The FXN (frataxin) gene is located at 9q21.11, contains 7 exons and spans about 80 kb. Frataxin promotes the biosynthesis of heme assembly and repair of iron-sulfur clusters by delivering Fe$^{2+}$ to proteins involved in these pathways. It may play a role in the protection against iron-catalyzed oxidative stress through its ability to catalyze the oxidation of Fe$^{2+}$ to Fe$^{3+}$. The oligomeric form but not the monomeric form of frataxin has in vitro ferroxidase activity. Depletion of FXN results in Friedreich ataxia, and hypertrophic cardiomyopathy with heart failure is the most common cause of early death in this disease. Approximately 95% of all Friedreich’s ataxia patients are homozygous for a GAA trinucleotide repeat expansion in the first intron of FXN. The remaining cases are compound heterozygous with a GAA expansion on one allele and a point mutation on the other. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for FXN point mutations. Individuals are tested by DNA sequencing of the coding exons of the FXN 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 Friedreich ataxia and hypertrophic cardiomyopathy.

### METHODOLOGY

Genomic DNA is analyzed for FXN mutations by DNA sequencing of the coding exons of the FXN 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></th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td><strong>Index Case (Male or Female)</strong></td>
<td>$600 per sample</td>
<td>81404</td>
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<tr>
<td><strong>Additional Family Members</strong></td>
<td>$300 per sample; Known familial mutation only</td>
<td>81403</td>
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</tbody>
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### SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-5 of FXN.

### 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