行政院國家科學委員會專題研究計畫 成果報告

維生素 B-6 及葉酸與大腸直腸息肉患者的基因多型性、抗氧化活性及甲基化作用關係的探討(第 3 年)
研究成果報告(完整版)

計 畫 類 別 ：個別型
計 畫 編 號 ：NSC 97-2320-B-040-031-MY3
執 行 期 間 ：99 年 08 月 01 日至 100 年 07 月 31 日
執 行 單 位 ：中山醫學大學營養學系（所）

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報 告 附 件 ：出席國際會議研究心得報告及發表論文

處 理 方 式 ：本計畫可公開查詢

中 華 民 國 100 年 10 月 20 日

行政院國家科學委員會補助專題研究計畫 ■成果報告 □期中進度報告

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計畫編號：NSC 97－2320－040－031－MY3
執行期間： 2008 年 8 月 1 日至 2011 年 7 月 31 日

執行機構及系所：中山醫學大學營養系

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中　華　民　國 100 年 10 月 20 日

中文摘要

大腸直腸癌目前已為台灣十大癌症死亡的第三名。腺瘤性息肉已被認為是發生大腸直腸癌的前身。葉酸與維生素 B_6 被認為在大腸直腸息肉形成中扮演重要角色。本計劃的主要目的為：1) 觀察及比較大腸直腸增殖性息肉及腺瘤性息肉受試者的維生素 B_6 及葉酸的營養狀況、抗氧化酵素活性的差異性。2) 探討維生素 B_6 及葉酸的營養狀況與大腸直腸息肉受試者的抗氧化酵素活性的關係。3) 探討維生素 B_6 及葉酸的營養狀況與罹患大腸直腸息肉的危險對比值。4) 評估及比較給予大腸直腸腺瘤性息肉受試者單獨維生素 B_6 或葉酸補充或合併補充後對抗氧化功能及 DNA 甲基化程度的差異及影響。

本研究設計方法是以醫院為基礎的橫斷面、病例-對照及隨機雙盲的補充劑介入試驗。本研究於中山醫學大學附設醫院肝膽胃腸科募集大腸直腸息肉受試者 (n = 48)及經年齡-性別配對之後的健康受試者 (n = 96)，並進一步詢問息肉受試者是否參加介入研究。介入研究將於受試者接受息肉切除後且經臨床醫師評估同意後進行。最後有 24 位受試者接受 12 週介入研究，並隨機分成以下三組，：1) 100 mg/d 維生素 B_6，n = 9；2) 5 mg/d 葉酸，n = 9 及 3) 維生素 B_6 (100 mg/d) 合併葉酸 (5 mg/d)，n = 6。大腸直腸息肉受試者的血液採集將於接受息肉切除後採集。參加介入研究的受試者的空腹血液採集將於第 0、4、12 週進行，血液樣本將進行臨床血液生化值 (白蛋白、肌酸酐、鹼性磷酸酶和高敏感度 C-反應蛋白) 及生化檢驗值 (血漿與紅血球磷酸比哆醛、血清與紅血球葉酸、血清維生素 B_{12} 及同半胱胺酸) 的分析，萃取 DNA 檢測 DNA 甲基化作用，及測定氧化壓力程度、脂質過氧化及抗氧化酵素活性。

在橫斷面試驗的部分，本研究發現血漿同半胱胺酸濃度對於大腸直腸息肉有顯著影響，在調整相關影響因子之後，影響依然顯著 (OR, 2.23; 95% CI, 1.23-4.03)。而 B-維生素營養狀況皆對罹患大腸直腸息肉無顯著影響。在不同型態的腺瘤性息肉或增生性息肉之間，兩組之臨床血液生化值、生化檢驗值、脂質過氧化、維生素 B_6 營養狀況及抗氧化酵素活性皆無顯著差異。進行 12 週的介入試驗後，無論是接受 100 mg/d 維生素 B_6，5 m/dg 葉酸或兩者同時補充的受試者，在臨床生化值，生化檢驗值，脂質過氧化程度及抗氧化酵素活性，三組間皆無顯著差異。可能是因為樣本數太小無法觀察到顯著影響。

本研究認為，血漿同半胱胺酸為大腸直腸息肉的獨立危險因子。並且給予 5 mg 葉酸介入 12 週後，可顯著降低血漿同半胱胺酸濃度。

關鍵詞：大腸直腸息肉、維生素 B_6、葉酸、DNA 甲基化程度、抗氧化活性

英文摘要

Colorectal cancer is now the third leading cause of cancer mortality among men and women in Taiwan. Colorectal adenomas are considered precursors of colorectal cancer, prevention of colorectal adenomas may decrease the occurrence of colorectal cancer. Vitamin B_6 and folate may play a critical role in the colorectal polyps progression. The specific aims of this proposal are: 1) to compare folate and vitamin B_6 status between colorectal hyperplastic polyps adenomatous polyps; 2) to compare and evaluate folate and vitamin B_6 status in relation to oxidative stress, antioxidant activities; 3) to evaluate the effect of vitamin B_6 and folate status on the risk of colorectal polyps; 4) to evaluate whether folic acid and/or pyridoxine supplementation had a beneficial effect on reducing oxidative stress, increasing antioxidant function and DNAmethylation in patients with colorectal adenomas.

This study was an observational case-control design. Forty-eight participants with colorectal polyps [29 adenomatous polyps , 19 hyperplastic polyps (HP)] and 96 age-, sex-matched healthy participants who met the inclusion criteria were recruited from Chung Shan Medical University Hospital and Taichung General Veterans Hospital. Fasting blood was drawn from each participant to measure hematological and biochemical parameters (plasma and erythrocytes pyridoxal 5'-phosphate (PLP), serum and erythrocytes folate, serum vitamin B_{12}, and plasma homocysteine). Subjects with polyps were blinded and randomly assigned to either the 1) 100 mg/d vitamin B_6 (n = 9) ; 2) 5 mg/d folic acid group (n=9); or 3) vitamin B_6 (100 mg/d) plus folic acid (5 mg/d)(n=6) for 12 weeks.

Participants with AP and HP had significantly higher plasma homocysteine levels than did healthy participants. There was no significant difference in serum folate and vitamin B_{12} and plasma PLP among the three groups. B-vitamins had no significant effect on the risk of developing colorectal polyps. However, participants with higher plasma homocysteine (OR, 2.23; 95% CI, 1.23-4.03) level exhibited significantly increased risk of developing colorectal polyps after adjusting for body mass index, diastolic blood pressure, total cholesterol and B-vitamins. There were no significant effect on DNA methylation, oxidative stress, antioxidant enzymatic activities, TBARS and oxidized low density lipoprotein levels among three groups after treated either vitamin B_6 or folic acid supplements. However, plasma homocysteine level has reduced by 14.2% in the folic acid group.

In conclusion, plasma homocysteine was a strong predictor for risk of developing colorectal polyps in subjects with adequate B-vitamins status. Treatment with 5 mg/d folic acid 12 weeks could significantly decrease plasma homocysteine level.

Keywords: colorectal polyps, vitamin B_6, folate, DNA methylation, antioxidant activities

前言

台灣的大腸直腸癌死亡率節節攀升，目前已是台灣地區男性及女性主要癌症死亡原因第三名。一般認為大腸直腸癌是由大腸的良性息肉，慢慢經年累月成長及癌化所造成。常見的大腸直腸息肉分別為增殖性息肉(hyperplastic polyps) 及腺瘤性息肉 (adenomatous polyps)。隨著息肉的變大，其發生癌化的比例也增加。大腸直腸息肉發生的原因雖然目前尚未十分清楚，不過可能與遺傳或營養素攝取有關，其中葉酸與維生素 B_6 和大腸直腸息肉形成的關係是非常值得探討的課題。

維生素 B_6 與葉酸缺乏被認為與許多癌症形成有顯著負相關，例如前列腺癌，肺癌，大腸直腸癌等 (Hartman et al., 2001; Wei et al., 2005; Larsson et al., 2005; Giovannucci et al., 1995; Choi & Mason, 2000)。Wei 等人 (2005) 在 Nurses' Health Study 的世代研究以鳥巢式病例對照 (nested case-control) 研究也觀察到高血漿磷酸比哆醇濃度與大腸直腸癌發生率呈顯著負相關 (RR, 0.42; 95% CI, 0.21 – 0.85)；即使調整葉酸，綜合維他命及甲硫胺酸 (methionine) 攝取量，顯著相關性依然存在 (RR, 0.38; 95% CI, 0.18 – 0.80)。葉酸在大腸直腸腫瘤生成占了相當重要的角色 (Mason & Choi, 2000; Eichholzer et al., 2001)，葉酸營養狀況也會影響大腸直腸腺瘤性息肉的形成及再發生。Kim 等人 (1998) 指出大腸直腸腺瘤性息肉患者的腸黏膜葉酸濃度顯著低於增殖性息肉的患者約 34% ($p = 0.006$)。Martinez 等人 (2004) 也發現若受試者有較高的的葉酸攝取量 (4^{th} quartile) 或血漿葉酸濃度 (4^{th} quartile) 其大腸直腸腺瘤性息肉再發生的勝算比只有葉酸攝取較少或血漿葉酸濃度較低 (1^{st} quartile) 的受試者的 0.61 倍 (OR, 0.61; 95% CI, 0.42 – 0.89; p for trend = 0.01) 及 0.66 倍 (OR, 0.66; 95% CI, 0.46 – 0.97; p for trend = 0.04)。因此，維生素 B_6 及葉酸營養狀況可能在大腸直腸息肉形成過程中扮演相當重要角色。

維生素 B_6 與葉酸在單碳代謝中也扮演重要角色。維生素 B_6 在合成 5,10-亞甲基四氫葉酸時作為絲胺酸羥基甲基轉移酶 (serine hydroxymethyltransferase, SHMT) 的依賴性輔酶，而 5,10-亞甲基四氫葉酸則是合成核酸所必須，且亞甲基四氫葉酸轉變成的醛基葉酸 (10-formyl-tetrahydrofolate)，則被當成單碳分子的傳遞者（圖 1）。以動物研究模式發現維生素 B_6 缺乏會降低單碳代謝作用的進行(Martinez et al., 2000; Scheer et al., 2005)。而 Kim 等人 (2001) 所執行的一項前瞻性研究，將 20 位接受幽門切除術後的腺瘤病人隨機分派到服用一年 5 mg/d 的葉酸補充劑或是安慰劑；分別在 6 個月及 1 年後發現服用葉酸補充劑的病人顯著增加 DNA 甲基化作用 ($p = 0.001$)。因此，若給予維生素 B_6 及葉酸補充或許能改善大腸直腸息肉受試者體內甲基化作用。

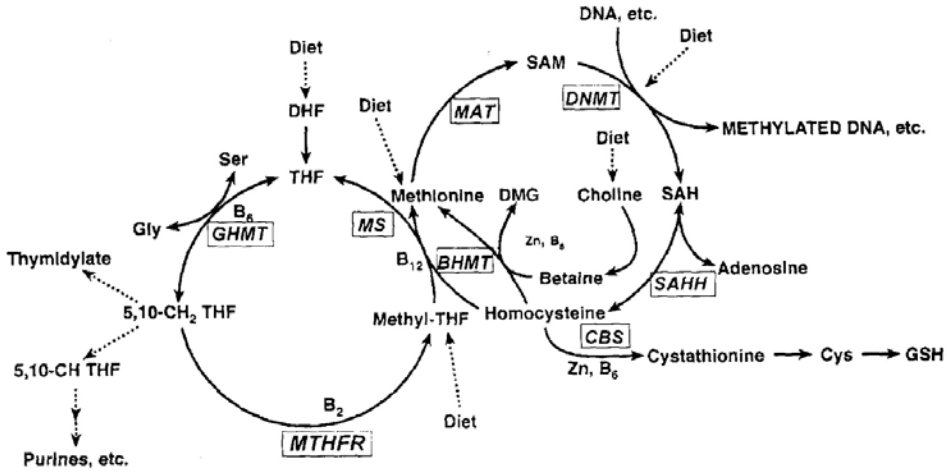

圖 1. Dietary factors, enzymes, and substrates involved in homocysteine and one-carbon metabolism. (Adapted from Davis & Uthus, 2004)

腸胃道，尤其是大腸直腸，因為內生性及外生性的物質來源，經常暴露於高的氧化壓力環境下 (Blau et al., 1999)。Reactive oxygen species (ROS) 為氧分子代謝後的產物，當細胞外過多的 ROS 形成過高的氧化壓力環境，則會造成基因調控失調及細胞傷害，因而導致細胞不正常的增生及癌細胞的形成 (Babbs, 1990)。研究指出大腸直腸癌患者組織的脂質過氧化程度，包括 lipid peroxides (2.78 ± 0.31 vs. 1.81 ± 0.29 nmol/mg)及 thiobarbituric acid reactive substances (TBARS) (0.86 ± 0.1 vs. 0.54 ± 0.08 nmol/mg) 的值均顯著高於健康受試者(Rainis et al., 2007)。若能增加大腸直腸息肉受試者的抗氧化壓力能力，或許能預防或降低癌化的形成。同半胱胺酸 (homocysteine) 代謝中的轉硫作用經由胱硫醚 β 合成酶 (cystathionine β-synthase, CBS) 催化絲胺酸 (serine) 轉成胱硫醚 (cystathionine)，進而由胱硫醚分解酶 (cystathionase) 水解成半胱胺酸 (cysteine)。胱硫醚 β 合成酶需要磷酸比哆醛做為輔酶 (coenzyme)，故為磷酸比哆醛依賴型酵素。半胱胺酸轉化成穀胱甘肽 (glutathione, GSH)，而穀胱甘肽是麩胱甘肽硫轉移酶 (glutathione *S*-transferase, GST) 及麩胱甘肽過氧化酶 (glutathione peroxidase, GSH Px) 的重要輔因子 (cofactor)，此兩個酵素為人體重要的抗氧化酵素，其功能包括去除許多致腫瘤化合物的毒性及保護細胞免於氧化壓力的傷害 (Hayes & McLellan, 1999; Matsubara et al., 2003)。大腸直腸息肉受試者可能會因有較低的維生素 B_6 營養狀況而影響 GSH 的合成，進而影響 GST 及 GSH Px 執行抗氧化壓力的能力。因此。若給予大腸直腸息肉患者維生素 B_6 補充或許能增加大腸直腸腺瘤性息肉受試者的的抗氧化活性。

