行政院國家科學委員會專題研究計畫 成果報告

探討維生素 B-6 對同半胱胺酸、氧化壓力、單碳代謝及甲基化作用之影響：大腸直腸癌的橫斷面、病例對照、介入及追蹤研究

研究成果報告(精簡版)

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計 畫 主 持 人：黃怡嘉
共 同 主 持 人：蔣鋒帆、王輝明
計畫參與人員：碩士班研究生-兼任助理人員：楊忞秀
碩士班研究生-兼任助理人員：藍郁淳

報 告 附 件 ：出席國際會議研究心得報告及發表論文

公 開 資 訊 ：本計畫可公開查詢

中 華 民 國 101 年 10 月 29 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。維生素 B-6、葉酸與同半胱胺酸被認為在大腸直腸癌形成中扮演重要角色。本研究目的：1）觀察及比較大腸直腸癌患者的維生素 B-6、葉酸、同半胱胺酸、氧化壓力程度及抗氧化酵素活性的差異性；2）探討維生素 B-6、葉酸、同半胱胺酸對大腸直腸癌患者的氧化壓力程度及抗氧化酵素活性的影響。本研究設計方法是以醫院為基礎的病例-對照研究。於台中榮總大腸直腸外科募集各期（第 0 期、第 1 期+第 2 期、第 3 期、第 4 期），共 168 位大腸直腸癌患者，並於體檢科募集 182 位健康受試者。收集所有受試者的體位測量及藥物疾病史的資料。大腸直腸癌患者的血液採集將於腫瘤切除或化療前採集，健康受試者的血液採集將於進行體檢時進行。血液樣本用來分析臨床血液生化值、維生素 B&not；-6 營養狀況、葉酸營養狀況、同半胱胺酸、脂質過氧化指標及抗氧化酵素活性。大腸直腸癌者中有 82 位為大腸癌，86 位為直腸癌。大腸直腸癌組與健康對照組的血漿 PLP 濃度無顯著差異，但大腸直腸癌組的血清葉酸、血漿同半胱胺酸及光胺酸濃度顯著高於健康對照組。血漿 MDA 濃度在兩組間沒有顯著差異。但是大腸直腸癌組的氧化型低密度脂蛋白(ox-LDL)濃度顯著高於健康對照組。大腸直腸癌組的總抗氧化能力及氧化物歧化酶(SOD)活性顯著高於健康對照組；但是穀胱甘肽過氧化酶(GPx)及穀胱甘肽硫轉移酶 (GST)活性則顯著低於健康對照組。調整年齡、性別、身體質量指數、收縮壓、總膽固醇及 C-反應蛋白後，血漿 PLP 顯著影響血漿 SOD 活性（beta = 0.03, p = 0.01），但與 GPx 及 GST 無顯著相關性。葉酸對氧化壓力及抗氧化能力指標並為顯著影響，但高血漿同半胱胺酸濃度顯著降低血漿 GPx 的活性（beta = -1.39, p < 0.05）。調整年齡、性別、身體質量指數、收縮壓、總膽固醇及 C-反應蛋白後，血漿 PLP 濃度對大腸直腸癌的危險性無顯著影響，但高血清葉酸（OR, 1.04, 95% CI, 1.01 - 1.07, p = 0.022）及高同半胱胺酸（OR, 1.31, 95% CI, 1.17－1.47, p < 0.001）濃度皆顯著增加大腸直腸癌發生的勝算比。高血漿同半胱胺酸及血清葉酸濃度是增加大腸直腸癌發生的重要危險因子。

中文關鍵詞：大腸直腸癌、維生素 B-6、葉酸、同半胱胺酸、氧化壓力、抗氧化能力

英文摘要：Colorectal cancer is now the third leading cause of cancer mortality among men and women in Taiwan. Vitamin B-6, folate and homocysteine may play a critical role in the colorectal cancer progression.

The purposes of this study were to: 1) to compare vitamin B-6, folate and homocysteine status, oxidative stress and antioxidant capacities between patients with colorectal cancer and healthy participants; and 2) to study the effects of vitamin B-6, folate and homocysteine status on oxidative stress and antioxidant capacities in colorectal cancer patients. This was designed as a hospital-based case-control study. One hundred sixty-eight patients with colorectal cancer and 182 healthy controls who meet the inclusion criteria were recruited from Taichung General Veterans Hospital. Hematological values, plasma and erythrocyte PLP, serum and erythrocyte folate, homocysteine, lipid peroxidation indicators [plasma malondialdehyde (MDA), oxidized-LDL], total antioxidant capacity and antioxidant enzymatic activities [glutathione peroxidase (GPx), glutathione S-transferase (GST), superoxide dismutase (SOD)] were measured. Eight-two patients were colon cancer, while 86 patients were rectal cancer. There was no significant difference in plasma PLP and MDA levels between two groups, while patients with colorectal cancer had significantly higher serum folate and plasma homocysteine concentrations when compared to healthy controls. Patients with colorectal cancer had significantly higher oxidized-LDL, total antioxidant capacities and SOD activities, while there were lower GPx and GST activities than did healthy controls. Plasma PLP significantly positively affected plasma SOD activity (beta = 0.03, $p = 0.01$) while plasma homocysteine negatively affected plasma GPx activity (beta = -1.39, $p < 0.05$) after adjusting age, gender, body mass index, systolic blood presser, total cholesterol and C-reactive protein. Plasma PLP had no significant effect on the risk of colorectal cancer; however, higher serum folate (OR, 1.04, 95% CI, 1.01 - 1.07, $p = 0.022$) and plasma homocysteine (OR, 1.31, 95% CI, 1.17-1.47, $p < 0.001$) significantly increased the risk of colorectal cancer after adjusting age, gender, body mass index, systolic blood presser, total cholesterol and C-reactive protein. Higher

serum folate and plasma homocysteine are two important factors to affect the risk of colorectal cancer.

英文關鍵詞： colorectal cancer, vitamin B-6, folate, homocysteine, oxidative stress, antioxidant capacity

行政院國家科學委員會補助專題研究計畫 □期中進度報告 ■期末報告

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計畫主持人：黃怡嘉 教授
共同主持人：王輝明 主治醫師 / 蔣鋒帆 主治醫師
計畫參與人員：楊忞秀 碩士生 / 藍郁淳 碩士生

本計畫除繳交成果報告外，另含下列出國報告，共 _1_ 份：
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■出席國際學術會議心得報告
□國際合作研究計畫國外研究報告

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中 華 民 國 101 年 10 月 30 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。維生素B-6、葉酸與同半胱胺酸被認為在大腸直腸癌形成中扮演重要角色。本研究目的：1) 觀察及比較大腸直腸癌患者的維生素B-6、葉酸、同半胱胺酸、氧化壓力程度及抗氧化酵素活性的差異性；2) 探討維生素B-6、葉酸、同半胱胺酸對大腸直腸癌患者的氧化壓力程度及抗氧化酵素活性的影響。本研究設計方法是以醫院為基礎的病例-對照研究。於台中榮總大腸直腸外科募集各期（第0期、第1期+第2期、第3期、第4期），共168位大腸直腸癌患者，並於體檢科募集182位健康受試者。收集所有受試者的體位測量及藥物疾病史的資料。大腸直腸癌患者的血液採集將於腫瘤切除或化療前採集，健康受試者的血液採集將於進行體檢時進行。血液樣本用來分析臨床血液生化值、維生素B-6營養狀況、葉酸營養狀況、同半胱胺酸、脂質過氧化指標及抗氧化酵素活性。大腸直腸癌者中有82位為大腸癌，86位為直腸癌。大腸直腸癌組與健康對照組的血漿PLP濃度無顯著差異，但大腸直腸癌組的血清葉酸、血漿同半胱胺酸及光胺酸濃度顯著高於健康對照組。血漿MDA濃度在兩組間沒有顯著差異。但是大腸直腸癌組的氧化型低密度脂蛋白(ox-LDL)濃度顯著高於健康對照組。大腸直腸癌組的總抗氧化能力及氧化物歧化酶(SOD)活性顯著高於健康對照組；但是穀胱甘肽過氧化酶 (GPx)及穀胱甘肽硫轉移酶 (GST)活性則顯著低於健康對照組。調整年齡、性別、身體質量指數、收縮壓、總膽固醇及C-反應蛋白後，血漿PLP顯著影響血漿SOD活性（$\beta = 0.03$, $p = 0.01$），但與GPx及GST無顯著相關性。葉酸對氧化壓力及抗氧化能力指標並為顯著影響，但高血漿同半胱胺酸濃度顯著降低血漿GPx的活性（$\beta = -1.39$, $p < 0.05$）。調整年齡、性別、身體質量指數、收縮壓、總膽固醇及C-反應蛋白後，血漿PLP濃度對大腸直腸癌的危險性無顯著影響，但高血清葉酸（OR, 1.04, 95% CI, 1.01 – 1.07, $p = 0.022$）及高同半胱胺酸（OR, 1.31, 95% CI, 1.17 – 1.47, $p < 0.001$）濃度皆顯著增加大腸直腸癌發生的勝算比。高血漿同半胱胺酸及血清葉酸濃度是增加大腸直腸癌發生的重要危險因子。

關鍵詞：大腸直腸癌、維生素B-6、葉酸、同半胱胺酸、氧化壓力、抗氧化能力

英文摘要

Colorectal cancer is now the third leading cause of cancer mortality among men and women in Taiwan. Vitamin B-6, folate and homocysteine may play a critical role in the colorectal cancer progression. The purposes of this study were to: 1) to compare vitamin B-6, folate and homocysteine status, oxidative stress and antioxidant capacities between patients with colorectal cancer and healthy participants; and 2) to study the effects of vitamin B-6, folate and homocysteine status on oxidative stress and antioxidant capacities in colorectal cancer patients. This was designed as a hospital-based case-control study. One hundred sixty-eight patients with colorectal cancer and 182 healthy controls who meet the inclusion criteria were recruited from Taichung General Veterans Hospital. Hematological values, plasma and erythrocyte PLP, serum and erythrocyte folate, homocysteine, lipid peroxidation indicators [plasma malondialdehyde (MDA), oxidized-LDL], total antioxidant capacity and antioxidant enzymatic activities [glutathione peroxidase (GPx), glutathione *S*-transferase (GST), superoxide dismutase (SOD)] were measured. Eight-two patients were colon cancer, while 86 patients were rectal cancer. There was no significant difference in plasma PLP and MDA levels between two groups, while patients with colorectal cancer had significantly higher serum folate and plasma homocysteine concentrations when compared to healthy controls. Patients with colorectal cancer had significantly higher oxidized-LDL, total antioxidant capacities and SOD activities, while there were lower GPx and GST activities than did healthy controls. Plasma PLP significantly positively affected plasma SOD activity（$\beta = 0.03$, $p = 0.01$）while plasma homocysteine negatively affected plasma GPx activity（$\beta = -1.39$, $p < 0.05$）after adjusting age, gender, body mass index, systolic blood presser, total cholesterol and C-reactive protein. Plasma PLP had no significant effect on the risk of colorectal cancer; however, higher serum folate（OR, 1.04, 95% CI, 1.01 – 1.07, $p = 0.022$）and plasma homocysteine（OR, 1.31, 95% CI, 1.17 – 1.47, $p < 0.001$）significantly increased the risk of colorectal cancer after adjusting age, gender, body mass index, systolic blood presser, total cholesterol and C-reactive protein. Higher serum folate and plasma homocysteine are two important factors to affect the risk of colorectal cancer.

