

Mucopolysaccharidosis Type II: *IDS* Gene Sequencing

Test Code: BQ

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Mucopolysaccharidosis type II (Hunter Syndrome) is a member of a group of inherited metabolic disorders collectively termed mucopolysaccharidoses (MPS's). The MPS's are caused by a deficiency of lysosomal enzymes required for the degradation of mucopolysaccharides or glycosaminoglycans (GAGs). Mucopolysaccharidosis type II or Hunter Syndrome (MPS II) is an X-linked disorder resulting from the deficiency of iduronate 2-sulfatase. The deficiency of iduronate sulfatase activity results in the lysosomal accumulation of heparan and dermatan sulfate. Mucopolysaccharides make up a large portion of the intercellular substance of connective tissue, therefore multiple organ systems are involved, including the musculoskeletal, integumentary, cardiovascular, pulmonary, and ocular systems. Symptoms may include coarse facial features, short stature, enlarged liver and spleen, progressive mental retardation, skeletal changes, joint stiffness, progressive airway obstruction, short neck, broad chest, large head, and progressive deafness. Two types of Hunter syndrome have been described, mild and severe, but individuals with intermediate severity who do not fit clearly in either the severe or the mild end of the spectrum have been described. It is now clear, based on current understanding of the enzyme and its gene, that MPS II comprises a wide spectrum of severity and that individuals may be categorized anywhere from severe to mild Hunter with many individuals having an intermediate form somewhere between severe and mild. Enzyme replacement therapy is FDA approved to treat the symptoms of Hunter patients. Because of the X-linked recessive pattern of inheritance, this is almost exclusively a disorder that affects males. Mutations to the *IDS* gene causes deficiency of iduronate 2-sulfatase. Diagnostic sequencing analysis of the *IDS* gene coding region is available for MPS type II patients and their at-risk relatives on a clinical basis. For questions about testing for MPS II, 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). Jonsson, J. J.; Aronovich, E. L.; Braun, S. E.; Whitley, C. B. Molecular diagnosis of mucopolysaccharidosis type II (Hunter syndrome) by automated sequencing and computer-assisted interpretation: toward mutation mapping of the iduronate-2-sulfatase gene. *Am. J. Hum. Genet.* 56: 597-607, 1995.
- 2). Upadhyaya, M.; Sarfarazi, M.; Bamforth, J. S.; Thomas, N. S. T.; Oberle, I.; Young, I.; Harper, P. S. : Localisation of the gene for Hunter syndrome on the long arm of X chromosome. *Hum. Genet.* 74: 391-398, 1986.
- 3). Froissart, R, Da Silva, IM, Maire, I. Mucopolysaccharidosis type II: an update on mutation spectrum. *Acta Paediatrica* 96: 71-77. 2007.

Genes

[IDS](#)

Indications

This test is indicated for:

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

Methodology

PCR amplification of 9 exons contained in the *IDS* 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

Clinical Sensitivity: Approximately 80% of mutations in the *IDS* gene are small mutations that will be detected by DNA sequencing. The remaining ~20% of *IDS* mutations are large gene deletions and/or rearrangements which may not be detected in females by this analysis[3]. Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of MPS II is not specifically known, but is likely to be rare and may vary by ethnicity.

Specimen Requirements

Submit only 1 of the following specimen types

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.

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.

Related Tests

- Mucopolysaccharide screen (urine GAG) (GA)
- Known mutation analysis (Custom Diagnostics) 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.