因此本研究分成以下兩部分進行探討

【第一部分】

研究目的

1. 觀察及比較大腸直腸增殖性息肉及腺瘤性息肉受試者的維生素 B_6 及葉酸的營養狀況、抗氧化酵素活性的差異性。
2. 探討維生素 B_6 及葉酸的營養狀況與大腸直腸息肉受試者的抗氧化酵素活性的關係。
3. 觀察及比較大腸直腸腺瘤性息肉受試者與年齡、性別配對後的健康受試者的維生素 B_6 及葉酸的營養狀況、抗氧化酵素活性的差異性。
4. 探討維生素 B_6 及葉酸的營養狀況與罹患大腸直腸息肉的危險對比值。

材料與方法

受試者

參與本研究之受試者是由中山醫學大學附設醫院胃腸科招募大腸直腸息肉受試者。納入條件為：1) 受試者須年滿 18 歲；且 2) 曾經接受大腸直腸鏡檢查並經過醫生診斷有大腸直腸息肉；且 3)診斷條件為有一顆以上的腺瘤存在。病人若有以下條件將排除在本研究外：1) 大腸直腸癌患者；2) 曾經有大腸直腸癌病史；3) 家族性腺瘤性息肉症(attenuated adenomatous polyposis coli；3) 發炎性腸道疾病(inflammatory bowel disease)；5) 代謝相關疾病（如肝腎疾病）；6) 服用非固醇類抗發炎藥物或葉酸阻抗性藥物（如：sulfasalazine, methotrexane）；7) 懷孕或哺乳；或 8)貧血或維生素 B_{12} 缺乏症(血清維生素 $B_{12} < 200$ *p*g/mL)。

資料收集

1) 基本資料

基本資料內容包括年齡、性別、抽菸習慣、酒精攝取量、家族病史及運動頻率。測量受試者的身高、體重、腰圍及臀圍，並計算受試者的身體質量指數 (body mass index, BMI; kg/m^2)。在受試者休息至少五分鐘後測量血壓。若血壓≥ 140/90 mmHg 或者最近有服用抗高血壓藥物者則定義為高血壓。另外紀錄其息肉切片組織相關資料，包括：病史、位置、數目、大小及組織型態 (villous, tubular 或 tubulovillous)。

2) 飲食紀錄

所有受試者將在空腹抽血後以 24 小時飲食回憶問卷紀錄其飲食攝取狀況。若受試者有服用任何營養補充劑，將會記錄其品牌、種類、劑量、及攝取頻率，並併入營養素總攝取量。

臨床血液生化值

使用不含及含有抗凝血劑 (EDTA 或 sodium citrate) 之真空採血管 (Becton Dickinson, Rutherford, NJ) 採集每位受試者 20 mL 的空腹血液，進行下列各項生化分析：肌酸酐 (creatinine)，高敏感度 C-反應蛋白 (high sensitivity CRP, hs-CRP)，禁食血糖，總膽固醇 (Total cholesterol, TC)，三酸甘油脂 (Triglyceride, TG)，高密度脂蛋白膽固醇 (high-density lipoprotein cholesterol, HDL-C)，低密度脂蛋白膽固醇(low-density lipoprotein cholesterol, LDL-C)。

血漿磷酸比哆醛濃度

血漿 PLP 及紅血球 PLP 參考 Talwar 等人(2003)的方法以高效能液相層析（high performance liquid chromatography, HPLC）分析。

血清葉酸濃度

血清葉酸濃度利用免疫競爭法分析，於室溫下進行化學發光的技術 (immunochemiluminometric methods)，採用專門分析葉酸的 kit 分析 (Chiron Diagnostics ACS:180 Automated Chemiluminescence Systems; Chiron Diagnostics Corporation, East Walpole, MA, USA)。紅血球葉酸則是使用放射性葉酸測定 kit 進行分析 (Bio- Rad, New England Nuclear (NEN), and RIA Products)。

血清維生素 B_{12} 濃度

血清維生素 B_{12} 將蛋白質結合競爭性放射 kits 分析 (Chiron Diagnostics Corporation, East Walpole, MA, USA)。

血漿同半胱胺酸之濃度

參考 Araki 及 Sako（1987）的方法，以 HPLC 來測量血漿同半胱胺酸的含量。

統計分析

所有的資料皆由 SAS statistical software (version 9.12; SAS Institute, Cary, NC, USA)的統計軟體執行分析。利用 one way analysis of variance 或是 Kruskal-Wallis one way analysis

of variance on ranks 比較腺瘤性息肉組、增生性息肉組及控制組間之體位測量值、臨床血液生化值及生化檢測值之差異性。類別變相則是利用卡方檢定 (chi-square test) 分析。

以 multiple linear regression analyses 分析血漿同半胱胺酸與/或 PLP、葉酸、及維生素 B_{12} 對於大腸直腸息肉數目的影響，並進一步調整年齡及性別。以 conditional logistic regression model 分析血漿同半胱胺酸、PLP、葉酸、及維生素 B_{12} 對罹患大腸直腸息肉的 odds ratio (ORs)，並計算信賴區間 (confidence intervals, CI) 表示相關強度及統計顯著性。

統計結果以 $p < 0.05$ 時具有統計上的意義。所有的資料將以 means ± standard deviation (SD) 表示。

結果

本研究總共募集了 48 位大腸直腸息肉受試者（12 女性，36 位男性）。有 29 位受試者為腺瘤性息肉，19 位受試者為增生性息肉。經過年齡性別配對後的控制組與息肉受試者之基本資料、體位測量等資料列於 Table 1。控制組的血壓顯著低於息肉受試者。

所有受試者的血液生化值、血漿同半胱胺酸濃度及 B-維生素營養狀況皆列於 Table 2。無論是腺瘤性息肉或增生性息肉受試者，血脂情況皆較控制組差（三較高的三酸甘油脂、總膽固醇及 LDL-C 濃度，較低的 HDL-C 濃度）。此外，相較於控制組，息肉受試者罹患高同半胱胺酸血症的比例較高。然而，血清 hs-CRP，葉酸及維生素 B_{12} 濃度在三組間皆無顯著差異。

由於腺瘤性息肉及增生性息肉兩組受試者之體位測量及健康狀況皆無顯著差異，因此將兩組受試者合併為一組，進一步分析血漿同半胱胺酸濃度，抽菸情形，及 B-維生素營養狀況與大腸直腸息肉數目之間的相關性。結果列於 Table 3。血漿同半胱胺酸濃度與抽菸情形與大腸直腸息肉數目有顯著正相關，但是調整了相關影響因子後，血漿同半胱胺酸濃度與息肉數目仍有顯著相關性，反之，抽菸情形與大腸直腸息肉數目的相關性則消失。血清葉酸、維生素 B_{12} 及 PLP 濃度皆與息肉數目無關。

Table 4 則是呈現血漿同半胱胺酸濃度及 B-維生素營養狀況（血清葉酸、維生素 B_{12} 及 PLP 濃度）對罹患大腸直腸息肉的影響。血漿同半胱胺酸濃度對於大腸直腸息肉有顯著影響，在調整相關影響因子之後，影響依然顯著。然而，B-維生素營養狀況皆對罹患大腸直腸息肉無顯著影響。

討論

過去的研究認為，B-維生素營養狀況如果處於正常的情況，可以預防大腸直腸息肉的發展 (Ashktorab et al., 2007; Kim et al., 1998; Martínez et al., 2004; Scheppach et al., 1999; Wei et al., 2005; Martínez et al., 2006)，然而本研究結果則與上述研究相反，血漿同半胱胺酸可能是較 B-維生素更為重要的影響因子。根據兩項大型的追蹤試驗結果顯示 (WBF and UDCA trials) (Martínez et al., 2006)，未服用綜合維生素補充劑的受試者，血漿同半胱胺酸對於大腸直腸息肉復發有顯著影響，但是服用綜合補充劑者則無。因此，推論 B-維生素可能是透過降低血漿同半胱胺酸濃度進而降低了罹患大腸直腸息肉的風險。

許多研究證實抽菸與大腸直腸腺瘤性息肉有關 (Ulvik et al., 2001; Giovannucci & Martinez, 1996)。Ji 等人 (2006) 也認為，抽菸者會增加大腸直腸腺瘤的發生。本研究也有觀察到相同結果，但是若調整了血漿同半胱胺酸濃度之後，則無顯著影響。推測抽菸是獨立於血漿同半胱胺酸的危險因子。因此，本研究認為，血漿同半胱胺酸為大腸直腸息肉的獨立危險因子。

Table 1. Characteristics of healthy participants and participants with colorectal polyps

Characteristics	Colorectal polyps (n = 48)				Healthy subjects (*n* = 96)	
	Adenomatous polyps (*n* = 29)		Hyperplastic polyps (*n* =19)			
	mean	SD	mean	SD	mean	SD
Age (y)	53.9	10.5	55.4	7.2	54.5	9.4
Gender (Female / Male)	6 / 23		6 / 13		24 / 72	
Height (cm)	165.3	8.7	164.7	6.3	164.7	7.8
Weight (kg)	67.6	10.4	68.9	7.0	64.6	10.6
Body mass index (kg/m^2)	24.7	2.6	25.4	2.3	23.7	3.1
Blood pressure (mmHg)						
Systolic	149.0[a]	16.4	133.3[a]	17.2	118.0[b]	17.3
Diastolic	95.8[a]	27.6	91.0[a]	13.0	74.1[b]	11.0
Numbers of polyps (n, %)	1 (n = 19, 65.5%) 2 (n = 5, 17.2%) 4 (n = 4, 13.8%) 17 (n = 1, 0.03%)		1 (n = 17, 89.5%) 2 (n = 1, 0.05%) 5 (n = 1, 0.05%)		0 (n = 96, 100%)	
Smoking (n, %)	12 (41.4%)		4 (21.1%)		19 (19.8%)	

Values with different superscript letter are significantly different among three groups; $p < 0.05$.

Table 2. Hematological measurements and levels of homocysteine and B-vitamins in healthy participants and participants with colorectal polyps

Characteristics	Colorectal polyps (n = 48)				Healthy participants (n = 96)	
	Adenomatous polyps (n =29)		Hyperplastic polyps (n =19)			
	mean	SD	mean	SD	mean	SD
Lipid profiles						
Triglycerides (mmol/L)	2.2[a]	3.1	1.6[a]	0.6	1.2[b]	0.8
Cholesterol (mmol/L)						
Total	5.4[a]	1.4	4.9[a,b]	0.7	4.8[b]	0.9
LDL	3.5[a]	0.9	3.4[a]	0.6	2.7[b]	0.9
HDL	1.1[a] ±	0.4	1.1[a]	0.3	1.6[b]	0.4
Hs-CRP (mg/dL)	0.2	0.4	0.3	1.0	0.1	0.3
Serum glucose (mmol/L)	5.9[a]	2.6	5.9[a]	2.7	5.5[b]	1.7
Serum creatinine (μmol/L)	83.5[a,b]	27.9	82.4[a]	2.7	94. 9[b]	13.8
Homocysteine (μmol/L)	14.2[a]	5.5	14.5[a]	7.4	9.8[b]	2.1
> 14 μmol/L (n, %)	10, 34.5%		7, 36.8%		3, 0.03%	
Plasma PLP (nmol/L)	111.0	101.2	141.9	149.0	135.3	118.4
< 20 nmol/L (n, %)	0, 0%		0, 0%		0, 0%	
Serum folate (nmol/L)	23.9	17.2	18.6	9.0	19.7	11.0
< 6.8 nmol/L (n, %)	2, 6.9%		2, 10.5%		1, 1.0%	
Serum vitamin B-12 ($p$mol/L)	333.6	188.9	354.6	162.1	373.0	205.4
< 125.5 $p$mol/L (n, %)	5, 17.2%		2, 10.5%		0, 0%	

Values with different superscript letter are significantly different among three groups; $p < 0.05$.

