

Mucopolysaccharidosis Type VII: *GUSB* Gene Sequencing

Test Code: SGUSB

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Mucopolysaccharidosis type VII (MPS VII) is a member of a group of inherited metabolic disorders collectively termed mucopolysaccharidoses (MPSs). The MPSs are caused by a deficiency of lysosomal enzymes required for the degradation of mucopolysaccharides also called glycosaminoglycans (GAGs) within the lysosome. When functioning normally, the lysosomal enzymes break down these GAGs, however when the enzyme is deficient, the GAG build up in the lysosomes causing damage to the body's tissues. The MPSs share a chronic progressive course with multisystem involvement, several physical features, laboratory findings, and radiographic abnormalities; these include facial coarsening, hepatomegaly, excretion of urinary GAG fragments, and leukocyte inclusion bodies.

Mucopolysaccharidosis type VII (MPS VII) is an autosomal recessive that occurs when certain mucopolysaccharides, specifically dermatan, heparan, and chondroitin sulfates accumulate in lysosomes due to a deficiency of the enzyme beta-glucuronidase. Unlike other lysosomal storage disorders in which patients begin life with a period of normal development, patients with MPS VII have a high incidence of hydrops fetalis [1]. Clinical features of MPS VII vary widely between patients and include short stature, coarse facial features, hepatosplenomegaly, respiratory difficulties, hearing loss, and mental retardation.

Mutations in the *GUSB* gene cause deficiency of beta-glucuronidase leading to MPS VII. A pseudodeficiency allele, a mutation that reduce enzyme activity but does not cause disease, has been described [2] and will be detected by this sequencing analysis. Diagnostic sequencing analysis of the *GUSB* gene coding region is available for MPS type VII patients and their at-risk relatives on a clinical basis.

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

For questions about testing for MPS VII, call EGL Genetics at (470) 378-2200 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.

References:

1. Muenzer, J., The mucopolysaccharidoses: a heterogeneous group of disorders with variable pediatric presentations. *J Pediatr*, 2004. 144(5 Suppl): p. S27-34.
2. Vervoort, R., M.R. Islam, W. Sly, A. Chabas, R. Wevers, J. de Jong, I. Liebaers, and W. Lissens, A pseudodeficiency allele (D152N) of the human beta-glucuronidase gene. *Am J Hum Genet*, 1995. 57(4): p. 798-804.
3. Vervoort, R., N.R. Buist, W.J. Kleijer, R. Wevers, J.P. Fryns, I. Liebaers, and W. Lissens, Molecular analysis of the beta-glucuronidase gene: novel mutations in mucopolysaccharidosis type VII and heterogeneity of the polyadenylation region. *Hum Genet*, 1997. 99(4): p. 462-8.
4. Yamada, S., S. Tomatsu, W.S. Sly, R. Islam, D.A. Wenger, S. Fukuda, K. Sukegawa, and T. Orii, Four novel mutations in mucopolysaccharidosis type VII including a unique base substitution in exon 10 of the beta-glucuronidase gene that creates a novel 5'-splice site. *Hum Mol Genet*, 1995. 4(4): p. 651-5.
5. Vervoort, R., M.R. Islam, W.S. Sly, M.T. Zabot, W.J. Kleijer, A. Chabas, A. Fensom, E.P. Young, I. Liebaers, and W. Lissens, Molecular analysis of patients with beta-glucuronidase deficiency presenting as hydrops fetalis or as early mucopolysaccharidosis VII. *Am J Hum Genet*, 1996. 58(3): p. 457-71.

Genes

[GUSB](#)

Indications

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

Methodology

PCR amplification of 12 exons contained in the *GUSB* 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.

Detection

Clinical Sensitivity: 10/10 mutations identified in 5 patients [3], 4/4 mutations identified in 2 Caucasian patients [4], 34/34 mutations identified in 17 patients from various ethnic groups; Analytical Sensitivity: ~99%

Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of MPS VII is not specifically known, but is likely to be rare and may vary by ethnicity.

Targeted CGH Array:

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. 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: 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.

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.

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 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)
- Lysosomal Enzyme Screening Panel (LS)
- 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.
- Known Mutation Analysis (KM) is available to test family members.
- 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.