SNX3 (Sorting nexin 3) gene, located on chromosome 6q21, belongs to the sorting nexin family, which is involved in intracellular protein trafficking. It contains four exons and spans around 50 kb of genomic sequences. Sorting nexins are a family of phosphoinositide-binding proteins that play critical roles in many cellular pathways including nutrient uptake, signal transduction, and development. A pseudogene of this gene is present on the sex chromosomes. Alternative splicing results in multiple distinct isoforms. The mutations in SNX3 gene has been found in patients with microcephaly, microphthalmia, ectrodactyly, and prognathism (MMEP) and mental retardation, demonstrating that SNX3 plays an important role in the genesis of these organs during development. SNX3 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 SNX3 mutations. Individuals are tested by DNA sequencing of the coding exons of the SNX3 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 disorders related to CHD.

### METHODOLOGY

Genomic DNA is analyzed for SNX3 mutations by DNA sequencing of the coding exons of the SNX3 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>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$600</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300</td>
</tr>
<tr>
<td></td>
<td>per sample; known familial mutation only</td>
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</tbody>
</table>

### SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-4 of SNX3.

### 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