The SYNE1 gene encodes a member of the spectrin family of structural proteins that link the plasma membrane to the actin cytoskeleton. The SYNE1 gene contains 147 exons and spans around 550 kb genomic distance that was mapped to chromosome 6q25. Defects in this gene are the cause of Emery-Dreifuss muscular dystrophy 4 (EDMD4). Emery-Dreifuss muscular dystrophy is a degenerative myopathy which is characterized by the triad of (1) slowly progressive muscle wasting and weakness with humeroperoneal distribution in the early stages; (2) early contractures of the elbows, Achilles tendons, and postcervical muscles; and (3) cardiomyopathy. The cardiac conduction defect in EDMD patients is the most serious and life-threatening clinical manifestation of the disease. Emery-Dreifuss muscular dystrophy is inherited as an X-linked recessive disorder. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for SYNE1 mutations. Individuals are tested by DNA sequencing of the coding exons of the SYNE1 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 Emery-Dreifuss muscular dystrophy 4 (EDMD4) and cardiomyopathy.

**METHODOLOGY**

Genomic DNA is analyzed for SYNE1 mutations by DNA sequencing of the coding exons of the SYNE1 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>
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</thead>
<tbody>
<tr>
<td></td>
<td>$4000 per sample</td>
<td>81408</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
<td>81403</td>
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</tbody>
</table>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-147 of SYNE1.

**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 and Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire

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