A gly170ser missense mutation and reduced RNA expression of dihydropteridine reductase gene detected in Chinese hyperphenyloalaninemia.

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Dihydropteridine reductase (DHPR) reduces the quinonoid dihydrobiopterin to tetrahydrobiopterin (BH_4), the essential cofactor required in aromatic amino acids hydroxylation. Defect in DHPR will result in BH_4-deficient hyperphenylalaninemia (HPA). Two Chinese DHPR deficient families were detected from about 300 Chinese hyperphenylalaninemia cases collected from Southern (Taiwan and Canton) and Northern (Shanghai and Beijing) China. To characterize the molecular basis of DHPR deficient HPA in Chinese, total RNA isolated from PHA-stimulated lymphocyte was amplified by reverse transcription (RT)-polymerase chain reaction (PCR). A single base transition 508G>A (Gly170Ser) on DHPR cDNA was identified in two consanguineous DHPR deficient siblings. None of 100 normal alleles screened were found to have this 508G>A substitution. With regard to the other Chinese DHPR deficient family, no nucleotide alteration could be found in the DHPR coding region. However, the quantitative RT-PCR analysis indicated a reduced DHPR mRNA expression. This reduced mRNA quantities were also found both in the maternal and the paternal families and tightly linked to the heterozygotes determined by DHPR activity in blood. This result indicates that the mutation might lie in the regulatory region of the DHPR gene.