NIPBL (Nipped-B-Like Protein) gene, encodes a protein called delangin, which plays an important role in human development, with broad roles in sister chromatid cohesion, chromosome condensation, and DNA repair. NIPBL gene contains 46 coding exons and spans 189.66 Kb genomic distance on chromosome 5p13.2. Mutations in this gene result in Cornelia de Lange syndrome, a disorder characterized by dysmorphic facial features, growth delay, limb reduction defects, and mental retardation. Congenital anomalies include malformations of the upper limbs, gastrointestinal malformation/rotation, pyloric stenosis, diaphragmatic hernia, heart defects and genitourinary malformations. Congenital heart disease (CHD) has been reported to occur in a significant number of individuals with Cornelia de Lange syndrome. NIPBL 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 NIPBL mutations. Individuals are tested by DNA sequencing of the coding exons of the NIPBL 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 Cornelia de Lange syndrome and NIPBL-related CHD.

**METHODOLOGY**
Genomic DNA is analyzed for NIPBL mutations by DNA sequencing of the coding exons of the NIPBL 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>
<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$1,400 per sample</td>
<td>81407</td>
</tr>
</tbody>
</table>

| Additional Family Members  | $300 per sample; known familial mutation only | 81403     |

**SENSITIVITY**
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 2-47 of NIPBL.

**SPECIMEN REQUIREMENTS**

- **Blood (preferred):** EDTA (purple-top) tubes:  
  - *Adult:* 5 cc  
  - *Child:* 5 cc  
  - *Infant:* 2-3 cc
- **Tissue:** Frozen (preferred), RNA later
- **Other Body Fluids or Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire