Condition Description

Mucopolysaccharidosis type IIIB (MPS IIIB, Sanfilippo syndrome type B), 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 or glycosaminoglycans (GAGs) within the lysosome. When functioning normally, the lysosomal enzymes break down these GAGs, however when the enzyme is deficient, the GAGs build up in the lysosomes causing damage to the body tissues. The MPSs share a chronic progressive course with multi-system involvement, characteristic physical features, laboratory findings, and radiographic abnormalities. MPS IIIB is an autosomal recessive caused by deficiency of the alpha-N-acetylgalactosaminidase enzyme and build up of heparin sulfate.

Clinical features of MPS IIIB begin in childhood with hyperactivity, aggressiveness, and developmental delays. Mental abilities decline as the disease progresses. Involvement of other organ systems tends to be mild and dysmorphic features are more subtle than those observed in other type of mucopolysaccharidosis [1]. A small number of late onset cases have been reported.

MPS IIIB is caused by mutations in the NAGLU gene, but is clinically indistinguishable from MPS IIIA, MPS IIIC, and MPS IIID, which are caused by mutations in other genes. All four forms of MPS III result in buildup of the same GAG, heparin sulfate. Diagnostic sequencing analysis of the NAGLU gene coding region is available for MPS type IIIB 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 (HZ).

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

Visit www.ThinkGenetic.com for patient-friendly information on mucopolysaccharidosis type III.

References:

Genes

NAGLU

Indications

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

Methodology

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

Full Gene Sequencing:
Clinical Sensitivity: 34/36 mutations identified in 18 patients [2], 36/36 mutations identified in 18 Greek families [3], 13/14 mutations identified in 7 Japanese families [4].
Analytical Sensitivity: ~99%

Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of MPS IIIB 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: 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: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Orangene™ 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.

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)
- Gene Sequencing for MPS IIIA (AW) and MPS IIID (BH)
- 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.
- 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.