

A High Frequency PAH Missense Mutation M276V in Kyushu Japanese Phenylketonuric Patients is Not Found Among Chinese Phenylketonuric Patients

C.-H. Chen^{1*}, S.-J. Wu³, K.-J. Hsiao^{2,3}

Department of Neurology and Psychiatry¹, Institute of Genetics², National Yang-Ming University; Department of Medical Research and Education³, Veterans General Hospital, Taipei, Taiwan 112, R.O.C.

Phenylketonuria (PKU) is an autosomal recessive inborn error of metabolism with manifestations of mental retardation. Classical PKU patients have elevated serum level of phenylalanine, which is due to the defects of phenylalanine hydroxylase (PAH). With the isolation of the human PAH cDNA and genomic DNA, the molecular defects of PAH gene causing PKU have been characterized. Recently, a new missense mutation M276V (A826G) in exon 7 of PAH gene, with high frequency in unrelated Japanese PKU patients from Kyushu island was reported by GoebelSchreiner and Schreiner (J Inher Metab Dis 16: 950-6, 1993). In their report, they suggested that one of the possibilities of the high frequency of M276V in Japanese PKU families, is a result of genetic drift, from southeastern China. To test this hypothesis, we decided to study the M276V mutation among Chinese classical PKU patients. A PCR-based restriction analysis was developed as screening method, because M276V obliterates a NlaIII restriction site. Genomic DNAs isolated from dried blood spots collected in filter paper were used as template, exon 7 of PAH gene with flanking intron sequences were PCR amplified. The 291 bp PCR products were subjected to restriction digestion with NlaIII. The digested PCR products were resolved in 4% agarose gel, and visualized with ethidium bromide. Positive control was generated by site-directed mutagenesis using "meg-primer" method. After restriction digestion, normal allele generates three fragments of 171 bp, 106 bp and 14 bp; whereas M276V mutant allele generates two fragments of 171 bp and 120 bp. After screening 72 cases of Chinese classical PKU patients from Taiwan (N=22) and mainland China (N=50), we do not identify any Chinese PKU patients with M276V mutation. Our results do not support the hypothesis that the frequent M276V missense mutation of PAH in Japanese PKU patients is due to genetic drift from southeastern China.

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