Keywords: colorectal cancer, vitamin B-6, folate, homocysteine, oxidative stress, antioxidant capacity

前言

大腸直腸癌

大腸直腸是消化道的末端，廣義的大腸包括結腸和末端的直腸。最常見的大腸直腸癌，乃是由腸粘膜細胞不受控制的增生，細胞成不規則排列並向周邊組織侵犯，甚至向身體各處轉移，造成腸道出血、阻塞並耗盡正常組織。大腸直腸癌較易發生於年紀大者，從 40 – 45 歲開始隨年紀增加而增加其罹患率。隨著經濟進步、飲食習慣逐漸西化，台灣的大腸直腸癌死亡率節節攀升，目前已是台灣男性及女性主要癌症死亡原因的第三名。在所有營養素中，目前已知維生素 B-6 及葉酸與大腸直腸癌形成有顯著的相關性。不過維生素 B-6 及葉酸是直接參與大腸直腸癌的形成，或者是間接透過其他機制影響大腸直腸癌的形成則需要進一步的研究。

葉酸 vs. 維生素 B-6 與大腸直腸癌

葉酸在人體主要是以具有活性的四氫葉酸的輔酶型式參與單碳及胺基酸代謝、合成嘌呤及嘧啶，進一步合成 DNA 等。世代研究及病例對照研究皆指出葉酸營養狀況（包括飲食及血清營養狀況指標）與大腸直腸癌的發生率呈顯著負相關（Giovannucci et al., 1995; Giovannucci et al., 1998; Mason & Choi, 2000; Le Marchand et al., 2009; Wei et al., 2005）。Giovannucci 等人（1995）指出即使受試者的酒精攝取量每天大於 2 份，但若葉酸攝取量高時其大腸直腸癌發生的危險性可被抵銷。在 Nurses' Health Study ，女性服用> 400 g/d 葉酸可顯著降低 31% 大腸直腸癌的罹患率（RR, 0.69; 95% CI, 0.52 - 0.93）（Giovannucci etal., 1998）。但是並非所有的研究都認為高葉酸與低大腸直腸癌罹患率有相關性（Watkins et al.,2000; Otaniet al., 2005; Martinez et al., 2006; Zhang et al., 2006）。美國癌症協會的 Cancer Prevention Study II cohort 指出葉酸與大腸直腸癌的發生並無顯著相關性（Watkins et al., 2000）。Women's Healthy Study 結果發現即使給予受試者服用含有葉酸的綜合維生素長達十年，與大腸直腸癌的發生仍無顯著相關（Zhang et al., 2006）。

動物及人體研究指出葉酸在細胞癌化的過程可能扮演雙重的角色，在早期癌化的進展階段，也就是在腸道的腫瘤病灶（neoplastic foci）出現前，高葉酸濃度有助於降低癌症的進程；但若是前腫瘤傷害（preneoplastic lesions）已出現，此時高濃度葉酸反而會促進大腸直腸腫瘤的加速發展（Kim 2004; Kim 2007）。上述理論或許可說明為何葉酸與大腸直腸癌的關係有不一致性的結果。Martinez 等人（2006）指出血漿葉酸濃度的高低對大腸直腸癌的復發無顯著影響，雖然此研究沒有探討維生素B-6，但作者認為維生素B-6的營養狀況可能相較於葉酸在大腸直腸癌復發的過程中扮演更重要的角色。維生素B-6在大腸直腸癌進展過程中扮演的是否也如葉酸一樣是雙重的角色或者是單一的影響？另外維生素B-6是獨立於葉酸外影響大腸直腸癌的發生？或是與葉酸有協同作用後再進而影響大腸直腸癌的發生？以上的議題皆須要進一步的探討。

維生素B-6 是2-甲基-3-羥基-5-羥甲基比哆胺的衍生物總稱，主要以3 種自由型式：比哆醇（pyridoxine, PN），比哆醛（pyridoxal, PL），比哆胺（pyridoxamine, PM），及其磷酸鹽型式：磷酸比哆醇(pyridoxine phosphate, PNP)，磷酸比哆胺（pyridoxamine phosphate , PMP），及磷酸比哆醛（pyridoxal 5'-phosphate, PLP）存在。鹽酸比哆醇則是商業販售的補充劑型式。維生素B-6 主要的代謝物是比哆酸（4-pyridoxic acid, 4-PA）。磷酸比哆醛為具有生物活性的輔酶，擔任胺基酸、核酸、肝醣、比咯紫質及脂肪代謝過程中的輔酶（Leklem, 1988）。因此，PLP 對於荷爾蒙的調節，紅血球的生成，免疫功能及神經系統的功能有很重要的影響（Leklem, 1988）。除了上述功能外，維生素B-6 在同半胱胺酸代謝、氧化壓力、發炎反應過程中所扮演的角色，進而與許多慢性疾病形成的關係近年來已引起廣泛的注意及討論。

維生素B-6 已被大多數研究證實與大腸直腸癌發生有關。以動物為研究對象的結果指出適度的維生素B-6 攝取（1 –35 mg PN- HCl/kg diet）可以顯著降低大腸直腸癌的發生（Coburn, 1994; Komatsu et al., 2001; Reeves et al., 1993）。一個分析七個國家調查資料的生態研究指出，高維生素B-6 攝取量與大腸直腸癌的發生率呈顯著負相關（OR, 0.84,95% CI, 0.71-0.99）（Jansen et al., 1999）。Wei等人（2005）在Nurses' Health Study的世代研究中以鳥巢式病例對照（nested case-control）觀察到高血漿PLP 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）。以族群為基礎的世代研究（The Swedish Mammography Cohort），也呈現相似的結果（*p* valuefor trend = 0.002）（Larsson et al., 2005）。日本的世代研究結果指出男性若每天攝取1.91 mg 的維生素B-6 會比每天只攝取1.09 mg 的男性顯著降低大腸直腸癌發生的危險性（HR, 0.69; 95% CI, 0.48 –0.9 8; *P* trend = 0.03）（Ishihara et al., 2007）。一個癌症預防的世代研究（α-Tocopherol, β-Carotene Cancer Prevention cohort Study）的研究結果指出血清維生素B-6 與大腸癌的罹患率呈顯著負相關（OR, 0.3; 95% CI, 0.11 - 0.82）; 但是葉酸對大腸癌的罹患率則無顯著的相關（Weinstein et al., 2008）。另一個包含多種族的大型世代研究（n > 215,000）（Multiethnic Cohort）結果指出血漿PLP 濃度若 > 101 nmol/L時會顯著降低大腸直腸癌的發生（OR, 0.49; 95% CI, 0.29 –0.83）；即使調整血漿葉酸濃度後，其顯著性仍不受影響（OR, 0.52; 95% CI, 0.29 –0.92）（Le Marchand et al., 2009）。最近剛發表的一篇系統性分析研究（meta-analysis）指出每增加100 *p*mol/mL 的血漿PLP 濃度會降低49% 的大腸直腸癌發生率（RR, 0.51; 95% CI, 0.38-0.69）（Larrson et al., 2010）。但是並非所有證據皆支持維生素B-6 與大腸直腸癌發生有關。在Iowa Women's Healthpopulation-based 的世代研究（追蹤期> 13 y），維生素B-6 與大腸直腸癌的發生並無顯著相關（Harnack et al., 2002）。Otani等人（2005）以醫院族群為基礎的病例對照研究，也觀察到大腸直腸癌患者（n = 107）與經年齡性別配對後的健康受試者（n = 224）的維生素B-6攝取量與大腸直腸癌發生率並無顯著相關。另一世代研究（the Women's Health Study）也發現維生素B-6總攝取量（含飲食及補充劑）及綜合維生素補充劑的使用與大腸直腸癌發生率無顯著相關性（Zhang et al., 2006）。

綜合上述，維生素B-6 與大腸直腸癌的關係似乎需進一步確認。若維生素B-6 與大

腸直腸癌的發生有顯著相關性，則值得進一步探討維生素B-6 是直接或是間接透過其他途徑（如：氧化壓力、同半胱胺酸代謝）而影響大腸直腸癌的發生。

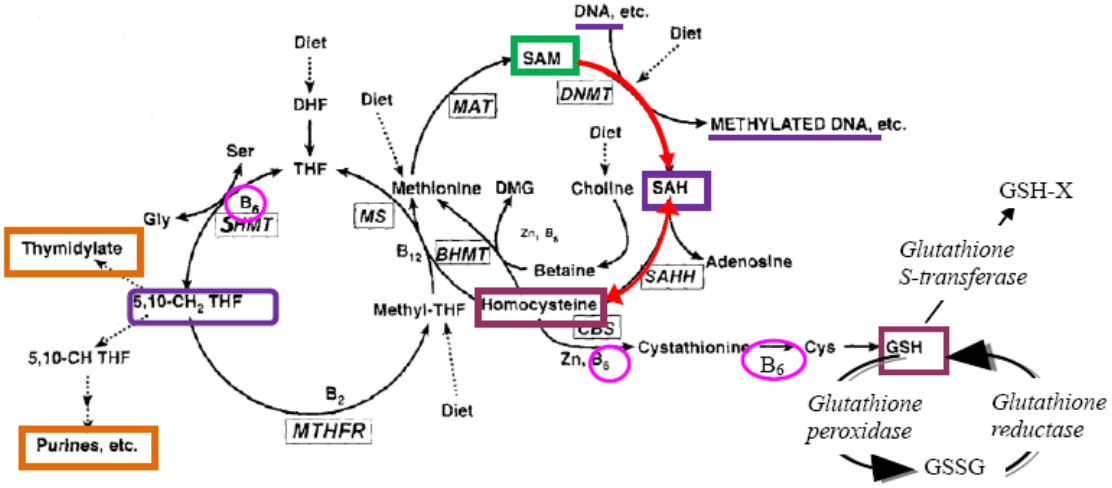
維生素B-6 與氧化壓力

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）。活性氧（reactive oxygen species, ROS）為氧分子代謝後的產物，包括帶有未成對電子，例如：超氧離子、氫氧離子，或能從其他分子接受電子形成過氧化氫等分子。當細胞外過多的ROS 形成過高的氧化壓力環境，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, 1992）。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）的值（0.86 ± 0.1 vs. 0.54 ± 0.08 nmol/mg）均顯著高於健康受試者（Rainis et al., 2007）。若能增加大腸直腸癌受試者的抗氧化壓力能力，或許能預防或降低癌症的復發或提高存活率。

