Molecular aspects of Mucopolysaccharidosis IVA in Taiwan

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ABSTRACT

Background：Mucopolysaccharides (MPS) are long unbranched polysaccharides consisting of a repeating disaccharide unit. They are throughout the body, often in mucus and in fluid around the joints. When the body cannot break down mucopolysaccharides, a condition called mucopolysaccharidosis MPSoccurs. MPS refers to a group of inherited disorders of metabolism. People with MPS do not have any, or enough of an enzyme needed to break down the sugar molecule chains. MPS type IVA (Morquio A syndrome) is an autosomal recessive lysosomal storage disease. It is induced by a deficiency of the enzyme *N*-acetyl- galactosamine-6-sulfatase (GALNS) and accumulates keratan sulfate, and chondroitin 6-sulfate in lysosomes. All of mucopolysaccharides are gross excretion in the urine. The symptoms include: severe skeletal dysplasia, short stature, motor dysfunction.

Methods：In this study, 12 MPS IVA patients were investigated. Genomic DNA was extracted from each patient's peripheral blood leukocytes. To identify possible exonic mutations in the target gene, *GALNS*, the entire coding sequence of the DNA fragments, each covering an exon and its flanking regions, was amplified and subjected to direct sequencing.

Results：The sequencing result of 12 MPS IVA patients revealed that one was homozygous, the others were compound heterozygous. Mutation types included one nonsense, two small deletion and seven missense. Although more than 180 mutations have been reported, three unique mutations (p.A64T, c.245-56_250del62, p.Q483K) were

only found in our population. The c.245-56_250del62 and p.M318R were common mutations in this group of MPS IVA patients, accounting for 41.7% of the total number of mutant alleles.

Conclusion：This study extended the spectrum of *GALNS* mutations and our results also suggested that *GALNS* gene mutation profile in Taiwanese MPS IVA patients may be little different from other countries. Therefore, *GALNS* gene profiling may be useful in genetic counseling for families affected by MPS IVA.