Analisis Varian Ekson 1--7 Gen Galactosamine (N-Acetyl)-6-Sulfatase (GALNS) pada Pasien Mukopolisakaridosis IVA di Indonesia = Variant Analysis for Exon 1--7 of Galactosamine (N- Acetyl)-6-Sulfatase (GALNS) Gene in Mucopolysaccharidosis IVA Patients in Indonesia

Nurul Muhammad Prakoso, author

Abstrak

Mukopolisakaridosis IVA (MPS IVA; Sindrom Morquio A) merupakan penyakit metabolik yang diturunkan secara autosomal resesif. Penyakit MPS IVA terjadi akibat defisiensi enzim N-acetylgalactosamine-6-sulfatase (GALNS) yang menyebabkan senyawa keratan sulfat (KS) dan kondroitin-6-sulfat (K6S) tidak terdegradasi dan terakumulasi di dalam lisosom. Defisiensi enzim GALNS terjadi karena varian patogenik pada gen galactosamine (N-Acetyl)-6-sulfatase (GALNS) yang terletak di lokus 16q24.3. Jenis varian yang ditemukan pada penelitian sebelumnya meliputi single nucleotide variation (SNV) dan varian frameshift. Namun sampai saat ini belum ada penelitian analisis varian yang telah dilakukan pada pasien MPS IVA di Indonesia. Penelitian ini bertujuan untuk mengetahui variasi genetik ekson 1--7 gen GALNS pada pasien MPS IVA di Indonesia. Penelitian dilakukan menggunakan empat pasien MPS IVA dan 50 individu normal sebagai kontrol. Daerah ekson 1--7 gen GALNS dari seluruh sampel yang telah diamplifikasi menggunakan teknik polymerase chain reaction (PCR) lalu disekuensing menggunakan teknik automated fluorescence DNA sequencing. Berdasarkan hasil analisis sekuensing DNA, variasi genetik ekson 1--7 gen GALNS pada populasi Indonesia berhasil diidentifikasi. Sebanyak 11 varian intronik, yaitu yaitu c.121 – 139G>A, c.244 + 86G>A, c.566 + 5T>C, IVS5 + 134G>A, c.633 + 85C>T, c.633 + 91T>C, c.633 + 125A>G, c.633 + 138C>A, c.634 – 20C>T, c.634 – 19G>A, dan c.634 – 130T>C berhasil diidentifikasi. Sementara itu, sebanyak empat varian eksonik berhasil ditemukan, yaitu c.503G>T (p.(Gly168Val)), c.510C>T (p.Tyr170=), c.751C>T (p.Arg251*), dan c.708C>T (p.His236=).

.....Mucopolysaccharidosis IVA (MPS IVA) or Morquio A Syndrome, is a lysosomal storage disorder caused by the deficiency of N-acetylgalactosamine-6-sulfatase (GALNS) enzyme, resulting in accumulation of keratan sulfate (KS) and chondroitin-6-sulfate (C6S) in the lysosome and leads to tissue or organ damage. The enzyme deficiency occurs due to mutations in the galactosamine (N-Acetyl)-6-sulfatase (GALNS) gene located at locus 16q24.3. Variants identified by previous studies consisted of single nucleotide variation (SNV) and frameshift. This study aims to identify the genetic variation of exon 1--7 of GALNS gene in MPS IVA patients in Indonesia. The study was conducted using previously diagnosed MPS IVA patients and 50 normal individuals as controls. Based on the results of DNA sequencing analysis, genetic variations of exon 1--7 of GALNS gene in MPS IVA patients in Indonesian population have been identified. A total of 11 intronic variants, namely c.121 – 139G>A, c.244 + 86G>A, c.566 + 5T>C, IVS5 + 134G>A, c.633 + 84C>T, c.633 + 91T>C, c.633 + 125A>G, c.633 + 138C>A, c.634 – 20C>T, c.634 – 19G>A, and c.634 – 130T>C. Four exonic variants were also found, namely c.503G>T (p.(Gly168Val)), c.510C>T (p.Tyr170=), c.751C>T (p.Arg251*), and c.708C>T (p.His236=).