• 系統編號	RN9611-4942
• 計畫中文名稱	幹細胞基因轉植與其在腫瘤診斷與治之動物模式研究(II)
• 計畫英文名稱	Stem Cell with Non-Invasive Gene-Assisted Pet Imaging for Cancer Diagnosis and Therapeutic Application (II)
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC95-NU-7038-001
• 執行機構	台北醫學大學生物醫學材料研究所
• 本期期間	9501 ~ 9512
• 報告頁數	8 頁
• 使用語言	中文
• 研究人員	鄧文炳; 洪士杰 Deng, Win-Ping; Hung, Shih-Chieh
• 中文關鍵字	肺部轉移腫瘤模式; 非侵入性造影; 第一型泡疹病毒胸腺嘧啶激脢基因; 人類間葉幹細胞
• 英文關鍵字	Lung metastases model; Noninvasive imaging; Herpes simplex virus thymidine kinase; Human mesenchymal stem cell; [131I]FIAU
• 中文摘要	本計畫爲兩年期計畫，第一年我們利用帶有第一型泡疹病毒胸腺嘧啶激脢的人類間葉幹細胞，結合微正子電腦斷層掃描非侵入性的監測其對於初期微小腫瘤的趨癌能力。由於在我們之前的實驗中已建立了表現有第一型泡疹病毒胸腺嘧啶激脢基因異種皮移植腫瘤的實驗動物模式，並且已經證明可應用[131I]FIAU 和非侵入性造影於監測此動物模式進行的癌症基因治療。所以在本年度的實驗中，我們應用相同的動物模式有效的以非侵入性的方式去監測肺部轉移模式，觀察其於不同時間點中，治療基因表現的位置、強度和持續時間。接著，我們利用非侵入性的造影技術監測結合人類間葉幹細胞和蛋白質疫苗所進行的癌症療法。爲了增加肺部轉移腫瘤的可偵測性，所以我們經由血管內送入表現有第一型泡疹病毒胸腺嘧啶激脢基因的 NG4TL4 纖維肉瘤細胞（NG4TL4-TK），以建立一個由血液產生的老鼠肺部轉移腫瘤實驗模式。利用單光子放射電腦斷層掃描和[131I]FIAU 非侵入性的監測，以評估肺部轉移腫瘤病灶處的生長。我們將 NG4TL4 纖維肉瘤細胞（NG4TL4-TK）種於老鼠的右腿皮下，利用人類間葉幹細胞的趨癌特性，結合蛋白質疫苗進行腫瘤治療，並利用分子造影技術進行非侵入性的監測。研究結果顯示經由靜脈注射利用[131I]FIAU 放射標定的 NG4TL4 細胞所建立的肺部轉移腫瘤模式，最早可於注射 24 小時後成功的被偵測到，接著於第 10 天利用靜脈注射[131I]FIAU 的長時間監測中仍可偵測到。而利用結合人類間葉幹細胞和蛋白質疫苗治療由老鼠肉瘤細胞形成的腫瘤的實驗中，平面影像和腫瘤生長速率分析的結果，老鼠右腿的訊號有明顯的減弱，腫瘤的生長也明顯的受到抑制。經由實驗結果，我們推斷此種活體造影方式將有助於未來肺部轉移腫瘤模式的研究及利用幹細胞趨癌特性來研發新的抗癌和抗癌症轉移的治療。
• 英文摘要	This study is a two-year project. First year, we utilized HSV1-tk-expressing human mesenchymal stem cell to target microscopic tumors and noninvasively monitored the homing ability of human mesenchymal stem cell with micro Positron Emission Tomography (.mu.PET). We have previously employed

[131I]FIAU and demonstrated the applicability of noninvasive imaging for monitoring cancer gene therapy in an experimental animal model of HSV1-tk-expressing tumor xenografts. In this year, we have now used the same animal model to effectively and noninvasively monitor the location, magnitude, and duration of therapeutic gene expression over time for lung metastases model. Next, we utilized noninvasive imaging techinque to monitor cancer treatment combined with mesenchymal stem cell and fusion protein vaccine. To improve the detectablility of lung metastases, an experimental blood-borne lung metastasis model in mice was established using intraveonously administered HSV1-tk-expressing NG4TL4 fibrosarcoma cells (NG4TL4-TK). The efficacy of noninvasively monitoring the 3 sites of development of lung metastatic lesions were assessed by SPECT imaging with [131I]FIAU. We subcutaneously inoculated HSV1-tk-expressing NG4TL4 fibrosarcoma cells (NG4TL4-TK) to the right flank of mice. We took advantage of the homing ability of mesenchymal stem cell combined with fusion protein vaccine, to noninvasively monitor and the treatment. The results of this study showed that lung metastases model of NG4TL4-TK cells could be successfully detected as early as 24 hours after i.v. injection of tumor cells radiolabeled with [131I]FIAU, and also subsequently detected by extended monitoring with the i.v. injection of [131I]FIAU on day 10. The combined treatment of mesenchymal stem cell and fusion protein vaccine by this study demostreted the eradication of murine sarcoma-derived tumor. The results of planar imaging and tumor growth rate analysis showed a significant reduction in signal observed at the right flank of mice ndicating the inhibition of tumor growth. We conclude that this in vivo imaging approach will be useful for future studies of lung metastases model and for the assessment of novel anti-cancer and anti-metastatic therapies.