- RN9305-0382
- PPAR
- Study on the Molecular Mechanisms of Anti-Carcinogenic and Anti-inflammatory Effects of Peroxisome Proliferator-Activated Receptor (PPAR) Ligands
- NSC90-2320-B038-050
- 9008 ~ 9107
- 16
- ; Liang, Yu-Chih; Lin, Jen-Kun
- ; ; JNK
- Prostaglandin; Apoptosis; JNK gene
- Peroxisome proliferator-activated receptor(PPAR) Eicosanoids Prostaglandin J2(PGJ2) 15-deoxy-12,14-PGJ2 (15d-PGJ2) PGA1 AGS PPARα PPARγ 15d-PGJ2 PGA1 15d-PGJ2 PGA1 PPAR 15d-PGJ2 PGA1 JNK Caspase-3 Dominant-negative c-Jun N-terminal kinase(DN-JNK) JNK Caspase-3 15d-PGJ2 PGA1 JNK JNK
- 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 that various eicosanoids on the inhibition of cell proliferation, and found that the terminal derivative of PGJ2 metabolism, 15-deoxy-G12,14-PGJ2 (15d-PGJ2), and PGA1 markedly inhibited growth and induced apoptosis in AGS gastric carcinoma cells. There were no significant increase in DNA-fragmentation in the cells with overexpression of PPAR \ or PPAR ^ plasmid, indicating 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 the caspase-3 activity in dose- and time-dependent manners. To further examine the role of JNK signaling cascades in apoptosis induced by 15d-PGJ2 and PGA1, we transfected dominant-negative (DN) mutants of JNK into the cells to analyze the apoptotic characteristics of cells expressing DN-JNK plasmid following exposure to 15d-PGJ2 and PGA1. Expression of DN-JNK proteins repressed both of endogenous JNK and caspase-3 activity, and subsequently inhibited apoptosis induced by 15d-PGJ2 and PGA1. These results suggest that CyPGs, such as 15d-PGJ2 and PGA1, activates the JNK signaling pathway, and that JNK activation may be involved in 15d-PGJ2 and PGA1 induced cell death.