The TSFM gene encodes a mitochondrial translation elongation factor (EFT) which catalyzes the nucleotide exchange reaction promoting the formation of EFTu/GTP from EFTu/GDP. The TSFM gene contains 7 exons mapped to chromosome 12q13-q14. A homozygous mutation in the TSFM gene has been identified in patients with combined oxidative phosphorylation deficiency-3 (COXPD3), which is characterized by onset of lactic acidosis and muscular hypotonia within 3 days after birth and death within the first few months of life. The patient with COXPD3 demonstrates encephalomyopathy and hypertrophic cardiomyopathy, as well as hepatomegaly. Fibroblasts and muscle tissue showed combined complex I, III, and IV deficiencies. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for TSFM mutations. Individuals are tested by DNA sequencing of the coding exons of the TSFM 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 combined oxidative phosphorylation deficiency-3 (COXPD3) and hypertrophic cardiomyopathy.

**METHODOLOGY**

Genomic DNA is analyzed for TSFM mutations by DNA sequencing of the coding exons of the TSFM 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>
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<th>Direct and Institutional Billing</th>
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<tr>
<td>Index Case (Male or Female)</td>
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<td>Additional Family Members</td>
<td>$300 per sample;</td>
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<td>Known familial mutation only</td>
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**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-7 of TSFM.

**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