The nuclear lamina is formed by a complex network of nuclear lamins, which are Type V intermediate filament proteins and can be divided into two classes, type A lamins and type B lamins. The A-type lamins are encoded by the gene \textit{LMNA}, which is composed of 12 exons and is located at 1q21.2-q21.3. Alternative splicing of the \textit{LMNA} gene product results in multiple protein products including the major protein products Lamin A and Lamin C. These two protein products have been shown to provide mechanical support to the nucleus and anchor heterochromatin to the inner nuclear membrane. However, multiple other functions for these proteins have been described or postulated.

Mutations in \textit{LMNA} have been described for a wide variety of diseases including Emery-Dreifuss muscular dystrophy, dilated cardiomyopathy with or without conduction system disease, limb-girdle muscular dystrophy type 1B, Dunnigan-type familial partial lipodystrophy, mandibuloacral dysplasia, Charcot-Marie-Tooth neuropathy type 2B1, Hutchinson-Gilford progeria syndrome and atypical Werner syndrome. These mutations include missense, nonsense, splicing, and deletion mutations. The pathogenesis of these mutations is still being investigated.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for \textit{LMNA} mutations. Individuals are tested by DNA sequencing of all 12 exons of the \textit{LMNA} gene. We strongly recommend initial testing of an 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 in order to identify additional at-risk family members and to discuss reproductive issues.

**REASONS FOR REFERRAL**

- Molecular confirmation of the diagnosis of Emery-Dreifuss muscular dystrophy, dilated cardiomyopathy with or without conduction system disease, limb-girdle muscular dystrophy type 1B, Dunnigan-type familial partial lipodystrophy, mandibuloacral dysplasia, Charcot-Marie-Tooth neuropathy type 2B1, Hutchinson-Gilford progeria syndrome, or atypical Werner syndrome

**METHODOLOGY**

Genomic DNA is analyzed for \textit{LMNA} mutations by DNA sequencing of all 12 exons of the \textit{LMNA} 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(s) by automatic fluorescent DNA sequencing.

**SERVICE FEES**

<table>
<thead>
<tr>
<th>Description</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$750 per sample</td>
<td>81406</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
</tr>
</tbody>
</table>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99% detection of mutations in exons 1-12 of \textit{LMNA}.

**SPECIMEN REQUIREMENTS**

- **Blood (preferred):** EDTA (purple-top) tubes: \textit{Adult}: 5 cc \textit{Child}: 5 cc \textit{Infant}: 2-3 cc
- **Tissue:** Frozen (preferred), RNA\textit{later}
- **Other Body Fluids and Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire

John Welsh Cardiovascular Diagnostic Laboratory • Section of Cardiology • Department of Pediatrics
Baylor College of Medicine • 1102 Bates Avenue, Suite 480.02 • Houston, TX 77030
PHONE: (832) 824-4155 • FAX: (832) 825-5159 • E-MAIL: yuxinf@bcm.edu
Web Site: [www.bcm.edu/pediatrics/welsh](http://www.bcm.edu/pediatrics/welsh)