Retinoic acid blocks pro-inflammatory cytokine-induced matrix metalloproteinase production by down-regulating JNK-AP-1 signaling in human chondrocytes

李建和

Ho LJ;Lin LC;Hung LF;Wang SJ;Lee CH;Chang DM;Lai JH;Tai TY

摘要

Abstract

The development of osteoarthritis (OA) has recently been implicated as a result of immune-mediated damage of chondrocytes and their supporting matrixes. Pro-inflammatory cytokines like interleukin (IL)-1 and tumor necrosis factor alpha (TNF-alpha) play pivotal roles in immunopathogenesis of OA. Because vitamins preserving anti-oxidative effects are Suggested to provide protection in OA patients from joint damage, in the present study, we examined the effects and mechanisms of all-trans retinoic acid (t-RA) in suppressing pro-inflammatory cytokine-induced matrix metalloproteinases (MMPS) production in human chondrocytes. Chondrocyles were prepared from cartilage specimens of OA patients receiving total hip or total knee replacement. The protein concentration was measured by ELISA, the mRNA expression by reverse transcriptase-polymerase chain reaction, the protein expression by Western blotting, the transcription factor DNA-binding activity by electrophoretic mobility shift assay and the protein kinase activity by kinase assay, We showed that both MMP-1 and MMP-13 mRNA expression, protein production and enzyme activity induced by either IL-1 or TNF-alpha were suppressed by t-RA or different retinoid derivatives. The molecular investigation revealed that the t-RA-mediated suppression was likely through blocking p38 kinase and c-Jun N-terminal kinase-activator protein-1 signaling pathways. In contrast, t-RA had no effect on extracellular signal-regulated kinase activity, nuclear factor kappaB (NF-kappa B)

DNA-binding activity and I kappa B alpha degradation. Furthermore, we showed that t-RA could reduce IL-1-induced TNF-alpha production in chondrocytes. Our results suggest that vitamin A may protect OA patients from pro-inflammatory cytokine-mediated damage of chondrocytes and their supporting matrixes. (c) 2005 Elsevier Inc. All rights reserved.