

Mucopolysaccharidosis Type I: *IDUA* Gene Sequencing

Test Code: BO

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Mucopolysaccharidosis type I or Hurler Syndrome (MPS I) is a progressive multisystem disorder with features that range over a continuum from mild to severe. MPS I is an autosomal recessive progressive disorder that results from the body's inability to make lysosomal alpha-L-iduronate, an enzyme that helps break down mucopolysaccharides. The enzyme deficiency found in MPS type I causes mucopolysaccharides to build up in the body, causing damage to many tissues and organs in the body.

MPS Type I is divided into three subtypes, but there is no clear distinction between the groups. Therefore, a classification based on disease severity has been suggested: Hurler as severe MPS I, Hurler-Scheie as intermediate MPS I, and Scheie as mild MPS I. Treatment is available through hematopoietic stem cell/bone marrow transplantation or enzyme replacement therapy.

MPS I is caused by mutations in the *IDUA* gene and the diagnosis relies on the demonstration of deficient activity of the lysosomal enzyme alpha-L-iduronidase in peripheral blood leukocytes or cultured fibroblasts. Diagnostic sequencing analysis of the *IDUA* gene coding region is now available for MPS type I 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 (LL).

For questions about testing for MPS I, 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). Beesley CE, Meaney CA, Greenland G, Adams V, Vellodi A, Young EP, Winchester BG (2001) Mutational analysis of 85 mucopolysaccharidosis type I families: frequency of known mutations, identification of 17 novel mutations and in vitro expression of missense mutations. *Hum Genet* 109:503-11
- 2). Muenzer J (2004) The mucopolysaccharidoses: a heterogeneous group of disorders with variable pediatric presentations. *J Pediatr* 144:S27-34

Genes

[IDUA](#)

Indications

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

Methodology

PCR amplification of 14 exons contained in the *IDUA* 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

Full Gene Sequencing:

Clinical Sensitivity: Two *IDUA* gene mutations were found in 81 (95%) families, one *IDUA* mutation in 3 (3.5%) families and none in 1 (1.1%) family as reported by Beesley CE, et al [1], Analytical Sensitivity: ~99% Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of MPS I 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: 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: 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)
- 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.