• 系統編號	RN9511-1528
• 計畫中文名稱	探討蛋白多醣對誘導小鼠胚胎幹細胞分化爲軟骨細胞之影響及作用機轉
• 計畫英文名稱	Studies of the Effect of Proteoglycans on the Chondrogenic Differentiation of Clonal Mouse Embryonic Cell
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC93-2320-B038-035
• 執行機構	臺北醫學大學生物醫學材料研究所
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• 研究人員	楊維中; 黃德揚 Yang, Wei-Chung; Huang,Teh-Yang
• 中文關鍵字	--
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• 中文摘要	現代生物醫學材料及組織工程領域發展的重點, 包括皮膚, 骨組織, 及神經組織的再生與移植, 及修復癌症或糖尿病患者身上難以癒合的傷口等。細胞外間質(extracellularmatrix, ECM), 誘導因子, 及未分化幹細胞, 被認爲是研究組織工程技術探討組織修補及移植所必須考慮之三要素。蛋白多醣(proteoglycan)由一條或多條直鏈粘多糖(glycosaminoglycan, GAG)，如硫化軟骨膠(chondritin sulfate), 硫化肝素 heparin sulfate)等及一核心蛋白(core protein)，共同組合而成, 存在於細胞外間質中與膠原蛋白(collagen), 纖維連接蛋白素(fibronectin)，纖維蛋白原(fibrinogen), 並列爲結締組織中之主要成分。細胞外間質的組成, 往往影響細胞的生長、形態、及分化。近年來膠原蛋白已應用爲促進骨組織再生之生物材料, 被認爲可促進細胞附著與增生。如以蛋白多醣中之粘多糖成分如硫化軟骨膠與膠原蛋白並用, 比單獨使用膠原蛋白能更加促進細胞的活化及再生。而一些研究亦證實蛋白多醣又比其組成分之一粘多糖，更能符合生物環境促進組織再生。因其不但能與其他細胞間質分子行交互作用，提供細胞附著及生長所需的生物物理特性，且可與周邊細胞組織分泌出的生長因子及細胞膜蛋白行交互作用，調節細胞內外之訊息傳遞，提供組織再生及修復工程中所需的化學性質。但是，蛋白多醣之萃取分析及製備技術，需要專業及有經驗之研究人員及設備方可施行。本計劃主持人在美具備多年研究蛋白多醣之經驗並於回國後積極建立製備蛋白多醣及醣質分析實驗室及設備並與國內外實驗室合作, 於先期研究已發現蛋白多醣在誘導幹細胞分化確有比傳統使用其成分之一,粘多糖更具生物活性也更能製造接近體內細胞外間質之環境。此初步研究成果論文已被第七屆世界生物材料大會接受,將於2004 年於澳洲雪梨大會中發表。本計劃將以完整的蛋白多醣取代單純的粘多糖爲研究對象，分析及研究其誘發未分化幹細胞株成軟骨細胞的效能並探討蛋白多醣誘發軟骨細胞分化之機轉。此計畫將有助於研發促進關節軟骨組織再生及修補之生物醫學材料, 並對於以幹細胞治療退化性關節炎之理論基礎作更深入之建立與探討。.

- 英文摘要

A perfect work for tissue engineering is determined by three key factors, extracellular matrix (ECM), growth factors, and the stem cells. Modern biomaterials for tissue repair must consider the biocompatibility, bioresorbability/biodegradability, and bioactivity. Proteoglycan consisting of a core protein to which one or more linear polysaccharide, glycosaminoglycan (GAG) is covalently attached. Proteoglycans play a central role in ECM remodeling and tissue repair through their bindings of either core protein or GAG with the other matrix molecules, growth factors, cytokines, adhesion receptors, enzymes, and enzyme inhibitors in the extracellular matrix. The designed material mimic the ECM will provide physical and chemical stimuli for tissue regeneration. Previous reports have shown that the GAG, by itself, can be used as a carrier material for the transplant engineering of cartilage-like tissue. However, the GAG alone may not fully replace the activity of the intact proteoglycan including the core protein and the GAG provides both the structural and biochemical effect on reconstitution of the complicate matrix assembly for tissue repair and remodeling. Preliminary study from our laboratory has extracted and purified various proteoglycans and exaimed their inductive activity on the chondrogenic cells differentiation to the chondrocytes, suggesting that the intact proteoglycan may cooperate with the chondrogenic growth factors and regulate the chondrogenesis. Part of the data will be present in the 7thWorld Biomaterials Congress, Sydney, Australia in 2004. This research aims to characterize the effect of proteoglycans on induction of chondrogenesis using an embryonic stem cell derived ATDC5 cells as a research model. The induction mechanism of the proteoglycan in chondrogenesis will be also studied. The obtained information will be helpful on developing a biomimic material for cartilage repair and for better understanding of the stem cell therapy in cartilage repair. The specific aims are listed as follows, I. Extraction, purification, and characterization of various proteoglycans from tissues. II. Study the induction of proteoglycans on chondrogenesis of ATDC5 cells. III. Identifications of the pathway of typical proteoglycan induced chondrogenesis