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• 中文摘要

近年來小腸移植已成為小腸衰竭病患之治療方式之一。台灣每年有近百位病患因短腸綜合病症或小腸衰竭，需依賴長期或居家全靜脈營養存活，這些病患很可能需靠小腸移植，才能避免或治療長期全靜脈營養所引發之嚴重併發症，並改善其生活品質。因小腸再生是小腸移植成功之重要因素之一，如何促進腸道大量切除及小腸移植後之小腸再生，已成為醫界最重要的研究課題之一。小腸移植必經缺血/再充血損傷，以及可能有排斥作用的傷害，均會造成小腸移植的失敗，而缺血/再充血損傷及排斥作用，均會引發腸道細胞基因表現之改變。為了提升小腸移植後，移植腸道及病患之存活率，篩檢出腸道大量切除、缺血/再充血損傷、以及排斥作用等之正向及負向調控基因，並研發其基因調控路徑，進行基因治療以促進小腸再生，已是必要方向之一。然而，至今尚無相關大量篩檢基因表現及基因調控路徑之報告。本計劃以重約 15 公斤之雄性迷你豬動物模式作研究。豬體經小腸大量切除（第一年）、小腸移植加抗排斥藥劑 FK506 等藥物（第二年）、小腸移植未加任何抗排斥藥劑（第三年）及小腸造瘻口等術式，於術前及術後第 1、2、3、5、7 天，及第 2、3、4、8、12 週採血及小腸組織作檢測。關鍵基因之定義為基因表現之變化，必需與小腸再生所有指標之變化平行，且其基因表現，需超過手術前之兩倍，或低於手術前之二分之一。本研究初步成果為：(1) 扣除手術後上腸繫膜動脈血栓引發小腸移植失敗三次，共七次小腸移植成功，其中一隻嚴重排斥於術後 7 天死亡，其他存活 24 天至 199 天(犧牲解剖)，並無小腸滲漏、粘黏、或腸造瘻口併發症等；(2)以修正 Paul-Mikuliz 迴腸造口術方式可方便迴腸(包括原腸段及移植段)之組織取樣檢查；(3)共有 17 種基因（11 種為正向調控，6 種為負向調控）很可能為關鍵基因。這些基因究竟為腸道大量切除、小腸移植之缺血/再充血損傷、或排斥作用所引發之基因表現差異，則尚待進一步研究查証。

• 英文摘要

Primary dysfunction of small intestinal grafts induced by I/R injury and rejection is still one of the main obstacles in clinical ITx. Gene expression profile of small bowel graft may change a lot after I/R injury and rejection. For improving the survival rate of graft and patient after ITx, detecting the up-regulated and down-regulated key genes, and conducting gene therapy to stimulate regeneration process should be essential in a patient with SBS after MR, I/R injury or rejection during ITx. However, the key genes and gene-control pathways for IReg among the effects of MR, I/R injury, and rejection is still unclear. Male minipigs weighing around 15kg were used as subject. 70% MR (1st year), ITx with FK506 and other immunosuppressant (2nd year), and ITx without any immunosuppressant agents (3rd year) will be performed. The blood sample and intestinal specimen from enterostoma will be taken on day 0, 1, 2, 3, 5, 7, and week 2, 3, 4, 8, 12, after surgical intervention. We define the key genes in the gene-control mechanism of MR as follows: the variations of key genes expressions should be: (1) parallel to all regeneration indicators in time sequence after 70% MR; (2) the changes are more than twice (up-regulated) or less than half (down-regulated) of preoperative level. In the first year study, we found that: (1) The early 10 pairs of ITx, 3 pairs died of failed technique due to superial mesenteric artery thrombosis. In the 7 successful technique ITx, one died of severe rejection, other survived for 24 days to 199 days (sacrificed by autopsy for sample study). There were no complications such as anastomotic leakage, adhesion ileus, or ileostoma failure; (2) Modified Paul-Mikuliz ileostomy enable us to obtain tissue samples of both the graft and the native ileum without disturbing the natural bowel conduit; (3) Under the definition of key genes expressions which should be parallel to all IReg indicators in time sequence after MR, and the variations should be more than twice or less than half of preresection gene levels, we have preliminarily demonstrated seventeen genes detected by cDNA microarray to be the possible key genes in the gene-control pathway during IReg after MR and ITx. Eleven are up-regulated and six are down-regulated genes. However, the differences of these genes changes between the effects of MR, I/R injury, and rejection of ITx, and the true roles in the gene-control mechanism during IReg after MR and ITx is still unclear.