Table 3. The associations between plasma homocysteine, B-vitamins and numbers of colorectal polyps

	Numbers of colorectal polyps (No.)[1] (*n* = 144)	Plasma homocysteine (μmol/L)[2] (n = 144)
	β (*p* value)	
Plasma homocysteine (μmol/L)		
Model 1[3]	0.05 (<0.001)	—
Model 2[4]	0.12 (<0.001)	—
Model 3[5]	0.11 (0.001)	—
Number of colorectal polyps (No.)		
Model 1	—	0.86 (<0.001)
Model 2	—	0.81 (<0.001)
Model 3	—	0.72 (0.001)
Smoking (yes/no)		
Model 1	0.43 (0.007)	1.34 (0.109)
Model 2	0.68 (0.047)	0.69 (0.435)
Model 4[6]	0.60 (0.065)	0.25 (0.781)
Serum folate (nmol/L)		
Model 1	0.01 (0.336)	-0.13 (0.056)
Model 2	-0.03 (0.277)	-0.12 (0.078)
Model 4	-0.01 (0.561)	—
Model 5[7]	—	-0.08 (0.239)
Serum vitamin B_{12} (*p*mol/L)		
Model 1	-0.00 (0.309)	-0.00 (0.003)
Model 2	-0.00 (0.080)	-0.00 (0.009)
Model 4	-0.00 (0.299)	—
Model 5	—	-0.00 (0.079)
Plasma PLP[8] (nmol/L)		
Model 1	-0.00 (0.570)	-0.00 (0.208)
Model 2	-0.00 (0.503)	-0.00 (0.156)
Model 4	-0.00 (0.768)	—
Model 5	—	-0.00 (0.561)

[1]Multiple linear regression analysis with numbers of colorectal polyps as the dependent variable after adjusting potential confounders. *β*, regression coefficient.
[2] Multiple linear regression analysis with plasma homocysteine concentration as the dependent variable after adjusting potential confounders.
[3]No confounders were adjusted.
[4]Adjusted for age and gender, body mass index, diastolic blood pressure, serum total cholesterol and creatinine.
[5]As in model 2 and additionally adjusting for the three B-vitamins (i.e., folate, vitamin B_{12} and PLP).
[6]As in model 2 and additionally adjusting for plasma homocysteine.
[7]As in model 2 and additionally adjusting for numbers of colorectal polyps and the other two B-vitamins.
[8]PLP, pyridoxal 5'-phosphate.

Table 4. The odds ratios (ORs) for risk of colorectal polyps

	No adjusted			BMI-, DBP-, TC-, creatinine-, smoking and/or hcy-, folate-, PLP, vitamin B_{12}- adjusted		
	OR	95% CI	*P*	OR	95% CI	*P*
Homocysteine (μmol/L)	1.80	1.37, 2.38	< 0.0001	1.87	1.13, 3.08	0.01
Plasma PLP (nmol/L)	1.00	1.00, 1.00	0.71	1.00	0.99, 1.01	0.45
Serum folate (nmol/L)	1.04	0.97, 1.11	0.30	1.07	0.91, 1.27	0.41
Serum vitamin B_{12} (*p*mol/L)	1.00	1.00, 1.00	0.63	1.00	0.99, 1.01	0.93

BMI, body mass index; DBP, diastolic blood pressure; TC, total cholesterol; hcy, homocysteine; PLP, pyridoxal 5'-phosphate.

【第二部分】

研究目的

評估及比較給予大腸直腸腺瘤性息肉受試者單獨維生素 B_6 或葉酸補充或合併補充後對抗氧化功能及 DNA 甲基化程度的差異及影響。

材料與方法

受試者

參加此研究的息肉受試者將詢問是否參加介入研究。受試者將會被隨機分派至以下四組，以雙盲試驗進行 16 週的介入研究：1) 100 mg 維生素 B_6 組；2) 5 mg 葉酸組；3) 維生素 B_6 ＋葉酸組：維生素 B_6 (100 mg/d) 與葉酸 (5 mg/d)。

資料收集

1) 基本資料

同第一年橫斷面研究的方法內容。

2) 飲食紀錄

於第 0、4、16 週回診時以 24 小時飲食回憶法紀錄飲食攝取狀況，以確定每一位受試者在實驗期間都有維持其日常飲食。其餘同第一年橫斷面研究的方法內容。

3) 血液樣本採集

使用不含及含有抗凝血劑 (EDTA) 之真空採血管 (Becton Dickinson, Rutherford, NJ) 採集每位受試者 20 mL 的空腹血液。血液採集將於在第 0、4、16 週進行。其餘同第一部分橫斷面研究的方法內容。

4) 生化分析方法

各項生化值檢驗方法如第一年橫斷面研究的方法內容。

脂質過氧化

參考 Jialal & Scaccini (1992) 的方法，利用 TBA (thiobarbituric acid) 與脂質過氧化產物-丙二醛 (malondialdehyde, MDA) 於酸性高溫下會形成紅色復合物質，測定螢光值(excitation: 515 nm; emission: 553 nm)。

抗氧化酵素活性

麩胱甘肽過氧化酶 (glutathione peroxidase) 及胱甘肽硫轉移酶 (glutathione *S*-transferase) 活性是利用商業套組檢測 (Cayman Chemical Company, Michigan, USA)。

DNA 甲基化程度

DNA 純化是在血液抽取後以 DNA 純化 kit (Gentra System, Minneapolis, MN) 進行。白血球 DNA 所含的 methyl-cytosine 濃度將以高效能液相層析進行分析，偵測 2-Deoxycytidine (2-DC) 與 5-methyldeoxycytidine (5-MDC) 的濃度，並以 5-MDC/(5-MDC+2DC)*100% 代表甲基化程度。紫外光-可見光偵測器之波長為 284 nm (Gehrke et al., 1984; Samlowski et al., 2005)。

統計分析

以 one-way analysis of variance (ANOVA)或是 Kruskal-Wallis one-way analysis on ranks 計算各組之間第 0 (baseline)、4 及 16 週的差異。以 one-way repeated measures analysis of variance 或 Friedman repeated measures analysis of variance on ranks 比較各組內第 4 及 16 週的各項血液生化值濃度與 baseline（第 0 週）時的差異。統計結果將以 $p < 0.05$ 時具有統計上的意義。所有的資料將以 means ± standard deviation (SD) 表示。

結果

總共有 24 位大腸直腸息肉受試者參加介入研究。分別隨機分派到以下三組：1) 100 mg 維生素 B_6 組；n = 9；2) 5 mg 葉酸組；n = 9；3) 維生素 B_6 ＋葉酸組：維生素 B_6 (100 mg/d) 與葉酸 (5 mg/d)；n = 6。受試者之基本資料、體位測量等資料列於 Table 1。在年齡、性別、血壓等三組間皆無顯著差異。

進行 12 週的介入之後，所有受試者的血液生化值列於 Table 2。葉酸組在第 12 周血中總膽固醇及 LDL-c 濃度有顯著降低，維生素 B-6 組則是血中 LDL-c 濃度顯著降低。在發炎指標及血中肌酸酐濃度各組間無顯著差異。

血漿同半胱胺酸濃度及 B-維生素營養狀況在介入 12 週後的結果呈現在 Table 3。介入葉酸 12 週後，血清及紅血球葉酸濃度皆有顯著增加，血漿同半胱胺酸有顯著降低 14.2%。維生素 B-6 組在第 12 週的血清及紅血球葉酸濃度有顯著降低。無論介入維生素 B_6 或葉酸，DNA 甲基化程度則無顯著變化。

抗氧化酵素及脂質過氧化程度的變化呈現於 Table 4。介入維生素 B_6 或/及葉酸，血中 ox-LDL 及 TBARs 濃度都沒有顯著的改變。

討論

由於受試者參與研究的意願未如預期，導致未能達到預期人數，可能因為人數的關係而無法觀察到顯著的影響。無論如何，給予葉酸的介入 12 週後，仍可以顯著降低大腸直腸息肉患者的血漿同半胱胺酸濃度，或許可以幫助減少息肉復發的危險。另外，本研究之受試者，皆有完成全大腸鏡的檢查，介入期間順從度皆有達 80%，且完成所有生化數據分析。因此所得到的資料依然具其可信度，仍可嘗試撰寫文獻投稿至期刊。

Table 1. Characteristics of vitamin B-6 and folic acid supplement groups[1]

Characteristics	Vitamin B-6 group (n =9)	Folic acid group (n =9)	The combination group (n =6)
Age (y)	52.7 ± 3.8	50.6 ± 2.6	48.5 ± 10.3
Gender (Female / Male)	3/6	1/8	2/4
Height (cm)	166.9 ± 3.8	165.5 ± 2.2	166.3 ± 8.1
Weight (kg)	69.1 ± 4.6	68.0 ± 2.1	71.8 ± 16.8
Body mass index (kg/m^2)	24.5 ± 0.8	25.0 ± 1.0	24.5 ± 3.4
Blood pressure (mmHg)			
Systolic	149.8 ± 12.1	139.4 ± 7.519	129.8 ± 18.6
Diastolic	94.4 ± 3.2	94.2 ± 8.0	83.7 ± 10.4

[1]Values are means ± standard deviation. Values with different superscript letter are significantly different among three groups; $p < 0.05$.

Table 2. Hematological measurements of vitamin B-6 and folic acid supplement groups [1]

Characteristics	Vitamin B-6 group (*n* =9)		Folic acid group (*n* =9)		The combination group (*n* =6)	
	Week 0	Week 12	Week 0	Week 12	Week 0	Week 12
Lipid profiles						
Triglycerides (mg/dL)	161.8 ± 27.7	158.1 ± 29.3	170.1 ± 61.0	201.8 ± 69.8	133.2 ± 65.6	121.5 ± 80.5
Cholesterol (mg/dL)						
Total	191.2 ± 9.9	159.1 ± 4.9	213.7 ± 26.6	172.6 ± 17.7*	183.8 ± 31.1	188.5 ± 20.4
LDL	138.1 ± 11.9	91.4 ± 7.8*	141.6 ± 18.9	99.5 ± 11.5 *	121.6 ± 36.9	112.0 ± 19.6
HDL	43.0 ± 5.4	49.1 ± 6.6	49.1 ± 6.6	38.8 ± 3.3	43.2 ± 11.9	52.2 ± 14.0
Hs-CRP (mg/dL)	0.3 ± 0.1	0.2 ± 0.1	0.3 ± 0.2	0.3 ± 0.1	0.1 ± 0.1	0.1 ± 0.1
Serum creatinine (mg/dL)	1.0 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	1.1 ± 0.0	0.920 ± 0.228	0.967 ± 0.186

[1]Values are means ± standard deviation.
*Values with superscript letter are significantly different among weeks; $p < 0.05$. LDL, low-density lipoprotein. HDL, high-density lipoprotein. Hs-CRP, high sensititve C-reactive protein

Table 3. Response of plasma PLP and serum folate to vitamin B-6 and folic acid supplement at week 0, week 4 and week 12[1]

[1]Values are means ± standard deviation. Values with different superscript letter are significantly different among three groups; $p < 0.05$.

Colorectal polyp risk factors	Vitamin B-6 group ($n = 9$)			Folic acid group ($n = 9$)			The combination group ($n = 6$)		
	Week 0	Week 4	Week 12	Week 0	Week 4	Week 12	Week 0	Week 4	Week 12
Homocysteine (μmol/L)	12.6 ± 0.6	15.3 ± 3.4	14.0 ± 1.0	14.7 ± 1.5[a]	12.5 ± 3.5[b]	12.6 ± 1.2[b]	14.5 ± 4.5	14.5 ± 5.1	14.8 ± 3.7
Plasma PLP (nmol/L)	97.7 ± 17.9[a]	340.5 ± 157.9[b]	434.3 ± 92.3[b]	88.1 ± 19.3[a]	45.6 ± 25.1[b]	55.1 ± 10.8[b]	176.0 ± 183.8	176.9 ± 164.2	264.5 ± 179.7
Serum folate (ng/mL)	9.8 ± 1.7[a]	8.8 ± 5.8[a,b]	6.7 ± 1.3[b]	6.7 ± 0.8[a]	69.1 ± 77.6[b]	35.3 ± 11.9[b]	8.3 ± 4.5[a]	16.4 ± 3.0[a,b]	44.3 ± 33.0[b]
RBC folate (ng/mL)	529.9 ±133.7[a]	485.2 ± 142.8[ab]	439.6 ± 116.8[b]	398.9 ± 76.2[a]	537.2 ± 249.0[ab]	719.5 ± 305.2[b]	578.4 ± 149.3[a]	666.4 ± 173.2[a]	862.8 ± 173.8[b]
Vitamin B_{12} (pmol/mL)	514.6 ± 136.1	480.8 ± 160.1	847.9 ± 1489.4	462.9 ± 152.1	401.3 ± 123.8	362.4 ± 156.2	309.6 ± 320.4	175.8 ± 127.5	356.2 ± 267.8
DNA methylation (%)	7.1 ± 3.3[a]	-	15.5 ± 1.9[a]	9.6 ± 9.7[a b]	-	17.0 ± 4.3[b]	19.3 ± 11.1[b]	-	14.5 ± 7.1[b]

[a,b,c]Values with superscript letter are significantly different among weeks; $p < 0.05$. PLP, pyridoxal 5'-phosphate

Table 4. Response of lipid oxidation and antioxidant enzymes to vitamin B-6 and folic acid supplement at week 0, week 4 and week 12[1]

Colorectal polyp risk factors	Vitamin B-6 group (n = 9)			Folic acid group (n = 9)			The combination group (n = 6)		
	Week 0	Week 4	Week 12	Week 0	Week 4	Week 12	Week 0	Week 4	Week 12
TBARS (μM)	0.7 ± 0. 2	0.7 ± 0.1	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.1	0.8 ± 0.2	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.1
Ox-LDL (U/L)	39.0 ± 9.9	12.0 ± 6.6	31.5 ± 13.4	45.4 ± 23.6	11.2 ± 3.5	37.4 ± 12.7	36.9 ± 15.3	12.4 ± 1.7	39.0 ± 15.1
GST activity (nmol/min/mL)	3.6 ± 1.0	6.8 ± 11.3	8.2 ± 12.6	5.2 ± 3.1	3.4 ± 1.8	7.0 ± 7.2	7.8 ± 9.9	10.9 ± 5.1	14.0 ± 4.5
GPX activity (nmol/min/mL)	86.9 ± 18.1	80.3 ± 19.7	68.3 ± 20.9	94.1 ± 18.2	88.5 ± 17.9	70.0 ± 34.0	84.9 ± 57.3	55.5 ± 17.8	65.1 ± 18.1
SOD (U/mL)	8.9 ± 4.2	38.1 ±5.5	13.6 ± 9.9	9.9 ± 3.2	37.1 ± 11.1	14.2 ± 6.1	13.9 ± 6.3	36.4 ± 13.1	11.1 ± 1.9

