ZFPM2 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

ZFPM2 (Zinc Finger Protein, FOG Family Member 2) gene, located on chromosome 8q23.1, encodes a protein that is a widely expressed member of the FOG family of transcription factors that plays a central role in heart morphogenesis and development of coronary vessels from epicardium, by regulating genes that are essential during cardiogenesis. The family members also modulate the activity of GATA family proteins acting through the formation of a heterodimer with transcription factors of the GATA family, which are important regulators of hematopoiesis and cardiogenesis. Such heterodimer can either activate or repress transcriptional activity, depending on the cell and promoter context. Mutations in ZFPM2 have been identified in patients with congenital heart diseases, such as tetralogy of fallot (TOF) and double outlet right ventricle (DORV), and may also be related to congenital diaphragmatic hernia. ZFPM2 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 ZFPM2 mutations. Individuals are tested by DNA sequencing of the coding exons of the ZFPM2 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.

METHODOLOGY

Genomic DNA is analyzed for ZFPM2 mutations by DNA sequencing of the coding exons of the ZFPM2 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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<tbody>
<tr>
<td>$750 per sample</td>
<td>81405</td>
<td></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 1-8 of ZFPM2.

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