有文獻指出維生素B-6 可保護細胞免於氧化壓力的威脅且其抗氧化能力甚至可能超過維生素C 及E (Bilski et al., 2000)。U937 單核細胞實驗指出維生素B-6 可以避免因添加過氧化氫所生成的氧自由基及脂質過氧化（Kannan & Jain, 2004）。若添加維生素B-6 於高同半胱胺酸血症的大鼠所食的葉酸缺乏但甲硫胺酸過多的的飲食，發現可降低氧化壓力的指標（如：血清TBARS）（Mahfouz & Kummerow, 2004）。雖然目前維生素B-6 清除氧自由基以及抑制脂質過氧化的機制尚不十分清楚，但維生素B-6 或許可被視為直接或間接的抗氧化營養素。維生素B-6 的化學結構因含有氫氧基（－OH）及胺基（$-NH_2$），被認為可直接與過氧自由基結合進而清除自由基及降低脂質過氧化（Bilski et al., 2000; Kannan & Jain, 2004; Ohta & Foote, 2002）。另外，維生素B-6 也可以透過穀胱甘肽（glutathione）抗氧化系統間接進行抗氧化功能。同半胱胺酸經轉硫作用形成半胱胺酸（cysteine）的過程中需要維生素B-6 作為輔酶，半胱胺酸會進而轉換形成穀胱甘肽(圖一)。穀胱甘肽是穀胱甘肽硫轉移（glutathione *S*-transferase, GST）及穀胱甘肽過氧化酶（glutathione peroxidase, GPx）的重要輔因子。研究指出維生素B-6 缺乏的大鼠其肝臟組織的穀胱甘肽、穀胱甘肽硫轉移酶及穀胱甘肽過氧化酶濃度皆低於正常組的大鼠（Taysi, 2005）。但是也有動物（Lima et al., 2006）及人體（Davis et al., 2006; Lamers et al., 2009）試驗指出即使維生素B-6 攝取不足不僅不影響血漿半胱胺酸濃度，且還會增加血漿胱硫醚及穀胱甘肽濃度；推測可能是因處在高氧化壓力或發炎狀態下，大量消耗維生素B-6 而增加穀胱甘肽的生成或從肝臟貯存釋放到血漿利用。目前有關維生素B-6 與穀胱甘肽的關係大部分皆是動物試驗或僅有以健康受試者為對象的研究。大腸直腸癌患者是否有可能因維生素B-6 攝取不足或血漿磷酸比哆醛缺乏而降低清除自由基及脂質過氧化的能力，進而增加癌症復發或減少存活率？或者是經由降低或增加半胱胺酸及穀胱甘肽的形成進而改變其抗氧化能力？若給予大腸直腸癌手術切除後的患者維生素B-6 的補充，是否有助於降低氧化壓力及提高抗氧化能力是值得進一步研究的。

維生素B-6 與同半胱胺酸

同半胱胺酸代謝途徑包含再甲基化（remethylation）與轉硫作用（trans-sulfuration）。當空腹狀態時，身體傾向再甲基化作用合成甲硫胺酸，再轉換成S-腺核苷甲硫胺酸（S-adenosyl-methionine, SAM），為甲基的提供者，由SAM進行去甲基化作用後形成S-腺核苷同半胱胺酸（S-adenosyl-homocysteine, SAH），此反應雖為可逆反應，但是較偏向SAH 的合成（圖一）。當甲硫胺酸濃度已足夠人體需求時，過剩的甲硫胺酸會促使同半胱胺酸進行轉硫作用，經由胱硫醚β-合成酶（cystathionine β-synthase）-磷酸比哆醛的依賴型酵素，催化絲胺酸轉成胱硫醚，由胱硫醚分解酶水解形成半胱胺酸，因此若維生素B-6 缺乏可能會導致同半胱胺酸蓄積，造成血漿同半胱胺酸濃度上升（圖一）。美國兩個大腸直腸癌的相關研究 [wheat bran fiber (WBT) trial & ursodeoxycholic acid (UDC) trial] 指出未服用綜合維生素補充劑的受試者若有較高的血漿同半胱胺酸濃度有顯著較高的大腸直腸癌復發率（WBT trial: OR, 2.25; 95% CI, 1.38–3.66; UDCA trial: OR,1.93; 95% CI, 1.07–3.49）（Martinez et al. 2006）。最近的研究也指出高血漿同半胱胺酸濃度會增加大腸直腸癌復發的機率（OR, 2.11; 95% CI, 1.01–4.40）（Bobe et al., 2010）。高同半胱胺酸促進癌症生成的機制被認為可能是直接經由活化NF-κB，進而促使前發炎細胞激素及癌化促進基因的表現（Zhou & Austin, 2009）；或是間接因為參與同半胱胺酸代謝的維生素B-6及葉酸也參與單碳代謝，因此高同半胱胺酸也會影響DNA的合成以及甲基化作用，進而導致癌症的形成（Lucock, 2006; Zhou & Austin, 2009）。同半胱胺酸在罹患大腸直腸癌過程中扮演的直接或間接的角色是需要進一步研究的。



圖一：單碳代謝、同半胱胺酸代謝及穀胱甘肽生成
(Adapted and modified from Davis & Uthus, 2004)

研究目的

過去二十年，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。但是，有關維生素B-6 與大腸直腸癌患者的葉酸營養狀況、同半胱胺酸及氧化壓力程度的相關研究卻很少或仍有爭議。因此，本研究的目的為：1) 觀察及比較大腸直腸癌患者的葉酸、同半胱胺酸、氧化壓力程度及抗氧化酵素活性的差

異性；2) 探討葉酸、同半胱胺酸對大腸直腸癌患者的氧化壓力程度及抗氧化酵素活性的影響。

研究方法

受試者

本研究於台中榮總大腸直腸外科招募大腸直腸癌患者。納入條件為：1) 受試者須年滿20 歲；且2) 病理切片組織經醫生診斷為大腸直腸癌。病人若有以下條件則排除在本研究外：1) 懷孕或哺乳。本研究經過台中榮總人體試驗委員會核准進行。大腸直腸癌病程分為五期，第零期：腫瘤僅局限於大腸直腸黏膜表面，可手術切除；第一期：侵犯黏膜下層及肌肉層，無淋巴腺轉移，可手術切除；第二期：穿透肌肉層進入漿膜層，無淋巴腺轉移，可手術切除，若有危險因子，須於術後化學治療；第三期：癌細胞已轉移到附近淋巴腺，手術切除後合併術後化療；第四期：腫瘤已經有遠端轉移(如肝、肺)，主要以化學治療並輔以手術或放射治療。本研究依患者病理診斷分期及腫瘤位置進行分組。依腫瘤分期後的結果，分為四組：第0 + 1期；第2期；第3期及第4期。

健康受試者於台中榮總體檢科募集。受試者完成所有的生理檢查，包括大腸直腸鏡檢查。受試者納入條件為：1) 無心臟、肝臟、腎臟、腸胃道、糖尿病、酒精中毒、癌症或其他代謝疾病；2) 過去無使用過荷爾蒙療法及無服用任何會干擾維生素 B-6 及葉酸代謝的藥物；3) 血液生化值皆正常，包括：尿素氮 < 24 mg/dL、肌酸酐 < 1.4 mg/dL、鹼性磷酸酶< 130 IU/L、丙胺酸轉胺酶 < 40 IU/L、天門冬胺酸轉胺酶< 40 IU/L、三酸甘油脂 < 190 mg/dL、總膽固醇 < 230 mg/dL、低密度脂蛋白< 130 mg/dL 及高密度脂蛋白 > 35 mg/dL；4) 酒精攝取 ≤ 2 份/天（一份酒精=12 oz 啤酒，6 oz 紅酒，1 oz 白酒）；5) 無抽菸；6) 過去一年內的體重變化沒有超過± 4 公斤；7) 目前體重不超過理想體重 20%。若受試者有以下條件將排除在本研究外：1) 懷孕或哺乳中的婦女；2) 受試者經全大腸鏡檢查發現息肉或疑似腺瘤。

資料收集

包括年齡、性別、抽菸習慣、酒精攝取量、家族病史。測量受試者的身高、體重、腰圍及臀圍，計算其身體質量指數（body mass index, BMI; kg/m^2）。受試者休息至少五分鐘後測量血壓，若血壓＞140/90 mmHg 或者有服用抗高血壓藥物者則定義為高血壓。

血液生化值分析

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，進行各項生化分析，包括：白血球 (white blood cell, WBC)、總淋巴球計數 (total lymphocyte count, TLC)、嗜中性球 (neutrophils)、血紅素 (hemoglobin)、血比容 (hematocrit)、白蛋白(albumin)、肌酸酐 (creatinine)、高敏感度C-反應蛋白（high sensitivity CRP, hs-CRP）、總膽固醇(total cholesterol, TC)、高密度脂蛋白膽固醇 (high density lipoprotein-cholesterol, HDL)、低密

度脂蛋白膽固醇 (low density lipoprotein-cholesterol, LDL)、三酸甘油酯 (Triglyceride, TG)、血清葉酸、血漿同半胱胺酸及胱胺酸、血漿丙二醛（malondialdehyde, MDA）、血漿氧化型低密度脂蛋白 (ox-LDL)、血漿總抗氧化能力、血漿穀胱甘肽過氧化酶 (GPx)活性、血漿穀胱甘肽硫轉移酶 (GST)活性及血漿超氧化物歧化酶(SOD)活性。

