

• 計畫中文名稱	補益類中藥保護幹細胞及影響癌病患腫瘤細胞之免疫相關之功能基因體研究(2-1)		
• 計畫英文名稱	A Functional Genomic Study of Some Bu-Yi Chinese Herbs? Pharmacologic Effects on Protection of Tissue Stem/Progenitor Cells and Immuno-Modulation of Patient?S Cancer Cells (2-1)		
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• 執行機構	台北醫學大學細胞及分子生物研究所		
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• 研究領域	基礎醫學類, 生物技術, 生物科學類		
• 研究人員	施子弼		
• 中文關鍵字	癌症細胞之免疫調控因子；人體組織幹/母細胞；補益類中藥方劑；；；；		
• 英文關鍵字	Cancer cell’s immuno-modulation；Human tissue stem/progenitor cell；Bu-Chi Chinese medicine；；；；		
• 中文摘要	在臨床上，傳統中藥對人體疾病已有廣泛應用，而在許多重大疾病的西醫治療上，中藥亦具有輔助效果，例如目前已知，中藥對於輔助癌症化療後的生理系統恢復，效果明顯。然而到目前為止，對於中藥在細胞組織生理的影響，了解仍非常有限。而近年來，幹細胞的研究已顯示成體幹細胞具多組織修復再生功能，小自身體日常組織細胞之更新，大至提供個體受傷之組織再生功能，都由幹細胞主導。在人體生理恢復過程中，幹細胞之增殖分化調節顯得格外重要，特別是在組織細胞面對環境壓力時，其幹細胞更是扮演著重要角色。本計畫旨在以系統分子醫學的角度，應用藥物基因體醫學之分析，探討並比較補益類中藥對於正常組織幹原細胞與腫瘤細胞的細胞生理及分子基因層面之影響，並藉而建立補益類中藥對人體組織幹原細胞基因體表達功能影響之資訊。在過去的研究中，本實驗室已建立數種人體組織幹細胞分離鑑定及培養之平台—從骨髓、脂肪、臍帶血、包皮、頭皮、羊膜等組織來源分離取得幹細胞，有效率地提供各組織幹細胞之生長、分化及分析檢測。已運用此細胞技術平台於中藥研究之計劃目標分類如下;(1)針對單方藥材如黃耆、西洋參、三七、柴胡、紅景天及複方中藥如人蔘養榮湯、十全大補湯及生脈散等活血化瘀藥材，分析此類中藥對於促進造血及間質幹細胞生長及分化等細胞活性之藥效分析。(2) 針對單方藥材如黃耆、西洋參、三七、柴胡、紅景天，何首烏及複方中藥如補中益氣湯、四物湯及生脈散等藥材。分析此類中藥對於造血及間質幹細胞受癌症醫療傷害的保護或修復性藥理基因體及蛋白體醫學之分析。本計畫擬繼續探討補益類防護人體幹細胞分子藥理，同時亦將平行比對分析補益類中藥對癌組織細胞之影響。本計劃擬針對補中益氣湯，或生脈散及四物湯等複方中藥，探討比較上述藥方作用於正常幹原細胞(例如:間質幹細胞及纖維母細胞)與腫瘤細胞(例如:乳癌或前列腺癌的初代細胞或細胞株)之細胞生理及分子基因層面之影響。具體上將利用細胞激素蛋白微陣列或酵素連結免疫吸附分析法探討補中益氣湯，或生脈散影響前		

