• 計畫中文名稱	大豆異黃酮(Isoflavones)對急性胰臟炎誘發肺損傷之保護作用及機轉之探討		
• 計畫英文名稱	The Protective Effects of Isoflavones on the Pancreatitis-Associated Lung Injury and the Mechanisms Involved		
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• 英文關鍵字	soy bean； isoflavones； pancreatitis； lung injury； antioxidant		
• 中文摘要	豆渣爲大豆製油後之副產品，其中含有高量的有機成分諸如異黃酮素（isoflavones）、皂苷及類黃酮素等。它們具有抗氧化、抗發炎、抑制癌細胞生長及抗老化之效果。Isoflavones 可促進血管內膜一氧化氮合成酶(eNOS)的表現，進而增加血液中一氧化氮含量以降低心血管疾病發生率。Isoflavones 也可基於抗氧化和抗炎症的特性而具有減少肺損傷的功能。動物實驗證明定期食用大豆異黃酮可有效降低猪隻氣喘發作時肺組織內和支氣管沖洗液嗜伊紅白血球的增加，有效降低肺炎症所誘發之呼吸道痙攣反應。本研究團隊也證實大豆萃取物可減少內毒素（LPS）所誘發之炎症反應。經過餵食大豆萃取液的老鼠，在 LPS 誘發腹膜炎的過程中，可有效降低血液中白血球數目及 IL-1β、IL-6 等之表現，並減少氮化壓力（nitrosative stress）的產生。因此大豆異黃酮具備了減少炎症反應、減少細胞素、減少氮化壓力及氧化壓力之功用。對於不同模式之肺部損傷也可產生一部份之保護作用。急性胰臟炎常會造成系統性之發炎反應，造成肺部病變或多器官損傷。本研究室藉著在胰管內注射 glycodeoxycholic acid 加上靜脈內注射膽囊收縮素類似物 cerulein 以引發急性胰臟炎。其中之損傷機轉伴隨著發炎反應，白血球活化，細胞素大量分泌，氧化壓力以及誘發型一氧化氮合成酶之大量表現等。此外，急性胰臟炎造成之肺功能改變包括: 一.阻塞型之肺功能改變：肺總量，功能肺餘量之上升，吐氣流速變小或是氣道阻力之上升。 二.限制型之通氣功能改變：肺順應性減少，肺容量下降，呼吸功上升以及肺瀰散量下降等二種模式。因此,本研究中我們擬探討(1)在急性胰臟炎造成肺部炎症反應中、氧游離基、一氧化氮之產生，細胞素 IL-1、IL-6、TNF-α 之變化以及肺組織內發炎反應物質諸如 iNOS、TNF-α、COX-2 之核酸及蛋白質之表現。（2）在服用不同劑量之大豆異黃酮下，探討它們對急性胰臟炎導致肺損傷之干預作用，並探討大豆異黃酮之抗氧化、抗氮化及抗發炎之效用及機轉之探討。我們將利用 Real-time PCR 分析及西方墨漬法之協助以了解在急性胰臟炎下之肺損傷有那些重要的基因及蛋白質參與其中。透過本研究將對於大豆異黃酮在此肺損傷模式下之保護效用及可能之作用機轉。		
• 英文摘要	Soy bean cake , side product of the soy bean oil extraction, contains high amount of organic components such as isoflavones, saponins and flavonoids. These components have antioxidative, antiinflammative, tumor cell suppressing and anti-aging effects. Isoflavones could induce expression of endothelial nitric oxide synthase so that blood nitric oxide concentration elevated and		

	cardiovascular diseases are attenuated. From the animal's data it proved that regular administration of isoflavones could effectively attenuate the asthmatic attacks in pigs and attenuate the eosinophils sequestered in the lung tissues and lung lavage fluid. They are also proved to attenuate airway reactivity by decreasing the lung inflammation. In our early study we proved that isoflavones cold attenuate lipopolysaccharide (LPS)-induced lung inflammation. Isoflavones significantly attenuated the white cell count, blood concentrations of IL-1β, IL-6 and nitrosative stress in the LPS exposed animals. So far, isoflavones proved to have attenuating effects on the inflammation, cytokine production, oxidative stress and nitrosative stress. They have been proved that they have protective effects on the different lung injury models. Acute pancreatitis always induced systemic inflammatory response syndrome, with lung injury and multiple organ injury ensued. In our lab, we successful set up the pancreatitis-associate lung injury model by injection of glycodeoxycholic acid into pancreatic duct and i.v. injection of Cerulein. This injury model accompanied with inflammatory response, white cell activation, cytokine release, respiratory burst and inducible nitric oxide synthase expression. Bedsides, acute pancreatitis also induced obstructive and/or restrictive ventilatory insufficiency. In this study we will study the systemic inflammation response syndrome (SIRS) in pancreatitis-associated lung injury, kinetic changes of oxygen radicals, nitric oxide, cytokines of IL-1, IL-6 and TNF-α will be measured. The mRNA and protein expression of iNOS, TNF-α, COX-2 will also be analyzed. The effects of pharmacologic interventions on the SIRS by different doses of isoflavones will also be studied. Real time polymerase chain reaction and Western blot will be utilized to analyze mRNA and protein expression of the inflammatory mediators. Through this study, we will understand the effects of isoflavones on the pancreatitis-associated lung injury and the possible protective mechanisms involved.