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• 計畫中文名稱	研發新型可注射性骨架合併間質幹細胞的混合物重建顱顏骨的缺損		
• 計畫英文名稱	Development of New Injectable Bone Scaffold Combination with Mesenchymal Stem Cell on Bone Regeneration for Craniofacial Surgery		
• 主管機關	行政院國家科學委員會	• 計畫編號	NSC96-2314-B182A-076-MY3
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• 研究人員	陳建宗； CHEN CHIEN-TZUNG；		
• 中文關鍵字	間葉幹細胞；纖維素膠；聚甲殼糖；玻尿酸；多甘醇酸；多糖乳酸		
• 英文關鍵字	mesenchymal stem cell；fibrin glue；Chitosan；polyglycolic acid；polylacticacid		
• 中文摘要	外傷後的骨缺損處的骨再生是骨科及顏面外科常見的問題尤其是腫瘤切除或嚴重外傷後導致大量的骨缺損. 傳統上常需要自體的骨移植以達到美觀的目的及功能回復，然而這些自體移植骨有不可預期的吸收率及產生供應區的 morbidity. 除了自體骨移植以外其他選擇包括異種異體， 同種異體骨移植，或是生物材質.近年來生物材質特別受到注意因其可避免免疫排斥或是感染某些傳染疾病的可能性. 這種生物材質刻可當作骨架具有骨傳導能力. 為了避免手術帶來更多的創傷，可注射性骨架搭載自體骨並結合內視鏡手術的方法在未來是需要發展的.液態性基質不像傳統多孔性陶製的骨架具有易塑型的優點，相較於傳統手術也有不具侵入性的優勢，除此之外它可搭載骨再生激素進而促進骨生長.本實驗的目的是要（1）發展新型可注射性骨架例如聚甲殼素及玻尿酸聚合物,多甘醇酸及多糖乳酸聚合物,和自體纖維素膠（2）了解這些聚合物能結合間質幹細胞是否能促使骨再生及癒合及比較不同可注射性骨架對於骨再生能力的優缺點(3) 測試不同可注射性骨架合併間質幹細胞，將來在顱顏手術運用的可能性本計畫計利用裸鼠，兔及豬為不同時期的實驗模型. 鼠的幹細胞由大腿骨髓抽取而兔及豬則從腸骨骨髓抽取約 10 ml 含間葉幹細胞的骨髓液，並將其分離出來在室溫下培養，當間葉幹細胞逐漸增生倍增時再以培養骨細胞之培養液誘導幹細胞分化成骨原使先驅細胞,當細胞濃度達到每毫升千萬個細胞，再與纖維蛋白原及凝血酵素混合成幹細胞/纖維素膠的混合液. 或是聚甲殼素及玻尿酸聚合物或是多甘醇酸及多糖乳酸聚合物以注射方式打入裸鼠皮下,兔子的顱骨骨缺損處，豬的頭蓋骨缺損處等三種不同實驗模型.結果發現最適合幹細胞的材料還是人體自行合成的組織膠,其他兩種化學合成的溫敏感水膠雖在小動物實驗也有骨修復的作用,但大型動物實驗卻不如組織膠好.經由此實驗我們建議以自體組織膠結合幹細胞可以從事臨床骨修復的試驗.也可進一步結合市售人工骨進行更大範圍的骨修復實驗.		
• 英文摘要	The regeneration of bone defect for the repair of fracture or bone defect is a common problem in orthopedic and craniomaxillofacial surgeons. Traditionally, autogenous materials are the gold standard to induced bony regeneration. However, they have some disadvantages that limit their use such as donor site morbidity, variable degree of resorption and the need for a secondary surgery exposure. The alternative to the use of autogenous graft are xenograft , or allograft and biomaterials. The biomaterials are particular interesting and popular in craniofacial surgery. To minimize surgical trauma, an injectable scaffold, conveying autogenous bone to craniofacial skeleton with combination of endoscopic surgery was needed to be developed to fulfill such requirement. A liquid support matrix that polymerized to a gel would be shaped easily and molded for custom reconstruction or augmentation, and much less invasive without an open surgical procedure.Besides, a liquid material may incorporate various therapeutic agents such as bone morphogenetic proteins to enhance bone regeneration. The aim of this study was to develop several new injectable scaffold such as chitosan-hyaluronic acid hydrogel, polylactide/polyglycolide (PLA /PGA) copolymer and autogenous fibrin glue. Secondly, this study tries to understand if these copolymer hydrogel have potential combination with stem cell to facilitate osteogenic cell proliferation and generate new bone both in vitro and in vivo. Furthermore, this technique has potential to be applied to reconstruct the bone defect on craniofacial surgery in future. Rat mesenchymal cell were harvested from the femur bone marrow and rabbit and pig MSCs were aspirated from the ilium. The cells were expanded and induced into osteoprogenitor cell with osteogenic cell culture medium. The cells were mixed with different new scaffold such as chitosan-hyaluronic acid hydrogel, polylactide/polyglycolide (PLA /PGA) copolymer and autogenous fibrin glue as experimental groups. The different admixtures were injected into rat dorsum, rabbit skull defect and pig skull bone defect to the ability of bone regeneration. The results showed that in the small animal study, the two synthetic materials all showed good bone regeneration. However, in the large pig animal, we can find the BMSCs regenerate better in nature fibrin glue than in synthetic materials. We recommended using natural fibrin glue as BMSCs carrier for clinical study and larger defect study.		