Beta-Mannosidosis: MANBA Gene Sequencing

Test Code: AI
Turnaround time: 4 weeks
CPT Codes: 81479 x1

Condition Description

Beta-mannosidosis is a rare autosomal recessive disorder that is due to deficiency in the lysosomal enzyme beta-mannosidase. The enzyme is responsible for catalyzing the removal of mannose sugar residues from proteins that contain sugar groups (called glycoproteins), such as oligosaccharides. Deficiency of the beta-mannosidase activity results in accumulation of mannose-rich oligosaccharide chains, leading to swelling of the lysosome and impairment of normal cellular functions.

Patients with beta-mannosidosis have coarse facial features, mild bone disease, delayed speech development, hyperactivity, and mental retardation (1). There is significant variability in clinical presentation.

Mutations in the MANBA are responsible for beta-mannosidosis (2). Only 13 cases in 10 families have been identified with beta-mannosidosis. Two mutations in the MANBA gene have been described thus far (3).

For questions about testing for beta-mannosidosis, 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.

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

References:

Genes

MANBA

Indications

- Confirmation of a clinical diagnosis of beta-mannosidosis.
- Prenatal testing for known familial mutation(s).
- 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

Clinical Sensitivity: Only 13 cases in 10 families have been identified with beta-mannosidosis.
Analytical Sensitivity: ~99%
Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of beta-mannosidosis 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: 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 24 hours of collection. Do not refrigerate or 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.

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

- 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.