血漿PLP以高效能液相層析 (HPLC)分析（Talwar et al, 2003）。螢光偵測器之excitation與emission波長分別為320及420 nm。維生素B-6測定過程在微弱黃光下進行，避免光的破壞。當血漿PLP濃度< 20 nmol/L表體內維生素B-6缺乏 (Food and Nutrition Board, 1998; Leklem, 1990)。血清葉酸濃度是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)。當血清葉酸濃度< 3 ng/mL代表葉酸缺乏。血漿同半胱胺酸及胱胺酸濃度的分析是參考Araki及Sako (1987) 的方法，利用HPLC 分析。使用的分離管柱為LiChrospher® 100 RP-18e (250 mm × 4 mm I.D，Merck)。移動相為0.1 M KH2PO4，3.5% acetonitrile，pH＝3.5，流速為1.2 mL/min，螢光檢測器之excitation 波長為385 nm，emission波長為515 nm。當自由基攻擊細胞膜的多元不飽和脂肪酸後會進行自由基的連鎖反應，導致體內脂質過氧化作用。參考Jialal & Scaccini (1992) 的方法，取90 μL血漿加入160 μLPBS 緩衝液，而後分別加入0.1N HCl 及10% 磷鎢酸 (phosphotungstic acid) 使蛋白質變性，之後加入0.7 % TBA (thiobarbituric acid) 混合，於100℃加熱30 分鐘，待冷卻後，加入正丁醇，離心（2,000 rpm，10 分鐘），利用正丁醇萃取TBA 與脂質過氧化產物-MDA形成的紅色複合物質，測定螢光值(excitation: 515 nm; emission: 555 nm)。MDA 越多表示氧化程度越嚴重。低密度脂蛋白的氧化狀況 (ox-LDL) 是利用市售ox-LDL ELISA kit (Mercodia AB, Uppsala, Sweden) 分析，利用酵素免疫分析儀於450 nm 波長讀取吸光值，並由標準品曲線以求得ox-LDL 濃度。血漿總抗氧化能力的分析是參考Erel（2004）的方法。穀胱甘肽過氧化酶 (GPx) 是利用商業套組檢測 (glutathione peroxidase assay kit, Cayman Chemical Company, Michigan, USA)。在340 nm 波長下吸光值減少的速率可作為其穀胱甘肽過氧化酶的活性。穀胱甘肽硫轉移酶 (GST) 活性是以商業套組檢測 (glutathione *S*-transferase assay kit, Cayman Chemical Company, Michigan, USA)。在340 nm 波長下吸光值增加的速率可作為其穀胱甘肽硫轉移酶的活性。超氧化物歧化酶 (SOD) 是利用商業套組檢測 (superoxide dismutase, Cayman chemical company, Ann Arbor, MI, USA)。於波長450 nm下，測定之吸光值可表示超氧化物歧化酶清除超氧陰離子的能力，因此可作為超氧化物歧化酶活性。

<u>統計分析</u>

資料皆利用SAS 統計軟體 (version 9.12; SAS Institute, Cary, NC, USA)分析。利用Chi-square、Student *t*-test 比較兩組間體位測量值及及生化檢測值之差異性。以multiple linear regression analyses 調整干擾因子後，分析維生素B-6、葉酸或同半胱胺酸對大腸直腸癌患者的氧化壓力程度及抗氧化酵素活性的影響。以logistic regression model計算維生素B-6、葉酸、同半胱胺酸對罹患大腸直腸癌的odds ratio，以95%信賴區間表示相關

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mean ± standard deviation（SD）表示。

結果

本研究總共募集了 168 位大腸直腸癌受試者（65 位女性，103 位男性），182 位健康對照受試者。大腸直腸癌者中有 82 位為大腸癌，86 位為直腸癌。大腸直腸癌與健康者之基本資料列於 Table 1。大腸直腸癌組的年齡及血壓皆顯著高於健康對照組，但身高及體重則顯著低於健康對照組。

Table 2 中，健康對照組的淋巴球、血紅素、血球容積比、白蛋白及總膽固醇值皆顯著高於大腸直腸癌組，但 C-反應蛋白濃度則顯著低於大腸直腸癌組。

Table 3顯示維生素B-6、葉酸、氧化壓力指標及抗氧化能力程度。大腸直腸癌組與健康對照組的血漿PLP濃度無顯著差異，但大腸直腸癌組的血清葉酸、血漿同半胱胺酸及光胺酸濃度顯著高於健康對照組。血漿MDA濃度在兩組間沒有顯著差異。但是大腸直腸癌組的氧化型低密度脂蛋白濃度顯著高於健康對照組。在抗氧化酵素活性的部分，大腸直腸癌組的總抗氧化能力及SOD活性顯著高於健康對照組；但是GPx 及GST活性則顯著低於健康對照組。

以multiple linear regression analyses 調整年齡、性別、身體質量指數、收縮壓、總膽固醇及C-反應蛋白後，血漿PLP顯著影響血漿SOD活性（$\beta = 0.03$, $p = 0.01$），但與GPx及GST無顯著相關性（data not shown）。葉酸對氧化壓力及抗氧化能力指標並為顯著影響（data not shown），但高血漿同半胱胺酸濃度顯著降低血漿GPx的活性（$\beta = -1.39$, $p < 0.05$）。

以logistic regression調整年齡、性別、身體質量指數、收縮壓、總膽固醇及C-反應蛋白後（Table 4），血漿PLP濃度對大腸直腸癌的危險性無顯著影響，但高血清葉酸（OR, 1.04, 95% CI, 1.01 – 1.07, $p = 0.022$）及高同半胱胺酸（OR, 1.31, 95% CI, 1.17 – 1.47, $p < 0.001$）濃度皆顯著增加大腸直腸癌發生的勝算比。

討論

大腸直腸癌患者的確較健康對照組承受較高的氧化壓力（高同半胱胺酸、高氧化型LDL）及較低的過去的研究維生素B-6可直接或間接扮演抗氧化的角色）（Bilski et al., 2000; Kannan & Jain, 2004; Ohta & Foote, 2002; Taysi, 2005）。本研究也發現維生素B-6可直接顯著增加血漿SOD活性。維生素B-6與穀胱甘肽抗氧化系統的GPx及GST並無顯著相關性，因此應不是間接透過穀胱甘肽抗氧化系統扮演抗氧化的功能。雖然維生素B-6會顯著增加SOD活性，但對大腸直腸癌發生的危險性並無影響。相對於維生素B-6，高血漿同半胱胺酸及血清葉酸似乎才是增加大腸直腸癌發生的重要危險因子。血漿同半胱胺酸可能是較維生素B-6更為重要的影響大腸直腸癌發生的因子。過去的研究結果顯示高血清葉酸可降低大腸直腸癌發生的危險性（Giovannucci et al., 1995; Giovannucci et al., 1998; Mason & Choi, 2000; Le Marchand et al., 2002; Wei et al., 2004; Sanjoaquin, et al., 2005），但本研究結果卻與上述研究相反。動物及人體研究指出葉酸在細胞癌化的過程

可能扮演雙重的角色，在早期癌化的進展階段，也就是在腸道的腫瘤病灶（neoplastic foci）出現前，高葉酸濃度有助於降低癌症的進程；但若是已造成前腫瘤傷害（preneoplastic lesions），此時高濃度葉酸反而會促進大腸直腸腫瘤的加速發展（Kim 2004; Kim 2007; Ulrich & Potter , 2007）。本研究為病例對照研究，在因果關係上很容易錯置，因此上述理論或許可說明為何本研究觀察到高血清葉酸與大腸直腸癌發生的危險性呈顯著正相關。有關葉酸與大腸直腸癌的關係有再進一步釐清的必要性。

大腸直腸癌患者的維生素B-6與健康對照受試者並無顯著差異，但較健康對受試者有較高的血漿同半胱胺酸及血清葉酸濃度。高血漿同半胱胺酸及血清葉酸濃度是增加大腸直腸癌發生的重要危險因子。

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Table 1. Characteristics of patients with colorectal cancer and healthy participants

Characteristics	Colorectal cancer (n = 168)	Healthy participants (n = 182)
Age (y)	60.8 ± 12.1[a]	48.2 ± 9.9[b]
Gender (Male / Female)	65 / 103	90 /92
Height (cm)	160.7 ± 8.1[a]	164.7 ± 8.5[b]
Weight (kg)	62.4 ± 10.6[a]	65.4 ± 12.7[b]
Body mass index (kg/m^2)	24.1 ± 3.2	24.0 ± 3.8
Blood pressure (mmHg)		
Systolic	140.3 ± 18.1[a]	117.5 ± 16.9[b]
Diastolic	82.4 ± 11.4[a]	75.4 ± 12.2[b]
Cancer location		
Colon	82 (48.8%)	
Rectum	86 (51.2%)	
Stage at diagnosis		
Stage o + 1	22 (13.6%)	
Stage 2	45 (27.8%)	
Stage 3	67 (41.3%)	
Stage 4	28 (17.3%)	
Smoking (n, %)		
Yes	25 (14.9%)	35 (19.8%)
No	143 (85.1%)	142 (80.2%)
Drinking (n, %)		
Yes	15 (8.9%)	51 (28.8%)
No	153 (91.1%)	126 (71.2%)
Family history (n, %)		
Yes	14 (8.3%)	13 (7.3%)
No	154 (91.7%)	164 (92.7%)

Values are means ± standard deviation. Values with different superscript letter are significantly different between two groups; $p < 0.05$

Table 2. Hematological measurements in patients with colorectal cancer and healthy participants

	Colorectal cancer (n = 168)	Healthy participants (n = 182)
White blood cell (mm^3)	5771.3 ± 1734.1	5608.8 ± 1767.7
Lymphocytes (%)	30.0 ± 8.9[a]	32.7 ± 7.9[b]
Neutrophils (%)	58.1 ± 10.2	56.9 ± 8.7
Hemoglobin (g/dL)	13.3 ± 1.8[a]	13.9 ± 1.6[b]
Hematocrit (%)	39.2 ± 5.1[a]	41.2 ± 4.3[b]
Albumin (g/dL)	4.3 ± 0.3[a]	4.5 ± 0.2[b]
Creatinine (mg/dL)	0.9 ± 0.3	0.8 ± 0.2
C-reactive protein (mg/dL)	0.3 ± 0.7[a]	0.1 ± 0.3[b]
Total cholesterol (mg/dL)	188.0 ± 37.1[a]	198.2 ± 39.6[b]
High density lipoprotein cholesterol (mg/dL)	56.4 ± 16.3	57.5 ± 16.4
Low density lipoprotein Cholesterol (mg/dL)	104.8 ± 31.1	112.5 ± 34.6
Triglycerides (mg/dL)	131.6 ± 69.8	140.7 ± 130.4

Values are means ± standard deviation. Values with different superscript letter are significantly different between two groups; $p < 0.05$

Table 3. Vitamins, indicators of oxidative stress and antioxidant capacity in patients with colorectal cancer and healthy participants

	Colorectal cancer (n = 168)	Healthy participants (n = 182)
Plasma PLP (nmol/L)	121.2 ± 122.9	96.2 ± 103.0
Serum folate (nmol/L)	20.0 ± 12.8[a]	15.1 ± 8.4[b]
Plasma cysteine (μmol/L)	193.3 ± 38.8[a]	175.7 ± 31.0[b]
Oxidative stress indicators		
MDA (μmol/L)	0.9 ± 0.2	0.9 ± 0.2
Oxidized-LDL (U/L)	40.1 ± 12.0[a]	33.8 ± 10.5[b]
Plasma homocysteine (μmol/L)	15.6 ± 5.7[a]	11.5 ± 3.9[b]
Antioxidant capacities		
Total antioxidant capacity (μmol/L)	4378.2 ± 426.3[a]	4286.5 ± 437.6[b]
GPx (nmol/mL/min)	107.8 ± 44.1[a]	148.4 ± 35.9[b]
GST (nmol/mL/min)	24.5 ± 16.6[a]	41.8 ± 29.5[b]
SOD (U/mL)	13.4 ± 6.6[a]	11.9 ± 3.3[b]

LDL, low density lipoprotein cholesterol; MDA, malondialdehyde; GPx, glutathione peroxidase; GST, glutathione *S*-transferase; SOD, superoxide dismutase.
Values are means ± standard deviation. Values with different superscript letter are significantly different between two groups; $p < 0.05$.

