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• 計畫英文名稱	Study on the Molecular Mechanisms of Anti-Carcinogenic and Anti-inflammatory Effects of Peroxisome Proliferator-Activated Receptor (PPAR) Ligands
• 主管機關	行政院國家科學委員會
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• 中文關鍵字	前列腺素; 細胞凋亡; JNK 基因
• 英文關鍵字	Prostaglandin; Apoptosis; JNK gene
• 中文摘要	花生四烯酸的多種前列腺素衍生物已知可經由活化 Peroxisome proliferator-activated receptor(PPAR)或其他路徑引起細胞凋亡。本研究計畫試驗了多種 Eicosanoids 對細胞增殖的抑制能力。結果發現 Prostaglandin J2(PGJ2)的代謝衍生物 15-deoxy-12,14-PGJ2 (15d-PGJ2)及 PGA1，可有效抑制胃腫瘤細胞株 AGS 的生長，且造成此細胞凋亡。過渡表現 PPARα 或 PPARγ 的細胞，並不會增加 15d-PGJ2 及 PGA1 所造成的細胞凋亡，顯 15d-PGJ2 及 PGA1 引起細胞凋亡非經由活化 PPAR 的路徑。然而 15d-PGJ2 及 PGA1 會依濃度及時間的增加，提昇 JNK 及 Caspase-3 的活化；若細胞先轉殖 Dominant-negative c-Jun N-terminal kinase(DN-JNK)則可減少 JNK 及 Caspase-3 的活性且降低細胞凋亡的數目，這些結果顯示 15d-PGJ2 及 PGA1 可活化 JNK，且活化 JNK 與造成細胞凋亡有相關性。
• 英文摘要	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.