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A prevalence study of single nucleotide polymorphisms in the promoter of the apolipoprotein E gene in different ethnic groups in Malaysia

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Abstract

Background and Objective: The promoter of the apolipoprotein E (*APOE*) gene is polymorphic at positions -491A/T, -427C/T and -219G/T. These single nucleotide polymorphisms may alter transcriptional activity and impact *APOE* expression due to differential binding of transcription factors. It has been suggested that the -491 A, -427 C and -219 T alleles are associated with a high risk of developing Alzheimer's disease. This study aims to investigate the frequencies of *APOE* promoter polymorphisms in three major ethnic groups (Malay, Chinese and Indian) in Malaysia. *Method:* DNA was extracted from blood obtained from 290 healthy people (Malay: *n*= 92; Chinese: *n*= 105; and Indian: *n*= 93), and the promoter region was amplified using PCR and genotyped by direct sequencing. *Result:* The Indian group has the lowest frequencies of - 491 A, - 427 C and - 219 T alleles (83.9%, 3.2% and 56.5%, respectively) compared to the Chinese group with the highest frequencies (97.1%, 11.9% and 67.1%, respectively). The frequencies in the Malay group were somewhere in between (94.6%, 8.2% and 61.4%, respectively). Moreover, for the - 491 and - 427 positions, the frequencies of possible genotypes viz., AA or AT or TT and CC or CT or TT, respectively, were statistically significant ($P < 0.05$, Chi- Square Test) between the 3 ethnic groups.
Conclusion: Based on the frequency of *APOE* promoter polymorphisms alone, the ethnic Indian may be predisposed to lower risks for AD than the Chinese or Malay.

INTRODUCTION

Apolipoprotein E (*ApoE*) is a polymorphic protein with three common isoforms encoded by three alleles (ε2, ε3 and ε4) of the *APOE* gene on chromosome 19q13.2.[1] *ApoE* represents a major lipoprotein within the central nervous system where it is synthesized by astrocytes.[2,3] It has been suggested that one role of *ApoE* in the brain may be neuronal homoestasis[4], particularly, mobilization of cholesterol in the central nervous system, where it is required for neuronal plasticity.[5,6] ApoE is also postulated to play a role in neuronal repair by mediating the recycle of damaged cell membranes.[4]

In-vivo and *in-vitro* studies have suggested an association of certain alleles of the *APOE* with a higher risk for Alzheimer's disease (AD).[4,7-12] The *APOE* ε4 allele is associated with both early- and late-onset AD. Factors that regulate *APOE* transcription, such as selected single nucleotide polymorphisms in the promoter or transcriptional regulatory region of *APOE*, may also contribute to an individual's risk for AD. Three single nucleotide polymorphisms in the gene promoter at positions -491 A/T, -427 C/T, and -219 G/T (also known as Th1/E47cs) have been variously reported to confer an increased risk for AD.[13-18,23,25,26] The various genotypes (allelic combinations) for each position are: -491 AA or -491 AT or -491 TT; -427 CC or -427 CT or -427 TT; -219 GG or -219 GT or -219 TT.

The allelic polymorphism at position -491 is the most thoroughly investigated. Several studies have shown that the -491 A allele is associated with an increased risk of AD that is independent of the *APOE* ε4 status.[13-17] Others have reported significant linkage disequilibrium between the -491 alleles and *APOE* ε4 polymorphisms but no independent association.[18-24] To date, the -427 allelic polymorphism has been the subject of five investigations, only two of which have shown an independent association between the -427 C allele

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