ARSB Gene Analysis in Maroteaux-Lamy Syndrome/ Mucopolysaccharidosis VI (MPSVI)

Clinical Features:

Mucopolysaccharidosis VI (MPSVI) or Maroteaux-Lamy syndrome is a lysosomal storage disorder with a wide spectrum of features ranging from a severe, rapidly progressing form to a relatively mild, slowly progressing form. Symptoms can include short stature, skeletal deformities, stiff and contracted joints, hepatosplenomegaly, coarse facial features, respiratory difficulties, hearing loss, corneal clouding, and cardiac abnormalities. Neurological development is generally normal. The rapidly progressing form is characterized by onset before 2 or 3 years, impaired mobility by 10 years, delayed puberty, an adult height less than 120 cm, cervical spinal cord compression, respiratory insufficiency, surgical complications and frequently death in the 2nd or 3rd decade due to heart failure.[1] The slowly progressing form is characterized by later onset of symptoms with a diagnosis being made after 5 years of age; however, some patients are not diagnosed until the 2nd or 3rd decades. These patients may also develop skeletal complications including carpal tunnel syndrome, joint disease and a decrease in their overall functional status, and most will develop more serious complications of MPSVI at some point including joint degeneration, cardiac valve disease, sleep apnea, decreases in pulmonary function and reduced endurance.[1] Birth prevalence estimates for MPS VI range from 0.5 to 4.3 per million live births, with the exception of a very high rate in Turkish immigrants in Germany (2.3 per 10^5 live births). [1]

Genetics:

Autosomal Recessive. MPSVI is caused by pathogenic variants in the *ARSB* gene encoding the arylsulfatase B (ASB) or *N*-acetylgalactosamine 4-sulfatase enzyme that hydrolyzes the C4 sulfate ester from the glycosaminoglycans (GAG) dermatan sulfate and chondroitin sulfate during their lysosomal degradation. Patients with MPSVI generally have ASB activity that is 10% or less than controls in leukocytes or cultured fibroblasts, leading to their intralysosomal storage and excretion in the urine. Higher urinary GAG concentrations (>200 µg/mg creatinine) have been associated with a more severe phenotype, while lower concentrations (<100 µg/mg creatinine) have been associated with a slower disease progression.[1]The *ARSB* gene is located on chromosome 5q13-5q14 and has 8 exons.

Test Methods:

Variant analysis of the *ARSB* gene is performed on genomic DNA from the submitted specimen using bi-directional sequence analysis of coding exons and corresponding intron/exon boundaries. If sequencing identifies a variant on only one allele of the *ARSB* gene, and if clinically indicated, reflex deletion/duplication testing (ExonArrayDx) will be performed at no additional charge to evaluate for a deletion/duplication of one or more exons of this gene.

Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis or another appropriate method.

Test Sensitivity:

In clinically affected patients with deficient enzyme activity and/or increased urinary excretion of dermatan and chondroitin sulfate, sequence analysis of the ARSB gene identified pathogenic variants on greater than 95% of alleles.[2]

References:

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