GM1 Gangliosidosis: \textit{GLB1} Gene Sequencing

**Test Code:** DU  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 x1

### Condition Description

GM1-gangliosidosis and Morquio B disease are both rare autosomal recessive lysosomal storage disorders caused by a deficiency of the enzyme beta-galactosidase (\textit{GLB1}; E.C.3.2.1.23) due to mutations in the \textit{GLB1} gene. The enzyme has a catalytic effect on the ganglioside GM1, keratan sulfate, and glycopeptides, and the enzyme is absent or reduced in GM1-gangliosidosis and Morquio B patients. Morquio B patients show reduced catalytic activity for keratan sulfate and oligosaccharides but normal activity for ganglioside GM1. Ganglioside GM1 is mainly stored in neuronal tissue, while keratan sulfate mainly accumulates in cartilage. GM1-gangliosidosis has been classified into three major clinical forms according to age of onset and severity of symptoms: type I (infantile), type II (late infantile/juvenile) and type III (adult) [Suzuki et al., 2001]. Type I is the most severe and is associated with developmental arrest observed within 3 to 6 months of birth, macular cherry-red spots, skeletal dysplasia and death usually within the first two years of life.

Morquio B disease or mucopolysaccharidosis type IVB (MPS IVB) is characterized by progressive, generalized skeletal dysplasia without central nervous system involvement and no clinical signs of storage disease in neuronal tissues.

More than 50 disease-causing mutations and several polymorphisms have been described in the \textit{GLB1} gene. There are very few mutational studies in specific populations, such as those of patients from Italy [Cacciotti et al., 2003; Morrone et al., 2000] or Brazil [Silva et al., 1999]. Furthermore, less than 30 Morquio B patients worldwide have been characterized for their DNA mutations [Bagshaw et al., 2002; Paschke et al., 2001]. Diagnostic sequencing analysis of the \textit{GLB1} gene coding region is available for GM1 patients and their at-risk relatives on a clinical basis.

For questions about testing for GM1, 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.

### References:

### Genes

**GLB1**

### Indications

- Confirmation of clinical diagnosis of GM1.
- Prenatal testing for known familial mutation(s).
- Assessment of carriers in high risk family members - known mutation analysis.

### Methodology

PCR amplification of 16 exons contained in the \textit{GLB1} gene coding region will performed on patient genomic DNA. Direct sequencing of amplification products is performed in both the forward and reverse directions using automated fluorescence deoxyxideoxy 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 be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### Detection

**Clinical Sensitivity:** 6/6 mutations identified in GM1 patients [1]. 21/21 mutations identified in Spanish patients.  
**Analytical Sensitivity:** ~99%

### 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

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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: 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™ 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.

**Related Tests**

- Mucopolysaccharide screen (urine GAG) (GA)
- Lysosomal Enzyme Screening Panel (LS)
- 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.