[1]Values are means ± standard deviation. Values with different superscript letter are significantly different among three groups; $p < 0.05$.
TBARS, thiobarbituric acid reactive substances. Ox-LDL, oxidative low density lipoprotein. GST, glutathione S-transferase. GPX, glutathione peroxidase. SOD, *superoxide dismutase.*

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國科會補助專題研究計畫項下出席國際學術會議心得報告

日期：2009 年 10 月 30 日

計畫編號	NSC 97－2320－040－031－MY3		
計畫名稱	維生素 B-6 及葉酸與大腸直腸息肉患者的基因多型性、抗氧化活性及甲基化作用關係的探討 (第二年)		
出國人員姓名	黃怡嘉 / 陳芳霈	服務機構及職稱	中山醫學大學營養系 教授 / 博士生
會議時間	2009 年 10 月 4 日至 2009 年 10 月 9 日	會議地點	泰國曼谷
會議名稱	第 19 屆營養國際會議（19th International Congress of Nutrition, ICN 2009）		
發表論文題目	1. Serum folate is a more sensitive predictor of hyperhomocysteinemia than erythrocyte folate in healthy young Taiwanese adults. 2. High high-density lipoprotein cholesterol is associated with decreased risk of coronary artery disease in patients with rheumatoid arthritis. 19th International Congress of Nutrition		

一、參加會議經過

第 19 屆營養國際會議(19th International Congress of Nutrition, ICN 2009)於 2009 年 10 月 4-9 日在泰國曼谷召開。來自世界各地大約有 3000 位左右的營養及膳食研究相關的專家學者、政府機關相關人員、業者、研究人員及研究生齊聚一堂。此次因獲得國科會專題研究計畫補助出席國際學術會議的經費，計畫主持人(黃怡嘉教授)與其博士班博士候選人陳芳霈榮幸能參與此次的國際研討會，與營養及食品等相關領域學者齊聚一堂，分享彼此研究心得及聆聽大會邀請的國際著名講者精湛的演說。

此次大會的主題為「Nutrition Security for All」(圖一)，6 天的議程涵蓋目前最新及最熱門的營養相關議題(圖二)。大會的 keynote topic 為「Addressing Nutrition and Health Challenges for the 21st Century」。有 5 個 plenary topics，包括 plenary I: Global Efforts Towards Achieving the Millennium Development Goals (MDGs) and Nutrition Well-being; Agriculture, Food Supply Systems and Trade for Nutrition Security;

plenary II: Molecular Genetics, Environment, and Diet-Related Diseases; plenary III: Global Partnerships for Combating Obesity and Chronic Diseases; plenary IV: Nutrition, Lifestyle and Cancer; 及 plenary V: Nutrition as a Sound Investment for Human Capital。

每天議程開場以 plenary 揭開序幕，邀請在其研究領域中的佼佼者做其專題演講，讓與會者有當日主題的概括輪廓，之後與會者可以選擇依自己有興趣的副題參與聆聽及討論。從主題中延伸出 3 個相關的副題，涵蓋：cascade I: Scientific-based knowledge and model in nutrition science and food-based strategies (a. nutrient requirements & metabolism, b. nutritional assessment, c. clinical nutrition); cascade II: Integrating agriculture, food systems, indigenous cuisines and diet quality (d. food-based strategies/interventions for optimal nutrition, e. agriculture and food systems, f. food cultures, cuisines, and indigenous diets, g. right to adequate food); 及 cascade III: Application of knowledge to policy formulation, problem solving, disease prevention and health promotion (h. nutrition and the triple "I", i. obesity and non-related chronic diseases, j. nutrition throughout the life course, k. evidence-based policies & programs to address the global health and nutrition goals, l. food & nutrition interventions for health, m. frontiers in nutrition research)。大會對其內容的安排非常多元、緊湊且充實，讓參與者有如置身學術研究的殿堂，透過聆聽演講與其他研究者的心得交流，讓我獲益良多，博士生大開眼界。

此次除了參加每日的演講外，也與博士生一起參與 2 個研究成果的壁報展示(poster presentation)，主題分別為：

1. Huang YC, Chen FP, Cheng CH. Serum folate is a more sensitive predictor of hyperhomocysteinemia than erythrocyte folate in healthy young Taiwanese adults. 19th International Congress of Nutrition. Ann Nutr Metab 2009;55(suppl):306.
2. Huang SC, Wei JCC, Huang YC. High high-density lipoprotein cholesterol is associated with decreased risk of coronary artery disease in patients with rheumatoid arthritis. 19th International Congress of Nutrition. Ann Nutr Metab 2009;55(suppl):152.

二、與會心得

壁報展示當天與參觀的研究學者展開熱烈的討論，互留名片，期待將來也許有國際合作的機會。營養國際會議 (International Congress of Nutrition)，為每 4 年才舉行一次的國際會議，此次非

常榮幸能獲得國科會專題計畫的出席國際會議的差旅費用補助，讓我及博士生可以至泰國曼谷參與此次營養界的盛會，有幸能與食品、營養與生化等相關領域學者齊聚一堂，共同聆聽台上講者精湛的演講並參與討論。此次的參與國際營養界的學術盛會，不僅增加與國外學術研究學者的交流，也開拓對自己的研究深度及廣度，真是不虛此行。再次感謝國科會的經費補助。

三、攜回資料名稱及內容

圖一:

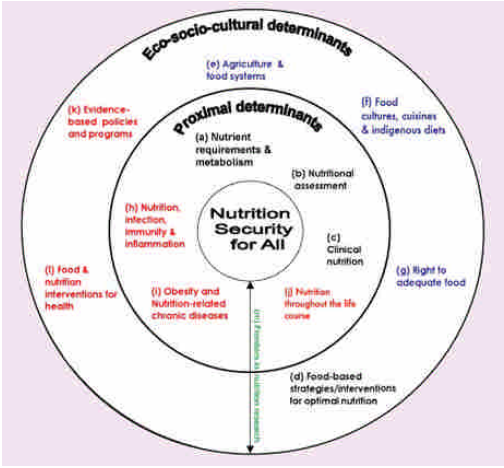
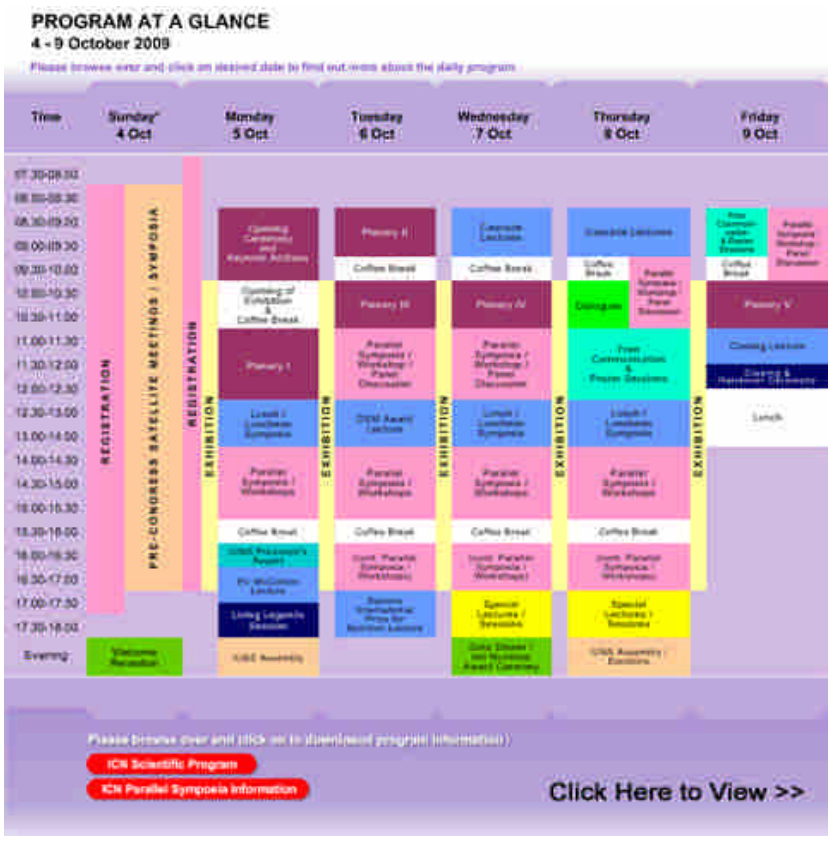


圖 二:



四、論文被接受發表之大會證明文件

Yi-Chia Huang
Professor of School of Nutrition
Chung Shan Medical University
No. 110, Sec. 1, Jianguo N. Rd.,
Taichung, Taiwan 402

Subject: Invitation to the International Congress of Nutrition 2009

Dear Dr. Yi-Chia Huang:

On behalf of the Nutrition Association of Thailand, I wish to invite you to the 19th International Congress of Nutrition (ICN 2009) to be held from 4-9 October 2009 at Bangkok Trade and Exhibition Center, Bangkok - Thailand.

Themed *"Nutrition Security for All"*, the 19th International Congress of Nutrition aims to bring together over 3,000 nutrition scientists, practitioners, and researchers from all over the world. The event will provide the highest quality scientific program featuring internationally recognized speakers and experts in the field. A cascading of the most up-to-date nutrition-related issues will be covered in the plenary lectures, debates, parallel symposia, workshops, as well as oral and poster presentations.

Your participation in the high-level discussions at this conference will help bring important nutrition issues to the forefront of the global nutrition agenda, focusing on the pressing theme of our time - *Nutrition Security for All*.

In the IUNS tradition, ICN 2009 will also feature social networking opportunities, which includes various cultural tours of Bangkok and surroundings, as well as welcome reception and Gala dinner.

The conference secretariat has received your registration. For more information on the congress, please do visit our website, www.icn2009.com. Please note that costs incurred in relation to your participation at the congress will not be borne by the ICN 2009 organizers.

We look forward to welcoming you to Bangkok to experience our vibrant city with its unique blend of Eastern and Western cultures.

Thank you and we look forward to seeing you in October.

Sincerely yours,

Prof. Kraisid Tontisirin

President, 19th International Congress of Nutrition (ICN 2009)

Chairman of the Organizing Committee

五、發表之論文摘要

1. Huang YC, Chen FP, Cheng CH. Serum folate is a more sensitive predictor of hyperhomocysteinemia than erythrocyte folate in healthy young Taiwanese adults. 19th International Congress of Nutrition. Ann Nutr Metab 2009;55(suppl):306.

摘要：

Objective: The present study was undertaken to assess which B-vitamin status indicator [serum folate, red blood cell (RBC) folate, serum vitamin B-12 or plasma pyridoxal 5'-phosphate (PLP)] is the most reliable indicator of fasting plasma homocysteine status in young Taiwanese adults. Methods: This study had a cross-sectional design. Healthy young adults were divided into either a hyper-homocysteinemia (≥ 14.9 μmol/L) (HHcy, n = 13), borderline hyper-homocysteinemia (fasting homocysteine, 14.9 – 10.2 μmol/L) (BHcy, n = 52), or normo-homocysteinemia (fasting homocysteine < 10.2 μmol/L) (NHcy, n = 65) group based on fasting homocysteine levels. The concentrations of plasma fasting homocysteine, serum folate, RBC folate, vitamin B-12 and plasma PLP were measured. Results: Fasting homocysteine was only significantly and inversely affected by serum folate ($\beta = -0.21$, $p < 0.05$) concentration after adjusting for potential confounders. Only serum folate concentration remained to decrease the risk of fasting hyperhomocysteinemia (OR, 0.73, CI, 0.56 – 0.95) after the other B-vitamins were additionally adjusted. Serum folate also had the highest area under the receiver operating characteristic curve (AUC) to predict the risk of hyperhomocysteinemia (AUC, 0.81) and hyper-borderline- hyperhomocysteinemia (AUC, 0.77). Conclusion: Serum folate is a reliable indicator of fasting hyperhomocysteinemia in the young adult population.

HIGH HIGH-DENSITY LIPOPROTEIN-CHOLESTEROL IS ASSOCIATED WITH DECREASED RISK OF CORONARY ARTERY DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Shih-Chien Huang[1], James Cheng-Chung Wei[2], Yi-Chia Huang[1]

[1]School of Nutrition, Chung Shan Medical University, [2]Division of Allergy, Immunology and Rheumatology, Chung Shan Medical University Hospital, Taichung, Taiwan.

Abstract

The cause of increased risk of coronary artery disease (CAD) in patients with RA is still highly controversial and also unclear. The purpose of this study was to investigate which factor might be a significant indicator for developing CAD in patients with RA. This study was a case-control design. Twenty-nine RA patients with normal endothelial function and 33 patients with CAD were recruited. Risk factors of CAD were measured. Patients with RA had significantly higher high-density lipoprotein-cholesterol (HDL-C) and lower systolic blood pressure (SBP), triglycerides (TG) and serum folate values than patients with CAD. The association of SBP and TG level with the risk of CAD disappeared after HDL-C (OR, 0.83, 95% CI, 0.74 –0.93) was additionally adjusted into the model. Increased HDL-C was significantly associated with decreased risk of CAD in patients with RA. Patients with RA should try to increase their HDL-C level in order to reduce the risk of CAD.

Introduction

Rheumatoid arthritis (RA) is characterized by a high cardiovascular mortality, which exceeds that of the general population. Traditional risk factors such as age, gender, hypertension, lipid profiles and diabetes are the most widely recognized risk factors for cardiovascular disease and have been observed in RA patients. Other studies, however, indicated that traditional risk factors for cardiovascular diseases were independent of RA. In addition to these traditional risk factors, poor B-vitamins status and elevated plasma homocysteine concentrations were seen in with rheumatoid arthritis may contribute to their increased risk of cardiovascular disease. Since the cause of increased risk of cardiovascular disease in patients with RA is still highly controversial and also unclear. The purpose of this study was to investigate which factor might be a significant indicator for developing CAD in patients with RA.