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

	Unadjusted			**Age-, gender-adjusted**			**Age-, gender-, BMI-, SBP-, TC-, CRP- adjusted**		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Plasma PLP (nmol/L)	1.00	0.997- 1.007	0.387	1.00	0.997- 1.007	0.363	1.00	0.997- 1.007	0.388
Serum folate (nmol/L)	1.04	1.022-1.066	<0.001	1.05	1.020-1.071	<0.001	1.04	1.005-1.071	0.022
Plasma homocysteine (μmol/L)	1.24	1.165-1.319	<0.001	1.17	1.091-1.254	<0.001	1.31	1.168-1.468	<0.001

CI, confidence interval; OR, odds ratios. BMI, body mass index; SBP, systolic blood pressure; TC, total cholesterol; CRP, C-reactive protein.

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

（說明：本計畫原申請為 3 年期計畫，但因只獲得 1 年的專題研究計畫經費補助，故無法如原 3 年期計畫內容所述執行完全部的計畫內容。但樣本數分析及數據分析仍然順利進行，就一年期計畫而言，本研究結果已達成目標。）

□ 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：

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）

目前正在撰寫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）

過去二十年，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。但是，有關維生素 B-6、葉酸及同半胱胺酸與大腸直腸癌患者的氧化壓力程度及抗氧化能力的相關研究卻很少或仍有爭議。本研究結果顯示大腸直腸癌患者的維生素 B-6 與健康對照受試者並無顯著差異，但較健康對受試者有較高的血漿同半胱胺酸及血清葉酸濃度。高血漿同半胱胺酸及血清葉酸濃度是增加大腸直腸癌發生的重要危險因子。雖然有關葉酸及大腸直腸癌的關係需要再進一步釐清，但此研究結果應可提供臨床醫師在預防及治療大腸直腸癌發生的危險性的重要參考。

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：2012 年 4 月 30 日

計畫編號	NSC 100-2320-B-040 -004		
計畫名稱	探討維生素B-6對同半胱胺酸、氧化壓力、單碳代謝及甲基化作用之影響：大腸直腸癌的橫斷面、病例對照、介入及追蹤研究		
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	2012 年 4 月 21 日至 2012 年 4 月 25 日	會議地點	美國聖地牙哥
會議名稱	Experimental Biology 2012		
發表論文題目	Adequate vitamin B-6 is associated with increased antioxidant enzyme activities in critically ill surgical patients. FASEB J 2012;26:1017.3. (poster presentation)		

一、參加會議經過

2012 年 Experimental Biology 會議於 4 月 21－25 日在美國聖地牙哥召開。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（100-2320-B-040-004）補助出席國際學術會議，計畫主持人(黃怡嘉教授)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：Energy Balance: A New Paradigm、Strategic, Global Approaches to Improve Breastfeeding Rates、Adopting Healthy and Sustainable Food Service Guidelines、Carotenoids and Health、The Role of Dietary Components in Leptin Resistance、Sustainability in the 21st Century: Food, Nutrition, Agriculture, Economics and the Environment、Metabolic Regulation by Amino Acids for Optimal Health、Health Impact of Whole Grains, Bran and Cereal Fiber、Establishing and Evaluating Health Claims for Probiotics、Monounsaturates - The Forgotten Fats、Adipose Dysfunction: Interaction of ROS and Inflammation、Expanding the Frontiers of Nutrition Research、The Future of Nutrition Research、Clinical Nutrition Update 2012、FNB Update: Not At All Quiet on the Labeling Front, and Remarques about Sodium、Scientific Career

Advancement for Early Stage Investigators 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，也以壁報的形式（poster presentation）發表研究成果，發表的作者及標題為：Huang YC, Cheng CH, Chen FP, Chiang TU. Adequate vitamin B-6 is associated with increased antioxidant enzyme activities in critically ill surgical patients. FASEB J 2012;26:1017.3.

在展示的過程中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，此會議共有 6 個學會一同參與，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

SATURDAY, APRIL 21st			
	8:00-10:00 AM	**10:30 AM -12:30 PM**	**3:00-5:00 PM**
Ballroom 20 D	**8:30 am- 12:00 pm Energy Balance: A New Paradigm** 1. *Milner and D. Tancredi*		**Controversies Regarding Reported Trends: Has the Obesity Epidemic Leveled Off in the U.S.?** 1. *Wang and W. Dietz*

31 **ABC**	**Helpful or Harmful: Soy, Isoflavones, and Cancer Risk** 1. *Lindshield and M. Messina*	1. **Strategic, Global Approaches to Improve Breastfeeding Rates** *Lutter and A. Morrow*	**Adopting Healthy and Sustainable Food Service Guidelines** *J. Kimmons and A. Lederer*
Education Track **Room 29AB**	**9:00 AM -10:30AM Clinical Emerging Leaders Award Competition**	**11:00AM - 1:00 PM** **The Postdoctoral Research Award Competition**	**2:00-5:00 PM Graduate Student Research Award Competition**
All minisymposia are programmed in rooms 32B â€“ 29C			
32B	Carotenoids and Health	Carotenoids: Bioavailability and Metabolism	Carotenoids: Eye and Brain Health
32A	The Experience of Household Food Insecurity	Creating Healthy Food Environments	Regulation of Food Intake
30D	Policies and Programs to Improve Children's Nutrition	Fat Soluble Vitamins and Chronic Disease	
30C	Animal Research Models for Macronutrient Metabolism	Protein and Amino Acid Metabolism	
29D		Nutrition and Inflammation	
29C		Breastfeeding and Human Milk: Effects on the Recipient Infant and/or Lactating Mother	

SUNDAY, APRIL 22nd			
	8:00-10:00 AM	**10:30 AM -12:30 PM**	**3:00-5:00 PM**
Ballroom 20 D	**The Role of Dietary Components in Leptin Resistance** 1. *Vasselli*	**Presidential Symposium & DANONE Award:** **Nutrition and the Human Gut Microbiome** 1. *Donovan and Award Winner, J.I. Gordon*	**Fructose, Sucrose and High Fructose Corn Syrup: Relevant Scientific Findings and Health Implications** 1. *Kris-Etherton*
31 **ABC**	**Sustainability in the 21st Century: Food, Nutrition, Agriculture, Economics and the Environment** 1. *Auestad and J.M Gazzaniga-Moloo*		**Food Insecurity and Health Across the Lifespan** 1. *Johnson and J.S. Lee*
Education Track	**Utilizing a Multi-level Team Approach: Lessons Learned from the Vitamin D**		**Zinc Nutrition: From Discovery to Global Health Impact**

Room 29AB	**DRI-setting Activity** 1. *Moran and V.V. Potter*		1. *H. Sandstead*
32B	Mechanisms of Action and Molecular Targets of Dietary Bioactive Comp. I		Bioavailability, Metabolism and Biomarkers of Dietary Bioactive Comp.
32A	Redefine Obesity â€“ Body Weight vs. Adiposity		Obesity, Inflammation and Chronic Disease Modulation by Dietary Phytonutrients
30D	Micronutrient Interventions		B Vitamins and One-Carbon Metabolism
30C	Immune Modulating Nutraceuticals and Functional Foods		Nutritional Immunology
30B	Epigenetics and Nutrition		Maternal Programming of Gene Expression
30A	Risk Factor Modification in Chronic Disease II: Nuts, Pulses, and Flavanols		Application of Novel Statistical Methods for Use in Nutritional Epidemiology
29D	What should I eat? Nutritional Effects of Foods		Breast Feeding, Early Child Feeding, Diet and Growth Trends
29C	Longitudinal and Cross-Sectional Analysis of Associations between Diet and Health Outcome		Innovative Tools for Assessment of Diet, Physical Activity, and Related Behaviors

MONDAY, APRIL 23rd

	8:00-10:00 AM	**10:30 AM -12:30 PM**	**3:00-5:00 PM**
Ballroom 20 D	**GPEC Forum: Using Interdisciplinary Tools to Evaluate Nutr. Interventions** 1. Haas and G.S. Marquis	**Probiotics for Optimal Nutrition. From Efficacy to Guidelines** S.M.Donovan and G.S.Howarth ***E.V. McCollum Lecture 12:45-1:45**	**Frontiers in Fiber Nutrition Research and Application** 1. Kuo and C.L. Pelkman
31 **ABC**	**Real-world Nutrition Translation Blended with Food Science** 1. Ferruzzi and R. Clemens	**Metabolic Regulation by Amino Acids for Optimal Health** S.M Hutson and T.G. Anthony	**Communication Techniques of Effective Speakers** 1. Swanson and J. Engel
Education	**Health Impact of Whole**	**Utilizing a Stepwise Procedure**	**Development of Career**