發炎因子、細胞激素、趨化激素、介白素及細胞生長因子等蛋白表達之分析以瞭解乳癌腫瘤細胞附著分子，細胞間交互作用分子及受體等蛋白表達之功能基因體變化影響。將同時也利用螢光免疫染色、RT-PCR、及基因晶片等技術，探討致癌基因、腫瘤抑制基因、細胞凋亡基因、前驅細胞早期基因及細胞週期基因等基因體之變化。並整合基因晶片資訊完成系統分析，藉此建立評估中藥對於正常及惡性體幹細胞生理與功能影響之資訊。本研究延續之前探討補益類中藥於癌症醫療中保護人體正常幹細胞之系統分析，得知部份補益類對人體幹細胞之正面防護效用。本計畫擬將分二年時間，針對女性乳癌及男性前列腺癌為例。深入探討補益類防護人體幹細胞分子藥理之同時對癌組織細胞在中藥輔助醫療之可能影響。期望能瞭解中藥補益類在癌症醫療輔助效益之系統生物學研究。本計畫如能順利執行，將對中藥在個體幹細胞生理調節上有更完整了解，提供中藥醫療作用於人體組織幹細胞之分子生理系統效用評估範例，並提供中藥應用於生理維護與組織修復機制及效用提供更有效之論證。建立一現代化中藥藥理鑑定的新方向，以助中藥之國際化發展。

The objective of this proposal study is to investigate and compare the molecular pharmacologic effects of the traditional chinese Bu-Yi medicine on normal stem cells and cancer cells in cancer patients. At mean time, to initiate and collect the molecular data for establishing a pharmacologic informatics bank of Chinese drugs effects on human tissue stem cell and malignant cells. We have previously established several human tissue stem/progenitor cell primary cultures for molecular studies on their lineage specific differentiation potentials. In vitro cell lineage specific differentiation culture studies on hematopoietic stem/ progenitor cells (peripheral blood, umbilical cord blood, and fetal liver) and on mesenchymal stem/progenitor cells derived from various tissues (bone marrow, peripheral blood, fat, scalp, foreskin, and amniotic membrane tissue) have been examining. We have also initiated a series of test on some selected chinese drugs such as Anax astragali, Anax quinoquefolius, Anax notoginseng, Lueureum chinese, Anax kirilowii and some Bu-Yi prescriptions, and analyzing their influences on hematopoietic erythroid maturation, mesenchymal tissue cell differentiations and proliferation for determining their tissue protection and repairing functions. We have also analyzed these Bu-Yi Chinese herb's pharmacologic effect on protection and repair of tissue stem/progenitor during cancer therapy in functional genomic and proteomic level. In this proposal study we plan to pursue a completely study focusing on investigating the molecular pharmacology of certain Bu-Yi prescription, which are well known their components in promoting human body physiological performance by the neutralizing and tonifying tissue organ cells. In this study, normal stem cells (e.g. hematopoietic, mesenchymal stem cells and fibroblast) and primary cancer cells (e.g. breast cancer and prostate cancer) will be simultaneously investigated to evaluate application of these herb's effects on adjuvant cancer therapy. We will focusing on study the pharmagenomic mechanism of effective Bu-Yi prescriptions by comparison and substractional analyses of gene expression and protein profile changes under influences of Bu-Yi drugs. The drug effect on the molecular basis of proliferation and differential patterns in the primary culture of hematopoietic and mesenchymal stem/progenitor cells will be qualitatively and quantitatively evaluated by cytokine protein array, immunofluorescence stain, and cDNA expression microarray. Specifically, we will also focus on the the expression of oncogenes, tumor suppressor genes, apoptotic genes, early genes, cell adhesion/interaction molecules, proinflammatory factor, cytokines and growth factors . After systemic integration with bioinformations from results of protein array and cDNA microarray. These informations will be organized and served as a pharmacogenomic evaluation reference for application of Chinese herbs on promoting normal stem cell and eliminating cancer cell in cancer patients. We have analyzed these Bu-Yi Chinese herbs' pharmacologic effect on protection and repair of tissue stem/progenitor during cancer therapy in functional genomic and proteomic level. This proposal will further focus on the distinct pharmacologic effects of Bu-Yi herbs on human normal and malignant cells. Upon completions of the

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	proposal study will enhance our better insights into the Chinese drug prescription function by means of the molecular pharmacological understanding on their influences to the tissue stem/progenitor cells and tumor cells. The successful of this study may show the feasibility of using tissue progenitor based primary cell culture drug testing system as an additional useful method for Chinese drug analysis which will be also aid to the
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