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• 計畫英文名稱	Studies of the Anti-Tumoral and the Cell Differentiational Effects of Peroxisome Proliferator-Activated Receptor (PPAR) Ligands---in vitro and in vivo Investigations		
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• 研究人員	梁有志 Liang, Yu-Chih		
• 中文關鍵字	血基質氧化甲; 前列腺素; 乙醯胱胺酸; 二硫糖醇; 穀胱甘		
• 英文關鍵字	Heme oxygenase-1; Prostaglandin; N-Acetyl-L-cysteine; Dithiothreitol; Glutathione.		
• 中文摘要	細胞在受到氧化壓力時,會引起 heme oxygenase-1 (HO-1)蛋白的表現 ，使細胞傷害降至最低。利用一系列前列腺素衍生物 ，我們發現 peroxisome proliferator-activated receptor (PPAR) 內生性配位體 15-deoxy- 12,14- prostaglandin J2 (15d-PGJ2),可引起 HO-1 的大量表現。其可能機制與活化 MAPKs 路徑無關 ； 並且不經由其受體 PPAR。進一步的研究發現,15d-PGJ2 可顯著降低細胞內還原態穀胱甘, 若細胞先處理硫基還原劑,如乙醯胱胺酸及二硫糖醇,則可有效恢復細胞內還原態穀胱甘,並且抑制 HO-1 的表現。結果顯示 PPAR 配位體 15d-PGJ2 是先影響細胞內硫基氧化還原狀態 ， 進而引起 HO-1 的表現。		
• 英文摘要	Heme oxygenase-1 (HO-1) is induced as a beneficial and adaptive response in cells and tissues exposed to oxidative stress. Herein we examined how various eicosanoids affect the induction of HO-1, and the possible mechanism underlying 15-deoxy- 12,14- prostaglandin J2 (15d-PGJ2)-induced HO-1 expression. PGH2, PGD2 and its metabolites of the PGJ2 series, and PGA1 markedly induced the protein expression of HO-1. Arachidonic acid (AA), docosahexaenoic acid (DHA), PGE2, PGF2, and thromboxane B2 (TXB2) were shown to have no effect on the induction of HO-1. 15d-PGJ2 was the most potent activator achieving significance at 5 um. Although 15d-PGJ2 significantly activated the MAPKs of JNK and ERK, the activation of JNK and ERK did not contribute to the induction of HO-1 as determined using transfection of dominant-negative plasmids and MAPKs inhibitors. Additional experiment indicated that 15d-PGJ2 induced HO-1 expression through peroxisome proliferator-activated receptor		

(PPAR)-independent pathway. 15d-PGJ2 significantly decreased the intracellular level of reduced glutathione; and the thiol antioxidant, N-acetyl-L-cysteine (NAC), and the thiol-reducing agent, dithiothreitol (DTT), inhibited the induction of HO-1 by 15d-PGJ2. Finally, NAC and DTT exhibited significant inhibition of HO-1 mRNA and HO-1 promoter reporter activity induced by 15d-PGJ2. These results suggest that thiol antioxidant and reducing agents attenuate the expression of HO-1 induced by 15d-PGJ2, and that the cellular thiol-disulfide redox status may be linked to HO-1 activation.