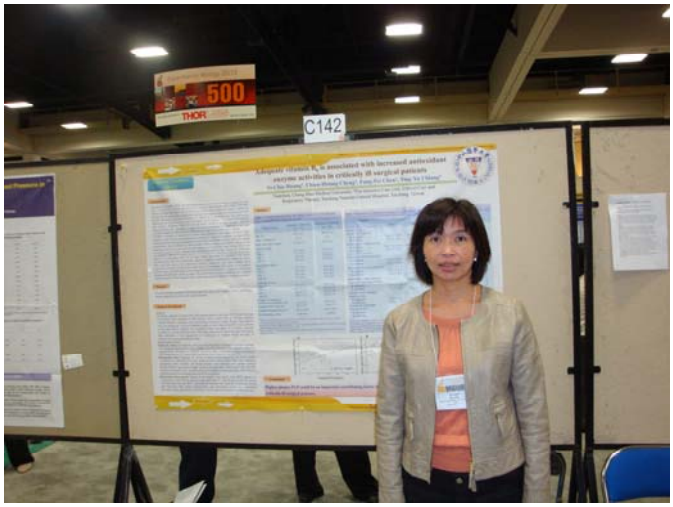
Track **Room 29AB**	**Grains, Bran and Cereal Fiber** 1. Klurfeld and I.S. Kim	**to Design Effective Nutrition Education** 1. Goodell ***1:00PM-2:30PM** **Establishing and Evaluating Health Claims for Probiotics** 1. Donovan and M.E. Sanders	**Through Successful Mentor-Mentee Relationships** 1. Chai
32B	Epidemiologic and Systems Biology Approaches	Mechanisms of Action and Molecular Targets of Dietary Bioactive Comp. II	Antioxidant and Anti-inflammatory Effects of Dietary Bioactive Components
32A	Preventing Childhood Obesity	Obesity and Metabolic Syndrome	Preventing Early Childhood Obesity
30D	Se 1: Selenoprotein Synthesis, Metabolism, and Function	Se II: Selenium in Cancer, Inflammation, and Oxidative Stress	Animal Research Models in Nutr. & Musculoskeletal Dev.
30C	Lipid and Fatty Acid Metabolism and Trans.	Dietary Factors Affecting Lipid Metabolism	Polyunsaturated Fatty Acids and Hlth.
30B	Nutrient Gene Interactions	Nutrient Gene Interaction in Models of Neurodegenerative/ Neuromuscular Disease	Nutrition Science Translation: Impacts â€¦
30A	Osteoporosis and Bone Metabolism in Aging	Applications and Challenges of Public Use Data Sets for Secondary Data Analysis Nutrition Research	Milk Bioactive Comp.
29D	Community Nutrition Programs and Policies for Older Adults	Weight Management in Real Life	Carbohydrate Metabolism
29C	Development of Evidence-based Nutrition Education	Influences of Water and Beverage Consumption on Nutrition and Health Outcomes	Advancing Nutrition Policy and Improving the Effects of Nutrition Programs

TUESDAY, APRIL 24th

	8:00-10:00 AM	**10:30 AM -12:30 PM**	**3:00-5:00 PM**
Ballroom 20 D	**Monounsaturates - The Forgotten Fats** 1. *Heber*	**Adipose Dysfunction: Interaction of ROS and Inflammation** 1. *Picklo, K. Claycombe*	1. **Emerging Biomarkers for Cardiovascular Disease: Beyond LDL Cholesterol** 2. *Park and B.H. Rice*

		and M.Meydani ***W.O. Atwater Lecture 12:45-1:45*** From Instinct to Intellect: 150 Years in the Evolution of Energy Balance in Man *J.O. Hill*	
31 **ABC**	**Expanding the Frontiers of Nutrition Research** *D. Pelletier and C. Porter*	**The Future of Nutrition Research** *S.M Hutson*	**Intervention Points in Obesity: Worksite Interventions for Weight Control** 1. *Roberts and N. Krebs*
Education Track **Room 29AB**	**FNB Update: Not At All Quiet on the Labeling Front, and Remarques about Sodium** *L. Meyers and* *D.M Bier*	**Clinical Nutrition Update 2012** 1. *Saltzman, C.W. Bales and M.A. Johnson*	**Scientific Career Advancement for Early Stage Investigators** *V.V. Potter*
32B	Effects of Dietary Bioactive Comp. on Experimental Models of Chronic Disease Risk	Dietary Bioactive Components	Cardiovascular Effects of Dietary Bioactive Components
32A	Obesity, Inflammation and Nutrigenomics	Childhood Obesity: When Should We Intervene?	Vitamin D and Obesity: From Cellular to Clinical Trials
30D	Micronutrient Bioavailability	Intestinal Physiology and Digestive Function	Risk Factor Modification in Chronic Disease I: Macronutrient Manipulation
30C	Diet and Cancer: Molecular Targets	Diet and Cancer: Animal Studies	Diet and Cancer: Translation, Clinical and Survivorship
30B	Nutrition and Cognitive and Physical Function in Older Adults	Translation of Nutrition Science to Public Health	Revitalizing Local Food Systems
30A	Breastfeeding: Determinants of Initiation, Durationâ€¦	Global Health: Dietary Intakes and Health Outcomes in Diverse Pop.	Lactation: Biology of Milk Production and Secretion
29D	Energy Balance, Macronutrients & Weight Management	Dietary Supplements as a Population Exposure to the Prev/Mgmt of Disease	Feeding Young Children
29C	Child Nutrition and Growth: Issues and Challenge	Behavioral Science and Eating Behavior Change	Micronutrients: Measurement, Interventions and Outcomes

WEDNESDAY, APRIL 25th		
	8:00-10:00 AM	**10:30 AM -12:30 PM**
Ballroom 20 D	**Nutritional Prevention of Cognitive Decline** 1. *Arab and R.Bailey*	**Macronutrients as Tools to Counter Age-related Changes in Skeletal Muscle** 1. *W. Campbell*
31 ABC	**Nutritional Regulation of Epigenetic Change** 1. *D. F. Romagnolo and T. Ziegler*	



圖一：研討會會場暨壁報展示

四、大會邀請函及論文被接受之證明文件

Experimental Biology 2012

Translating Science for Tomorrow's Health

April 21-25
San Diego, CA

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

Boston, MA
April 20 - 24, 2013

San Diego, CA
April 26 - 30, 2014

Boston, MA
March 28 - April 1, 2015

San Diego, CA
April 2 - 6, 2016

April 02, 2012

Yi-Chia Huang
SCHOOL OF NUTRITION, CHUNG SHAN MEDICAL UNIVERSITY
No. 110, Sec. 1, Jianguo N. Rd
Taichung, Taiwan

Passport Number: 302497881
Date of Birth: 10/03/1967

Dear Yi-Chia:

We would like to extend to you an invitation to attend and participate in the Experimental Biology 2012 Annual Meeting scheduled April 21 - 25, in San Diego, CA. Much thought and effort has gone int2 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 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 23, 2012.

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
Meeting Manager
FASEB Scientific Meetings and Conferences

9650 Rockville Pike • Bethesda, MD 20814-3998
Telephone 301-634-7010 • FAX 301-634-7014
www.experimentalbiology.org • E-mail: eb@faseb.org

EXPERIMENTAL BIOLOGY 2012

ABSTRACT CONFIRMATION OF POSTER PRESENTATION-ASN

Diego Convention Center - 111 W. Harbor Drive, San Diego, California 92101

The following will confirm the day, date, time, and location of your poster presentation. Please advise co-authors of the time and place of the presentation as they will not receive a separate notification. A copy of this email has been sent to your sponsor.

POSTER PRESENTATION INFORMATION: (read carefully)

Abstract Number: 1070

Abstract Title: Adequate vitamin B-6 is associated with increased antioxidant enzyme activity in critically ill surgical patients

First Author: Yi-Chia Huang

Poster Session Title: Antioxidant Micronutrients

Day of Presentation: Tuesday April 24, 2012

Program Number: 1017.3

Poster Board Number: C142

Authors must be present at their posters from: 12:45-1:45PM (I)

Location: San Diego Convention Center, Exhibit Hall

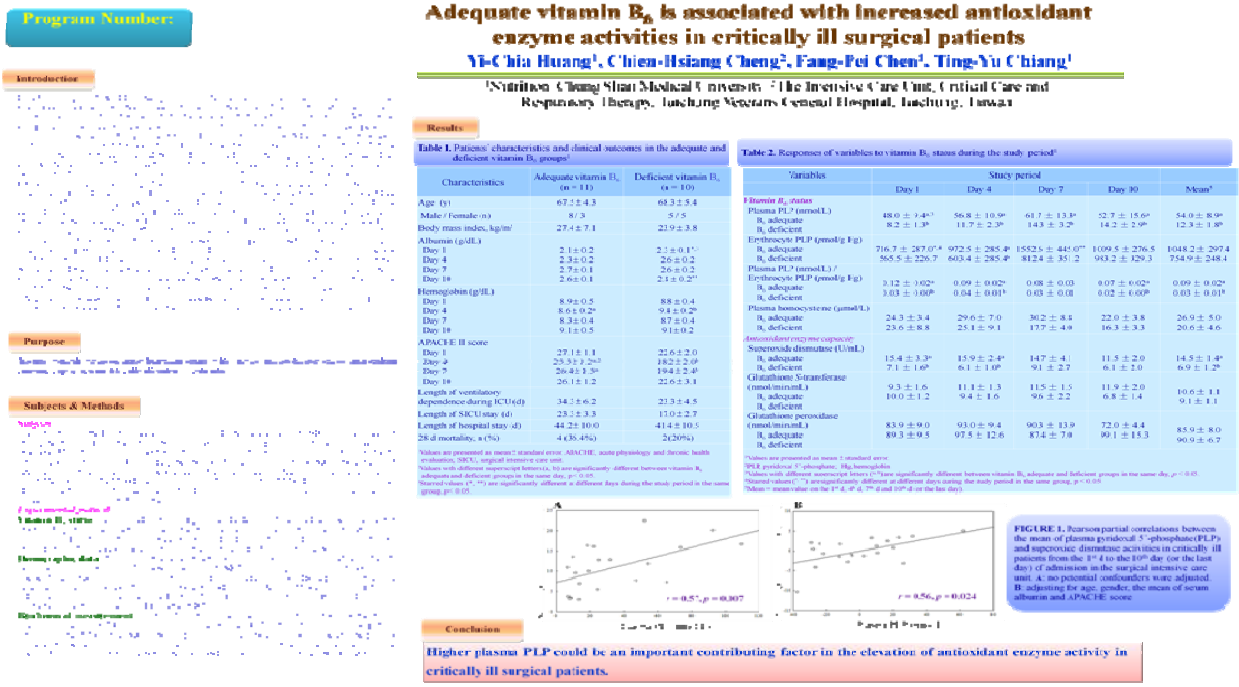
The early registration deadline is Thursday, February 23.

五、發表之論文摘要

Adequate vitamin B_6 is associated with increased antioxidant enzyme activities in critically ill surgical patients

Yi-Chia Huang[1], Chien-Hsiang Cheng[2], Fang-Pei Chen[1], Ting-Yu Chiang[1]. [1]School of Nutrition, Chung Shan Medical University, [2]The Intensive Care Unit, Critical Care and Respiratory Therapy, Taichung Veterans General Hospital, Taichung, Taiwan

Inadequate vitamin B_6 status may increase oxidative stress and compromise antioxidant capacity. The purpose of this study was to understand the association between vitamin B_6 status and oxidative stress, antioxidant enzyme capacities in critically ill surgical patients. Patients were allocated into either adequate B_6 (n = 11) or deficient B_6 (n = 10) group based on their fasting plasma pyridoxal 5'-phosphate (PLP) concentration at admission to the surgical intensive care unit (SICU). Plasma and erythrocyte PLP, serum malondialdehyde (MDA), total antioxidant capacity (TAC), superoxide dismutase (SOD), glutathione *S*-transferase (GST) and glutathione peroxidase (GPx) were determined on the 1st, 4th, 7th and 10th d of admission. There was no significant difference in TAC and MDA levels, GST and GPx activities between the 2 groups on the 1st, 4th, 7th and 10th in the SICU. The mean SOD activity level was significantly higher in the adequate B_6 group when compared to the deficient B_6 group on the 1st and 4th after admission. The change of plasma PLP (r_s = 0.68, p < 0.01) significantly correlated with the change of SOD activities after adjusting for the potential confounders. Higher plasma PLP at admission would be an important contributing factor to increased antioxidant enzyme activity in SICU patients. This study was supported by Taichung Veterans General Hospital (TCVGH-994101B), Taiwan.



