

**PRKAG2-Related Disorders via *PRKAG2* Gene Sequencing -- Test #199**  
**Wolff-Parkinson-White Syndrome**  
**Hypertrophic Cardiomyopathy with Wolff-Parkinson-White Syndrome**  
**Glycogen Storage Disease of Heart, Lethal Congenital**

**Brief Description of Disorders:** Wolff-Parkinson-White Syndrome (WPW, OMIM 194200), also called pre-excitation syndrome is characterized by short PR intervals and prolonged QRS. Age of onset varies between 11 and 50 years of age. WPW syndrome occurs in isolation or with hypertrophic cardiomyopathy (HCM-WPW, OMIM 600858). HCM-WPW is characterized by juvenile to adult onset, atrial fibrillation, atrioventricular conduction block, and electrophysiological abnormalities, especially preexcitation (Gollob et al. N Engl J Med 344:1823-1831, 2001; Blair et al. Hum Mol Genet 10:1215-1220, 2001). The Lethal Congenital form of Glycogen Storage Disease of Heart (OMIM 261740) is characterized by fetal onset, electrocardiographic abnormalities, cardiomegaly, and pulmonary compression resulting in heart failure and ultimately death (Regalado et al. Pediatr Cardiol, 20:304-307, 1999).

**Genetics:** WPW, HCM-WPW and the lethal congenital form of Glycogen Storage Disease of the Heart may be caused by heterozygous mutations in the *PRKAG2* gene. To date, about 15 pathogenic mutations have been reported. While the WPW and HCM-WPW causative mutations are inherited in an autosomal dominant manner (Gollob et al. N Engl J Med 344:1823-1831, 2001; Blair et al. Hum Mol Genet 10:1215-1220, 2001), the Glycogen storage disorder of the heart is caused by *de novo* mutations (Burwinkel et al. Am J Hum Genet 76:1034-1049, 2005; Akman et al. Pediatr Res 62:499-504, 2007). All *PRKAG2* mutations reported to date are missense, except for a single in-frame codon insertion, situated in a highly conserved domain of the protein, and predicted to introduce a leucine residue (Blair et al. 2001).

**Description of This Particular Test:** The *PRKAG2* gene encodes the gamma-2 regulatory subunit of AMP-activated protein kinase, which regulates substrate use for energy production. This test involves bidirectional DNA sequencing of all 16 coding exons and splice sites of the *PRKAG2* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced.

**Reference Sequences:** Genomic: NC\_000007.13 mRNA: NM\_016203.3 Protein: NP\_057287.2 (CCDS 5928.1)

**Indications for Test:** Patients with WPW syndrome (OMIM 194200), patients with HCM and WPW (OMIM 600858), and patients with Lethal Congenital Glycogen Storage Disease of Heart (OMIM 261740).

**Sensitivity of Test:** The sensitivity of this test is not currently known.

**Turnaround Time:** Maximum of 40 days, although many tests are completed in 2-3 weeks.

**Specimen Requirements:** See page 4 of the Requisition Form.

**Price:** Sequencing of *PRKAG2* Gene, Exons 1, 3-17 \$ 870

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x16	83898 \$ 250	Sequencing x16	83904 \$ 380
Separation x1	83894 \$ 60	Interpretation/Report x1	83912 \$ 110

**Accreditation Info.** CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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