LEFTY2 (Left-Right Determination Factor 2) gene encodes a member of the TGF-beta family of proteins. The encoded protein is secreted and plays a role in left-right asymmetry determination of organ systems during development as well as a role in endometrial bleeding. LEFTY2 gene contains 4 coding exons and spans about 4.9 kb long of genomic sequence. It has been mapped to chromosome 1q42.12. Mutations in this gene have been associated with left-right axis malformations, particularly in the heart and lungs. Alternate splicing results in multiple transcript variants. LEFTY2 mutations demonstrate autosomal dominant 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 LEFTY2 mutations. Individuals are tested by DNA sequencing of the coding exons of the LEFTY2 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 and heterotaxy.

METHODOLOGY
Genomic DNA is analyzed for LEFTY2 mutations by DNA sequencing of the coding exons of the LEFTY2 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>
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<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>$500 per sample</td>
<td>81404</td>
</tr>
<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 1-4 of LEFTY2.

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