TBX3 (T-box 3) gene is a member of a phylogenetically conserved family of genes that share a common DNA-binding domain, the T-box. T-box genes encode transcription factors involved in the regulation of developmental processes. Human studies have demonstrated that TBX3 is required for the development of the heart, limbs, mammary glands and other tissues and organs. The protein encoded by TBX3 gene is a transcriptional repressor and is thought to play a role in the anterior/posterior axis of the tetrapod forelimb. TBX3 gene is located on chromosome 12q24.21 and contains 8 exons, covering around 13.9 Kb of genomic sequence. Mutations in this gene cause ulnar-mammary syndrome, with multiple developmental defects including cardiac defects. TBX3 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 TBX3 mutations. Individuals are tested by DNA sequencing of the coding exons of the TBX3 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 and ulnar-mammary syndrome.

**METHODOLOGY**
Genomic DNA is analyzed for TBX3 mutations by DNA sequencing of the coding exons of the TBX3 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></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>$750 per sample</td>
<td>81405</td>
</tr>
<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 1-8 of TBX3.

**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

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John Welsh Cardiovascular Diagnostic Laboratory • Section of Cardiology • Department of Pediatrics
Baylor College of Medicine • 1102 Bates Avenue, Suite 480.02 • Houston, TX 77030
PHONE: (832) 824-4155 • FAX: (832) 825-5159 • E-MAIL: yuxinf@bcm.edu
Web Site: www.bcm.edu/pediatrics/welsh