### Alpha-Mannosidosis: MAN2B1 Gene Sequencing

**Test Code:** AL  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 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 1, 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.

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

#### 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

PCR amplification of 24 exons contained in the MAN2B1 gene is 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: In 43 individuals, mainly of European origin, with alpha mannosidosis, Bert et al. identified 62 mutations, giving a detection rate of 72% [2].

Analytical Sensitivity: ~99%

Prevalence: The estimated prevalence of all lysosomal storage disorders is 2-5 per 100,000. The prevalence of alpha-mannosidosis disease is not specifically known, but is likely to be rare and may vary by ethnicity.

#### Reference Range

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
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™ 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.
- 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.