• 系統編號	RN9604-3902		
• 計畫中文名稱	同半胱胺酸誘發血管平滑肌細胞增生的分子機制		
• 計畫英文名稱	Molecular Mechanism of Homocysteine-Induced Proliferation in Aortic Smooth Muscle Cells		
• 主管機關	行政院國家科學委員會	• 計畫編號	NSC94-2314-B038-040
• 執行機構	臺北醫學大學內科		
• 本期期間	9408 ~ 9507		
• 報告頁數	14 頁	• 使用語言	中文
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• 中文關鍵字	同半胱胺酸; 細胞增生; 內皮素; 訊息傳遞; 血管平滑肌細胞； 活性氧族群		
• 英文關鍵字	Homocysteine, Proliferation, Endothelin-1, Signal transduction		
• 中文摘要	血液中的「同半胱胺酸」(homocysteine)與血管硬化的進行有非常密切的關係，據估計至少有 10%的心臟血管疾病與同半胱胺酸過量有關。細胞培養的實驗結果進一步發現同半胱胺酸有誘發鼠血管平滑肌細胞增生的作用，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,而且與高血壓及心血管疾病如冠狀動脈硬化的形成有密切關聯,血管平滑肌細胞亦存在著內皮素的接受器。然而有關同半胱胺酸對於內皮素基因的表現作用，在血管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，釐清內源性的內皮素於同半胱胺酸所誘發血管平滑肌細胞增生的作用中所扮演的角色，並了解同半胱胺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，據以解釋血液中同半胱胺酸過高易致高血壓及心血管疾病發生的分子機制，並且深入探討同半胱胺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	Homocysteine is a sulfur-containing amino acid produced from methionine during processing of dietary protein. It has gained considerable attention recently because elevated concentration of total homocysteine are believed to be associated with an increased risk of cardiovascular disease, including coronary artery, cerebrovascular, and peripheral vascular disease. There is evidence that homocysteine can induce vascular smooth muscle cell proliferation in vitro. However, the molecular mechanism(s) of homocysteine 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 arterial hypertension and cardiovascular diseases, such as atherosclerosis. Abundant ET-1 receptors present on vascular smooth muscle cells. Recent evidence indicates that reactive oxygen species (ROS) may function as intracellular messengers to modulate signaling pathways. Homocysteine also		

induces oxidative stress in vascular smooth muscle cells. We previously demonstrated that ROS mediate the induction of ET-1 gene, raised the possibility of its transcriptional regulation by homocysteine in vascular smooth muscle cells. Therefore, it is tempting to hypothesize that endogenous ET-1 mediates the effects of homocysteine and ROS do play a role in homocysteine-induced ET-1 gene expression. However, the direct effect of homocysteine on ET-1 gene expression and the role of ROS in homocysteine-induced cell proliferation and ET-1 gene expression have not been well examined in vascular smooth muscle cells. In this project, we found that endogenous ET-1 mediates homocysteine-induced vascular smooth muscle cell proliferation and explored the detailed intracellular signal transduction pathway of homocysteine-induced ET-1 gene expression in rat aortic smooth muscle cells.