RYR2-related Disorders: RYR2 Gene Deletion/Duplication

**Test Code:** DRYR2  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

### Condition Description

**Catecholaminergic Polymorphic Ventricular Tachycardia**  
Catecholaminergic polymorphic ventricular tachycardia (CPVT) is characterized by cardiac electrical instability. This instability can be exacerbated by acute activation of the adrenergic nervous system, such as during exercise or extreme emotional events. These episodes have an underlying cause of ventricular tachycardia, which may progress into ventricular fibrillation. Two genes are known to cause CPVT. Mutation of the RYR2 gene cause autosomal dominant CPVT while mutations of the CASQ2 gene cause autosomal recessive CPVT.

**Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy**  
Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is an autosomal dominant condition characterized by abnormalities in cardiac structure and rhythm. The fibrofatty replacement of myocardium can predispose affected individuals to ventricular tachycardia and sudden death in young individuals and athletes. Common presenting features include heart palpitation, syncope, and death. Other diagnostic criteria include right ventricular dilation and reduction of right ventricular function, and right ventricular aneurysms. The phenotype of ARVD/C is very variable and while it primarily affects the right ventricle, it may involve the left ventricle as well. Eight genes are known to cause ARVD/C; TGFβ3, RYR2, TMEM43, DSP, PKP2, DSG2, DSC2, and JUP.

Please note that this is for the RYR2 (1q42.1-q43) gene only.

For patients with suspected RYR2-related disorders, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

### References

- GeneReviews  
- OMIM #180902: RYR2 gene  
- OMIM #604772: CPVT  
- OMIM #600996: ARVD/C

### Genes

**RYR2**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of RYR2-related disorders in an individual in whom sequence analysis was negative.  
- Carrier testing in adults with a family history of RYR2-related disorders in whom sequence analysis was negative.

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type:** Whole Blood

**Specimen Requirements:**

In EDTA (purple top) tube:  
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the RYR2 gene is available and is required before deletion/duplication analysis.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.