Subjects & Methods

Forty-three RA patients (≥18 y) were recruited from the Division of Allergy, Immunology and Rheumatology of Chung Shan Medical University Hospital, which is a teaching hospital in Taiwan. Patients were diagnosed as having RA according to the 1991 American College of Rheumatology criteria for RA. Thirty- three CAD patients were recruited from the cardiology clinic of the Taichung Veteran General Hospital. Informed consent was obtained from each subject, and the study protocol was approved by the Institutional Review Board of Chung Shan Medical University.

All patients' age, gender, smoking and drinking habits, family history, medication uses and blood pressure were recorded or measured. Fasting blood samples were drawn from each subject to estimate hematological entities [serum creatinine, total serum cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides] and novel (i.e., plasma homocysteine and B-vitamins) risk factors for CAD were estimated.

Results

Table 1 Characteristics of all subjects

Characteristics	Normal endothelial function with rheumatoid arthritis patients (n = 29)	Cardiovascular disease patients (n = 33)
Age	52.0 ± 7.8 [a]	58.8 ± 8.3 [b]
Sex (Male / Female)	2 / 27 [a]	10 / 23 [b]
Body mass index (kg/m²)	24.2 ± 3.8	25.4 ± 3.6
Smoking	6.9 %	18.2 %
Drinking	6.9 %	15.2 %
Disease duration (y)	2.5 ± 1.7	
Rheumatoid factor (IU)	25.3 ± 26.2	
Number of painful joints	7.7 ± 7.2	
Number of swollen joints	2.3 ± 3.1	
Disease activity score 28	4.0 ± 1.0	
Visual analog scale	49.3 ± 19.6	

Values are means ± SD. Values with different superscript letters ([a],[b]) are significantly different within the group; $P < 0.05$

Table 2 Traditional and novel risk factors for coronary artery disease in all subjects

Characteristics	Normal endothelial function with rheumatoid arthritis patients (n = 29)	Cardiovascular disease patients (n = 33)
Hypertension (yes / no) (%)	4/25 (16 %) [a]	33/0 (100 %) [b]
SBP (mmHg)	111.8 ± 16.4 [a]	134.8 ± 23.2 [b]
DBP (mmHg)	69.0 ± 13.9	74.6 ± 14.7
Lipid profiles		
Total cholesterol (mg/dL)	193.9 ± 46.1	197.0 ± 56.2
HDL-C (mg/dL)	38.8 ± 9.8 [a]	60.2 ± 15.1 [b]
LDL-C (mg/dL)	119.34 ± 44.7	121.8 ± 37.6
Triglycerides (mg/dL)	106.6 ± 38.0 [a]	193.3 ± 129.4 [b]
Hs-CRP (mg/L)	2.1 ± 2.2	4.9 ± 7.6
Plasma PLP (nmol/L)	47.7 ± 52.1	37.0 ± 38.0
Serum folate (ng/mL)	14.7 ± 35.6 [a]	17.1 ± 11.4 [b]
Serum vitaminB12 (pg/mL)	605.2 ± 352.7	574.7 ± 194.6
Plasma Hcy (μmol/L)	10.3 ± 4.1	11.4 ± 5.6

Values are means ± SD. Values with different superscript letters ([a],[b]) are significantly different within the group; $P < 0.05$. SBP, Systolic blood pressure; DBP, Diastolic blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; Hs-CRP, high sensitivity C-reactive protein; PLP, pyridoxal 5'-phosphate; Hcy, homocysteine

Table 3 The odds ratios (ORs) for cardiovascular disease

Cardiovascular risk factors	Age, gender, BMI and creatinine adjusted			Age, gender, BMI, creatinine, and HDL adjusted		
	OR	95% CI	P-value	OR	95% CI	P-value
Blood pressure						
SBP (mmHg)	1.07	1.02-1.12	0.01	1.11	0.99-1.23	0.08
DBP (mmHg)	1.03	0.98-1.08	0.20	1.03	0.96-1.10	0.39
Lipid profiles						
Total cholesterol (mg/dL)	1.00	0.98-1.01	0.50	1.00	0.99-1.02	0.98
HDL-C (mg/dL)	0.83	0.74-0.93	0.00			
LDL-C (mg/dL)	1.00	0.98-1.01	0.63	1.00	0.98-1.01	0.63
Triglycerides (mg/dL)	1.01	1.00-1.03	0.04	1.01	0.99-1.03	0.32
Hs-CRP (mg/dL)	1.13	0.91-1.41	0.28	1.10	0.82-1.48	0.53
Plasma PLP (nmol/L)	0.99	0.97-1.00	0.07	0.98	0.96-1.00	0.10
Serum folate (ng/mL)	0.99	0.97-1.01	0.39	1.01	0.98-1.04	0.57
Serum vitamin B_{12} (pg/mL)	1.00	1.00-1.00	0.86	1.00	1.00-1.01	0.72
Plasma Hcy (μmol/L)	0.86	0.70-1.06	0.15	0.83	0.62-1.10	0.19

Adjusted for age, gender, body mass index, creatinine and homocysteine. SBP, Systolic blood pressure; DBP, Diastolic blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; Hs-CRP, high sensitivity C-reactive protein; PLP, pyridoxal 5'-phosphate; Hcy, homocysteine

Conclusion

Higher HDL-C was independently significantly associated with decreased risk of CAD in patients with RA. Patients with RA should try to increase their HDL-C level in order to reduce the risk of CAD.

References

García-Gómez C, Nolla JM, Valverde J, et al. Conventional lipid profile and lipoprotein(a) concentrations in treated patients with rheumatoid arthritis. J Rheumatol 2009; 36: 1365-70.

2. Huang SC, Wei JCC, Huang YC. High high-density lipoprotein cholesterol is associated with decreased risk of coronary artery disease in patients with rheumatoid arthritis. 19th International Congress of Nutrition. Ann Nutr Metab 2009;55(suppl):152.

摘要：

The cause of increased risk of coronary artery disease (CAD) in patients with RA is still highly controversial and also unclear. The purpose of this study was to investigate which factor might be a significant indicator for developing CAD in patients with RA. This study was a case-control design. Twenty-nine RA patients with normal endothelial function and 33 patients with CAD were recruited. Risk factors of CAD were measured. Patients with RA had significantly higher high-density lipoprotein-cholesterol (HDL-C) and lower systolic blood pressure (SBP), triglycerides (TG) and serum folate values than patients with CAD. The association of SBP and TG level with the risk of CAD disappeared after HDL-C (OR, 0.83, 95% CI, 0.74 –0.93) was additionally adjusted into the model. Increased HDL-C was significantly associated with decreased risk of CAD in patients with RA. Patients with RA should try to increase their HDL-C level in order to reduce the risk of CAD.

SERUM FOLATE IS A MORE SENSITIVE PREDICTOR OF HYPERHOMOCYSTEINEMIA THAN ERYTHROCYTE FOLATE IN HEALTHY YOUNG TAIWANESE ADULTS

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[2]Critical Care and Respiratory Therapy, Taichung Veterans General Hospital, Taichung, Taiwan

Abstract

Objective: The present study was undertaken to assess which B-vitamin status indicator [serum folate, red blood cell (RBC) folate, serum vitamin B-12 or plasma pyridoxal 5'-phosphate (PLP)] is the most reliable indicator of fasting plasma homocysteine status in young Taiwanese adults. Methods: This study had a cross-sectional design. Healthy young adults were divided into either a hyper-homocysteinemia (≥ 14.9 μmol/L) (HHcy, n = 13), borderline hyper-homocysteinemia (fasting homocysteine, 14.9 – 10.2 μmol/L) (BHcy, n = 52), or normo-homocysteinemia (fasting homocysteine < 10.2 μmol/L) (NHcy, n = 65) group based on fasting homocysteine levels. The concentrations of plasma fasting homocysteine, serum folate, RBC folate, vitamin B-12 and plasma PLP were measured. Results: Fasting homocysteine was only significantly and inversely affected by serum folate (β = -0.21, p < 0.05) concentration after adjusting for potential confounders. Only serum folate concentration remained to decrease the risk of fasting hyperhomocysteinemia (OR, 0.73, CI, 0.56 – 0.95) after the other B-vitamins were additionally adjusted. Serum folate also had the highest area under the receiver operating characteristic curve (AUC) to predict the risk of hyperhomocysteinemia (AUC, 0.81) and hyper-borderline- hyperhomocysteinemia (AUC, 0.77). Conclusion: Serum folate is a reliable indicator of fasting hyperhomocysteinemia in the young adult population.

Introduction

B-vitamins (folate, vitamin B-6 and B-12) are required for homocysteine metabolism. Previous studies have postulated that S-adenosylmethionine favors folate and vitamin B-12-dependent homocysteine conversion to methionine in the fasting state; plasma pyridoxal 5'-phosphate (the physiologically active coenzyme form of vitamin B-6) deficiency does not affect S-adenosylmethionine, and homocysteine is then removed by the remethylation pathway in the nonfasting state. Serum folate thus has been shown to be a much stronger determinant of fasting plasma homocysteine concentration than vitamin B-12 and B-6. In addition to the strong correlation between serum folate and plasma homocysteine, red blood cell folate has also been shown to be significantly correlated with plasma homocysteine. Serum folate concentrations fluctuate rapidly with recent dietary folate intakes even when body folate stores remain stable; folate is taken up by the developing erythrocyte in the bone marrow; therefore, Erythrocyte folate concentration is considered to be a better index of tissue folate stores and could be a long- term status indicator.

Purpose

To assess which B-vitamin status indicator [serum folate, erythrocyte folate, serum vitamin B-12 or plasma pyridoxal 5'-phosphate (PLP)] could better reflect fasting plasma homocysteine status in the young Taiwanese adult population.

Materials & Methods

Subjects

Young adults were recruited from the university community by advertisements. The inclusion criteria were as follows: age between 19 and 35 y, no pregnancy and normal blood biochemical values, including fasting blood glucose < 6.1 mmol/L (110 mg/dL), blood urea nitrogen < 7.9 mmol/L (22.1 mg/dL), creatinine < 123.8 μmol/L (1.4 mg/dL), alkaline phosphatase < 150 U/L, glutamic oxaloacetic transaminase < 35 U/L, and glutamic pyruvate transaminase < 45 U/L. Exclusion criteria were as follows: current illness or history of cardiovascular, liver, renal or other metabolic diseases, diabetes or cancer and taking B-vitamins supplements within 6 mo. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Institutional Review Board of Chung Shan Medical University. Written informed consent was obtained from all subjects.

Experimental protocol

Design: Subjects were assigned to 3 groups based on their fasting plasma homocysteine concentrations: 1. hyperhomocysteinemia, borderline hyperhomocysteinemia and normo-homocysteinemia) were set at more than the 90th percentile (> 14.9 μmol/L); 2. 60th to 90th percentile (14.9 – 10.2 μmol/L); 3. less than 50th percentile (< 10.2 μmol/L).

Demographic data: All subjects' weight and height were measured; the body mass index was then calculated. Blood pressure was measured after a resting period of at least 5 min. Fasting venous blood samples were obtained to estimate hematological and vitamin status.

Biochemical measurement: RBC, hemoglobin, hematocrit, urea nitrogen, serum glucose, creatinine, GOT, GPT, triacylglycerol, total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol were measured by using an automated biochemical analyzer. Plasma homocysteine and PLP concentrations were measured by using high performance liquid chromatography.

Result

Table 1 Demographic characteristics and hematological values for the hyper-, borderline- and normo-homocysteinemia groups[1]

Characteristics	Hyper-homocysteinemia (n = 13)	Borderline hyperhomocysteinemia (n = 52)	Normo-homocysteinemia (n = 65)
Male / Female	10 / 3	35 / 17	5 / 60
Age (y)	23.1 ± 2.0 (23.0)	23.1 ± 3.0 (22.0)	24.8 ± 9.6 (22.0)
Body mass index (kg/m²)	24.0 ± 3.6[a] (23.7)	25.3 ± 3.6[a] (22.4)	21.3 ± 3.0[b] (20.2)
Red blood cell (10^6/mm³)	5.0 ± 0.5[a]	5.0 ± 0.5[a]	4.6 ± 0.4[b]
Hemoglobin (g/dL)	15.2 ± 1.5[a]	15.1 ± 1.5[a]	13.7 ± 1.2[b]
Hematocrit (%)	45.5 ± 4.4[a]	45.2 ± 3.9[a]	41.6 ± 3.4[b]
Blood pressure			
systolic (mmHg)	123.8 ± 12.4[a] (126.0)	119.3 ± 11.3[a] (120.0)	107.8 ± 10.3[b] (110.0)
diastolic (mmHg)	78.0 ± 12.1[a] (76.0)	73.8 ± 9.8[a] (70.0)	67.9 ± 9.7[b] (70.0)
Total Cholesterol (mg/dL)	188.8 ± 30.8 (189.0)	182.9 ± 31.1 (183.5)	183.2 ± 28.3 (180.0)
LDL Cholesterol (mg/dL)	107.8 ± 32.2 (107.0)	104.3 ± 26.6 (104.3)	99.3 ± 23.4 (100.4)
HDL Cholesterol (mg/dL)	68.6 ± 16.6[a] (62.0)	63.8 ± 11.2[a] (64.0)	72.9 ± 14.7[b] (74.0)
Triacylglycerol (mg/dL)	90.0 ± 39.3[a] (89.0)	92.9 ± 47.8[a] (80.0)	73.6 ± 30.0[b] (66.0)
Serum creatinine (mg/dL)	1.1 ± 0.2[a] (1.1)	1.1 ± 0.2[a] (1.0)	0.8 ± 0.1[b] (0.8)

Values are means ± standard deviation with median in the parentheses. Values with different superscript letters ([a], [b]) are significantly different between two groups. P < 0.05. LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol.

