Genomic Structure of 6-Pyruvoyl-tetrahydropterin Synthase Gene and a T/C polymorphism Detected in Chinese

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Deficiency in 6-pyruvoyl-tetrahydropterin synthase (PTPS) activity is a major cause of the tetrahydrobiopterin (BH_4) deficient hyperphenylalaninemia (HPA). A 23-bp deletion (164-186del) was found to occur in the lymphoblast PTPS cDNA of the PTPS-deficient HPA as well as in that of the normal subjects. This finding suggests that the 23-bp deletion might be an alternative splicing in the PTPS transcripts of lymphoblasts instead of a mutation causing PTPS-deficiency. The genomic structure of PTPS gene was characterized, starting from this skipped 23-bp exon, by polymerase chain reaction using human genomic DNA as template. Its coding region consists of six exons and is approximately 7.5 kb in length. A T- to -C substitution polymorphism, in intron 2 at 14 nt downstream of the 5'- splice donor site, was found in the Chinese population in Taiwan with 14% heterozygosity. This polymorphic marker may provide an aid for linkage analysis.

Key words: 6-pyruvoyl-tetrahydropterin synthase; tetrahydrobiopterin; hyperphenylalaninemia; gene structure; polymorphism.

Introduction

Phenylketonuria (PKU) and hyperphenylalaninemia (HPA) may be caused by deficiency of phenylalanine hydroxylase (EC 1.14.16.1) or the tetrahydrobiopterin (BH_4) cofactor required in the aromatic amino acids hydroxylation. In addition to mental retardation manifested in phenylalanine hydroxylase deficient HPA, deficiency of BH4 may also lead to severe neurological disorders due to deficit of neurotransmitter derivatives of tyrosine and tryptophan [1]. The overall incidence (~1/33,000) of PKU among the Chinese population in Taiwan [2] was found to be lower than that in general Caucasian populations (1/10,000) [1]. However, about one third of these southern Chinese HPA is caused by BH4 deficiency [3, 4], which is much more

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