The TMEM70 gene encodes trans-membrane protein 70 (TMEM70) which contributes to oligomycin-sensitive ATP hydrolysis, ADP-stimulated respiration, mitochondrial ATP synthesis and ADP-induced decrease of mitochondrial membrane potential. The TMEM70 gene contains 3 exons mapped to chromosome 8q 21.11. Homozygous mutations in this gene have been detected in affected individuals with neonatal mitochondrial encephalocardiomyopathy associated with complex V deficiency (MC5DN2). MC5DN2 is caused by inborn defects of complex V due to nuclear genome mutations characterized by a selective inhibition of ATP synthase biogenesis. Most cases present with neonatal-onset hypotonia, lactic acidosis, hyperammonemia, hypertrophic cardiomyopathy, and 3-methylglutaconic aciduria. Many patients die within a few months or years. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for TMEM70 mutations. Individuals are tested by DNA sequencing of the coding exons of the TMEM70 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 mitochondrial encephalocardiomyopathy associated with complex V deficiency (MC5DN2).

**METHODOLOGY**

Genomic DNA is analyzed for TMEM70 mutations by DNA sequencing of the coding exons of the TMEM70 gene, as well as the exon/intron junctions and a portion of the 5' and 3' untranslated regions. 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>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$500 per sample</td>
<td>81404</td>
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</tbody>
</table>

| Additional Family Members | $300 per sample;               | 81403     |
|                          | Known familial mutation only   |           |

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-3 of TMEM70.

**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