

Mucopolysaccharidosis Type VI: *ARSB* Gene Sequencing

Test Code: BI

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Mucopolysaccharidosis type VI (MPS VI), also known as Maroteaux-Lamy Syndrome, is a lysosomal storage disorder caused by absence or dysfunction of the enzyme arylsulfatase B (N-acetylgalactosamine 4-sulfatase). This enzyme is one of a group responsible for the degradation of dermatan sulfate, a glycosaminoglycan (GAG) normally broken down in the lysosomes. In MPS VI, insufficient enzyme activity is available and the degradation of dermatan sulfate is blocked, leading to accumulation of this substrate in the lysosomes of several tissues.

The clinical presentation can vary from mild to severe. The major clinical manifestations are corneal clouding, joint stiffness, and a skeletal dysplasia known as dysostosis multiplex. Unlike most lysosomal storage disorders, intelligence is unaffected. Macrocephaly and sternal abnormalities can be present at birth, and inguinal/umbilical hernias are common. Restriction of joint movement develops sometime in the first few years of life, and a typical crouched posture is assumed. Hepatomegaly, corneal clouding, claw-hand deformities, cardiac valve involvement, decreased pulmonary function, and sleep apnea become evident as the child ages. Respiratory infections are common. Growth in height is usually less than normal, but variable with the severity of disease. Facial features become more coarse with age, and individuals with MPS VI often resemble one another. Deafness, both sensorineural or conductive, is seen in all types of mucopolysaccharidoses, including MPS VI. Spinal cord compression is a typical complication in older children and adults. Carpal tunnel syndrome and nerve compression is also seen in older children and adults. Enzyme replacement therapy (ERT) for MPS VI has been approved by the FDA and is available for treatment of this disorder.

Mutations in the *ARSB* gene result in reduced activity of the arylsulfatase B enzyme. Diagnostic sequencing analysis of the *ARSB* gene coding region is available for MPS VI patients and their at-risk relatives on a clinical basis.

For questions about testing for MPS VI, call EGL Genetics at (404) 778-8499 or (855) 831-7447. For further clinical information about lysosomal storage diseases, including management and treatment, call the Emory Lysosomal Storage Disease Center at (404) 778-8565 or (800) 200-1524.

For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array (LZ).

References:

- 1). Litjens, T. and Hopwood, JJ. Mucopolysaccharidosis Type VI: Structural and Clinical Implication of Mutations in N-Acetylgalactosamine-4-Sulfatase. 2001. *Hum. Mut.* 18:282-295.
- 2). Karageorgos, L. et al. Mutational analysis of mucopolysaccharidosis type VI patients undergoing a trial of enzyme replacement therapy. 2004. *Hum. Mutat.* 23: 229-233.

Indications

- Confirmation of a clinical diagnosis of MPS VI (Maroteaux-Lamy).
- Prenatal testing for known familial mutations.
- Assessment of carrier status in high risk family members known mutation analysis.

Methodology

PCR amplification of 8 exons contained in the *ARSB* gene coding region will be performed on patient genomic DNA. Direct sequencing of amplification products is performed in both the forward and reverse directions using automated fluorescence dideoxy sequencing methods. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then classified as mutations, benign variants unrelated to disease or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members.

This assay does not interrogate the promoter region, deep intronic regions or other regulatory elements. Large deletions are not detected by this analysis. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Detection

Clinical Sensitivity: In 7 patients undergoing enzyme replacement therapy for MPS VI, 13 mutations were identified, giving a detection rate of 93% [2]. Analytical Sensitivity: ~99% Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of MPS VI is not specifically known, but is likely to be rare and may vary by ethnicity. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: Whole Blood (EDTA)**Specimen Requirements:**

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: DNA, Isolated**Specimen Requirements:**

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions

Submit copies of diagnostic biochemical test results with the sample. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

Related Tests

- Mucopolysaccharide screen (urine GAG) (GA)
- Known mutation analysis (Custom Diagnostics) is available to test family members.
- A deletion/duplication assay is available separately for individuals where mutations are not identified by sequence analysis. Refer to the test requisition or contact the laboratory for more information.
- Prenatal testing is available for known familial mutations only.
- Please call the Laboratory Genetic Counselor for specific requirements for prenatal testing before collecting a fetal sample.