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：2012 年 4 月 30 日

計畫編號	NSC 100-2320-B-040 -004		
計畫名稱	探討維生素B-6對同半胱胺酸、氧化壓力、單碳代謝及甲基化作用之影響：大腸直腸癌的橫斷面、病例對照、介入及追蹤研究		
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	2012 年 4 月 21 日至 2012 年 4 月 25 日	會議地點	美國聖地牙哥
會議名稱	Experimental Biology 2012		
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一、參加會議經過

2012 年 Experimental Biology 會議於 4 月 21－25 日在美國聖地牙哥召開。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（100-2320-B-040-004）補助出席國際學術會議，計畫主持人(黃怡嘉教授)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：Energy Balance: A New Paradigm、Strategic, Global Approaches to Improve Breastfeeding Rates、Adopting Healthy and Sustainable Food Service Guidelines、Carotenoids and Health、The Role of

Dietary Components in Leptin Resistance、Sustainability in the 21st Century: Food, Nutrition, Agriculture, Economics and the Environment、Metabolic Regulation by Amino Acids for Optimal Health、Health Impact of Whole Grains, Bran and Cereal Fiber、Establishing and Evaluating Health Claims for Probiotics、Monounsaturates - The Forgotten Fats、Adipose Dysfunction: Interaction of ROS and Inflammation、Expanding the Frontiers of Nutrition Research、The Future of Nutrition Research、Clinical Nutrition Update 2012、FNB Update: Not At All Quiet on the Labeling Front, and Remarques about Sodium、Scientific Career Advancement for Early Stage Investigators 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，也以壁報的形式（poster presentation）發表研究成果，發表的作者及標題為：Huang YC, Cheng CH, Chen FP, Chiang TU. Adequate vitamin B-6 is associated with increased antioxidant enzyme activities in critically ill surgical patients. FASEB J 2012;26:1017.3.

在展示的過程中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，此會議共有 6 個學會一同參與，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

SATURDAY, APRIL 21st			
	8:00-10:00 AM	**10:30 AM -12:30 PM**	**3:00-5:00 PM**
Ballroom 20 D	**8:30 am- 12:00 pm Energy Balance: A New Paradigm** 1. *Milner and D. Tancredi*		**Controversies Regarding Reported Trends: Has the Obesity Epidemic Leveled Off in the U.S.?** 1. *Wang and W. Dietz*
31 **ABC**	**Helpful or Harmful: Soy, Isoflavones, and Cancer Risk** 1. *Lindshield and M. Messina*	1. **Strategic, Global Approaches to Improve Breastfeeding Rates** *Lutter and A. Morrow*	**Adopting Healthy and Sustainable Food Service Guidelines** *J. Kimmons and A. Lederer*
Education Track **Room 29AB**	**9:00 AM -10:30AM Clinical Emerging Leaders Award Competition**	**11:00AM - 1:00 PM** **The Postdoctoral Research Award Competition**	**2:00-5:00 PM Graduate Student Research Award Competition**
All minisymposia are programmed in rooms 32B â€“ 29C			
32B	Carotenoids and Health	Carotenoids: Bioavailability and Metabolism	Carotenoids: Eye and Brain Health
32A	The Experience of Household Food Insecurity	Creating Healthy Food Environments	Regulation of Food Intake
30D	Policies and Programs to Improve Children's Nutrition	Fat Soluble Vitamins and Chronic Disease	
30C	Animal Research Models for Macronutrient Metabolism	Protein and Amino Acid Metabolism	
29D		Nutrition and Inflammation	
29C		Breastfeeding and Human Milk: Effects on the Recipient Infant and/or Lactating Mother	

SUNDAY, APRIL 22nd			
	8:00-10:00 AM	**10:30 AM -12:30 PM**	**3:00-5:00 PM**
Ballroom 20 D	**The Role of Dietary Components in Leptin Resistance** 1. *Vasselli*	**Presidential Symposium & DANONE Award:** **Nutrition and the Human Gut Microbiome** 1. *Donovan and Award Winner, J.I. Gordon*	**Fructose, Sucrose and High Fructose Corn Syrup: Relevant Scientific Findings and Health Implications** 1. *Kris-Etherton*
31 **ABC**	**Sustainability in the 21st Century: Food, Nutrition, Agriculture, Economics and the Environment** 1. *Auestad and J.M Gazzaniga-Moloo*		**Food Insecurity and Health Across the Lifespan** 1. *Johnson and J.S. Lee*
Education Track **Room 29AB**	**Utilizing a Multi-level Team Approach: Lessons Learned from the Vitamin D DRI-setting Activity** 1. *Moran and V.V. Potter*		**Zinc Nutrition: From Discovery to Global Health Impact** 1. *H. Sandstead*
32B	Mechanisms of Action and Molecular Targets of Dietary Bioactive Comp. I		Bioavailability, Metabolism and Biomarkers of Dietary Bioactive Comp.
32A	Redefine Obesity â€“ Body Weight vs. Adiposity		Obesity, Inflammation and Chronic Disease Modulation by Dietary Phytonutrients
30D	Micronutrient Interventions		B Vitamins and One-Carbon Metabolism
30C	Immune Modulating Nutraceuticals and Functional Foods		Nutritional Immunology
30B	Epigenetics and Nutrition		Maternal Programming of Gene Expression

30A	Risk Factor Modification in Chronic Disease II: Nuts, Pulses, and Flavanols		Application of Novel Statistical Methods for Use in Nutritional Epidemiology
29D	What should I eat? Nutritional Effects of Foods		Breast Feeding, Early Child Feeding, Diet and Growth Trends
29C	Longitudinal and Cross-Sectional Analysis of Associations between Diet and Health Outcome		Innovative Tools for Assessment of Diet, Physical Activity, and Related Behaviors

MONDAY, APRIL 23rd

	8:00-10:00 AM	**10:30 AM -12:30 PM**	**3:00-5:00 PM**
Ballroom 20 D	**GPEC Forum: Using Interdisciplinary Tools to Evaluate Nutr. Interventions** 1. Haas and G.S. Marquis	**Probiotics for Optimal Nutrition. From Efficacy to Guidelines** S.M.Donovan and G.S.Howarth ***E.V. McCollum Lecture 12:45-1:45**	**Frontiers in Fiber Nutrition Research and Application** 1. Kuo and C.L. Pelkman
31 ABC	**Real-world Nutrition Translation Blended with Food Science** 1. Ferruzzi and R. Clemens	**Metabolic Regulation by Amino Acids for Optimal Health** S.M Hutson and T.G. Anthony	**Communication Techniques of Effective Speakers** 1. Swanson and J. Engel
Education Track Room 29AB	**Health Impact of Whole Grains, Bran and Cereal Fiber** 1. Klurfeld and I.S. Kim	**Utilizing a Stepwise Procedure to Design Effective Nutrition Education** 1. Goodell ***1:00PM-2:30PM** **Establishing and Evaluating Health Claims for Probiotics**	**Development of Career Through Successful Mentor-Mentee Relationships** 1. Chai

		1. Donovan and M.E. Sanders	
32B	Epidemiologic and Systems Biology Approaches	Mechanisms of Action and Molecular Targets of Dietary Bioactive Comp. II	Antioxidant and Anti-inflammatory Effects of Dietary Bioactive Components
32A	Preventing Childhood Obesity	Obesity and Metabolic Syndrome	Preventing Early Childhood Obesity
30D	Se 1: Selenoprotein Synthesis, Metabolism, and Function	Se II: Selenium in Cancer, Inflammation, and Oxidative Stress	Animal Research Models in Nutr. & Musculoskeletal Dev.
30C	Lipid and Fatty Acid Metabolism and Trans.	Dietary Factors Affecting Lipid Metabolism	Polyunsaturated Fatty Acids and Hlth.
30B	Nutrient Gene Interactions	Nutrient Gene Interaction in Models of Neurodegenerative/ Neuromuscular Disease	Nutrition Science Translation: Impacts â€¦
30A	Osteoporosis and Bone Metabolism in Aging	Applications and Challenges of Public Use Data Sets for Secondary Data Analysis Nutrition Research	Milk Bioactive Comp.
29D	Community Nutrition Programs and Policies for Older Adults	Weight Management in Real Life	Carbohydrate Metabolism
29C	Development of Evidence-based Nutrition Education	Influences of Water and Beverage Consumption on Nutrition and Health Outcomes	Advancing Nutrition Policy and Improving the Effects of Nutrition Programs

