

## Arrhythmogenic Right Ventricular Cardiomyopathy/ Dysplasia via *DSG2* Gene Sequencing -- Test #205

**Brief Description of Clinical Features:** Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D, OMIM 107970) is a heart disease primary affecting the right ventricle. It is characterized by myocardial atrophy, fibrofatty replacement of the ventricular myocardium and inflammatory infiltrates. With disease progression and occasional left ventricle involvement, heart failure may result. The most common symptoms include ventricular arrhythmias, recurrent syncope, seizures and sudden death after physical or emotional stress. ARVC/D is present in ~20% of young sudden cardiac death victims (Corrado et al. N Engl J Med 339:364-369, 1998). ARVC/D affects between 1/1000 and 1/5000 people worldwide with a higher prevalence in men compared to women (Corrado and Thiene, Circulation, 113:1634-1637, 2006). See also the Cardiomyopathy Association at ([www.cardiomyopathy.org](http://www.cardiomyopathy.org)) and McNally et al. (GeneReviews, 2009, [www.genetests.org](http://www.genetests.org)).

**Genetics:** ARVC/D is a heterogeneous disease that is inherited in about 50% of the cases (Basso et al. Eur Heart J 25:531-534, 2004). The mode of inheritance is most often autosomal dominant with age- and gender-dependent penetrance. Autosomal recessive variants of ARVC/D with hair and skin abnormalities have been described (Protonotarios et al. Br Heart J 56:321-326, 1986). To date, eight genes have been implicated in ARVC/D. Mutations in three genes: *PKP2*, *DSP* and *DSG2*, encoding desmosomal proteins, account for the great majority of known genetic causes of ARVC/D (McNally et al. GeneReviews, 2009, [www.genetests.org](http://www.genetests.org); Bhuiyan et al. Circ Cardiovasc Genet 2:418-427, 2009). Over 30 heterozygous *DSG2* mutations, distributed throughout the entire coding region, have been reported. Although the majority of causative variants were missense or nonsense mutations, five small insertions/deletions and two splicing mutations were reported. ARVC/D patients with compound heterozygous mutations in the *DSG2* gene or digenic mutations in the *DSG2* and *DSC2* genes have been reported (Awad et al. Am J Hum Genet 79:136-142, 2006).

**Description of This Particular Test:** The *DSG2* gene encodes the desmoglein-2 protein, an important component of the cardiac desmosome that is expressed only in the myocardium. This test involves bidirectional DNA sequencing of all 15 coding exons and splice sites of the *DSG2* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced.

**Reference Sequences:** Genomic: NC\_000018.9 mRNA: NM\_001943.3 Protein: NP\_001934.2(CCDS 42423.1)

**Indications for Test:** All patients with symptoms suggestive of ARVC/D and no mutations in the *PKP2* or *DSP* genes.

**Sensitivity of Test:** This test will detect mutations in ~10% of patients with clinical diagnosis of ARVC/D (Pilichou et al. Circulation 113:1171-1179, 2006; Syrris et al. Eur Heart J 28:581-588, 2007).

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

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

<b>Price:</b>	<b>Sequencing of <i>DSG2</i> Gene, Exons 1- 15</b>	<b>\$ 940</b>
<b>CPT Codes:</b>		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x17	83898 \$ 280	Sequencing x17 83904 \$ 420
Separation x1	83894 \$ 70	Interpretation/Report x1 83912 \$ 100

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

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