Molecular Analysis of Thai Patients with Mucopolysaccharidosis Type I

Mucopolysaccharidosis type I (MPS I) is a rare autosomal recessive disorder resulting from the deficiency of alpha-L-iduronidase (IDUA; EC: 3.2.1.76) which is involved in the degradation of glycosaminoglycans (GAGs), namely heparin sulfate and dermatan sulfate. MPS I presents a wide variation of clinical manifestations from attenuated to severe forms, which can be divided in three distinct phenotypes: severe (Hurler), intermediate (Hurler-Scheie) and mild (Scheie). The gene encoding IDUA maps in chromosome 4p16.3 and contains 14 exons. Recently, more than 100 different IDUA mutations have been reported in the Human Gene Mutation Database (http://www.hgmd.org). This work was supported by Chulaborn Research Institute, Bangkok.

ABSTRACT

Mucopolysaccharidosis type I (MPS I) is a rare autosomal recessive disorder resulting from the deficiency of alpha-L-iduronidase (IDUA; EC: 3.2.1.76) which is involved in the degradation of glycosaminoglycans (GAGs), namely heparin sulfate and dermatan sulfate. MPS I presents a wide variation of clinical manifestations from attenuated to severe forms, which can be divided in three distinct phenotypes: severe (Hurler), intermediate (Hurler-Scheie) and mild (Scheie). The gene encoding IDUA maps in chromosome 4p16.3 and contains 14 exons. Recently, more than 100 different IDUA mutations have been reported in the Human Gene Mutation Database (http://www.hgmd.org). Six Thai unrelated patients with MPS I have been characterized using biochemical and molecular biology approaches in our facility. Two Hurler patients have previously reported: one was heterozygous for c.311G>A (p.A75T) and c.1986C>T (p.R89Q) and the other had a frameshift mutation 252insC and a nonsense mutation c.983G>T (p.E299X). Two patients were found to have homozgyous mutation for c.1183-1G>A (p.X654R) which caused the elongation of an extra 46 amino acid residues before the poly A tail signal and does not contain any stop codon in this extra sequence. The other two patients were compound heterozygotes of the mutation c.1183-1G>A (p.X654R) in association with either the mutation c.345G>A (p.R89Q) or the nonsense mutation c.1023G>A (p.W312X) which is novel. These findings, some of mutations were the first found in Thailand, expand the diverse set of defective IDUA genes in the Thai population that will be useful for molecular diagnosis and treatment of disease. This work was supported by Chulaborn Research Institute, Thailand.