TUESDAY, APRIL 24th

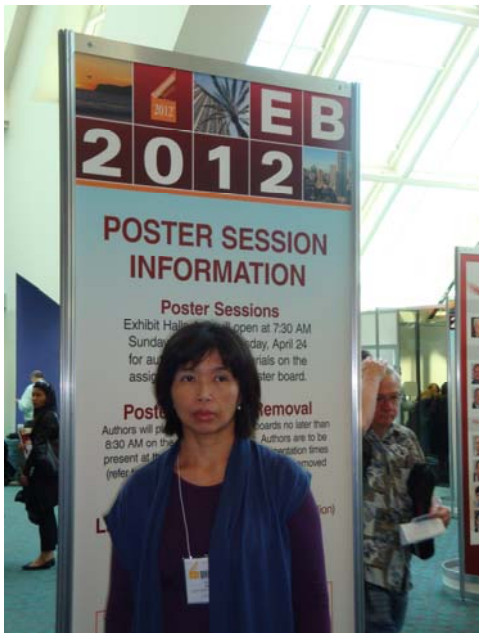
	8:00-10:00 AM	**10:30 AM -12:30 PM**	**3:00-5:00 PM**
Ballroom 20 D	**Monounsaturates - The Forgotten Fats** 1. *Heber*	**Adipose Dysfunction: Interaction of ROS and Inflammation** 1. *Picklo, K. Claycombe*	1. **Emerging Biomarkers for Cardiovascular Disease: Beyond LDL Cholesterol** 2. *Park and B.H. Rice*

		and M.Meydani ***W.O. Atwater Lecture 12:45-1:45*** From Instinct to Intellect: 150 Years in the Evolution of Energy Balance in Man *J.O. Hill*	
31 **ABC**	**Expanding the Frontiers of Nutrition Research** *D. Pelletier and C. Porter*	**The Future of Nutrition Research** *S.M Hutson*	**Intervention Points in Obesity: Worksite Interventions for Weight Control** 1. *Roberts and N. Krebs*
Education Track **Room 29AB**	**FNB Update: Not At All Quiet on the Labeling Front, and Remarques about Sodium** *L. Meyers and* *D.M Bier*	**Clinical Nutrition Update 2012** 1. *Saltzman, C.W. Bales and M.A. Johnson*	**Scientific Career Advancement for Early Stage Investigators** *V.V. Potter*
32B	Effects of Dietary Bioactive Comp. on Experimental Models of Chronic Disease Risk	Dietary Bioactive Components	Cardiovascular Effects of Dietary Bioactive Components
32A	Obesity, Inflammation and Nutrigenomics	Childhood Obesity: When Should We Intervene?	Vitamin D and Obesity: From Cellular to Clinical Trials
30D	Micronutrient Bioavailability	Intestinal Physiology and Digestive Function	Risk Factor Modification in Chronic Disease I: Macronutrient Manipulation
30C	Diet and Cancer: Molecular Targets	Diet and Cancer: Animal Studies	Diet and Cancer: Translation, Clinical and Survivorship
30B	Nutrition and Cognitive and Physical Function in Older	Translation of Nutrition Science to Public Health	Revitalizing Local Food Systems

	Adults		
30A	Breastfeeding: Determinants of Initiation, Durationâ€¦	Global Health: Dietary Intakes and Health Outcomes in Diverse Pop.	Lactation: Biology of Milk Production and Secretion
29D	Energy Balance, Macronutrients & Weight Management	Dietary Supplements as a Population Exposure to the Prev/Mgmt of Disease	Feeding Young Children
29C	Child Nutrition and Growth: Issues and Challenge	Behavioral Science and Eating Behavior Change	Micronutrients: Measurement, Interventions and Outcomes

WEDNESDAY, APRIL 25th

	8:00-10:00 AM	**10:30 AM -12:30 PM**
Ballroom 20 D	**Nutritional Prevention of Cognitive Decline** 1. *Arab and R.Bailey*	**Macronutrients as Tools to Counter Age-related Changes in Skeletal Muscle** 1. *W. Campbell*
31 ABC	**Nutritional Regulation of Epigenetic Change** 1. *D. F. Romagnolo and T. Ziegler*	



圖一：研討會會場暨壁報展示

四、大會邀請函及論文被接受之證明文件

Experimental Biology 2012

Translating Science for Tomorrow's Health

April 21-25
San Diego, CA

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

- Boston, MA
  April 20 - 24, 2013
- San Diego, CA
  April 26 - 30, 2014
- Boston, MA
  March 28 - April 1, 2015
- San Diego, CA
  April 2 - 6, 2016

April 02, 2012

Yi-Chia Huang
SCHOOL OF NUTRITION, CHUNG SHAN MEDICAL UNIVERSITY
No. 110, Sec. 1, Jianguo N. Rd
Taichung, Taiwan

Passport Number: 302497881
Date of Birth: 10/03/1967

Dear Yi-Chia:

We would like to extend to you an invitation to attend and participate in the Experimental Biology 2012 Annual Meeting scheduled April 21 - 25, in San Diego, CA. Much thought and effort has gone int2 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 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 23, 2012.

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
Meeting Manager
FASEB Scientific Meetings and Conferences

9650 Rockville Pike • Bethesda, MD 20814-3998
Telephone 301-634-7010 • FAX 301-634-7014
www.experimentalbiology.org • E-mail: eb@faseb.org

EXPERIMENTAL BIOLOGY 2012

ABSTRACT CONFIRMATION OF POSTER PRESENTATION-ASN

Diego Convention Center - 111 W. Harbor Drive, San Diego, California 92101

The following will confirm the day, date, time, and location of your poster presentation. Please advise co-authors of the time and place of the presentation as they will not receive a separate notification. A copy of this email has been sent to your sponsor.

POSTER PRESENTATION INFORMATION: (read carefully)

Abstract Number: 1070

Abstract Title: Adequate vitamin B-6 is associated with increased antioxidant enzyme activity in critically ill surgical patients

First Author: Yi-Chia Huang

Poster Session Title: Antioxidant Micronutrients

Day of Presentation: Tuesday April 24, 2012

Program Number: 1017.3

Poster Board Number: C142

Authors must be present at their posters from: 12:45-1:45PM (I)

Location: San Diego Convention Center, Exhibit Hall

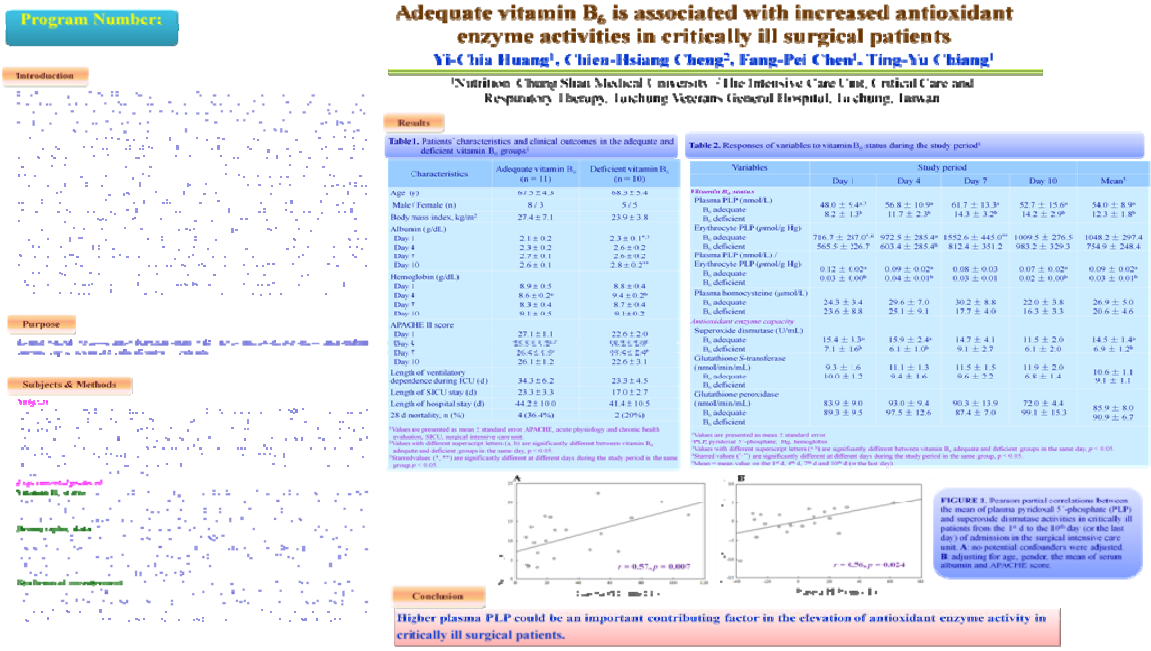
The early registration deadline is Thursday, February 23.

五、發表之論文摘要

Adequate vitamin B_6 is associated with increased antioxidant enzyme activities in critically ill surgical patients

Yi-Chia Huang[1], Chien-Hsiang Cheng[2], Fang-Pei Chen[1], Ting-Yu Chiang[1]. [1]School of Nutrition, Chung Shan Medical University, [2]The Intensive Care Unit, Critical Care and Respiratory Therapy, Taichung Veterans General Hospital, Taichung, Taiwan

Inadequate vitamin B_6 status may increase oxidative stress and compromise antioxidant capacity. The purpose of this study was to understand the association between vitamin B_6 status and oxidative stress, antioxidant enzyme capacities in critically ill surgical patients. Patients were allocated into either adequate B_6 (n = 11) or deficient B_6 (n = 10) group based on their fasting plasma pyridoxal 5'-phosphate (PLP) concentration at admission to the surgical intensive care unit (SICU). Plasma and erythrocyte PLP, serum malondialdehyde (MDA), total antioxidant capacity (TAC), superoxide dismutase (SOD), glutathione *S*-transferase (GST) and glutathione peroxidase (GPx) were determined on the 1st, 4th, 7th and 10th d of admission. There was no significant difference in TAC and MDA levels, GST and GPx activities between the 2 groups on the 1st, 4th, 7th and 10th in the SICU. The mean SOD activity level was significantly higher in the adequate B_6 group when compared to the deficient B_6 group on the 1st and 4th after admission. The change of plasma PLP (r_s = 0.68, p < 0.01) significantly correlated with the change of SOD activities after adjusting for the potential confounders. Higher plasma PLP at admission would be an important contributing factor to increased antioxidant enzyme activity in SICU patients. This study was supported by Taichung Veterans General Hospital (TCVGH-994101B), Taiwan.



國科會補助計畫衍生研發成果推廣資料表

日期:2012/07/31

國科會補助計畫	計畫名稱: 探討維生素B-6對同半胱胺酸、氧化壓力、單碳代謝及甲基化作用之影響：大腸直腸癌的橫斷面、病例對照、介入及追蹤研究
	計畫主持人: 黃怡嘉
	計畫編號: 100-2320-B-040-004- 學門領域: 保健營養

無研發成果推廣資料

100 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：100-2320-B-040-004-
計畫名稱：探討維生素 B-6 對同半胱胺酸、氧化壓力、單碳代謝及甲基化作用之影響：大腸直腸癌的橫斷面、病例對照、介入及追蹤研究	

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	1	100%		
		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	2	0	100%	人次	
		博士生	0	0	0%		
		博士後研究員	0	0	0%		
		專任助理	0	0	0%		
國外	論文著作	期刊論文	0	2	100%	篇	
		研究報告/技術報告	0	0	0%		
		研討會論文	0	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：

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)

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)

過去二十年，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。但是，有關維生素 B-6、葉酸及同半胱胺酸與大腸直腸癌患者的氧化壓力程度及抗氧化能力的相關研究卻很少或仍有爭議。本研究結果顯示大腸直腸癌患者的維生素 B-6 與健康對照受試者並無顯著差異，但較健康對受試者有較高的血漿同半胱胺酸及血清葉酸濃度。高血漿同半胱胺酸及血清葉酸濃度是增加大腸直腸癌發生的重要危險因子。雖然有關葉酸及大腸直腸癌的關係需要再進一步釐清，但此研究結果應可提供臨床醫師在預防及治療大腸直腸癌發生的危險性的重要參考。