MKKS (McKusick-Kaufman Syndrome) gene encodes a molecular chaperone protein which shares sequence similarity with other members of the type II chaperonin family. MKKS is a centrosome-shuttling protein and plays an important role in cytokinesis. This protein also interacts with other type II chaperonin members to form a complex known as the BBSome, which involves ciliary membrane biogenesis, and is involved in protein processing in limb, cardiac and reproductive system development. MKKS gene contains three coding exons and spans around 33.2 Kb of genomic sequence, it has been mapped to chromosome 20p12. Mutations in MKKS gene have been observed in patients with Bardet-Biedl syndrome type 6, also known as McKusick-Kaufman syndrome which is characterized by a combination of three features: extra fingers and/or toes (polydactyly), heart defects, and genital abnormalities. MKKS 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 MKKS mutations. Individuals are tested by DNA sequencing of the coding exons of the MKKS 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 MKKS mutations by DNA sequencing of the coding exons of the MKKS 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></th>
<th><strong>Direct and Institutional Billing</strong></th>
<th><strong>CPT Codes</strong></th>
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</thead>
<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$500 per sample</td>
<td>81404</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
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</tbody>
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### SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 3-6 of MKKS.

### SPECIMEN REQUIREMENTS

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