The LTBP4 gene encodes a protein which binds transforming growth factor beta (TGFB) as it is secreted and targeted to the extracellular matrix. The LTBP4 gene contains 33 exons that were mapped to chromosome 19. Mutations in this gene are associated with cutis laxa and severe pulmonary, gastrointestinal, and urinary abnormalities. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for LTBP4 mutations. Individuals are tested by DNA sequencing of the coding exons of the LTBP4 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 valvar and vascular disorders including cutis laxa and severe pulmonary, gastrointestinal, and urinary abnormalities.

**METHODOLOGY**

Genomic DNA is analyzed for LTBP4 mutations by DNA sequencing of the coding exons of the LTBP4 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></th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1,500 per sample</td>
<td>81407</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
<td>81403</td>
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</tbody>
</table>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the 33 coding exons of LTBP4.

**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