Molecular Analysis of Thai Patients with Mucopolysaccharidosis Type I

Mucopolysaccharidosis type I (MPS I) is an 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 into 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) which vary in several types: frameshift mutation 252insC and nonsense mutation c.983G>T (p.E299X) in a Japanese patient, 50 patients with homozgyote mutation c.345G>A (p.R89Q) in an American study, 3 patients with a frameshift variant c.983G>T (p.E299X) and nonsense mutation c.311G>A (p.A75T) in a Chinese study. MPS I patients have previously reported its existence in the Thai population; an MPS I patient with homozygous mutation c.983G>T (p.E299X) was reported from the Chulabhorn Research Institute, Bangkok, Thailand.

In this study, we have characterized four more Thai patients with MPS I who were diagnosed as MPS I. Two patients were found to have homozgyote mutation for c.983G>T (p.E299X), 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.1023G>A (p.W312X) 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 Chulabhorn Research Institute, Thailand.