Table 2 Homocysteine and B-vitamins in the hyper-, borderline- and normo-homocysteinemia groups[1]

Characteristics	Hyper-homocysteinemia (n = 13)	Borderline hyperhomocysteinemia (n = 52)	Normo-homocysteinemia (n =65)
Plasma homocysteine (μmol/L)	24.1 ± 14.6[a]	12.0 ± 1.3[b]	8.1 ± 1.2[c]
Serum folate (nmol/L)	8.3 ± 4.5[b]	12.1 ± 5.1[a]	17.4 ± 7.6[a]
Red blood cell folate (nmol/L)	387.3 ± 127.6[b]	476.5 ± 160.3[a]	569.7 ± 248.6[a]
Serum vitamin B-12 (pmol/L)	219.7 ± 77.5[a]	249.8 ± 80.5[a]	337.3 ± 176.7[a]
Plasma PLP (nmol/L)	58.7 ± 30.1	54.3 ± 19.8	55.6 ± 36.0

Values are means ± standard deviation. Values with different superscript letters ([a], [b], [c]) are significantly different between two groups. P < 0.05. PLP, pyridoxal 5'-phosphate.

Table 3 Multiple linear regression (β) analysis of fasting plasma homocysteine with B-vitamins in hyper-, borderline-, normo-homocysteinemia and pooled groups

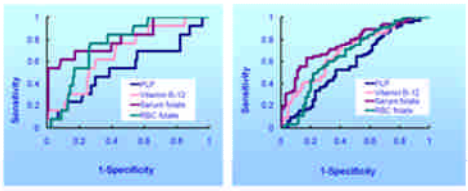
	Hyper-homocysteinemia (n = 13)	Borderline homocysteinemia (n = 52)	Normo-homocysteinemia (n = 65)	Pooled (n = 130)
	β[a]	β	β	β
Serum folate (nmol/L)				
Model 1[d]	1.35	-0.04	-0.03	-0.34[g]
Model 2[e]	-0.91	-0.06	-0.03	-0.24[g]
Model 3[f]	-4.65	-0.04	-0.00	-0.21[g]
Red blood cell folate (nmol/L)				
Model 1	-0.00	-0.00	-0.00	-0.01[g]
Model 2	-0.09[g]	-0.00	-0.00	-0.00
Model 3	0.02	-0.00	-0.00	-0.00
Serum vitamin B-12 (pmol/L)				
Model 1	-0.08	-0.00	-0.00	-0.01[g]
Model 2	-0.03	-0.00	-0.00	-0.01
Model 3	-0.08	-0.00	-0.00	-0.00
Plasma PLP (nmol/L)				
Model 1	-0.07	-0.00	-0.01	-0.03
Model 2	-0.04	-0.01	-0.01[g]	-0.03
Model 3	0.66	0.00	-0.01[g]	-0.01

[a] regression coefficient. [g] P < 0.05, [h] P < 0.01, [i] P < 0.001. [d] Not adjusting any confounders. [e] Adjusting for age, gender, body mass index, systolic blood pressure, red blood cell, triglycerides and creatinine. [f] As for model 2 and additionally adjusting for other two B-vitamins.

Table 4 Multivariate adjusted odds ratios for fasting hyperhomocysteinemia and borderline-hyperhomocysteinemia

	Factors adjusted[a]			Additional factors adjusted[b]		
	OR	95% CI	P	OR	95% CI	P
Serum folate (nmol/L)						
Hyperhomocysteinemia[c]	0.69	0.55 – 0.87	0.002	0.71	0.54 – 0.93	0.013
Hyper- and borderline-hyperhomocysteinemia[d]	0.82	0.73 – 0.91	< 0.001	0.84	0.73 – 0.95	0.006
Red blood cell folate (nmol/L)						
Hyperhomocysteinemia	0.99	0.99 – 1.00	0.009	0.99	0.99 – 1.00	0.074
Hyper- and borderline-hyperhomocysteinemia	1.00	1.00 – 1.00	0.058	1.00	1.00 – 1.00	0.759
Serum vitamin B-12 (pmol/L)						
Hyperhomocysteinemia	0.99	0.98 – 1.00	0.075	1.00	0.99 – 1.01	0.991
Hyper- and borderline-hyperhomocysteinemia	0.99	0.99 – 1.00	0.038	1.00	0.99 – 1.00	0.143
Plasma pyridoxal 5'-phosphate (nmol/L)						
Hyperhomocysteinemia	0.99	0.96 – 1.02	0.393	1.01	0.99 – 1.04	0.373
Hyper- and borderline-hyperhomocysteinemia	0.97	0.95 – 0.99	0.004	0.97	0.95 – 1.00	0.023

[a] Adjusting for age, gender, body mass index, systolic blood pressure, red blood cell, triglycerides and creatinine. [b] Additionally adjusting for the other B-vitamins. CI, 95% confidence interval; OR, odds ratio. [c] Hyperhomocysteinemia is defined as fasting plasma homocysteine concentration ≥ 14.9 μmol/L. [d] Hyper- and borderline-hyperhomocysteinemia is defined as fasting plasma homocysteine concentration ≥ 10.2 μmol/L.



Indicators	Estimated AUC and 95% confidence interval			
	Serum folate (nmol/L)	RBC folate (nmol/L)	Serum vitamin B-12 (pmol/L)	Plasma PLP (nmol/L)
AUC				
Hyperhomocysteinemia	0.81 (0.67 – 0.95)	0.76 (0.65 – 0.87)	0.68 (0.53 – 0.82)	0.54 (0.36 – 0.72)
Hyper- and borderline-hyperhomocysteinemia	0.79 (0.69 – 0.89)	0.66 (0.56 – 0.76)	0.69 (0.60 – 0.79)	0.58 (0.48 – 0.69)

Figure 1 Receiver operating characteristic (ROC) curve of serum folate, red blood cell folate, serum vitamin B-12 and plasma PLP concentrations for identifying subjects with hyperhomocysteinemia and borderline-hyperhomocysteinemia.

Conclusion

Serum folate was a more sensitive predictor of hyperhomocysteinemia in healthy young Taiwanese adults than RBC folate, serum vitamin B-12 and plasma pyridoxal 5'-phosphate.

School of Nutrition
Chung Shan Medical University

國科會補助專題研究計畫項下出席國際學術會議心得報告

日期：2011 年 4 月 30 日

計畫編號	NSC 97－2320－040－031－MY3		
計畫名稱	維生素 B-6 及葉酸與大腸直腸息肉患者的基因多型性、抗氧化活性及甲基化作用關係的探討 (第三年)		
出國人員姓名	黃怡嘉	服務機構及職稱	中山醫學大學營養系 / 教授
會議時間	2011 年 4 月 9 日至 2011 年 4 月 13 日	會議地點	美國華盛頓特區
會議名稱	Experimental Biology 2011		
發表論文題目	1. Higher plasma homocysteine is associated with increased risk of colorectal polyps. Experimental Biology 2011 (poster presentation) 2. Higher plasma homocysteine is associated with lower vitamin B-6 in critically ill surgical patients. Experimental Biology 2011 (oral presentation)		

一、參加會議經過

2011 年 Experimental Biology 會議於 4 月 9－13 日在美國華盛頓特區召開。Experimental Biology 是一年一度由美國的 6 個學會（解剖、生理、生化、病理及營養學會）共同召開的科學性國際會議。每年自世界各地大約有 13,000 位左右的專家學者、研究人員及研究生與會。此次因獲得國科會專題研究計畫（97-2320-B-040-031-MY3）補助出席國際學術會議，計畫主持人(黃怡嘉教授)與其博士候選人黃詩茜榮幸能參與此次的國際研討會（圖一），與營養及醫學等相關領域學者齊聚一堂，分享彼此研究心得及聆聽大會邀請的國際著名講者精湛的演說。

因為計畫主持人的專長及研究是在營養相關的領域，且本身也是美國營養學會（American Society for Nutrition）的會員（會員編號#30314），因此主要是參與美國營養學會所舉辦的 symposium 以及 mini-symposium。每天議程以 symposium 揭開序幕，邀請在其研究領域中的佼佼者做其專題演講，內容包括：Functional foods for health promotion, Neuroscience of food intake & obesity, ameliorating micronutrient deficiency through biofortification, biofortification of provitamin A in maize for Africa, Ethical issue in nutrition, Maternal obesity and long-term programming of offspring obesity risk, 2010 dietary

guidelines, NSC genetic polymorphisms, Metabolic regulation of immune cells, Maternal nutrition and breast milk quality, DRIs for calcium and vitamin D, Science of global beverage consumption and Enteric infections meet the mucosa 等；下午的議程主要是從 symposium 的主題所延伸出來的多個相關的副題（表一）；另外，有全天候的 poster 展示。大會對其內容的安排非常多元、緊湊且充實，讓參與者有如置身學術研究的殿堂，透過聆聽演講與其他研究者的心得交流，讓計畫主持人獲益良多，博士生大開眼界。

此次除了參加每日的演講外，也與博士生一起發表 2 個研究成果，一個成果是以口報告的型式(oral presentation)發表，另一個成果則是以壁報的形式(poster presentation)發表（圖二），發表的題目分別為：

1. Huang YC, Lin CC, Chen FP, Chen TH. Higher plasma homocysteine is associated with increased risk of colorectal polyps. Experimental Biology 2011 (poster presentation)
2. Huang SC, Hou CT, Wu YH, Huang PN, Huang YC. Higher plasma homocysteine is associated with lower vitamin B-6 in critically ill surgical patients. Experimental Biology 2011 (oral presentation)

不管是口頭發表還是壁報展示，皆有許多位的國外學者提出他們對我們的研究結果的問題及見解，並展開熱烈的討論，事後並且互留聯絡方式，期待將來也許有國際合作的機會。

二、與會心得

Experimental Biology，為每年在美國不同城市所舉行的國際聯合會議，此會意涵蓋了 6 個學會，除了自己本身所參與的學會外，也可以同時參與其他學會所舉辦的 symposium 或 mini-symposium，是一個非常大型且多元的國際研討會。此次非常榮幸能獲得國科會專題計畫的出席國際會議的差旅費用補助，讓我及博士生可以至美國華盛頓特區參與此次的學術盛會，有幸能與食品、營養與生化等相關領域學者齊聚一堂，共同聆聽台上講者精湛的演講並參與討論，不僅增加與國外學術研究學者的交流，也開拓對自己的研究深度及廣度，真是不虛此行。再次感謝國科會的贊助。

三、攜回資料名稱及內容

表一：美國營養學會的大會議程

THURSDAY, APRIL 7th	**FRIDAY , APRIL 8th**
1:00-5:00 PM	8:00 AM - 3:30 PM
The Global Nutrition Transition: The Role of Protein Supplementation *D. Heber*	"Heart Healthy Omega-3s for Food: Stearidonic Acid (SDA) as a Sustainable Choice." *R. Deckelbaum*

SATURDAY, APRIL 9th

8:00-10:00 AM	Intervention Points in Childhood Obesity: How and who should we treat? *S.B. Roberts and N. Krebs*	
8:30 am- 12:00 pm	ILSI Functional Foods for Health Promotion *J.A. Milner and B.D. Flickinger*	
9:00AM	Clinical Emerging Leaders session	
10:30AM - 12:30 PM	Policy- Improving the Food Environment *J.E. Kimmons and A.S. Wasserman*	
2:00-5:00 PM	NSC Graduate Student Research Award Session	
3:00-5:00 PM	MNC & Obesity RIS Neuroscience of Food Intake & Obesity *G. Blackburn and W.A. Walker*	Tackling Iron Deficiency in Malaria-Endemic Areas *L.M. Neufeld and A.G. Scrimgeour*
	Beverage consumption in nationally representative US samples. Co-chairs: *Jodi Stookey and Claire Zizza*	Research with dietary supplements. Co-chairs: *Regan Bailey and Ka He*
	Micronutrient bioavailability and biomarkers. Chair: *Danielle Greenberg*	New perspectives on the prevalence and determinants of micronutrient deficiency in populations. Chair: *Jere Haas and Parmi Sachdev.*
	Aligning nutrition education programs and research to effect change. Chair: Susan Baker; Co-Chair: Helen Chipman.	

SUNDAY, APRIL 10th

8:00-10:00 AM	Presidental SymposiumMicronutrient Deficiency Through Biofortification *R.M. Russell*	
10:30 AM -12:30 PM	Biofortification of Provitamin A in Maize for Africa *S.A.Tanumihardjo*	Ethical Issues in Nutrition Research *L.E.Caulfield and T.R. Ziegler*
	Carbohydrate digestion; energy boundary between plant and animal kingdoms. Chair: *Buford L. Nichols* and *Bruce R. Hamaker*	Energy balance, macronutrient and weight. Chairs: *Nancy L. Keim* and *Marta Van Loan*.

