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Identification of four novel mutations in five unrelated Korean families with Fabry disease

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Abstract

Fabry disease is a X-linked recessively inherited metabolic disorder, which results from the deficient activity of the lysosomal hydrolase α-galactosidase A leading to the systemic deposition of glycosphingolipids with terminal α-galactosyl moieties. Single-strand conformation polymorphism (SSCP) analysis was performed, followed by DNA sequencing of PCR amplified exons of the human α-galactosidase A gene in 5 unrelated Korean patients with classic Fabry disease. Five different mutations were identified; two nonsense mutations (Y86X and R342X), one missense mutation (D266N), and two small deletions (296del2 and 802del4). Except for R342X mutation, four were novel mutations (Y86X, D266N, 296del2, 802del4). A T to G transversion at nucleotide position 5157 in exon 2 caused a tyrosine-to-stop substitution at codon 86. A G to A transition at position 10 287 in exon 5 substituted an asparagine for an aspartate at codon 266. Mutation 296del2 in exon 2 resulted in a frame shift with a stop signal at the 22th codon downstream from the mutation, whereas mutation 802del4 resulted in a stop codon at the site of 4 bp deletion. In addition, the 802del4 was found to be a *de novo* mutation. This is the first report on mutation analysis of the human α-galactosidase A gene in Korean patients with Fabry disease.

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