Orthopedics & Rheumatology-2013
OMICS Group Conferences
Accelerating Scientific Discovery
2nd International Conference and Exhibition on
Orthopedics & Rheumatology
August 19-21, 2013 Embassy Suites Las Vegas, USA

Activation of the sapk/mapk pathway by il-6 family cytokines in the c28/i2 immortalized human juvenile chondrocyte line

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Abstract

The immortalized juvenile human chondrocyte line, C28/I2, was employed to determine if recombinant human IL-6 (rhIL-6), rh-oncostatin-M (rhOSM) and rh-adiponectin (rhAPN) activated the SAPK/MAPK pathway. Confluent C28/I2 chondrocytes were incubated in medium containing 0.1% fetal bovine serum (FBS) or 0.1%-FBS-containing medium and rhIL-6, rhAPN or rhOSM, (50ng/ml) for up to 60 min. Proteins were separated by electrophoresis on SDS-10% polyacrylamide gels. JNK, p38α, ERK1/2 and β-actin were localized on Western blots with anti-U- or anti-P-specific antibodies or with an anti-β-actin antibody. The ratio of U- or P-forms of these kinases to β-actin was determined using Metamorph® software. Three anti-U-JNK antibody-reactive bands of ~54kDa, 46kDa and 36kDa were identified. RhIL-6, rhOSM and rhAPN gradually increased the ratio of the U-JNK proteins to β-actin up to 30 min. The combination of SP600125 (20μM) and rhIL-6 did not alter this result. None of the IL-6-type cytokines increased the ratio of P-JNK to β-actin, nor did rhIL-6, rhOSM or rhAPN alter the ratio of U-p38α or P-p38α to β-actin. In contrast, rhOSM and rhAPN, but not rhIL-6, increased the ratio of P-ERK to β-actin by 57% and 35%, respectively. U0126 (1μM), an upstream inhibitor of ERK1/2 via MEK1/2 reduced the ratio of P-ERK to β-actin to the control level. Increasing the content of C28/I2 U-JNK *in vitro* by IL-6-type cytokines may yield additional transcription factor activity for regulating chondrocyte gene expression. The activation of ERK by rhOSM and rhAPN could be associated with regulating c-myc and apoptosis, and/or AP-1 and matrix metalloproteinase gene expression. (Support provided by Genentech/Roche Group and 5P30EY11373 from the National Eye Institute).

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, Dr. 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 190 papers, chapters 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.