The COL18A1 gene is composed of 41 exons and spans approximately 110 kb on chromosome 21q22.3. The protein encoded by this gene is the alpha chain of type XVIII collagen. This collagen is one of the multiplexins, extracellular matrix proteins that contain multiple triple-helix domains (collagenous domains) interrupted by non-collagenous domains. The proteolytically produced C-terminal fragment of type XVIII collagen is endostatin, a potent antiangiogenic protein. Alternatively spliced transcript variants encoding different isoforms have been found for this gene. COL18A1 mutations are associated with Knobloch syndrome type I. COL18A1 mutations demonstrate autosomal recessive 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 COL18A1 mutations. Individuals are tested by DNA sequencing of the coding exons of the COL18A1 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 congenital heart disease (CHD), Knobloch syndrome type I.

**METHODOLOGY**

Genomic DNA is analyzed for COL18A1 mutations by DNA sequencing of the coding exons of the COL18A1 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>Description</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>

**SENSITIVITY**


**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