Mucopolysaccharidosis Type I: IDUA Gene Sequencing

**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:

**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 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 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
interpreted in the context of the patient’s clinical and/or biochemical phenotype.

## Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

### Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

### Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection 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 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.