

Catecholaminergic Polymorphic Ventricular Tachycardia Testing via *RYR2* Exon Sequencing

Brief Description: Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) (OMIM 604772) is a heart disorder characterized by electrical instability induced by physical exercise or intense emotion (Napolitano and Priori 2004 www.geneclinics.org). The electrical instability may degenerate into cardiac arrest and sudden death. CPVT usually onsets in childhood or adolescence and often presents as syncope. Preventive drugs (beta-blockers) and other treatments are available for susceptible individuals.

Genetics: CPVT is inherited in an autosomal dominant manner. The most common known causes of CPVT are missense mutations in the *RYR2* gene. The large *RYR2* (ryanodine receptor type 2) gene with 105 exons encodes the cardiac muscle calcium release channel. Some patients have been reported to carry de novo mutations.

This particular test involves DNA sequencing of all *RYR2* exons that have been reported to contain causative mutations. Currently the test involves sequencing of the full coding segment plus adjacent intronic regions of 20 exons (8, 14, 15, 44, 45, 46, 47, 49, 50, 83, 88, 90, 93, 95, 97, 100, 101, 102, 103, and 105). We expect that the list of exons will grow as new mutations are reported.

Indications for Test: All individuals diagnosed with CPVT are candidates for this test. Individuals with exercise or stress induced cardiac arrest or even sudden unexplained death are also candidates. When dealing with affected families, PreventionGenetics recommends that gene testing be performed first in an affected family member. If a likely causative mutation is found in the affected individual, then other family members can be tested at much reduced cost.

Sensitivity of Test: Priori et al. (Circulation 106:69-74, 2002) reported that about 50% of CPVT patients have mutations in the *RYR2* gene. Tester et al. (Mayo Clin Proc 79:1380-1384, 2004) reported that 14% of sudden unexplained death cases had *RYR2* mutations.

SPECIMEN REQUIREMENTS

Collect a minimum of 1 ml of whole blood in EDTA (purple top tube) or ACD (yellow top tube).

Whole blood collected in Na Heparin is acceptable but not preferred.

Ship whole blood specimens at ambient temperature. Do not freeze blood tube.

During hot summer months, include a frozen ice pack in the shipping container. Do not allow the ice pack to come in direct contact with the specimen tubes. In winter, include an unfrozen ice pack to help moderate extremes in temperature. The DNA in whole blood is stable for at least 48 hours at 21°C, 5-7 days at 4°C.

Exon sequencing of the <i>RYR2</i> gene		\$1390.00
Molec Diag, Ascertainment	83890	
Molec Diag, Isolation	83891	
Molecular Diag, Amplif x 24	83898	
Mutat Id By Seq, Single Seg x 24	83904	
Molecular Diag, Separation	83894	
Interpretation And Report	83912	

Single exon sequencing for the presence of previously identified mutations in the *RYR2* gene will also be provided for \$230.

Accreditation Info. CLIA ID #: 52D1027685 (expires 1/18/07) (CAP#: 7185561, AU ID: 1407125 expires 12/20/06)

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