AMP-activated protein kinase (AMPK) is an important energy-sensing enzyme that monitors cellular energy status and functions by inactivating key enzymes involved in regulating de novo biosynthesis of fatty acid and cholesterol. It is a heterotrimeric protein composed of a catalytic alpha subunit, a noncatalytic beta subunit, and a noncatalytic regulatory gamma subunit. *PRKAG2* gene encodes the gamma 2 non-catalytic subunit with four cystathionine beta-synthase domains. *PRKAG2* gene contains 19 coding exons and spans 321.1 kb genomic distance which has been mapped to chromosome 7q36.1. Alternate transcriptional splice variants, encoding different isoforms, have been characterized. Mutations in *PRKAG2* gene have been associated with familial hypertrophic cardiomyopathy 6, lethal congenital glycogen storage disease of heart, ventricular pre-excitation (Wolff-Parkinson-White syndrome). *PRKAG2* 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 *PRKAG2* mutations. Individuals are tested by DNA sequencing of the coding exons of the *PRKAG2* 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 familial hypertrophic cardiomyopathy 6, lethal congenital glycogen storage disease of heart, ventricular pre-excitation (Wolff-Parkinson-White syndrome).

**METHODOLOGY**
Genomic DNA is analyzed for *PRKAG2* mutations by DNA sequencing of the coding exons of the *PRKAG2* 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>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1,300 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>
</tr>
</tbody>
</table>

**SENSITIVITY**
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-19 of *PRKAG2*.

**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 and Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire

---

John Welsh Cardiovascular Diagnostic Laboratory • Section of Cardiology • Department of Pediatrics
Baylor College of Medicine • 1102 Bates Avenue, Suite 480.02 • Houston, TX 77030
PHONE: (832) 824-4155 • FAX: (832) 825-5159 • E-MAIL: yuxinf@bcm.edu
Web Site: [www.bcm.edu/pediatrics/welsh](http://www.bcm.edu/pediatrics/welsh)