ZIC3 (Zic family member 3) encodes a member of the ZIC family of C2H2-type zinc finger proteins. This nuclear protein probably functions as a transcription activator in the earliest stages in both axial midline development and left-right (LR) asymmetry specification. ZIC3 gene contains three exons and spans about 11 kb of genomic distance and has been mapped to chromosome Xq26.3. Mutations in this gene cause X-linked visceral heterotaxy, which includes congenital heart disease and left-right axis defects in organs. ZIC3 mutations demonstrate X-linked 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 ZIC3 mutations. Individuals are tested by DNA sequencing of the coding exons of the ZIC3 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 X-linked visceral heterotaxy, which includes congenital heart disease and left-right axis defects in organs.

**METHODOLOGY**
Genomic DNA is analyzed for ZIC3 mutations by DNA sequencing of the coding exons of the ZIC3 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>
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<tr>
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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tr>
<td>Index Case (Male or Female)</td>
<td>$500 per sample</td>
<td>81404</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 1-3 of ZIC3.

**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