

Phosphodiesterase 4D (PDE4D) Gene Variants and Risk of Ischemic Stroke in the Taiwanese Population

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摘要

Abstract

Objectives: It has been suggested that genetic variants in the phosphodiesterase 4D (PDE4D) gene confer risk of ischemic stroke. However, the cerebral infarction/cerebral hemorrhage ratio is lower in Asian populations compared with those in Caucasian and black populations. Thus, the association between variations in the PDE4D gene and ischemic stroke in Taiwan needs to be replicated. In the present study, we evaluated whether the PDE4D gene polymorphism confers a risk of ischemic stroke in Taiwanese patients.

Methods: Two single-nucleotide polymorphisms (SNPs) covering the PDE4D gene were genotyped using genomic DNA sequencing and a high-throughput TaqMan PCR assay in 100 patients who had suffered an ischemic stroke and 270 healthy individuals.

Results: No significant associations with ischemic stroke were observed with the SNP87 (rs2910829) or SNP41 (rs152312) SNPs from PDE4D, which were a part of the Icelandic at-risk haplotypes.

Conclusions: The present data does not support a significant role for PDE4D polymorphisms in genetic susceptibility to ischemic stroke in the Taiwanese population.

Strokes are a major cause of adult disability and mortality in the elderly human

population worldwide.^{1,2} Strokes can be divided into 2 major categories: ischemic and hemorrhagic.³ The ischemic stroke is characterized by a sudden decrease in blood flow to 1 or more central nervous system areas, and it is the major type of stroke in Caucasians (80% to 90%). Compared with the Caucasian and black populations, the ratio of ischemic stroke/hemorrhagic stroke in Asian populations, including Chinese, Japanese, and Koreans, was much lower.⁴ Epidemiological studies revealed that strokes can be attributed to a variety of genetic and environmental risk factors.⁵ An epidemiologic study estimated the risk attributable for stroke in two-thirds of the population was due to genetic factors.⁶

Recently, a linkage and association study in Iceland showed that the chromosome 5q12 region was linked to ischemic stroke.⁷ The same group then reported that the phosphodiesterase 4D (PDE4D) gene variants were associated with ischemic stroke as results of a genome-wide screening for stroke-susceptibility genes in Iceland.⁸ PDE4D is involved in inflammation, cell proliferation, and migration—processes implicated in stroke occurrence.^{9–11} PDE4D is a large gene that spans 1.5 Mb and has 22 exons and 8 splice variants.¹² Six PDE4D single-nucleotide polymorphisms (SNPs) were significantly associated with strokes after adjusting for multiple comparisons.¹³ However, several replicated studies from different populations have provided apparently conflicting evidence as to the association between the PDE4D gene and stroke.^{13–21} For example, PDE4D is a risk factor for ischemic stroke and, in particular, for cardio-embolic (CE) stroke among whites and blacks.¹⁸ However, variants in the PDE4D gene are not a major risk factor for stroke in individuals from central Europe.¹⁴ Population differences in allelic and haplotype frequencies as well as linkage disequilibrium (LD) structure may contribute to the observed differences among populations.

Although of great potential importance, the association of PDE4D with strokes has not been investigated in the Taiwanese population. The aim of the present study was to evaluate the potential of the PDE4D genes to increase the risk of stroke in Taiwan..