Alpha-Mannosidosis: MAN2B1 Gene Deletion/Duplication

<table>
<thead>
<tr>
<th>Test Code</th>
<th>KU</th>
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<tbody>
<tr>
<td>Turnaround time</td>
<td>2 weeks</td>
</tr>
<tr>
<td>CPT Codes</td>
<td>81228 x1</td>
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</tbody>
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**Condition Description**

Alpha-mannosidosis is an autosomal recessive disorder due to deficiency in the lysosomal enzyme alpha-mannosidase. The enzyme is responsible for catalyzing the removal of the mannose sugar residues during the breakdown of proteins that contain sugar groups (called glycoproteins), such as oligosaccharides. Deficiency of the alpha-mannosidase activity results in accumulation of mannose-rich oligosaccharides chains, leading to swelling of the lysosome and impairment of normal cellular functions. Alpha-mannosidosis is a heterogeneous condition that is classified into overlapping types. Clinical symptoms of Type I, the mildest form, are typically noticeable after 10 years of age and do not include skeletal abnormalities. Clinical symptoms of Type 2, the intermediate form, include skeletal abnormalities and typically onset before 10 years of age. Type 3 is the most severe form with early childhood onset of symptoms and rapid progression of the disease, leading to death. Individuals with alpha-mannosidosis have: delayed motor development, mental retardation, hearing loss, typical facies (a Hurler-like face), bone disease, immunodeficiency, ocular findings and hepatosplenomegaly. In addition, psychiatric problems are common. Mutations in the MAN2B1 gene are responsible for alpha-mannosidosis(1). More than 20 different disease causing mutations have been identified. These mutations include missense, nonsense, splice site, frameshift and large deletions(2). These mutations lead to partial or complete loss of enzymatic activity.

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:**


**Genes**

MAN2B1

**Indications**

- Confirmation of a clinical diagnosis of alpha-mannosidosis
- Prenatal testing for known familial mutation(s).
- Assessment of carrier status in high risk family members - known mutation analysis.

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

**Detection**

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. Results of molecular analysis must interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Reference Range**

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 of EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: DNA, Isolated**

**Specimen Requirements:**

- **Microtainer**
- 3µg
- 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
- 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.