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• 計畫中文名稱	全身性發炎反應症候群致病機轉及治療之整合研究---全身性發炎反應症候群引起血小板及小神經膠細胞活的機轉探討：評估高壓氧及抗氧化劑的治療效果(I)
• 計畫英文名稱	Mechanisms Of SIRS-Induced Platelet And Microglia Activation---Evaluation Of Effectiveness Of HBO And Antioxidant Therapy
• 主管機關	--
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• 中文關鍵字	抗氧化劑；全身性炎症反應症候群；小神經膠細胞；高壓氧；血小板；發炎
• 英文關鍵字	Antioxidant；Systemic inflammatory response syndrome (SIRS)；Microglia；Hyperbaric oxygen (HBO)；Platelet；Inflammation
• 中文摘要	全身性發炎反應症候群(Systemic inflammatory response syndrome, SIRS)是指宿主遭受到某種病原菌入侵或因機械性、化學性的傷害而引起的初期全身性發炎反應稱之。人類全身性發炎反應可依發生的時間先後順序及病情的嚴重性可約略分爲四期：第一期爲如前述之 SIRS，接著產生敗血症(Sepsis)，若病情持續惡化可進一步轉變成敗血性休克(Septic shock)及最後轉變成最具致命性的多重器官衰竭(Multiple organ dysfunction)。有許多因素會引起全身性發炎反應症候群如格蘭氏陰性菌和陽性菌以及一些化學物質如 Oleic acid 等。其中格蘭氏陰性菌及陽性菌是引起 SIRS 的最主要原因。至目前爲止，一般相信格蘭氏陰性菌(Gram-negative)及其內毒素 Lipopo1ysaccharide (LPS)是造成敗血症的主要原因；另外格蘭氏陽性菌(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。引發敗血症的過程目前被認爲是因許多細胞(如白血球、血小板)被活化產生 Cytokines(如 IL-1β、PAF、TNFα 等)的結果；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。高壓氧氣治療(Hyperbaric oxygenation)是指運用大於常壓的氧氣作爲臨床治療之用途。高壓氧氣治療目前在臨床上正被廣泛的採用；許多證據顯示高壓氧氣可應用於治療包括減壓症、一氧化碳中毒、傷口癒合、燒燙傷及骨髓炎等臨床疾病。1987 年 Thom 等人初步研究發現，間歇給予高壓氧氣可減低敗血性休克造成的動物死亡率，並認爲高壓氧氣應可運用於敗血性休克的治療用途；但是此一臨床運用的系統性研究仍相當缺乏。同時對高壓氧氣應用於敗血性休克治療上的可行性及作用機轉亦不清楚。因此，我們在此計畫中將有系統性地研究高壓氧氣在實驗性敗血性休克老鼠的治療效果及詳細機制。在過去幾年中，本實驗室對格蘭氏陰性菌內毒素 LPS 在血小板上的作用機轉已有詳加的研究；另外對格蘭氏陽性菌毒素 LTA 對血小板的影響，亦有初步的研究結果。因此，在本年度中，我們將把重點放在探討陽性菌毒素 LTA 抑制血

	小板凝集作用的分子機轉探討及在活體動物內的作用。
• 英文摘要	SIRS (systemic inflammatory response syndrome) was developed to imply a clinical response arising from a non-specific insult and includes two or more defined variables. There is a continuum from the development of SIRS to the onset of sepsis and progression to septic shock and multiple organ dysfunctions. The SIRS caused predominantly by gram-negative and gram-positive bacteria. At present, it is widely believed that sepsis is caused predominantly by gram-negative organisms, and endotoxin LPS (lipopolysaccharide), a substance produced by these organisms. However, recent studies show an increasing evidence of gram-positive sources of sepsis. Lipoteichoic acid (LTA), a predominant component associated with the cell wall of gram-positive bacteria, can provoke marked stimulation of sepsis. Sepsis is believed to result from a complex mechanism involving activation of a number of cells, most notably leukocytes, platelets and mcroglia. Microglia are like macrophages, and reside in the CNS. Hyperbaric oxygenation (HBO) involves the use of oxygen under pressure greater than that found on earth's surface at sea level. HBO has been applied as an adjunct treatment for a variety of clinical problems such as decompression sickness, carbon monoxide poisons, burn injury and wound healing. On the other hand, Thom (1987) proposed that HBO might be beneficial in septicemia by a study showing that intermittent HBO reduced the mortality in experimental polymicrobial sepsis. Unfortunately, there is lacking of systematic studies that are designed to evaluate the therapeutic values of HBO in septic shock. However, the role of HBO plays in the treatment of septic shock is not clear and warrants further investigations. In the past few years, we have studied the inhibitory mechanisms of LPS in agonist-induced platelet aggregation. Furthermore, we also accomplished the preliminary studies of the influence of LTA on platelets. Therefore, this project will further explore the detailed mechanisms of LTA in platelet aggregation in vitro and in vivo experiments.