	Bioactive Components IV: Anti-oxidant and Anti-inflammatory functions I. Chairs: *Zeina Jouni and Richard Bruno; trainee: Jesse Solomon*	Biofortification of staple crops with micronutrients. Chair: *J. Haas; Co-chair: Elizabeth Johnson*.
	Nutrition and physical and cognitive function. Chairs: *Denise Houston and Christy Tangney and Steve Kritchevsky*	Changing retail environments. Chair: *Diego Rose and Elizabeth Racine.*
	Preventing childhood obesity. Chairs: *Barbara Lohse and Juhee Kim*	Selenium. Chair: *Roger Sunde*.
12:45- 2:45 PM	McCollum Lecture	
	Posters: Dietary Bioactive Components Including Botanicals Dietary Bioactive Components II: Mechanisms of Action and Molecular Targets I Dietary Bioactive Components III: Chronic Disease Risk Reduction II Dietary Bioactive Components V: Medicinal and Functional Foods Lipid and Fatty Acid Metabolism and Transport Dietary Factors Affecting Lipid Metabolism Carbohydrate Digestion: Energy Boundary between Plant and Animal Kingdoms Regulation of Food Intake Breastfeeding: Determinants and the Effects on Health Outcomes Human Milk Biology Sociocultural and Dietary Determinants of Obesity in Low and Middle Income Counties Dietary and Nutritional Assessment Comprehensive Weight Management Nutrition Interventions for Health Promotion Nutrition and Inflammation Aligning Nutrition Education Programs and Research to Effect Change Epigenetics and Nutrition Diet and DNA Methylation Dietary Bioactives and Gene Expression Innovative Dietary Assessment Tools: Including Use of Image and Visualization Methods Research with Dietary Supplementation Applications and Challenges of Public Use Data Sets for Secondary Data Analysis Nutrition Research Assessment of Child and Adolescent Nutritional Status, Growth and Obesity Beverage Consumption in Nationally Representative U.S. Samples Gene Environment Interactions in Obesity Muscle Metabolism, Exercise and Obesity Iron Micronutrient Interventions Nutrient Data Methods and Quality Understanding and Communicating Benefits/Risks of Natural-State Foods [e.g. Minimally Processed, Natural, Organic] Zinc	
3:00-5:00 PM	Maternal Obesity and Longterm Programming *T.M. Badger and J.C. King*	2010 Dietary Guidelines for Americans *A.M. Siega-Riz and P.M. Guenther* GPEC Education Forum *R. J. Wood*
	Human milk biology. Chair: *Lars Bode; Co-chair: Katherine Hunt.*	Lipid and fatty acid metabolism and transport. Chairs: *Richard Bazinet and Tom Brenna* .
	Dietary Bioactive Components IV: Anti-oxidant and Anti-inflammatory functions II. Chairs: *Joshua Bomser and Kelly Walsh; trannee Christopher*	Nutrition interventions for risk factor modification in chronic disease. Chairs: *Connie Bales and Christy Tangney..*

	Masterjohn.	
	Experiences in development and sustainability of nutrition in developing countries. Chair: *Lynette Neufeld and Helena Pachon.*	Animal research models for macronutrient metabolism. Chair: *Sung Woo Kim*
	Selenium and Cancer. Chair: *Cindy Davis and Matthew Jackson.*	

MONDAY, APRIL 11th

8:00-10:00 AM	NSC Genetic Polymorphisms *S.H. Zeisel and W.G. Bergen*	Assessing Evidence of Bioactives in Humans *D.Heber*
	Breastfeeding: determinants and the effect on health outcomes. Chair: Laurie Nommsen-Rivers; Co-chair: Yeon Bai.	Obesity and metabolic syndrome: Emerging concepts. Chair: *Sai Krupa Das and Nicholas Hays.*
	Dietary Bioactive Components II: Mechanisms of Action and Molecular Targets I. Chair: *Clint Allred and Guy Johnson Student Co-Chair: Rebecca Creasy*	Diet and Cancer - translational, clinical and survivorship issues. Chair: *Susan McCann; Co-chair: Jay Whelan*
	Assessment of child and adolescent nutritional status, growth and obesity. Co-chairs: Youfa Wang and Sibylle Kranz	HIV, infant growth, and food security. Chair: *Anna Lartey and Grace Marqui*s.
	Animal research models for nutrient digestion and absorption. Chair: *Matthew Waldron.*	Fat soluble vitamins. Chair: *Maret Traber*
10:30 AM -12:30 PM	INC Childhood Undernutrition *P. Menon and R. Stoltzfus*	Is "Processed" a Four Letter Word? *G.H. Johnson and J.C. King* Training Nutrition Educators for the Health Professions *M. Kohlmeier, D. Seidner and C. Lenders*
	Nutritional Immunology. Chair: *Elizabeth Gardner and David M. Duriancik*	Nutritional Immunology. Chair: *Elizabeth Gardner and David M. Duriancik*
	Dietary Bioactive Components II: Mechanisms of Action and Molecular Targets II. Chair: *G. K. Harris and Suzanne D. Johanningsmeier.*	Diet and Cancer: Animal studies. Chair: *Cindy Davis; Co-chair: Hang Xiao; trainee: Petra Tsuji*
	Advances in food insecurity research. Chairs: *Sonya Jones and Ed Frongillo*	Global health: Dietary intakes and health outcomes in diverse populations. Chair: *Youfa Wang and Lisa Troy.*
	Zinc. Chair: *Angus Scrimegeour*	
12:45- 2:45 PM	G.A. Leveille Lecture	
	Posters: Nutrition and Physical and Cognitive Function Community Nutrition and Aging Nutritional Assessment and Status in Older Populations Community and Public Health Nutrition	

	Diet, Food Security, and Health Promotion in Diverse Communities Dietary Bioactive Components I: Bioavailability and Metabolism of Biomarkers of Intake Dietary Bioactive Components II: Mechanisms of Action and Molecular Targets II Dietary Bioactive Components IV: Anti-oxidant and Anti-inflammatory Functions I Energy Balance, Macronutrient and Weight Biochemical and Molecular Factors The Effects of Food and Dietary Supplements Polyunsaturated Fatty Acids and Health Companion Animal Nutrition and Physiology Prevalence and Determinants of Micronutrient Deficiencies and Impact of Diverse Interventions Nutrition and Health Preventing Childhood Obesity Nutrient Gene Interactions Measures of Diet and Their Associations with Health Outcomes Nutritional Immunology Immune Modulating Nutraceuticals and Functional Foods Selenium Vitamin A, Carotenoids and Retinoids The Nutrient Physiology and Biomarkers Nutrition Knowledge and Behavior Body Composition and Energy Expenditure	
3:00-5:00 PM	Metabolic Regulation and Immune Cells *S.N. Meydani and M.A.Beck*	Recovery from Stunting after 2 Years *K. Dearden and E. Piwoz*
	Community, economic, social approaches to public health nutrition intervention. Chairs: *Kim Harding and Nurgul Fitgerald.*	Nutrient regulation of protein anabolism: mechanism and metabolic effects. Chairs: *Elena Volpi and Yves Boirie*
	Dietary Bioactive Components I: Bioavailability, metabolism and biomarkers of intake. Chair: *Susanne Talcott and Giuliana Noratto Student Co-Chair: Jenna Cramer*	Diet and Cancer: Molecular targets. Chair: *Rosalia Simmen; Co-chair: Niyati Parekh; trainee: Manal Elfakhani*
	Experiences in development and sustanablity of nutrition programs in developing countries II. Chair: *Laura Murray-Kolb and Doona Winham*	Nutritional assessment and status in older populations. Chairs: *Joseph Sharkey and Denise Houston.*
	Iron. Chairs: *James Swain and James McClung*.	

TUESDAY, APRIL 12th

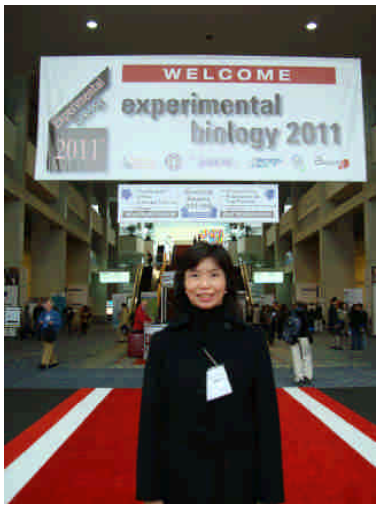
8:00-10:00 AM	Maternal Nutriton & Breast Milk Quality *L.Nommsen-Rivers and D. Chapman*	Global Food Aid and Micronutrient Nutrition *B.L. Rogers and P. Webb*	MNC. Clinical Nutrition Update *C. Bales, E. Saltzman, and M.A. Johnson*
	Regulation of food intake. Chairs: *Kevin Laugero and John Apolzan*		
	Bioactive Components III: Chronic Disease Risk Reduction I. Chair: *Sabrina Peterson and Kristie Canene-Adams and student chair: Cheryl Ainslie.*	Development of evidence-based nutrition education. Chair: *Cindy Fitch; Co-chair: Nancy Cohen*	
	Measures of diet and their associations with health outcomes. Co-chairs: *Ka He and Ana*	Nutrition and age-related changes in body composition. . Chairs: *Wayne Campbell and*	

	Maria Siega-Riz	*Richard Lewis*	
	Vitamin A, carotenoids and retinoids. Chair: *Sherry Tanumihardjo and Michael Green*		
	Maternal-Fetal programing of gene expression		
10:30 AM -12:30 PM	FNB Update: DRIs Calcium and Vit D *L. Meyers, C. Taylor and D. Biers*	MAC Health Disparities in Early NutritionR. *Perez-Escamilla and O.I. Bermudez*	SIG The Changing Face of Nutrition in US *R. Kopec*
	Inflammation and Obesity and obesity associated diseases. Chair: *Holly Wyatt*	Dietary factors affecting lipid metabolism. Chairs: *Kola Ajuwon and Kee-Hong Kim.*	
	Bioactive Components III: Chronic Disease Risk Reduction II. Chair: Cara Frankenfeld and *E. M. Seymour, trainee: Drew Brockman.*	*Nutrient-gene interactions. Chair: Y-X Pan; Co-chair: Dongmin Liu*	
	Innovative dietary assessment tools (including use of image and visualization methods). *Co-chairs: Carol Boushey and Lenore Arab*	Nutrition science translation for policy, practice and consumers. Chairs: *Patricia Williamson-Hughes and Donna Winham*	
	Micronutrient interventions. Chair: *Harold Sandstead and Harold Furr*	Carotenoids and health. Chair: *Lewis Rubin; Co-Chair: Mario Ferruzzi*	
12:45- 2:45 PM	W.O Atwater Lecture		
	Posters: Nutrition Interventions for Risk Factor Modification in Chronic Disease Nutrition and Age-Related Changes in Body Composition Changing Retail Environments Community and Public Health Nutrition Interventions Carotenoids and Health Biofortification of Staple Crops with Micronutrients Diet and Cancer: Animal Studies Diet and Cancer: Translational, Clinical and Survivorship Issues Diet and Cancer: Molecular Targets Bioactive Components III: Chronic Disease Risk Reduction I Bioactive Components IV: Anti-oxidant and Anti-inflammatory Functions II Diet, Lifestyle, and Intervention Effects Protein and Amino Acid Metabolism Metabolic Phenotyping, Metabolomics, and Biomarkers Animal Research Models for Macronutrient Metabolism International Nutrition Mathematical Modeling Nutrition Education in Diverse Populations Development of Evidence-Based Nutrition Education Maternal-Fetal Programming of Gene Expression Global Health: Dietary Intakes and Health Outcomes in Diverse Populations The Use of Consumer Insights to Guide Scientific Research Balancing Foods and Nutrients in the Diet [e.g. Nutrient Density, Ratios, Types] Nutrition Science Translation for Policy, Practice and Consumers Inflammation and Obesity and Obesity Associated Diseases Fat Soluble Vitamins Risk-Benefit Analysis of Micronutrient Supplementation		
3:00-5:00 PM	Science of Global Beverage Consumption *B.M. Popkins and G. Bray*	Enteric Infections meet the Mucosa *A.G. Scrimgeour and J. Baum*	

	Applications and challenges of public use data sets for secondary data analysis nutrition research. Co-chairs: *Niyati Parekh and Carol Boushey.*	Polyunsaturated fatty acids and health. Chairs: *Jay Whelan and Kate Claycombe.*
	Dietary bioactive components including botanicals. Co-Chair: *Nathan Matusheski and Andrew Shao Student Co-Chai*r: Angela Myracle	Nutrient-sensing mechanisms. Chair: *Hong Chen; Co-chair: Chaodong Wu*
	Immune modulating nutraceuticals and functional foods. Chair: *Patricia A Sheridan and Barry Ritz*	Advances in Measurement if Nutrition Behaviors. Chair: *Ed Frongillo and Christine Blake*
	Micronutrients and energy metabolism. Chair: Joyce Gilbert	

WEDNESDAY, APRIL 13th

8:00-10:00 AM	Evidence–based Review Methodology to Support Dietary Guidelines *J. Lua and L. Van Horn*	Blood Cholesteral and CVD Risk *M. Kanter and P. Kris-Etherton*
	Dietary Bioactive Components V: Medicinal and Functional Foods I. Chairs: Sang Woo Choi and Sang K. Noh. Trainee: Chi-Hua (Peter) Lu	
9:00am-3:30AM	NIST Micronutrient Measurement Quality Assuance Workshop. Chair: *Jeanice Brown Thomas*	
10:30 AM -12:30 PM	Evidence-Based Analysis-Controversy? *F. Coletta and C. Kapica*	Saturated Fat and CVD *K. Park*
	Dietary Bioactive Components V: Medicinal and Functional Foods II. Chairs: *Hyang Sook Chun and Yongsoon Park. Trainee: Alexandro Gianforcaro.*	



圖一：研討會會場　　圖二：壁報展示

四、論文被接受發表之大會證明文件

Experimental Biology 2011

Today's Research: Tomorrow's Health

April 9-13
Washington, DC

Annual Meeting of:

American Association of Anatomists (AAA)

The American Physiological Society (APS)

American Society for Biochemistry and Molecular Biology (ASBMB)

American Society for Investigative Pathology (ASIP)

American Society for Nutrition (ASN)

American Society for Pharmacology and Experimental Therapeutics (ASPET)

Guest Societies

Future Meetings

San Diego, CA
April 21 - 25, 2012

Boston, MA
April 20 - 24, 2013

2/5/2011

Yi-Chia Huang
Dr. Yi-Chia Huang
No. 110, Sec. 1, Jianguo N. Rd
Taichung
TAIWAN

Passport Number: 132226457
Date of Birth: 100367

Dear Yi-Chia Huang:

We would like to extend to you an invitation to attend and participate in the Experimental Biology 2011 Annual Meeting scheduled April 9–13, in Washington, DC. Much thought and effort has gone into the planning and organization of this meeting to make it one of the premier scientific meetings for researchers. The scientific program will cover current topics in many areas including anatomy, biochemistry, physiology, pathology, nutrition and pharmacology. For detailed program information please visit our website at http://www.experimentalbiology.org/

As part of U.S. security procedures, applications for visas are being sent to the State Department where they are reviewed. The website for the State Department is http://travel.state.gov/visa. We advise scientists traveling to the United States to apply for a visa as early as possible (at least three months before visa is needed). Because of the number of visas being processed and the need to be thorough with the reviews, this can take as long as 8–10 weeks. Please check with your local U.S. consulate or embassy to find out the earliest that you may apply.

