The *SPRED1* gene encodes a member of the Sprouty/SPRED family of proteins that regulate growth factor-induced activation of the MAP kinase cascade. The *SPRED1* gene contains 8 exons and was mapped to chromosome 15q13. Mutations in this gene are associated with Legius syndrome. Legius syndrome is an autosomal dominant disorder that manifests with Noonan-like facial features and *CBL* (Casitas B-lineage lymphoma), which associates to Noonan-like syndrome. Noonan syndrome (NS) is an autosomal dominant disorder characterized by short stature, facial dysmorphism, and a wide spectrum of congenital heart defects. Cardiac involvement is present in up to 90% of patients. Pulmonic stenosis and hypertrophic cardiomyopathy are the most common forms of cardiac disease, but a variety of other lesions are also observed. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for *SPRED1* mutations. Individuals are tested by DNA sequencing of the coding exons of the *SPRED1* 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 hypertrophic cardiomyopathy and Legius syndrome.

**METHODOLOGY**

Genomic DNA is analyzed for *SPRED1* mutations by DNA sequencing of the coding exons of the *SPRED1* 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>
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<tr>
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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<td>Index Case (Male or Female)</td>
<td>$600 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 1-8 of *SPRED1*.

**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