• 計畫中文名稱	應用幹原細胞探討中藥對人體組織修復再生功能之基因體研究(I)		
• 計畫英文名稱	A Pharmacogenomics Evaluation of Chinese Herb's Function Using Human Tissue Stem/Progenitor Cells		
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• 研究人員	施子弼		
• 中文關鍵字	人體組織幹/母細胞；中藥天然藥物；組織再生修復；造血及神經組織；重組基因轉殖；藥物基因體		
• 英文關鍵字	Human Tissue Stem/Progenitor Cells；Chinese Herbs；Tissue Regeneration；Hematopoietic and Neuron Tissue；Recombinate Gene Transfection；Pharmacogenomics		
• 中文摘要	目前一些中藥在臨床上對人體病害組織修復或再生療效已被認定，但其作用成分及藥理大都尚未明瞭。近年來幹原細胞的研究顯示體幹/母細胞具多樣性組織修復再生功能。本計畫之主旨在於應用人體組織幹/母細胞鑑定天然中藥有效成分，並應用幹細胞的分子生物實驗評估藥物對其基因體效用及毒性影響。具體上本計劃將針對與造血、筋骨及神經組織具修復相關效能中藥中萃取物，應用人體造血、間質及神經幹/母細胞分化培養中鑑定其藥效，並進而由培養分化中之細胞族群中探討其對人體組織幹/母細胞基因體影響之藥理。 本實驗室已初步利用新生兒臍帶血中分離之造血幹/母細胞，評估數種中藥萃取物對於造血細胞之增殖與分化中是否有促進血球系，如紅血球、巨噬細胞、顆粒性細胞，之群落生成等進行分析。初步發現某些中藥成分的確具有促進細胞生長之功能，但對於其是否具有影響其他組織幹/前驅細胞之分化功能目前尚未清楚。我們主要將探討中藥對存於各組織，如頭皮、骨髓、脂肪之表皮或間質幹/母細胞之分化研究。爲了進一步探討中藥對組織幹/母細胞基因體作用之藥理，我們初期將建立造血性幹/母細胞、頭皮表皮幹細胞、骨髓及脂肪間質幹細胞(mesenchymal stem cells)之體外培養系統，利用重組基因轉殖造血及神經相關細胞之生長因子來促進幹細胞神經組織生長與分化。初代培養(primary culture)的各組織細胞之分化初、中、後期之基因表達的細胞表面標記抗原及功能蛋白，將利用螢光免疫染色(immuno-florecent staining)、西方墨點法(Western blotting)與北方墨點法(Northern blotting)等作定量、定性分析。藥物對於不同組織幹/母細胞之細胞週期與增生、分化調控機轉亦將進一步作基因蛋白體分析探討。另外，我們亦將使用免疫缺陷鼠(NOD/SCID mice)，來檢測天然藥物是否於活體中仍具有促進特定（多重）組織分化與局部損傷修復之功效。本計劃之目標（一）：補氣、血及壯筋骨中藥之有效成分鑑定；（二）探討中藥對組織幹/母細胞分化作用之基因體研究。 本研究之完成將提供中藥醫療與人體組織幹細胞潛能應用之一結合橋樑，並透過人體初級細胞培		

	養及動物模型實驗，增加中藥天然物對於早期幹細胞功能影響的真正了解，並對中藥之藥理以現代化科技加以證實，以助中藥之國際化發展。
• 英文摘要	Some Chinese herbs for human disease, tissue repair and regernation have been identified in the past years, yet most of their effective components and action mechanisms remain under explored. Recent progresses on stem cell research have shown the tissue stem/ progenitor cells compose multipotency on tissue regeneration and repair. The goal of this study is to identify effective components of selected Chinese herbs by in vitro culture of human tissue/ progenitors and to evaluate their mediated genomic influences by molecular biology studies. This study will focused on the use of tissue Tem/ progenitor cells for herb screening on cell differentiation and proliferation of human hematopoietic, bone and neuron tissue formation. We will also investigate the genomic changes and molecular mechanism caused by drug treatment in established primary culture systems. We have previously evaluated the effect of several Chinese herb extracts on lineage specific cell growth (such as erythrocyte, marchrophage and granulocytes) and colony formation increase of cord blood hematopoietic stem/ progenitor cells by in vitro culture.This preliminary study, we found some herb extracts could changes the hematopoietic colony formation in size and/or number. However, the influences on cell growth or differentiation of other tissue stem/ progenitor cells were still der investigation. We propose to study the functional effects of Chinese herb components on cell growth or differentiation of in vitro cultured human cord blood HSCs, bone marrow MSCs, mesenchymal-like fat tissue derived PLAs and scalp epithelia progenitor cells. We will also transfect viral constructs carrying hematopoietic or neuron growth related genes to establish a stable cell line for long-term culture of hematopoiesis or neuron growth, which will benefit our drug screening and basic pharmaceutical studies. We will examine the early, middle and late stage specific surface antigen or marker expressions for cell differentiation cultures by immuno-florecent staining. Northern blotting and Western blotting will also be used for gene and protein expressional quantification. The molecular mechanism of drug induced gene expression changes will be studied by cDNA microarry and proteomic studies. On the other hand, we will use the immune deficient NOD/SCID mice model to evaluate the drug functions according to the primary culture results. We will use this animal model to evaluate their multipotent reconstitution in vivo and their tissue repair or regeneration potentials. The specific aims includes I) Extraction and evaluation of effective components of Chinese herbs in supporting hematopoiesis, immunology and bone tissue formation. II) Genomic studies of the Chinese herbs for differentiation of tissue stem/ progenitor cells. The success of our study will provide a linkage between therapeutically herbs and stem cell biology in clinical applications. We are therefore capable of getting better insight into the influences of nature compounds on tissue stem cells by primary culture system and animal study. Modern technologies applied in this study for functional evaluations and mechanical studies will advantage the internationalization development of Chinese herbs.