TWIST1 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

TWIST1 (Twist Family BHLH Transcription Factor 1) gene belongs to the basic helix-loop-helix (bHLH) class of transcriptional regulators family, and has been implicated in cell lineage determination and differentiation. TWIST1 gene is located on chromosome 7p21.2 and contains one exon which spans around 117.98Kb of genomic sequence. TWIST1 protein is essential for the formation of cells that give rise to bone, muscle and other tissues in the head and face in embryo development and also plays a role in the early development of the limbs. Mutations and deletions in TWIST1 gene are the cause of Saethre-Chotzen syndrome, an autosomal dominant form of craniosynostosis involving either unilateral or bilateral coronal sutures, and may also be involved in the pathogenesis of ventricular septal defect. TWIST1 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 TWIST1 mutations. Individuals are tested by DNA sequencing of the coding exons of the TWIST1 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, Saethre-Chotzen syndrome and ventricular septal defect.

METHODOLOGY
Genomic DNA is analyzed for TWIST1 mutations by DNA sequencing of the coding exons of the TWIST1 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>
<th>CPT Codes</th>
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<tr>
<td>Index Case (Male or Female)</td>
<td>$500 per sample</td>
<td>81403</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 of TWIST1.

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