The PLOD1 gene encodes lysyl hydroxylase which catalyzes the formation of hydroxylysine in collagens and other proteins with collagen-like amino acid sequences, by the hydroxylation of lysine residues in X-lys-gly sequences. The PLOD1 gene contains 19 exons that were mapped to chromosome 1p36. Mutations in this gene are associated with Ehlers-Danlos type VI. The Ehlers-Danlos syndromes (EDS) are a group of heritable connective tissue disorders that share the common features of skin hyperextensibility, articular hypermobility, and tissue fragility. In particular, Ehlers-Danlos type VI also named the kyphoscoliosis type is characterised by progressive curvature of the spine (scoliosis), fragile eyes, and severe muscle weakness. Affected individuals are at risk for rupture of medium-sized arteries and respiratory compromise if kyphoscoliosis is severe. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for PLOD1 mutations. Individuals are tested by DNA sequencing of the coding exons of the PLOD1 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 arrhythmia and Ehlers-Danlos syndromes VI.

METHODOLOGY

Genomic DNA is analyzed for PLOD1 mutations by DNA sequencing of the coding exons of the PLOD1 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>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1,100 per sample</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
</tr>
</tbody>
</table>

SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons of PLOD1.

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