

Editorial

Genetic Risks of Atherothrombotic Diseases in Taiwan

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Over the past years, many studies have evaluated the association between genetic variations and atherothrombotic disorders in the world. While ethnic background plays an important role in the study of genetic risk factors, data from Caucasians could not be directly applied to the Oriental populations.

In 1992, Cambien *et al.* first demonstrated a positive association between angiotensin-converting enzyme gene I/D polymorphism and myocardial infarction.¹ However, studies on the Chinese population failed to find such associations.^{2,3} In 2001, data from Taiwan also demonstrated the negative association between the C677T mutation of the methylenetetrahydrofolate reductase gene and the risk of coronary artery disease among Chinese.^{4,5} These results were also not consistent with those that had been reported in the West.

Recently, the genetic variants of thrombomodulin have become another focus of study. Thrombomodulin is an endothelial cell membrane-bound glycoprotein. Its main physiological function is to bind thrombin. Recently, several distinct mutations in the 5'-promoter region of human thrombomodulin gene have been identified, and Asians are particularly noted to carry these promoter mutations.⁶ The G-33A mutation in the thrombomodulin promoter region was a common genetic variant in Taiwan, with a prevalence about 13-15% in healthy controls.⁷ From reporter gene assay, this mutation was noted to be a functional genetic variant.⁸ Data from our research team found that the mutation might play a role as an independent risk factor for the occurrence of coronary artery disease, carotid atherosclerosis and myocardial infarction.^{7,8} The risk of premature myocardial infarction was remarkably increased, especially for heavy

smokers who carried the mutation.⁹ These findings established the significant role of genetic risk factors in the pathogenesis of atherothrombotic disorders in Taiwan.

In addition to those genetic polymorphisms of the genes involved in the renin-angiotensin system or coagulative and anticoagulative pathway, an association between the paraoxonase (PON-1)-191 polymorphism and coronary atherosclerosis has been suggested by reports that showed protection of oxidation of LDL cholesterol by HDL-associated PON1. The association between the polymorphism of PON1-191 and coronary artery disease was not consistent.¹⁰ In Taiwan, Ko *et al.* found no association between the Gln-Arg 191 polymorphism of human PON1 gene and CAD patients.¹⁰ However, the structurally related PON2 gene has been recognized as being functionally similar to PON1 in lipid metabolism. The data from Pan *et al.* in this issue¹¹ demonstrated that individuals with SS genotype of the codon 311 polymorphism of PON2 gene showed an increased risk of CAD. The result might suggest that the PON2 polymorphism is the other genetic risk factor for coronary artery disease in Taiwan. These findings are mainly from case-control studies in the hospital base. To establish the gene-disease relationship in Taiwan, further investigations are needed.

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