

Involvement of c-Jun N-terminal kinase activation in 15-deoxy-D12,14-prostaglandin J2 and prostaglandin A1-induced apoptosis in AGS gastric epithelial cells.

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摘要

Abstract

Cyclopentenone prostaglandins (CyPGs), derivatives of arachidonic acid, have been suggested to exert growth-inhibitory activity through peroxisome proliferator-activated receptor (PPAR)-dependent and -independent mechanisms. Here we examined various eicosanoids for growth inhibition and found that the terminal derivative of prostaglandin (PG) J2 metabolism, 15-deoxy-12,14-PGJ2 (15d-PGJ2), and PGA1 markedly inhibited the growth and induced apoptosis in AGS gastric carcinoma cells. There were no significant increases in cell death and DNA-fragmentation in the cells with overexpression of PPAR or PPAR, indicating the possibility that 15d-PGJ2 and PGA1 induced apoptosis through PPAR-independent pathway. Moreover, 15d-PGJ2 and PGA1 activated the c-jun N-terminal kinase (JNK) and caspase-3 activity in dose- and time-dependent manners. To examine further the role of JNK signaling cascades in apoptosis induced by 15d-PGJ2 and PGA1, we transfected dominant-negative (DN) mutants of JNK plasmid into the cells to analyze the apoptotic characteristics of cells overexpressing DN-JNK following exposure to 15d-PGJ2 and PGA1. Overexpression of DN-JNK significantly repressed both endogenous JNK and caspase-3 activity, and subsequently decreased apoptosis induced by 15d-PGJ2 and PGA1. These results suggested that CyPGs, such as 15d-PGJ2 and PGA1, activated JNK signaling pathway, and that JNK activation may be involved in 15d-PGJ2- and PGA1-induced apoptosis. © 2003 Wiley-Liss, Inc...