GLI3 MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

GLI3 (GLI Family Zinc Finger 3) gene encodes a protein which belongs to the C2H2-type zinc finger proteins subclass of the GLI family. These proteins are DNA binding transcription factors and mediate Sonic hedgehog signaling. GLI3 gene contains 17 coding exons which cover around 276.922 Kb of genomic sequence on chromosome 7p13. Mutations of the GLI3 gene cause Greig cephalopolysyndactyly syndrome, Pallister-Hall syndrome, preaxial polydactyly type IV, and postaxial polydactyly types A1 and B. GLI3 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 GLI3 mutations. Individuals are tested by DNA sequencing of the coding exons of the GLI3 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 congenital heart diseases (CHD).

METHODOLOGY

Genomic DNA is analyzed for GLI3 mutations by DNA sequencing of the coding exons of the GLI3 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>Index Case (Male or Female)</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>$1,200 per sample</td>
<td>81406</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
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SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 2-18 of GLI3.

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

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