Chondroprotective effects of glucosamine involving the p38 MAPK and Akt signaling pathways

謝銘勳

Lin;Y.C.;Liang;Y.C.;Sheu;M.T.;Lin;Y.C.;Hsieh;M.S.;Chen;T.F.

摘要

Abstract

The purpose of the present study was to elucidate the possible signal transduction pathway involved in the underlying mechanism of glucosamine (GLN)' s influence on the gene expression of matrix metalloproteinases (MMPs) in chondrocytes stimulated with IL-1 β. Using chondrosarcoma cells stimulated with IL-1 β, the effects of GLN on the mRNA and protein levels of MMP-3, the activation of JNK, ERK, p38, NF- κ B, and AP-1, the nuclear translocation of NF- κ B/Rel family members, and PI3-kinase/Akt activation were studied. GLN inhibited the expression and the synthesis of MMP-3 induced by IL-1 β, and that inhibition was mediated at the level of transcription involving both the NF- κ B and AP-1 transcription factors. Translocation of NF- κ B was reduced by GLN as a result of the inhibition of I κ B degradation. A slightly synergistic effect on the activation of AP-1 induced by IL-1 β was shown in the presence of GLN. Among MAPK pathways involved in the transcriptional regulation of AP-1, phosphorylation of JNK and ERK was found to increase with the presence of GLN under IL-1 β treatment, while that for p38 decreased. It was also found that GLN alone, but also synergistically with IL-1 β, was able to activate the Akt pathway. The requirements of NF- κ B translocation and p38 activity are indispensably involved in the induction of MMP-3 expression in chondrosarcoma cells stimulated by IL-1 β. Inhibition of the p38 pathway in the presence of GLN substantially explains the chondroprotective effect of GLN on chondrocytes that regulate COX-2 expression, PGE2 synthesis, and NO expression and synthesis. The chondroprotective effect of GLN through the decrease in MMP-3 production and stimulation of proteoglycan synthesis may follow another potential signaling pathway of Akt.