Alpha-Mannosidosis: MAN2B1 Gene Deletion/Duplication

Test Code: KU
Turnaround time: 2 weeks
CPT Codes: 81228 x1

**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 questions about testing for alpha-mannosidosis, call the Emory Genetics Laboratory at (404) 778-8500 or (800) 366-1502.

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.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. Results of molecular analysis must be 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 Emory Genetics Laboratory, 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

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:
In EDTA (purple top) or ACD (yellow 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\textsuperscript{TM} 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 of Emory Genetics Laboratory, 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.