All visitors traveling to the U.S. from visa waiver countries (i.e., Europe, Japan, Australia, etc.) will have to register online 3 days in advance of travel. This rule is mandatory as of January 12, 2009. For more information on the Electronic System for Travel Authorization (ESTA), as well as link to a list of visa waiver countries, please visit:
http://travel.state.gov/visa/temp/without/without_1990.html.

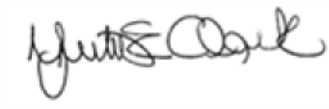
You should begin the visa process as early as possible. If your visa is denied, you will not be issued a refund of your paid registration fee if the cancellation is received after Friday, March 9, 2011.

If you followed the abstract submission guidelines please do not wait until you receive your program

confirmation before applying for your visa.

Although the meeting organizers do not have funds available to assist with your travel, housing, and registration, we hope you are able to attend. We look forward to your participation. If you have any questions or require further assistance, please contact eb@faseb.org.

Sincerely,



Yvette E. Clark
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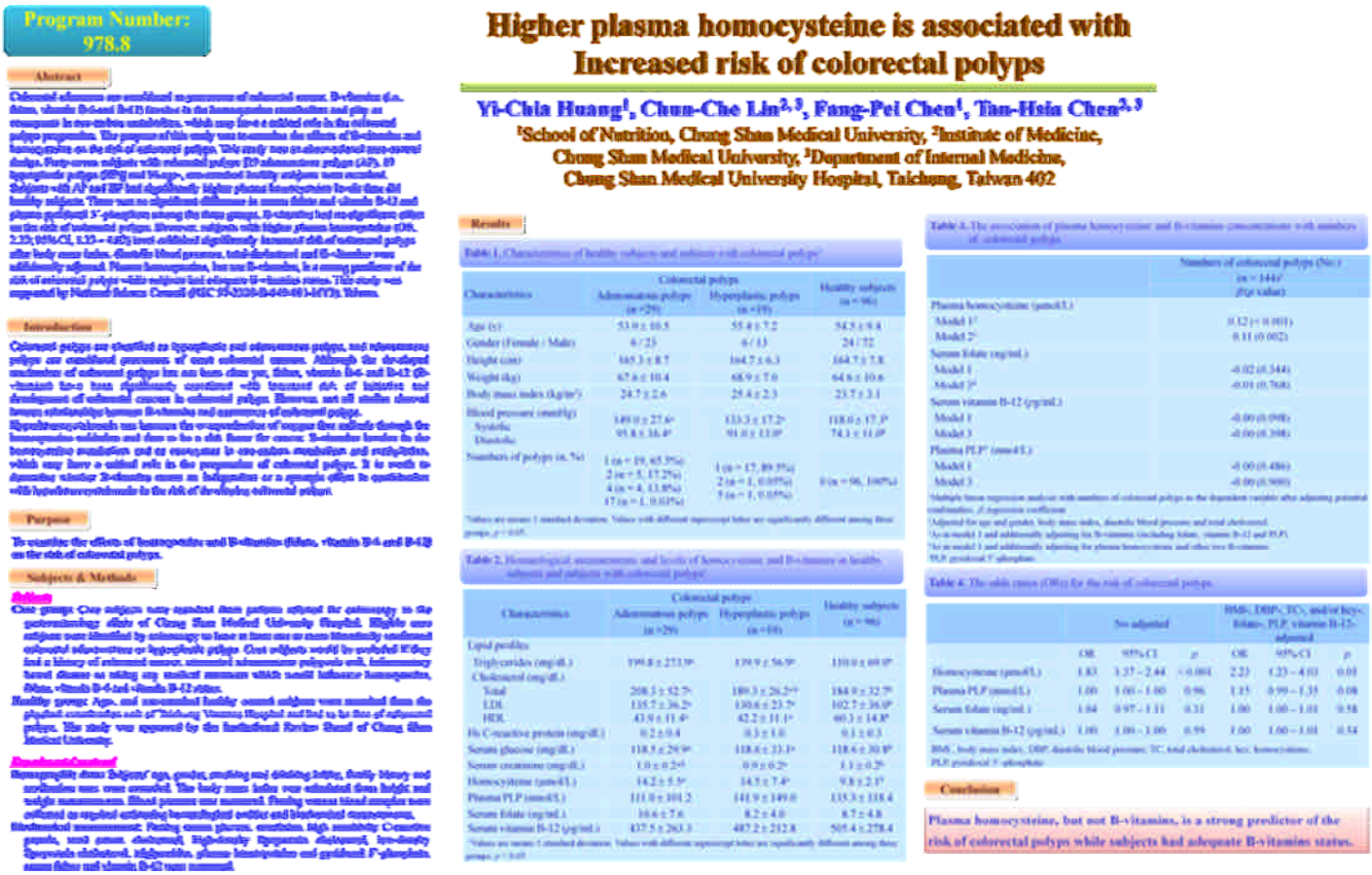
五、發表之論文摘要

Higher plasma homocysteine is associated with increased risk of colorectal polyps

Yi-Chia Huang[1], Chun-Che Lin[2, 3], Fang-Pei Chen[1], Tan-Hsia Chen[2, 3]: [1]School of Nutrition, Chung Shan Medical University, [2]Institute of Medicine, Chung Shan Medical University, [3]Department of Internal Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan 402

Colorectal adenomas are considered as precursors of colorectal cancer. B-vitamins (i.e., folate, vitamin B-6 and B-12) involve in the homocysteine metabolism and play as coenzymes in one-carbon metabolism, which may have a critical role in the colorectal polyps progression. The purpose of this study was to examine the effects of B-vitamins and homocysteine on the risk of colorectal polyps. This study was an observational case-control design. Forty-seven subjects with colorectal polyps [29 adenomatous polyps (AP), 18 hyperplastic polyps (HP)] and 95 age-, sex-matched healthy subjects were recruited. Subjects with AP and HP had significantly higher plasma homocysteine levels than did healthy subjects. There was no significant difference in serum folate and vitamin B-12 and plasma pyridoxal 5'-phosphate among the three groups. B-vitamins had no significant effect on the risk of colorectal polyps. However, subjects with higher plasma homocysteine (OR, 2.18; 95% CI, 1.23 - 3.88) level exhibited significantly increased risk of colorectal polyps after body mass index, diastolic blood pressure, total cholesterol and B-vitamins were additionally adjusted. Plasma homocysteine, but not B-vitamins, is a strong predictor of the risk of colorectal polyps while subjects had adequate B-vitamins status. This study was supported by National Science Council (NSC 97-2320-B-040-031-MY3), Taiwan.



Higher plasma homocysteine is associated with lower vitamin B-6 in critically ill surgical patients

Shih-Chien Huang[1], Chen-Tai Hou[2], Ying-Hsun Wu[3], Pei-Ning Huang[4], Yi-Chia Huang[1]: [1]School of Nutrition, Chung Shan Medical University, Taichung, [2] Critical Care, Changhua Christian Hospital, Changhua, [3]Burn Center, Changhua Cristian Hospital, Changhua, [4]Department of Nutrition, St. Martin De Porres Hospital, Chia-Yi, Taiwan

Stress, inflammation and clinical conditions may increase the utilization and metabolic turnover of B-vitamins (i.e., folate, vitamin B-6 and B-12). Hyperhomocysteinemia might be at least partially due to compromised B-vitamin status in critically ill patients. This cross-sectional study was to examine the association of plasma homocysteine with B-vitamins in critically ill surgical patients. Thirty-four patients in the surgical intensive care unit were enrolled. Disease severity (APACHE II score), albumin, C-reactive protein (CRP), serum folate and vitamin B-12, plasma and erythrocyte pyridoxal 5'-phosphate (PLP) were determined within 24 h of admission and again after 7 days. Plasma homocysteine, serum folate and vitamin B-12 concentrations significantly increased by day 7, whereas plasma and erythrocyte PLP remained constant throughout the study. Plasma homocysteine was not correlated with serum folate and vitamin B-12. However, plasma PLP concentration at admission had a significant effect on the 1st day (β = -0.06, $p < 0.05$) and 7th day (β = -0.05, $p < 0.05$) of plasma homocysteine after adjusting for age, gender, APACHE II score and CRP levels. Lower plasma PLP might be a major contributing factor in the increase of plasma homocysteine concentration in critically ill surgical patients. This study was supported by Changhua Christian Hospital and Chung Shan Medical University (97-CCH-CSMU-07), Taiwan.

國科會補助計畫衍生研發成果推廣資料表

日期:2011/10/15

國科會補助計畫	計畫名稱: 維生素B-6及葉酸與大腸直腸息肉患者的基因多型性、抗氧化活性及甲基化作用關係的探討
	計畫主持人: 黃怡嘉
	計畫編號: 97-2320-B-040-031-MY3　　學門領域: 保健營養

無研發成果推廣資料

97 年度專題研究計畫研究成果彙整表

計畫主持人：黃怡嘉	計畫編號：97-2320-B-040-031-MY3
計畫名稱：維生素 B-6 及葉酸與大腸直腸息肉患者的基因多型性、抗氧化活性及甲基化作用關係的探討	

成果項目			量化			單位	備註（質化說明：如數個計畫共同成果、成果列為該期刊之封面故事...等）
			實際已達成數（被接受或已發表）	預期總達成數(含實際已達成數)	本計畫實際貢獻百分比		
國內	論文著作	期刊論文	0	0	0%	篇	
		研究報告/技術報告	0	0	0%		
		研討會論文	0	0	0%		
		專書	0	0	0%		
	專利	申請中件數	0	0	0%	件	
		已獲得件數	0	0	0%		
	技術移轉	件數	0	0	0%	件	
		權利金	0	0	0%	千元	
	參與計畫人力（本國籍）	碩士生	0	0	0%	人次	
		博士生	1	0	100%		
		博士後研究員	0	0	0%		
		專任助理	1	0	35%		
國外	論文著作	期刊論文	1	2	100%	篇	
		研究報告/技術報告	0	0	0%		
		研討會論文	1	1	100%		
		專書	0	0	0%	章/本	
	專利	申請中件數	0	0	0%	件	
		已獲得件數	0	0	0%		
	技術移轉	件數	0	0	0%	件	
		權利金	0	0	0%	千元	
	參與計畫人力（外國籍）	碩士生	0	0	0%	人次	
		博士生	0	0	0%		
		博士後研究員	0	0	0%		
		專任助理	0	0	0%		

其他成果 (無法以量化表達之成果如辦理學術活動、獲得獎項、重要國際合作、研究成果國際影響力及其他協助產業技術發展之具體效益事項等，請以文字敘述填列。)	無

	成果項目	量化	名稱或內容性質簡述
科教處計畫加填項目	測驗工具(含質性與量性)	0	
	課程/模組	0	
	電腦及網路系統或工具	0	
	教材	0	
	舉辦之活動/競賽	0	
	研討會/工作坊	0	
	電子報、網站	0	
	計畫成果推廣之參與（閱聽）人數	0	

國科會補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現或其他有關價值等，作一綜合評估。

1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估

□達成目標

■未達成目標（請說明，以 100 字為限）

□實驗失敗

□因故實驗中斷

■其他原因

說明：

因大腸直腸息肉受試者參與研究意願未如原先預期，導致受試者募集人數未達原先預定之人數。雖然未達預期人數但樣本數分析及數據分析仍然順利進行，其結果仍可嘗試發表於 SCI 期刊。

2. 研究成果在學術期刊發表或申請專利等情形：

論文：□已發表 □未發表之文稿 ■撰寫中 □無

專利：□已獲得 □申請中 ■無

技轉：□已技轉 □洽談中 ■無

其他：（以 100 字為限）

已經撰寫一篇研究結果並已經將之投稿至 Nutrition Cancer，目前正接受審查中。另外正在撰寫第 2 篇研究成果並將投稿至 SCI 期刊。

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）（以 500 字為限）

本研究以大腸直腸癌為研究模式，透過給予患者單獨或合併維生素 B6 及葉酸補充劑觀察是否能增加免疫功能及改善 DNA 甲基化作用來釐清相關問題。進行完這一系列的研究可以提供更多有關大腸直腸癌的資訊，而使醫師、護士及營養師在大腸直腸癌病人的治療及照護上可利用給予維生素 B6 或葉酸的補充劑達到預防腫瘤生長，改善免疫功能，進而減少醫療費用的支出。此外，研究人員及學生可因參與此研究了解如何設計及執行人體的研究並進一步了解人體研究的複雜性。參與的研究人員可學習如何進行受試者的募集、維生素 B6 及葉酸補充劑介入、及各項生化指標的分析。研究人員另外可透過本研究的資料收集學習有關營養流行病學的統計分析方法。