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• 計畫中文名稱	敗血症致病因和治療之研究－敗血症引起血小板減少之機轉探討及其治療方法之研究(II)		
• 計畫英文名稱	Investigation of Pathogenic Mechanisms and Treatments of Thrombocytopenia in Sepsis (II)		
• 主管機關	行政院國家科學委員會	• 計畫編號	NSC87-2314-B038-023-M3
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• 研究人員	許準榕 Sheu, Joen-Ron		
• 中文關鍵字	敗血症；血小板減少症；擴散性血管內凝血症；血小板；細胞膜流動性；一氧化氮；蛋白激酶 C；磷酸肌酐		
• 英文關鍵字	Sepsis；Thrombocytopenia；Disseminated intravascular coagulation (DIC)；Platelet；Membrane fluidity；Nitric oxide (NO)；Protein kinase C (PKC)；Phosphoinositide		
• 中文摘要	在本實驗中,大腸桿菌的脂多醣體 LPS 依劑量(100-300.mu.g/ml)-及時間(10-60min)-相關性抑制活化劑所引起的血小板凝集反應。在人類的血小板中, LPS 亦明顯的抑制 Phosphoinositide 的分解及抑制細胞內鈣離子的移動。LPS(300.mu.g/ml)亦會抑制 Collagen 所引起的 Thromboxane A/sub 2/合成。再者,LPS 亦會明顯的影響血小板細胞膜的流動性;另外,LPS 會增加血小板 cyclic GMP 的含量,但卻無法增加 cyclic AMP 的含量。LPS(200.mu.g/ml)亦會明顯的增加血小板 NO 的合成;另一方面,LPS 亦會抑制 PDBu(50nM)所引起的血小板 Protein kinase C 的活化。由上述實驗結果顯示抑制血小板凝集反應有二個主要路徑:(1)首先影響到血小板細胞膜的流動性近而抑制 Phospholipase C 的活性;(2)LPS 直接活化 Nitric oxide(NO)/cyclic GMP 路徑,導致抑制血小板凝集反應。		
• 英文摘要	In this study, Escherichia coli LPS dose-dependently (100-300.mu.g/ml) and time-dependently (10-60 min) inhibited platelet aggregation in human platelets stimulated by agonists. LPS also dose-dependently inhibited the phosphoinositide breakdown and the intracellular Ca/sup +2/ mobilization in human platelets stimulated by collagen. LPS (300.mu.g/ml) also significantly inhibited the thromboxane A/sub 2/ formation stimulated by collagen in human platelets. Moreover, LPS (100-300.mu.g/ml) dose-dependently decreased the fluorescence of platelet membranes tagged with diphenylhexatrience. In addition, LPS (200 and 300.mu.g/ml) significantly increased the formation of cyclic GMP but not cyclic AMP in platelets. LPS (200.mu.g/ml) also significantly increased the production of nitrate within a 30-min incubation period. Rapid phosphorylation of a platelet protein of Mr. 47,000, a marker of protein kinase C activation, was triggered by PDBu (50nM). This		

phosphorylation was markedly inhibited by LPS (200. μ g/ml) within a 30-min incubation period. These results indicate that the antiplatelet activity of LPS may be involved in two important pathways. (1) LPS may be due to the induction of conformational changes in the platelet membrane, leading to change in the activity of phospholipase C. (2) LPS also activated the formation of NO/cyclic GMP in human platelets, resulting in inhibition of platelet aggregation. Therefore, LPS-mediated alteration of platelet function may contribute to bleeding diathesis in septicemic and endotoxemic patients.