TGFBR3 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

TGFBR3 gene encodes the transforming growth factor (TGF)-beta type III receptor, a glycoprotein existing in both a membrane-bound and a soluble form. The membrane bound proteoglycan often functions as a co-receptor with other TGF-beta receptor superfamily members, capturing and retaining TGF-beta for presentation to the signaling receptors. Ectodomain shedding produces soluble TGFBR3, which may inhibit TGFβ signaling. Decreased expression of this receptor has been observed in various cancers. The TGFBR3 gene contains 16 coding exons and spans about 226 Kb of genomic sequence. It has been mapped to chromosome 1p22.1. Alternatively spliced transcripts have been identified for this gene. Mutations in this gene are believed to be associated with familial cerebral saccular aneurysm and priapism. TGFBR3 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 TGFBR3 mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the TGFBR3 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 clinical diagnosis of cerebral saccular aneurysm, priapism and aortopathy.

METHODOLOGY

Genomic DNA will be analyzed for TGFBR3 mutations by automatic fluorescent DNA sequencing of the coding exons of the TGFBR3 gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated region. Patient DNA will be sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members will be analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

SERVICE FEES

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<thead>
<tr>
<th>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td></td>
<td>$1,200 per sample</td>
<td>81406</td>
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| Additional Family Members  | $300 per sample; known familial mutation only | 81403     |

SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 2-17 of TGFBR3.

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: Adult: 5 cc Child: 5 cc Infant: 2-3 cc
Tissue: Frozen (preferred), RNAlater
Formalin-fixed, Paraffin-embedded Tissue or Other Body Fluids: Call to inquire

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