NUBPL MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

NUBPL (Nucleotide Binding Protein-Like) gene encodes a member of the Mrp/NBP35 ATP-binding proteins family. The encoded protein is required for the assembly of the respiratory chain NADH dehydrogenase (complex I), an oligomeric enzymatic complex located in the inner mitochondrial membrane. NUBPL gene contains 11 coding exons and spans 299.8 kb genomic distance on chromosome 14q12. Mutations in this gene are associated with mitochondrial complex I deficiency, a disorder of the mitochondrial respiratory chain that causes a wide range of clinical manifestations including macrocephaly with progressive leukodystrophy, non-specific encephalopathy, cardiomyopathy, myopathy and liver disease. NUBPL mutations demonstrate autosomal dominant inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for NUBPL mutations. Individuals are tested by DNA sequencing of the coding exons of the NUBPL 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 CHD, mitochondrial complex I deficiency.

**METHODOLOGY**
Genomic DNA is analyzed for NUBPL mutations by DNA sequencing of the coding exons of the NUBPL 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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<tr>
<th></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>$1,000 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 1-11 of NUBPL.

**SPECIMEN REQUIREMENTS**

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

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