ZMPSTE24 (Zinc Metallopeptidase STE24) gene encodes a member of the peptidase M48A family. The encoded protein is a zinc metalloproteinase involved in the two step post-translational proteolytic cleavage of carboxy terminal residues of prelamin A to form mature lamin A. Mature lamin A is a component of the nuclear envelope that regulates the movement of molecules into and out of the cell nucleus. The ZMPSTE24 gene is located on chromosome 8q23 and contains 10 exons. Mutations in the ZMPSTE24 gene results in decreased enzyme function that cause a spectrum of diseases known as secondary laminopathies that share certain features of premature aging, such as mandibuloacral dysplasia and restrictive dermopathy, a neonatal lethal disorder. ZMPSTE24 mutations demonstrate autosomal recessive 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 ZMPSTE24 mutations. Individuals are tested by DNA sequencing of the coding exons of the ZMPSTE24 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.

**METHODOLOGY**

Genomic DNA is analyzed for ZMPSTE24 mutations by DNA sequencing of the coding exons of the ZMPSTE24 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>
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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tr>
<td>Index Case (Male or Female)</td>
<td>$800 per sample</td>
<td>81405</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 1-10 of ZMPSTE24.

**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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