• 系統編號	RN9511-0594
• 計畫中文名稱	(子計畫六)膀胱癌易罹癌基因之多發家族遺傳連鎖分析(II)
• 計畫英文名稱	Linkage Analysis of Susceptibility Genes for Bladder Cancer in Multiplex Families (II)
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC92-3112-B038-002
• 執行機構	臺北醫學大學公共衛生學系
• 本期期間	9205 ~ 9304
• 報告頁數	28 頁
• 使用語言	中文
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• 中文關鍵字	移形上皮細胞癌、砷、家族聚集研究
• 英文關鍵字	Transitional cell carcinoma; Inorganic arsenic; multiplex family study
• 中文摘要	無機砷是確認之人體肺癌與皮膚癌致癌物，包括台灣、美國、日本、阿根廷、智利及芬蘭等國家，均有研究指出砷暴露與泌尿道癌症的產生具有統計顯著相關存在。我們最近於台灣東北角的蘭陽盆地亦發現砷暴露與泌尿道癌，特別是移形上皮細胞癌(TCC)具有明顯的劑量效應關係存在。不過，引起膀胱癌之主要易感受基因及其功能目前並不清楚。因此本計畫的研究目的包括(1)透過癌症登記系統及各合作醫院確認的膀胱癌病例，以家族疾病史問卷作電話或家戶訪視，以尋找膀胱癌多發家庭。(2)以問卷訪視蒐集指標個案及其家庭成員之研究資訊並收集其血液、尿液等生物檢體。(3)分離、純化及分裝研究對象 DNA 並儲存在超低溫冷凍庫以供各子計畫使用。(4)針對過去 CGH 及 LOH 研究所獲得在染色體上與膀胱癌發生相關之 DNA 增加與缺失的部位，進行易感受基因多型性分析。(5)針對砷引起與非砷引起之膀胱癌，利用多發家庭連鎖分析，對相關易感受性基因進行定位。(6)分析可能的易感受基因與環境因子對膀胱癌發生危險性之交互作用。(7)建立遺傳流行病學與生物統計支援中心，協助各子計畫進行資料分析工作。本研究共分爲兩個部分，第一部分預備以三年時間在台南、嘉義、宜蘭三縣各合作醫院收集 150 位多發性家族之膀胱癌指標個案，及每一指標個案的十位一等親成員，合計 1500 位多發家庭成員。第二部分針對 150 個多發家庭(每一家庭除指標個案外，至少一名成員罹患膀胱癌)以問卷蒐集環境暴露等危險因子及生活史資料，以判定爲砷暴露及非砷暴露組。每一位研究對象亦將蒐集 35c.c.血液及 50c.c.尿液，以獲得研究所需的 DNA，DNA 將被分離、純化、儲存在超低溫冷凍庫中，以供各子計畫使用。本計畫亦將針對過去 CGH 及 LOH 研究所獲得在染色體上與膀胱癌發生相關之 DNA 增加與缺失的部位，進行易感受基因定位之連鎖分析，比較砷引起及非砷引起膀胱癌的易感受基因的部位之異同，供日後做預防與治療的基礎資料。
• 英文摘要	Inorganic arsenic has been well documented as a human carcinogen of skin and lung. A significant association between arsenic exposure and risk of urinary

cancer has also been reported in many epidemiological studies carried out in many countries of the world. Our recent study had also found a significant dose-response relationship between risk of cancers of urinary organs, especially for transitional cell carcinoma (TCC), and arsenic exposure through drinking well water in Lanyang Basin. However, the major susceptible gene(s) of bladder cancer from arseniasis-endemic and non-endemic areas and their functional changes that make a person to be a victim of arsenic-induced bladder cancer is still unclear. The objective of this subproject is to identify and differentiate the major susceptibility gene(s) for arsenic-induced and non-arsenic-induced bladder cancers through the linkage analysis of genetic markers in members of multiplex families. It will include following specific aims: 1) the ascertainment of multiplex families through the telephone or home-visit interview, based on a family history questionnaire, of bladder cancer cases reported to the national cancer registry and cases diagnosed and treated in collaborative medical centers; 2) the recruitment of probands and families members through home-visit personal questionnaire interview and biospecimen collection; 3) the purification, depository and inventory of DNA samples in central biospecimen bank; 4) the typing of genetic markers on chromosomes in which loss or gain have been observed through previous comparative genomic hybridization and loss of heterozygosity studies; 5) the mapping of susceptibility gene(s) through linkage analysis of multiplex family data for bladder cancer cases in arseniasis-endemic and non-endemic areas; 6) the examination of the effects of possible candidate genetic marker(s) and their synergistic interactions with environmental factors on bladder cancer; and 7) the establishment of Genetic Epidemiology and Biostatistics Supporting Core to provide methodological support to other subprojects. A total of 150 multiplex families of bladder cancer including 150 probands and 1500 first-degree relatives from arseniasis -endemic and non-endemic area will be recruited by the end of three year grant period. An informed consent will be obtained from each participant for the collection of risk factor information through questionnaire interview. A 35 mL blood and buccal cell specimen will be obtained from each consenting participant. DNA samples will be extracted from peripheral lymphocytes and buccal cells, aliquoted and frozen at -70.degree.C. Polymorphisms of genetics markers closely linked to the major susceptible gene(s) of bladder cancer will be typed. Analysis of Lod score, and transmission disequilibrium test will be carried out to map susceptible gene(s) of arsenic-induced and non-arsenic-induced bladder cancer based on multiplex family study.