GLB1 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR
DIAGNOSTIC LABORATORY

The GLB1 gene encodes beta-galactosidase-1, a lysosomal hydrolase that cleaves the terminal beta-galactose from ganglioside substrates and other glycoconjugates. The human GLB1 located on chromosome 3p21.33 and contains 16 exons spanning approximately 62.5 kb. The GLB1 gene encodes two alternatively spliced products, lysosomal beta-galactosidase (GLB1) and elastin-binding protein (EBP). Defects in this gene are the cause of GM1-gangliosidosis and Morquio B syndrome, inherited as autosomal recessive traits. To date, more than 130 mutations have been identified in the GLB1 gene. Although the EBP’s role in the development of GM1 gangliosidosis is unclear, the alteration of this protein may contribute to the weakened heart muscle (cardiomyopathy) found in some people with GM1 gangliosidosis. Current research showed that GLB1 mutations can be related to infantile GM1 with cardiac dysfunction. GLB1 mutation induce significant suppression of beta-galactosidase activity, correlating with severity of disease and presence of cardiomyopathy. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for GLB1mutations. Individuals are tested by DNA sequencing of the coding exons of the GLB1gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

REASONS FOR REFERRAL
Molecular confirmation of the diagnosis of cardiomyopathy.

METHODOLOGY
Genomic DNA is analyzed for GLA mutations by DNA sequencing of the coding exons of the GLB1 gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated region. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

SERVICE FEES

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<th>Service</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1100 per sample</td>
<td>81406</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
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SENSITIVITY
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-16 of GLB1.

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: Adult: 5 cc   Child: 5 cc   Infant: 2-3 cc
Tissue: Frozen (preferred) or RNAlater
Other Body Fluids or Formalin-fixed, Paraffin-embedded Tissue: Call to inquire

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