

Arrhythmogenic Right Ventricular Cardiomyopathy - Autosomal Dominant or Sporadic via Sequential Testing of Four Desmosomal Genes—Test # 207

Brief Description of Clinical Features: Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D, OMIM 107970) is a heart disease primarily 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) and McNally et al. (GeneReviews, 2009, www.genetests.org).

Genetics: ARVC/D is a heterogeneous disease that is inherited in roughly 50% of the cases (Basso et al. Eur Heart J 25:531-534, 2004). The mode of inheritance is most often autosomal dominant (AD) with age- and gender-dependent penetrance. 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). Mutations in the *DSC2* gene account for ~2% of patients with clinical diagnosis of ARVC/D (Bhuiyan et al. Circ Cardiovasc Genet 2:418-427, 2009).

Description of These Tests: PreventionGenetics offers sequencing of each of the four genes individually, or the Sequencing Panel described here. These tests involve bidirectional DNA sequencing of all coding exons of the genes listed below as well as ~ 50 bp of flanking DNA on either side. The default gene order is *PKP2*, *DSP*, *DSG2* and *DSC2*. However, the genes will be tested in a different order if requested by the client.

Gene	<i>PKP2</i>	<i>DSP</i>	<i>DSG2</i>	<i>DSC2</i>
Genomic_NC	000012.11	000006.11	000018.9	000018.9
mRNA	004572.3	004415.2	001943.3	024422.3
Protein	004563.2	004406.2	001934.2	077740.1

Indications for Test: Patients with symptoms suggestive of ARVC/D.

Sensitivity of Test: This Panel may detect mutations in up to 73% of patients with autosomal dominant or sporadic ARVC/D (McNally et al., 2009; Bhuiyan et al. Circ Cardiovasc Genet 2:418-427, 2009).

Turn Around Time: Maximum of 70 days.

Specimen Requirements: See page 4 of the Requisition Form

Prices: Sequential Testing of *PKP2*, *DSP*, *DSG2*, and *DSC2* genes \$ 820-3810

CPT Codes:

CPT	Description	<i>PKP2</i> Only	<i>DSP</i> Only	<i>DSG2</i> Only	<i>DSC2</i> Only	All Four Genes
83890	Sample Ascertainment	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)
83891	DNA Isolation	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)
83898	Amplification	\$ 240 (x14)	\$ 600 (x41)	\$ 280 (x17)	\$ 260 (x16)	\$1350 (x88)
83904	Sequencing	\$ 370 (x14)	\$ 900 (x41)	\$ 420 (x17)	\$ 400 (x16)	\$2030 (x88)
83894	Separation	\$ 60 (x1)	\$ 110 (x1)	\$ 70 (x1)	\$ 70 (x1)	\$ 190 (x1)
83912	Interpretation/Report	\$ 80 (x1)	\$ 140 (x1)	\$ 100 (x1)	\$ 100 (x1)	\$ 170 (x1)
	Totals	\$ 820	\$1820	\$ 940	\$ 900	\$3810

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

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