**LRP5 MUTATION ANALYSIS**

**JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY**

**LRP5 (Low Density Lipoprotein Receptor-Related Protein 5) gene** encodes a transmembrane low-density lipoprotein receptor that binds and internalizes ligands in the process of receptor-mediated endocytosis. LRP5 is a component of the Wnt-Fzd-LRP5-LRP6 complex that triggers beta-catenin signaling through inducing aggregation of receptor-ligand complexes into ribosome-sized signalsomes. This protein plays a key role in skeletal homeostasis and many bone density related diseases are caused by mutations in this gene. It also play a role in cardiomyocyte hypertrophy. **LRP5** gene contains 23 coding exons covering a 136.667 Kb genomic sequence on chromosome 11q13.4. Mutations in this gene cause osteoporosis and osteoporosis-pseudoglioma syndrome and familial exudative vitreoretinopathy. **LRP5** 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 **LRP5** mutations. Individuals are tested by DNA sequencing of the coding exons of the **LRP5** 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 **LRP5** mutations by DNA sequencing of the coding exons of the **LRP5** 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**

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<tr>
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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td><strong>Index Case (Male or Female)</strong></td>
<td>$1,200 per sample</td>
<td>81406</td>
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<tr>
<td><strong>Additional Family Members</strong></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 1-23 of **LRP5**.

**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