NPHP3 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

NPHP3 (Nephronophthisis 3) gene encodes a protein containing a coiled-coil domain, a tubulin-tyrosine ligase domain, and a tetratrico peptide repeat domain. The encoded protein interacts with nephrocystin, and it is required for normal ciliary development, and it also functions in renal tubular development. NPHP3 gene contains 27 coding exons and spans 40.8 kb genomic distance on chromosome 3q22.1. Mutations in this gene are associated with nephronophthisis type 3, a cystic renal disease that leads to end-stage renal failure; and also with renal-hepatic-pancreatic dysplasia, a lethal condition reminiscent of a ciliopathy that features cystic dysplasia of the pancreas and situs inversus, and Meckel syndrome type 7, which presents as clinical features: cystic renal disease, a central nervous system abnormality, and hepatic abnormalities. NPHP3 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 NPHP3 mutations. Individuals are tested by DNA sequencing of the coding exons of the NPHP3 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, nephronophthisis type 3, renal-hepatic-pancreatic dysplasia, and Meckel syndrome type 7.

**METHODOLOGY**
Genomic DNA is analyzed for NPHP3 mutations by DNA sequencing of the coding exons of the NPHP3 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>
<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>$1,200 per sample</td>
<td>81407</td>
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<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 1-27 of NPHP3.

**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 and Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire