PRKAB2 MUTATION ANALYSIS
JOHN WELSH CARDIOVASCULAR DIAGNOSTIC LABORATORY

PRKAB2 (Protein Kinase, AMP-Activated, Beta 2 Non-Catalytic Subunit) gene encodes the regulatory gamma-2 subunit of AMP-activated protein kinase (AMPK). AMPK is an important energy-sensing enzyme that monitors cellular energy status. In response to cellular metabolic stresses, AMPK activates energy-producing pathways and inhibits energy-consuming processes. It is active in many different tissues, including cardiac and skeletal muscles and may also regulate the activity of ion channels in the heart. PRKAB2 gene contains 7 coding exons and spans 17.44 Kb genomic distance on chromosome 1q21.1. Mutations in this gene cause atrioventricular septal defect (ASD), familial hypertrophic cardiomyopathy (HCM) and Wolff-Parkinson-White syndrome, a disease associated with supraventricular tachycardia and ventricular pre-excitation or atrial fibrillation. PRKAB2 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 PRKAB2 mutations. Individuals are tested by DNA sequencing of the coding exons of the PRKAB2 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 including atrioventricular septal defect, familial hypertrophic cardiomyopathy and Wolff-Parkinson-White syndrome.

METHODOLOGY
Genomic DNA is analyzed for PRKAB2 mutations by DNA sequencing of the coding exons of the PRKAB2 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

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<thead>
<tr>
<th>Service Description</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$600 per sample</td>
<td>81405</td>
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<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 2-8 of PRKAB2.

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