Tectonic Family Member 3 (TCTN3) gene encodes a protein that contains 595 amino acids which has an N-terminal signal peptide and a C-terminal transmembrane domain. Human TCTN3 gene contains 14 exons mapped within chromosome 10q24.1. Functional analysis indicated that TCTN3 was necessary for transduction of the SHH signaling pathway. Mutations in this gene are found in patients with orofaciodigital syndrome IV and Joubert syndrome. Orofaciodigital syndrome (OFDS) is an autosomal recessive inheritance disease characterized by premature termination and malformations of the face, oral cavity, digits and central nervous system. Thirteen clinical subtypes of OFDS are delineated. Severe forms of OFD IV have been reported in children or fetuses presenting additional features of cystic dysplastic kidneys and brain malformation that include occipital encephalocele. Joubert Syndrome-18 (JBTS18) can be caused by homozygous mutation in the TCTN3 gene presenting abnormal eye movements, breathing anomalies, severe mental retardation, and ventricular septal defect. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for TCTN3 mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the TCTN3 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, OFDS IV and JBTS18.

**METHODOLOGY**

Genomic DNA is analyzed for TCTN3 mutations by DNA sequencing of the coding exons of the TCTN3 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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<th>Direct and Institutional Billing</th>
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<td>Index Case (Male or Female)</td>
<td>$1,000 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 exons 1-14 of TCTN3.

**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