• 計畫中文名稱	加護病房敗血症患者營養生物標記評估: 蛋白質體學---單一核酸多型性-維生素訊息之應用		
• 計畫英文名稱	Nutritional Biomarkers Evaluation of Severe Sepsis in Intensive Care Units---Plasma Proteomic, Single Nucleotide Polymorphism and Vitamins Information to Clinical Application		
• 系統編號	PC9709-1201	• 研究性質	基礎研究
• 計畫編號	NSC97-2320-B038-032	• 研究方式	學術補助
• 主管機關	行政院國家科學委員會	• 研究期間	9708 ~ 9807
• 執行機構	臺北醫學大學保健營養學系		
• 年度	97 年	• 研究經費	500 千元
• 研究領域	基礎醫學類		
• 研究人員	李信昌,陳巧明,林景堉		
• 中文關鍵字	敗血症；營養生物標記；血漿蛋白質體學；維生素；單一核?酸多形性		
• 英文關鍵字	Sepsis； Nutritional biomarkers； Plasma proteomic； Vitamins； Single nucleotidepolymorphism		
• 中文摘要	敗血症（sepsis）主要是由於細菌感染所引起的症狀，釋放至血液中的毒素會引起全身性 嚴重的發炎反應，會導致體內細胞激素、腫瘤壞死因子等的產生，一連串激活了補體、白血 球和血管內皮細胞等，最後常導致患者血液凝結、多重器官衰竭及休克死亡。行政院衛生署 民國九十五年的死亡原因統計報告中指出，敗血症已躍升至國人主要死因的第十二位，通常 是加護病房患者的死亡主要原因。在臨床上，除了使用抗發炎藥、抗生素、血管收縮藥物、 大量點滴輸液等支持性治療外，目前並無有效的治療方式。敗血症在過去數十年間有數以萬 計的文獻被發表，平均每一位敗血症患者的治療費用約 22,500 美元，過去 10 年間製藥業已經 花費近 20 億美元在敗血症的治療研究，然而臨床應用試驗卻無明顯的療效。其原因爲大部份 的研究只著重在動物、體外細胞或細胞株間關鍵單一分子或相關分子變化，然而分子間的交 互作用與敗血症間的關聯性仍不清處。對於不同類型敗血症患者，如何診斷病理的發展乃至 於發炎的過程，最後導致器官多重衰竭的途徑，將有助於敗血症的治療及照護。本研究室以 蛋白質體學法進行血漿蛋白質圖譜發現，三位敗血症患者於加護病房緊急期及經治療後於普 通病房恢復期間，患者血漿二維蛋白質膠體電泳有顯著的變化，目前經由質譜分析(MS)及生 物資料庫分析比對後，已經找到一些新穎性蛋白質點可作爲診斷敗血症的生物標記。本計畫 第一年的研究擬增加敗血症患者收案人數，並利用西方點墨法評估差異蛋白質點作爲敗血症 指標的可行性。此外我們先前使用脂多醣誘發敗血症模式動物實驗發現，預先介入核黃素可 以提高敗血性小鼠的存活率，然而核黃素是否干擾脂多醣造成的毒素效應並不清楚，因此第 二年的研究我們將以細胞模型進行		

	transwell 進行假說驗證，並配合臨床營養師同時進行敗血 症患者臨床營養評估及以 HPLC 法追蹤患者血漿維生素消長變化，以提供第三年感染科醫師 臨床上介入相關維生素重要參考依據。從已經發表的文獻指出 TNF-α、IL-6、IL10、PAI-1、 APOE 及 CXCL2 基因的多型性與敗血症患者死亡風險有關，因此第三年的研究擬針對前二年 敗血症收樣患者白血球萃取其 DNA，以 DHPLC 法分析加護病房敗血症患者不同基因型是否影 響病人住院天數及營養素利用。本研究結合感染科醫師、醫檢師、營養師及生化研究人員， 從蛋白質及核酸層次，並配合相關生化指標數據以進行敗血症患者之臨床醫學研究，預期可 以探究敗血症的生化機轉及提供患者醫療照護更多的學理依據。
• 英文摘要	Sepsis is a condition that results from a harmful or damaging host response to infection. Excessive toxins in blood cause to serve inflammatory responses, including cytokines production and tumor necrosis factor-α (TNF-α) that lead to activation of innate immune system, complement system, coagulation system and adaptive immune system. Epidemiology report from Department of Health in Taiwan in 2006, sepsis has risen to the twelfth and is often the harbinger of multiple organ failure and constitutes the leading cause of mortality in intensive care unit. In clinical treatment, except for anti inflammation drug, antibiotics, vasoconstriction drugs and intravenous drip support, none effective methods in sepsis therapy. In the past ten years, numerous of papers were published in the immunopathogenesis of sepsis. The average cost to treat sepsis is estimated to be $22,500 per case in U.S.A. Pharmaceutical industry spent 20 hundred million in therapy of sepsis, however the therapeutic approaches used to treat sepsis with very limited success. Furthermore, most studies have focused on either a single molecule or a few related molecules in animal models or cell lines. A detailed understanding of how these components and pathways interaction to sepsis are still nebulous. In our previous proteomic profiles in septic shock serum, three patients have differential protein spots in plasma 2D analysis between intensive care unit to normal sickroom. These proteins were identified by MALDI-TOP analysis and could be as biomarkers in diagnosis in processing of sepsis. In order to evaluate these biomarkers accurately, the septic patients will enlarge with new septic cases and confirm by immunoblotting analysis in first year. The septic mice could elevate survival rate by riboflavin intervention had been proved in our previous study; however the mechanism was still unclear. We can explore how lipopolysaccharide and riboflavin interaction by transwell test. The nutrition evaluation by dietician related to vitamin status by HPLC in septic plasma will process in the second year. All clinical information will advantage clinical physician in vitamin intervention in third year. It has shown the single nucleotide polymorphism (SNP) in candidate genes such as TNF-α、IL-6、IL10、PAI-1、APOE and CXCL2 were related to survival rate of septic patient in papers. The extraction of genomic DNA from septic cases will be used in high-throughput SNP detection by using DNA pooling and denaturing high performance liquid chromatography (DHPLC). The working team will combine infectious physician, medical technologist and dietician assessment to evaluate septic patient in DNA variation, proteomic profile and biological value. This result will help us how to diagnosis and take care different type of septic patients.