

一、計畫中文摘要：請於五百字內就本計畫要點作一概述，並依本計畫性質自訂關鍵詞。

關鍵詞：AdipoQ, ApM1, adiponectin, 肥胖， 冠心病， X 症候群

肥胖長久以來已然被認定為冠狀動脈心臟病之重要危險因子。然而肥胖對粥狀動脈硬化的效應之生物機制至今仍然未明。近年來對脂肪細胞之生物學研究顯示脂肪組織不僅是能量儲存之油脂庫而且是一藉由荷爾蒙與細胞素與身體其他組織積極交互作用之”內分泌”器官。其分泌之物質中最佳的幾個例子是瘦素，纖維蛋白溶解酵素原活化物之抑制物-1 及甲型瘤壞死素，三者均具有極明顯之全身作用。

AdipoQ/apM1 蛋白大小約 28-30 Kd，在體內僅由脂肪組織所表達並分泌於血液中。其蛋白一次結構與膠原蛋白質、補體及哺乳類冬眠相關血漿蛋白質及其他蛋白質等有頗大之相似。此基因之生物功能大多仍然未明。然而有研究顯示其基因表現在 ob/ob 肥胖鼠中較低。在人類中，肥胖病人血漿 apM1 之濃度亦較正常控制組受試為低。近來亦有研究發現在細胞培養之系統中它可減低甲型瘤壞死素引起之單核球細胞附著於血管內皮細胞上並降低血管內皮細胞中某些黏著分子之基因表現。此外，在冠狀動脈心臟病之病人中，血漿 apM1 之濃度也較正常控制組受試為低。總結這些研究顯示 AdipoQ/ApM1 也許在肥胖及與其相關之病症，如 X 症候群及粥狀動脈硬化之病理生理中扮演一些角色。

過去一年中，吾等在人類研究中發現，血漿中之 apM1 (adiponectin) 濃度與 X 症候群之表現有密切相關，並與冠心病有關，同時也是肥胖與冠心病之遺傳因子，除此之外，吾等並發減重及以新型之糖尿病治療藥物有助提高血漿中之 apM1 (adiponectin) 濃度。是否有益病人之 X 症候群及粥狀動脈硬化之改善，則有待進一步之研究。同時吾等並發現其在培養細胞中與胰島素刺激血糖吸收有關。此一豐碩之成果並未獲心肺學門委員之青睞，至為惋惜。

二、計畫英文摘要：請於五百字內就本計畫要點作一概述，並依本計畫性質自訂關鍵詞。

Keywords : AdipoQ, ApM1, adiponectin, obesity, coronary heart disease, X syndrome

Obesity has long been well accepted as a major risk factor for coronary artery disease. However, the biological mechanisms mediating the effects of obesity on atherosclerosis remain obscure. Recent studies of the biology of adipocytes have shown that adipose tissue, rather than just a fat depot for energy storage, is an extremely active tissue constantly interacting with the other tissues by hormones and cytokines. The well-known examples of secreted products of adipose tissue are leptin, PAI-1 and TNF α , all of which have profound systemic effects.

Similar to leptin, AdipoQ/ApM1 protein (28-30 Kd) is exclusively expressed in and secreted by adipose tissue into blood circulation. Analysis of its primary peptide sequence revealed striking homology to those of collagens, complement and mammalian hibernation-associated plasma protein and others. The biological function of its product is mostly unclear. It was demonstrated that the expression of AdipoQ is down regulated in ob/ob mice. In human, the plasma level of apM1 in obese subjects was significantly lower than that in normal controls. Recently, it was shown to reduced TNF α -induced monocyte adhesion to endothelial cells and gene expression of certain adhesion molecules in endothelial cells *in vitro*. In addition, the plasma level of apM1 in patients with coronary artery disease was significantly lower than that in the normal controls. Taken together, these studies suggest that AdipoQ/apM1 may play a role in the pathophysiology of obesity and obesity-related disease processes, such as syndrome X and atherosclerosis.

In the last one year, we found in human study that the plasma levels of apM1 (adiponectin) intimately correlated with variables of X syndrome and coronary artery disease. It is also a genetic contributor to obesity and coronary artery disease. In addition, we demonstrated that weight reduction and treatment with a new anti-diabetic drugs raised plasma apM1 levels. Whether these may benefit patients with X syndrome and coronary artery disease awaits further studies. In cultured cells, we also found that apM1 may improve insulin-stimulated glucose uptake. However, these fruitful results did not impress the division of cardiovascular and pulmonary medicine of NSC. It is a regret the project was not further granted after one year.

三、結果：

Objectives: Hypo-adiponectin has been documented in subjects with obesity, diabetes mellitus (DM), or coronary heart disease (CHD), suggesting a potential use of plasma adiponectin to follow the clinical progress in subjects with metabolic syndrome (MS). In this study, we investigated the plasma adiponectin levels in relation to the variables of MS among overweight/obese Asian subjects.

Research Methods and Procedures: The plasma adiponectin, anthropometric and biochemical measurements, oral glucose tolerance tests (OGTT), and modified insulin suppression tests (IST) were performed on 180 overweight/obese Asian subjects ($BMI \geq 23 \text{ kg/m}^2$), including 47 subjects with morbid obesity ($BMI \geq 40 \text{ kg/m}^2$).

Results: The plasma adiponectin levels negatively correlated with BMI, waist-hip ratio (WHR), fasting plasma glucose, insulin, triglyceride, uric acid levels, hyperinsulinemia and glucose intolerance in OGTT; but positively with HDL-C. In contrast, they were not related to blood pressure and total cholesterol. Moreover, insulin sensitivity measured by QUICKI or in IST correlated with the plasma adiponectin levels significantly. Among morbidly obese subjects, only the WHR correlated with the plasma adiponectin levels. Using multivariate linear regression models, the area under curve of plasma glucose in OGTT and HDL-C among the overweight/obese subjects; and WHR among the morbidly obese subjects were related to the plasma adiponectin levels significantly after adjustment for other variables.

Conclusions: In overweight/obese Asians, the plasma adiponectin levels significantly correlated with various indices of MS except hypertension. Whether the plasma adiponectin level could be a suitable biomarker for following the clinical progress of MS warrants further investigation.