TGFB3 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

TGFB3 gene encodes the transforming growth factors beta 3, a member of the TGF-beta family of proteins. TGFB3 protein is secreted and is involved in embryogenesis and cell differentiation. The TGFB3 gene contains 7 exons and spans around a 24.8 kb genomic distance that was mapped to chromosome 14q24.3. Mutations in TGFB3 gene are associated with familial arrhythmogenic right ventricular dysplasia/cardiomyopathy type 1 (ARVD/C1). ARVD/C is an autosomal dominant disease characterized by partial degeneration of the myocardium of the right ventricle, electrical instability and sudden death. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for TGFB3 mutations. Individuals are tested by DNA sequencing of the coding exons of the TGFB3 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 familial arrhythmogenic right ventricular dysplasia/cardiomyopathy type 1 (ARVD/C1).

METHODOLOGY

Genomic DNA is analyzed for TGFB3 mutations by DNA sequencing of the coding exons of the TGFB3 gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated regions. 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>
</tr>
</thead>
<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$800 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>
</tr>
</tbody>
</table>

SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-7 of TGFB3.

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 and Formalin-fixed, Paraffin-embedded Tissue: Call to inquire

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