• 計畫中文名稱	建立體外腦內皮細胞和體內動物腦損傷模式以評估健康食品對腦血管功能的保健功效		
• 計畫英文名稱	Establishing the in vitro cerebral endothelial cells and in vivo brain-injury models to evaluate the		
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• 中文關鍵字	健康食品；腦血管功能；血腦障蔽；腦內皮細胞；保健功效；；；		
• 英文關鍵字	Health food；Cerebrovascular functions；Blood-brain barrier；Cerebral endothelial cells；Protective effects；；；		
• 中文摘要	隨著經濟的發展與生活水準的提高，現代人日益重視養身之道，除了日常飲食之外，強調各種保健功效的健康食品(health food)亦陸續出現在市面上。然而許多健康食品所強調的保健功效，常缺乏相關明確的科學數據做爲輔證。爲提供消費者對於健康食品保健功效的科學憑據，以及產業界對於健康食品保健功效多樣化的訴求，開發健康食品可能具有的不同保健功效的評估項目與方法實屬重要。近幾年以來，因腦部相關疾病而死亡者，一直高居國人十大死亡之因的前幾名。腦血管(cerebrovessels)中的血腦障壁(blood-brain barrier; BBB)是維持中樞神經系統恆定的重要構造，一旦 BBB 受到破壞，大量的水份或有害物質將進入腦組織造成嚴重且不可逆的傷害。腦內皮細胞(cerebral endothelial cells)是組成腦血管 BBB 的主要組成細胞，其爲一種特化的內皮細胞，會於腦血管內排列成一緊密的構造(tight junction)，並能維持腦內外血流的恆定，以及阻擋血液中的有害物質進入腦組織。當腦內皮細胞受到傷害時，BBB 的功能將會受損。所以，保護腦內皮細胞免於血液中有害物質的傷害，當能降低 BBB 的損傷和腦疾病的發生率。腦血管發生缺血-再灌流(ischemia-reperfusion)現象，常會造成腦血管和神經組織因氧化壓力(oxidative stress)的升高而發生損傷。本實驗室已成功自 ICR 小鼠(ICR mice)腦微血管中分離出腦內皮細胞，並加以證實其會被氧化態低密度脂蛋白(oxidized low-density lipoprotein)所誘導發生的活氧物質所傷害(Chen et al., 2007)。而在我們的先期實驗中更進一步發現，健康食品白藜蘆醇(resveratrol)可以保護腦內皮細胞免於氧化壓力的破壞。所以，本研究計劃將嘗試建立 in vitro 腦內皮細胞模式和 in vivo 動物腦損傷模式，以探討健康食品是否可以保護腦血管 BBB 功能免於氧化壓力所造成的傷害。在 in vitro 部份，將以分離出的腦內皮細胞爲研究模式，並分別以氧化物 donors 包括 menadione (superoxide anion donor)和 t-BHP(hydroxyl radical donor)處理細胞，模擬細胞受到缺血-再灌流的損傷，以研究健康食品如白藜蘆醇對腦內皮細胞存活率(viability)和		

	形成 tight junction 功能，是否具有保健功效。當在 in vitro 得到保健功效的證實後，將進行建立 in vivo 驗證模式。先以健康食品如白藜蘆醇餵食實驗動物 ICR mice 後， 施以側腦室注射(intracerebroventricular injection; ICV injection)活氧物質 donors (menadione and t-BHP)，使腦組織受到氧化壓力的傷害，再由靜脈注射 Even blue 後將動物犧牲，並評估 Even blue 在腦組織的分部情形，以及腦血管 tight junction 結構的完整性，以評估該健康食品對腦血管 BBB 功能的保護功效。經由此計畫的執行，將可建立健康食品對腦血管功能保健功效的 in vitro 和 in vivo 評估方法，並能將其應用在相關產品之可行性及應用性之評估，以利相關健康食品的開發。
• 英文摘要	Accompanying with the development of economy, the modern people take much more attention at how to keep their health. Thus, more and more health food has been developed. Meanwhile, there is so much health food, which is not evaluated and validated by scientific methods. To meet the requirements from the consumers and the bio-companies about the protective effects of health food, establishing the evaluation methods are needed. In the passed years, the cerebral disease is usually the major cause of death in Taiwan. The blood-brain barrier (BBB) is a specified tissue in cerebrovessels, which forms a tight junction to maintain the homeostasis of blood flow across the barrier and to protect brain tissues against damages induced by the toxicants in the blood. Cerebral endothelial cells are the major components in BBB. Injuries in cerebral endothelial cells can lead to BBB dysfunction and brain damage. Ischemia-reperfusion, commonly occurring in cerebral vessels, can augment the levels of reactive oxygen species and induce vascular and brain dysfunction. In our lab, we have successfully isolated cerebral endothelial cells from the cerebral microvessels of ICR mice and demonstrated that oxidized low-density lipoprotein can enhance oxidative stress in the cells and induce apoptotic insults (Chen et al., 2007). Our further study showed that resveratrol can protect cerebral endothelial cells from oxidized low-density lipoprotein-induced oxidative insults. Therefore, in this study, we try to establish in vitro and in vivo models to evaluate the protective effects of health food such as resveratrol on cerebrovascular functions, especially in BBB. At first, we will use the in vitro model of cerebral endothelial cells to test the protective effects of health food against reactive oxygen species-induced insults to cell viability and tight junction permeability. Then, we will establish in vivo animal brain-injury model (ICR mice) to evaluate the protective effects of health food on the integrity of BBB tight junction and brain damage in rats intracerebroventricularly injected with menadione (superoide anion donor) and t-BHP (hydroxyl radical donor). After performing this study, we expect to have established in vitro and in vivo models to evaluate the protective effects of health food on cerebrovascular functions.