• 系統編號	RC9012-0135
• 計畫中文名稱	探討 Mitogen-Activated Protein Kinases 在氧化低密度脂蛋白及發炎性細胞激素對內皮與巨噬細胞誘發'Matrix Metalloproteinase 活化之角色'
• 計畫英文名稱	The Studies of the Roles of Mitogen-Activated Protein Kinases on Oxidized LDL-or Inflammatory Cytokines-Induced the Activation of Matrix Metalloproteinase in Endothelial Cells and Macrophages
• 主管機關	--
• 計畫編號	NSC89-2320-B038-058
• 執行機構	台北醫學院藥理科
• 本期期間	8908 ~ 9007
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• 使用語言	中文
• 研究人員	蕭哲志；許準榕 Hsiao, George；Sheu, Joen-Rong
• 中文關鍵字	有絲分裂劑；蛋白激脢；發炎性細胞激素；基質金屬蛋白脢；氧化性低密度脂蛋白；內皮細胞
• 英文關鍵字	Mitogen；Protein kinase；Inflammatory cytokine；Matrix metalloproteinase (MMP)；Oxidized low density lipoprotein；Endothelial cell
• 中文摘要	基質金屬酵素在許多疾病中扮演相當重要的角色，尤其癌症的轉移與血管斑塊剝離在臨床上更受到重視。本計畫之目的在探討分裂素活化蛋白酵素是否在細胞激素或氧化型人類低密度脂蛋白所誘發細胞基質金屬酵素的表現與活化上所扮演的角色。從實驗結果發現，的確細胞激素(如腫瘤壞死因子)能使單核球細胞引發大量基質金屬酵素的表現與活化，尤其第九型基質金屬酵素的表現特別明顯。我們也發現兩種分裂素活化蛋白酵素抑制劑(PD98059 與 SB203580)二者均能抑制電泳酵素分析之基質金屬酵素的分解作用，且隨濃度增高而抑制性越強。但二者對於第九型基質金屬酵素之酵素活性並不影響。而這些抑制作用也不是源自於細胞傷害。另外，未刺激之人類臍帶靜脈內皮細胞能持續釋放多量的第二型基質金屬酵素，二者抑制劑對此基質金屬酵素之活化並不影響。初步活體大鼠總頸動脈氣球擴張損傷後，血管明顯提高 MMP-9 的生成與釋放。從這些結果可提供有關分裂素活化蛋白酵素在不同血管性細胞基貿金屬酵素活化過程時之重要性，以利活體穩定血管(Vascular stability)或癌症實驗之參考。
• 英文摘要	Matrix metalloproteinases (MMPs) have the important role in the pathogenesis of atherosclerotic plaque destabilization. The purpose of this study was to determine if mitogen-activated protein kinase might involve in the cytokine- or oxLDL-induced MMPs activation, and thus represents an attractive therapeutic target. Exposure monocyte (THP-1) to TNFα (10 ng/ml) increased MMP-9 protein expression as measured by gelatinolytic activity as determined by zymography. We found that treatment with MAPK. inhibitors (PD 98059 or SB 203580) significantly decreased MMP-9

gelatinolytic at a concentration-dependent manner. However, both inhibitors were without any inhibition on MMP-9 activity. These inhibitory actions on gelatinolytic activity by MAPK inhibitors were not mediated by reduction of cellular viability. Differently, non-stimulated HUVEC could expressed much amount of MMP-2. Such constitutive expression of MMP-2 was no clearly affected by MAPK. inhibitors. On the other hand, according to preliminary animal studies, the MMP-9 activity was clearly elevated on the balloon-injuried common carotid artery. These data demonstrate that MAPK play an important role on induction of different MMPs. This newly described action of MAPK. inhibition might prove useful to inhibit matrix degradation and to improve vascular stability, or even cancer invasion.