• 系統編號	RN9704-1300
• 計畫中文名稱	白蘆藜醇對血管收縮素所誘發心臟纖維化的作用
• 計畫英文名稱	Effect of Resveratrol on Angiotensin II-Induced Cardiac Fibrosis
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC95-2314-B038-027
• 執行機構	台北醫學大學醫學系
• 本期期間	9508 ~ 9607
• 報告頁數	15 頁
• 使用語言	中文
• 研究人員	劉如濟; 鄭志鴻 Liu, Ju-Chi
• 中文關鍵字	白蘆黎醇; 血管收縮素; 內皮素; 心臟纖維細胞; 活性氧族群; 訊息傳遞
• 英文關鍵字	Resveratrol; Angiotensin II; Endothelin-1; Cardiac fibroblast; Reactive oxygen species; Signal transduction; ERK (extracellular signal-regulated kinase)
• 中文摘要	廣泛的流行病學的研究報告顯示，適度紅酒的飲用有助於降低冠心疾病的發生率，而紅酒中所含的有效成分之一爲白蘆黎醇(resveratrol) 。白蘆黎醇據有許多生物活性有助於降低冠心疾病的發生率， 在最近相關的文獻報告，以及計劃提案人最近於血管內皮細胞的研究結果顯示：白蘆黎醇亦具有抗氧化的作用，然而，目前對於其在心血管系統的細胞作用與分子生物機轉仍有許多不明確處。近來實驗發現；血管收縮素(angiotenisn II; Ang II)可增加心臟纖維細胞增生及內皮素-1(endothelin-1；ET-1)的基因表現。而此種作用與細胞內活性氧族群(reactive oxygen species;ROS)有關。所以本實驗即以血管收縮素誘發心臟纖維細胞增生及內皮素基因表現來探究白蘆黎醇對於培養中鼠心臟纖維細胞內皮素基因表現的影響與其分子生物機轉。本實驗發現：白蘆黎醇可抑制血管收縮素誘發心臟纖維細胞增生、ROS 的產生、以及 ET-1 基因的表現；探究上述作用的細胞內訊息傳導路徑，發現白蘆黎醇可抑制血管收縮素誘發表皮生長因子接受器轉活化以及胞外訊號激脢的磷酸化，此抑制作用與白蘆黎醇對抗血管收縮素誘發 SHP-2 去磷酸脢的氧化作用有關。
• 英文摘要	Objectives: The aims of this study were to examine whether resveratrol influences the proliferation of cardiac fibroblasts and to identify the molecular target of resveratrol. Background: Resveratrol is a phytoestrogen naturally found in grapes and is the major constituent of wine thought to have a cardioprotective effect. Cardiac fibroblasts regulate myocardial remodeling by proliferating and secreting extracellular matrix proteins and growth factors such as endothelin-1 (ET-1). Prolonged activation of cardiac fibroblasts

leads to cardiac fibrosis and reduced myocardial contractile function. However, the molecular mechanisms that resveratrol affects cardiac fibroblast proliferation still remains to be clarified. Methods: Cultured neonatal rat cardiac fibroblasts were preincubated with resveratrol then stimulated with angiotensin II, after which [3H]thymidine incorporation and endothelin-1 gene expression were examined. The intracellular mechanism of resveratrol in cellular proliferation and endothelin-1 expression was elucidated by examining the level of angiotensin II-induced epidermal growth factor (EGF)-receptor transactivation and extracellular signal-regulated kinase (ERK) phosphorylation. Results: Resveratrol (1–100 .mu.M) inhibited angiotensin II-induced DNA synthesis and endothelin-1 secretion. The inductive properties of angiotensin II on EGF-receptor transactivation and ERK phosphorylation were found reversed with resveratrol and antioxidants such as N-acetyl-cysteine. We also examined the effect of angiotensin II on Src homology 2-containing tyrosine phosphatase (SHP-2) in cardiac fibroblasts using a modified malachite green phosphatase assay. SHP-2 was oxidized during angiotensin II treatment, and this oxidization could be repressed by resveratrol treatment. Conclusions: In summary, we speculate that resveratrol inhibits angiotensin II-induced cell proliferation which involves the disruption of the ERK pathway via activation of SHP-2.