Screening, Diagnosis and Molecular Genetics of Methylmalonic Acidemia in Chinese

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Methylmalonic acidemia caused by methylmalonyl CoA mutase deficiency (MIM 251000; mut type MMA) is a common disorder of organic acid metabolism. Voluntary neonatal screening for MMA by tandem mass spectrometry (MS/MS) was performed since 2001.8 by three neonatal screening centers in Taiwan. Confirmatory and differential diagnosis for MMA were performed by detecting methylmalonic acid in urine, incorporation assay of propionic acid in fibroblasts and measurement of methylmalonyl CoA mutase in lymphocytes. One case of MMA was detected from 216,000 newborns between 2001.8 and 2003.10 by MS/MS screening. This case was differentially diagnosed as a mut type MMA by analyzing mutase activity. Prenatal diagnosis for six families suffering from MMA were performed by measuring methylmalonic acid and/or propionylcarnitine in amniotic fluids, propionic acid incorporation in amniocytes, determining mutase activity in amniocytes and/or chorionic villi and molecular genetic analysis. Nine mutations in the MUT gene, designated c.316A>C (T106P), c.682C>T (R228X), c.683G>A (R228Q), c.1106G>A (R369H), c.1280G>A (G427D), [c.1630G>T+c.1631G>A] (G544X), c.1741C>T (R581X), c.1046-058del (A349delX368), and IVS9-1G>A, were identified in eight unrelated Chinese mut type patients. Among which, the c.316A>C, c.1280G>A, [c.1630G>T+c.1631G>A], c.1741C>T, c.1046-058del, and IVS9-1G>A alterations are novel mutations found in the MUT gene. The allele frequency of both c.1280G>A and [c.1630G>T+c.1631G>A] mutations were 15% (3/20) in Chinese mut type MMA. These two mutations were all linked to the 190bp allele of a short tandem repeat marker (STR) D6S269 that was found to be a rare allele in normal Chinese population. These data suggested that c.1280G>A and [c.1630G>T+c.1631G>A] mutations might have founder effects in Chinese mut type MMA patients.

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Application New

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Using tandem mass sp
categories of fatty acid oxid
be diagnosed simultaneousl
have screened about 210,0
acidemias (propionic acide
carboxylase deficiency), 7 w
long-chain acyl-CoA dehydr
and 7 with amino acidopath
All of 7 patients with propi
residual enzyme activities, a
a protein-restricted diet. T
neurological crises under th
FAODs are important targe
believed very rare based on t
been developing without n
episodes of hypoglycemia. C
the elevations of the selected
did not have the characteristi
should be tested further.