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• 計畫中文名稱	尿酸誘發心臟纖維細胞增生的分子機制探討		
• 計畫英文名稱	Molecular Mechanisms of Uric Acid-Induced Proliferation in Rat Cardiac Fibroblasts		
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• 中文關鍵字	尿酸; 細胞增生; 內皮素; 訊息傳遞; 心臟纖維細胞； 活性氧族群		
• 英文關鍵字	Uric acid, Proliferation, Endothelin-1, Signal transduction, Cardiac fibroblasts, Reactive oxygen species		
• 中文摘要	臨床研究報告指出：血液中尿酸濃度與心血管疾病的發生有密切的相關性，細胞培養的實驗結果進一步發現尿酸有誘發鼠心臟纖維細胞增生的作用，然而其作用的相關細胞分子機轉，目前尚不是很清楚。內皮素爲目前已知具有強力促進血管收縮作用的內生性物質,而且與心血管疾病如心臟纖維化的形成有密切關聯，心臟纖維細胞亦存在著內皮素的接受器。然而有關尿酸對於內皮素基因的表現作用，在心臟纖維細胞上作用的相關機轉，目前相關的文獻仍付之闕如。本研究計劃，經由釐清內源性的內皮素於尿酸所誘發心臟纖維細胞增生的作用中所扮演的角色，並了解尿酸可以經由增加細胞內活性氧族群，進一步活化內皮素基因表現，據以解釋血液中尿酸過高易致心血管疾病發生的分子機制，並且深入探討尿酸對內皮素基因表現的作用，其細胞內訊息傳遞的機轉。		
• 英文摘要	Serum uric acid is frequently elevated in subjects at cardiovascular risk. Literature indicates that soluble uric acid can induce rat cardiac fibroblast proliferation in vitro. However, the molecular mechanism(s) of uric acid in the pathogenesis of cardiovascular diseases remains to be further examined. Endothelin-1 (ET-1) is one of the most potent vasopressors identified to date. It was studied in depth in relation to cardiovascular diseases, such as cardiac fibrosis. Abundant ET-1 receptors present on cardiac fibroblasts. Recent evidence indicates that reactive oxygen species (ROS) may function as intracellular messengers to modulate signaling pathways. Literature indicates the ability of antioxidants to inhibit uric acid-induced monocyte chemoattractant protein-1 production suggested involvement of intracellular redox pathways in vascular smooth muscle cells. Recently, we also found that ROS mediate		

the induction of ET-1 gene, raised the possibility of its transcriptional regulation by uric acid in cardiac fibroblasts. Therefore, it is tempting to hypothesize that endogenous ET-1 mediates the effects of uric acid and ROS do play a role in uric acid-induced ET-1 gene expression. Thus, ET-1 antagonism; endothelin-converting enzyme inhibitor and antioxidants may offer an additional weapon for therapeutic interventions aimed at preventing cardiovascular damage. In this project, we found endogenous ET-1 mediates uric acid-induced cardiac fibroblast proliferation and explore its molecular mechanism in culture system.