TBX1 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR
DIAGNOSTIC LABORATORY

T-BOX 1 (TBX1) is a member of a phylogenetically conserved family of genes that share a common DNA-binding domain T-box. The box genes are transcription factors involved in the regulation of developmental processes. TBX1 acts as an intrinsic rheostat of BMP signaling. Human TBX1 gene contains 8 exons that were mapped to chromosome 22q11.2. Mutations in this gene are found in patients with conotruncal anomaly face syndrome/velocardiofacial syndrome and DiGeorge syndrome (both belong to the 22q11.2 deletion syndrome which is caused by the deletion of a small piece of chromosome 22). The patients have typical conotruncal anomaly face and velopharyngeal insufficiency, tetralogy of Fallot, pulmonary atresia, atrial septal defect and major aortopulmonary collateral artery. TBX1 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 TBX1 mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the TBX1 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 arrhythmia, CHD.

METHODOLOGY

Genomic DNA is analyzed for TBX1 mutations by DNA sequencing of the coding exons of the TBX1 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>$800 per sample</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
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SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exon 2-9 of TBX1.

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

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