Study of Restriction Frament Length Polymorphisms At the Human Dihydropteridine Reductase Locus and Its Application in Prenatal Diagnosis of Dihydropteridine Reductase Deficien Phenylketonuria in Chinese

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Dihydropteridine reductase (DHPR; E.C. 1.6.99.7) is an essential enzyme in the pterin-dependent aromatic acid hydroxylating systems. Deficiency of DHPR activity will cause tetrahydiopterin deficient forms of phcnylketonuria. Using a human DHPR cDNA probe, we have determined the restriction fragment length polymorphisms (RFLPs) with the restriction enzymes, *Nco*I, *Ava*II, *Msp*I and *Hinf*I in 50 unrelated and apparently normal Chinese. With *Nco*I and *Ava*II, we observed two sets of polymorphisms for each enzyme, but only one set of polymorphisms was found for each of *Msp*I and *Hinf*I. The allele frequencies are 0.34/0.66 for Ncol 10/7.8+2.2 kb, 0.31/0.69 for Ncol 6.6/5.9+0.7 kb, 0.69/0.31 for *Ava*II 9.0/7.0 kb, 0.29/0.71 for *Ava*II 5.7/4.3 kb, 0.4/0.6 for *Msp*I 1.3/1.2 kb, and 0.1/0.9 for *Hinf*I 1.1/0.9 kb.These results are different form those reported in Caucasians, but similar with those reported in Japanese, especially with *Msp*I and *Hinf* I. The frequency of the observed heterozygosity is approximately 86%, lower than the expected 95%. AvaII 9.0 kb and 4.3 kb were found in strong linkage disequilibrium with *Nco*I 7.8+2.2 kb and 5.9+0.7 kb, respectively. No major DNA insertion, deletion or rearrangemeng of DHPR lous was observed in two DHPR deficent families in Taiwan. The abnormal alleles in these families were found belong to different haplotypes, which indicates that the DHPR mutations in Taiwan are not in linkage disequilibrium to one partcular haplotype. RFLPS of these families are fully informative for prenatal diagnosis of DHPR deficiency. A carrier fetus was correctly prenatal diagnosed by this RFLPS analysis with DNA obtained form amniotic cells.

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