

國科會計畫

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應用毛細管電泳、液相層析-質譜以及聚苯乙烯微粒子開發新方法來研究氧化性低密度脂蛋白及磷脂質對於血管內皮細胞產生的 C-反應蛋白的影響

Determine the Effects of Oxidized Low-Density Lipoproteins and Phospholipids on the Endothelial Expression of C-Reactive Protein by Ce, Lc-Esi Mass and Polystyrene Microspheres

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中文摘要

氧化性低密度脂蛋白以及 C-反應蛋白都與心血管疾病非常有關聯。C-反應蛋白是急性發炎的生物指標，高濃度的 C-反應蛋白可預測心血管疾病。很多研究也發現氧化性低密度脂蛋白沉積在動脈硬化病人的動脈硬塊中。C-反應蛋白可藉著氧化的縮醛磷脂醯膽鹼 (oxidized phosphatidyl choline) 與氧化的低密度脂蛋白及死亡細胞的細胞膜結合，但是 C-反應蛋白不與沒受氧化的低密度脂蛋白及活細胞結合。目前，科學家們尚未清楚 C-反應蛋白是否直接參與動脈硬化疾病的發展。我們推測氧化性低密度脂蛋白破壞血管內皮細胞的同時，也促進血管內皮細胞分泌 C-反應蛋白。這個反應可能是藉著類似凝集素的氧化性低密度脂蛋白接受器(lectin-like oxidized low-density lipoprotein receptor-1; LOX-1) 進行的。我們的初步結果顯示以硫酸銅氧化的低密度脂蛋白刺激血管內皮細胞產生 C-反應蛋白。很多研究指出磷脂質是具有生化活性的。但是，我們還是不清楚位於氧化的低密度脂蛋白上之磷脂質是否在這個反應中扮演著重要的角色。我們想要瞭解不同的氧化性低密度脂蛋白及磷脂質分子對於血管內皮細胞釋放 C-反應蛋白的影響。我們將應用毛細管電泳、聚苯乙烯微粒子以及液相層析-電漿噴灑質譜，來合理的設計及開發新的分析方法。希望我們能促進人們瞭解氧化性低密度脂蛋白、磷脂質、血管內皮細胞及 C-反應蛋白四者間的關係，也希望能對瞭解 C-反應蛋白在動脈硬化的過程中是否扮演直接的角色有所貢獻。期待這個研究能夠增進人們對動脈硬化的瞭解、預防及治療。

關鍵字：氧化性低密度脂蛋白;氧化性磷脂質;C-反應蛋白;血管內皮細胞;毛細管電泳;聚苯乙烯微粒子;液相層析-電漿噴灑質譜

Abstract

Both oxidized low-density lipoproteins (ox-LDL) and C-reactive protein (CRP) are found to be closely associated with cardiovascular disease. CRP is an acute-phase inflammatory biomarker, and high plasma level of CRP is a strong predictor for cardiovascular disease. Ox-LDL is found to accumulate in the plaques of arterial lesions of atherosclerotic patients. CRP was shown to bind to ox-LDL and apoptotic cell membranes through oxidized phosphatidyl choline (ox-PC), but not bind to native LDL and viable cells. However, it is not clear if CRP directly participates in the development of atherosclerosis. We hypothesize that ox-LDL induced endothelial dysfunction may also promote endothelial CRP expression mediated by lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1). Our preliminary results show that CuSO₄ oxidized LDL stimulates the release of CRP from endothelial cells. Many lines of evidences indicate that phospholipids are biologically active. However, it is not clear whether oxidized phospholipids on LDL particles play a key role on the CRP expression. We seek to understand the effects of various in vitro oxidized LDL particles and phospholipid molecules on the endothelial secretion of CRP. By rational method design and development of capillary electrophoresis, polystyrene microspheres and LC-ESI Mass, we hope that we will contribute to the understanding of the relationships among ox-LDL, ox-phospholipids, endothelial cells and CRP as well as whether CRP plays a direct role in atherosclerosis. This study will improve our understanding, prevention and efficacy of treatment for atherosclerosis.

Key words : Oxidized low-density lipoproteins; Oxidized phospholipids; C-reactive protein; Endothelial cells; Capillary electrophoresis; Polystyrene microspheres; LC-ESI Mass