GLA MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

GLA gene encodes alpha-galactosidase A protein. GLA is located on the X chromosome at Xq22.1 and more than 300 mutations have been reported in all 7 exons to cause Fabry disease (FD), an X-linked lysosomal storage disorder due to the deficient activity of α-galactosidase. While classical FD is a multi-system disorder, some patients with FD present with isolated hypertrophic cardiomyopathy (HCM). HCM affects about 1 in 500 individuals, and is genetically heterogeneous. Three percent of males with left ventricular hypertrophy (LVH), and up to 6% of men diagnosed with HCM after 40 years of age have FD. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for GLA mutations. Individuals are tested by DNA sequencing of the coding exons of the GLA gene. 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 Fabry Disease, HCM, and LVH.

METHODOLOGY

Genomic DNA is analyzed for GLA mutations by automatic fluorescent DNA sequencing of the coding exons of the GLA 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

<table>
<thead>
<tr>
<th>Description</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>$600 per sample</td>
<td>81405</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 1-7 of GLA.

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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