• 系統編號	RN9406-0546
• 計畫中文名稱	研究分析罹患子宮內膜異位症婦女之特異表現基因---嘗試尋找子宮內膜異位症之標記分子
• 計畫英文名稱	Global Analysis of Specific Expressed Genes in Women with Endometriosis---To Find the Markers for Endometriosis
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC92-2314-B038-060
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• 研究人員	曾啓瑞 Tzeng, Chii-Ruey
• 中文關鍵字	子宮內膜位症; 細胞凋亡; 基因晶片; cDNA 微陣列; 基因表現; 類促性腺激素
• 英文關鍵字	Endometriosis; Apoptosis; Genechip; cDNA microarray; Gene expression; Gonadotropin-releasing hormone analog (GnRHa)
• 中文摘要	子宮內膜位症 (Endometriosis)，是一種常的婦科疾病，約有 40%的孕婦患有子宮內膜位症，Gonadotropin-releasing hormone analog (GnRHa)是目前床上普遍使用於治子宮內膜位症的一種藥物。但對子宮內膜位症致病機轉與診斷的標誌分子，至今仍清楚。本篇研究中，用 cDNA 基因晶片 (cDNA microarray) 技術，分析比較 GnRHa 治前後的位(Ectopic)子宮內膜組織-巧克囊腫(Chocolate cyst)之基因表現差。經過台醫學大學附設醫院人體試驗委員會核准及病人同意下，取得實驗所需之位子宮內膜組織檢體。位子宮內膜組織檢體分別取自於接受過 GnRHa 治及未經過 GnRHa 治的子宮內膜位症病人(n=4)。萃取其 mRNA 後，進 cDNA 基因晶片分析。用人 cDNA 基因晶片 (包含 9600 個基因及 EST)並結合酵素呈色系統 (Colorimetric detection system) 分析基因表現差。接著用即時定 PCR (Real time quantitative RT-PCR)、免疫 組 織 染 色 (Immunohistochemistry)和西方點墨法 (Western blotting)確認這些基因的差性表現。根據 cDNA 基因晶片的分析結果，75 個基因的表現在經過 GnRHa 治療後，其表現會減少；216 個基因的表現則會增加 (up-regulated)。 與細胞生長(如：PCNA、topoisomerase II alpha 和 CDC2 delta T)、細胞轉化(Pituitary tumor-transforming gene) 及細胞侵入(Enolase 1 alpha)相關的基因，皆高表現於未經 GnRHa 治之位子宮內膜組織。進一步以免疫組織染色方法分析細胞增殖標誌 PCNA (Proliferative cell nuclear antigen)的表現，經過 GnRHa 治之位子宮內膜組織 PCNA 表現減少。根據 cDNA 基因晶片、即時定 PCR 及西方點墨法的分析結果，確認 Enolase 1 alpha, Pituitary tumor-transforming gene, H-cadherin 及 Keratin 19 在 GnRHa 治前後的子宮內膜位症病人之位子宮內膜組織、腹腔液及血清檢體，皆具有差性表現。用 cDNA 基因晶片確認這些表現差的基因，將有助於我們對子宮內膜位症導致不孕之致病機轉的瞭解，且也許能夠提供尋找診斷或治標誌分子的相關資訊。
• 英文摘要	Endometriosis is one of the most common gynecological diseases and about 40 % of infertile women have endometriosis. The gonadotropin-releasing

hormone analog (GnRHa) has been widely used in the treatment of endometriosis for many years. However, the genetic mechanisms and diagnostic marker of endometriosis are still unclear. In this study, the global gene expression profiles in ectopic endometrium (chocolate cysts) which have been treated with or without GnRHa were analyzed by using cDNA microarray technology. Institutional review board approval was obtained before initiation of this investigation by the Taipei Medical University Hospital (Taipei, Taiwan). Endometric tissues were obtained from endometriosis patients have been treated with or without GnRHa (n=4). The mRNA was extracted for cDNA microarray analysis. The human cDNA microarray system (9,600 genes, including known regulatory genes and expressed sequence tag, EST) with colorimetric detection system was used to identify the differentially expressed genes. The real time quantitative RT-PCR, Immunohistochemistry and Western blotting were used to confirm the cDNA microarray data. According to cDNA microarray analysis, we have identified 75 genes whose expression was down regulated in endometric tissues with GnRHa treatment, and 216 genes were up regulated. The genes related to cell growth (PCNA, CDC2 delta T, and topoisomerase II alpha), cell transformation (Pituitary tumor transforming), and cell invasion (Enolase 1 alpha) were highly expressed in the endometric tissues without GnRHa treatment. Immunohistochemistry was used to confirm the cell proliferating marker, PCNA, was decreased following GnRHa treatment. According to the results from cDNA microarray, real time quantitative RT-PCR, and Western blotting, we defined that Enolase 1 alpha, Keratin 19, Pituitary tumor-transforming gene, and H-cadherin were consisted expressed differentially in endometriotic tissues, peritoneal fluid, and serum from patients with or without GnRHa treatment. To identify these differentially expressed genes globally by cDNA microarray add to our understanding of the pathological mechanisms about endometriosis-induced infertility and might provide the information to find the diagnostic markers or therapeutic targets for endometriosis.