as well as the extent to which TCZ differentially inhibits these STAT3 isoforms.

### **Biography**

Charles J Malemud has received Bachelor of Science degree from Long Island University in 1966 and PhD from George Washington University in 1973. He has completed his Postdoctoral studies in Experimental Pathology in 1977 at the State University of New York at Stony Brook. Since 1977, he has been a Member of the Faculty at the Case Western Reserve University School of Medicine where he is presently a Professor of Medicine & Anatomy in the Division of Rheumatic Diseases and Senior Investigator in the Arthritis Research Laboratory. He has published well over 225 papers, chapters and reviews primarily in the fields of chondrocyte biology, matrix metalloproteinase gene regulation, signal transduction and controlled cell death. 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 and Global Vaccines and Immunology.

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