• 系統編號	RC9101-0102
• 計畫中文名稱	比較格蘭氏陰性及陽性菌毒素對刺激小神經膠細胞、白血球及血小版釋放 Cytokines 及 Nitricoxide 的相對活性(II)
• 計畫英文名稱	The Detailed Mechanisms and Relative Acitivites of Induction of Cytokines and Nitric Oxide Release in Microglia, Leukocytes, and Platelets by Gram-negative and Positive Toxins (II)
• 主管機關	--
• 計畫編號	NSC89-2320-B038-069-M53
• 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	許準榕 Sheu, Joen-Rong
• 中文關鍵字	細胞激素；一氧化氮；小神經膠細胞；血小板；白血球；脂磷壁質酸
• 英文關鍵字	Cytokine；Nitric oxide (NO)；Microglia；Platelet；Leukocyte；Lipoteichoic acid (LTA)
• 中文摘要	至目前爲止，一般相信格蘭氏陰性菌(Gram-negative)及其內毒素 Lipopolysaccharide (LPS)是造成敗血症的主要原因；較常見且具高致命性的反應如引起低血壓，血小板減少症，瀰漫性血管內凝血以及最後常導致許多器官的衰竭而死亡。另一方面，在最近幾年的研究中亦發現格蘭氏陽性菌(Gram-positive)所引起的細菌感染亦能引發全身性的細菌感染與敗血性休克；據統計約有 1/3 到 1/2 的敗血症是由陽性菌所引起的，並且相信在未來的幾年中其所占的比例還會再繼續增加。引發敗血症的過程目前被認爲是因許多細胞被活化產生 Cytokines(如 IL-1β，PAF，TNFα 等)的結果；主要參與這些反應的細胞如單核球(Monocyte)，淋巴球(Lymphocyte)，嗜中性白血球(PMN)及血小板(Platelet)等；在中樞神經系統中，最明顯的反應是小神經膠細胞(Microglia)的活化；此細胞不論在細胞型態，免疫表型或生理功能上都與單核球/巨噬細胞(Macrophage)相似。研究陽性菌引發敗血症最困難的一點在於不同菌種間其細胞壁的成份各有不同。其中 Lipoteichoic acid (LTA)爲陽性菌細胞壁中最重要的成份之一，目前被認爲在陽性菌引起敗血症的過程中，LTA 扮演非常重要的角色。因此本計畫的重點主要在探討及比較陰性菌的主要內毒素 LPS 和陽性菌的 LTA 對於 Microglia，各種白血球以及對血小板的作用差異性；並由其中的實驗可瞭解 LPS 和 LTA 的相對作用強度及個別作用機轉。
• 英文摘要	At present, it is a widely believed that sepsis in caused predominantly by gram-negative organisms, and endotoxin LPS (lipopolysaccharide), a substance produced by these organisms. The progression of sepsis is cardiovascular dysfunction (i.e., hypotension, thrombocytopenia, disseminated intravascular coagulation) and multiple organ by dysfunction syndrome (MODS), finally associated with an increase in the

mortality. Up to now, the important of gram-negative organisms in the genesis of sepsis has been emphasized. However, recent studies show an increasing evidenced of gram-positive sources of sepsis. On the basis of this evidence, it seems reasonable to conclude that between one third and one half of all cases of sepsis are currently caused by gram-positive organisms and that the incidence of gram-positive sepsis should continue to rise for at least the nest few years. Sepsis is believed to result from a complex mechanism involving activation of a number of cells, most notably monocytes, lymphocytes, neutrophils and platelets as well as microglia. Microglia are like macrophages in that they are derived from mononuclear myeloid progenitors, they reside in the CNS in a ramified, quiescent states, but can readily migrate to sites of inflammation in the CNS. One of the chief difficulties in elucidating how gram-positive organisms cause sepsis is that they are considerable differences in cell wall composition among various gram-positive species. Lipoteichoic acid (LTA), a predominant component associated with the cell wall of gram-positive bacteria, can provoke marked stimulation of sepsis. The present project is designed to compare the relative activities of LPS and LTA in stimulation of cytokines (i.e., IL-1β, TNFα) and NO release in microglia, monocytes, lymphocytes, neurophils and platelets in vitro and ex vivo, respectively.