SUPPLEMENTAL MATERIAL

Online supplemental materials for “Comprehensive Desmosome Mutation Analysis in North Americans with Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy”

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Supplemental Methods: None. All methods are provided in the text.

Supplemental Tables:

Supplemental Table 1 - Clinical and genetic characteristics of patients with ARVD/C

Supplemental Table 2 – Non-conserved desmosome variants excluded as mutations

Supplemental Table 3 - Clinical and genetic characteristics of patients with suspected ARVD/C

Supplemental Figures: None

Supplemental References: None

Supplemental Table I: Clinical and genetic characteristics of patients with ARVD/C

Case	Gene	Nucleotide change	Gender	Age first symptom	Family History	Depol	Repol	Arrhyth	Struct	Tissue
1	*PKP2*	c.145_148delCAGA	M	28	-	++	+	-	++	-
2	*PKP2*	c.145_148delCAGA	M	31	++	++	+	+	++	ND
3	*PKP2*	c.235C>T	F	26	-	+	+	+	+	ND
4	*PKP2*	c.235C>T	F	?	+	-	+	+	+	-
5	*PKP2*	c.1171-2A>G	M	19	++	++	+	+	++	ND
6	*PKP2*	c.1237C>T	F	33	+	+	+	-	+	ND
7	*PKP2*	c.1271T>C	F	30	+	-	+	+	+	-
8	*PKP2*	c.1307_1315del-ins8	M	22	-	+	+	+	+	ND
9	*PKP2*	c.1368delA	F	15	-	+	+	+	++	-
10	*PKP2*	c.1613G>A	F	18	-	+	+	+	++	ND
11	*PKP2*	c.1613G>A	M	30	-	+	+	+	++	ND
12	*PKP2*	c.1613G>A	M	35	-	++	+	+	+	+
13	*PKP2*	c.1613G->A	M	26	-	++	+	+	++	ND
14	*PKP2*	c.1613G->A	M	45	-	++	+	+	++	ND
15	*PKP2*	c.1643delG	M	30	++	-	+	-	+	ND
16	*PKP2*	c.2013delC	F	11	+	+	+	+	++	-
17	*PKP2*	c.2146-1G->C	M	20	+	++	+	+	-	ND
18	*PKP2*	c.2146-1G->C	M	31	++	++	+	+	+	ND
19	*PKP2*	c.2146-1G->C	M	26	-	++	+	+	++	++
20	*PKP2*	c.2146-1 G>C	F	34	+	+	+	+	+	ND
21	*PKP2*	c.2146-1G->C	F	34	-	++	+	-	++	ND
22	*PKP2*	c.2146-1G->C	M	47	-	++	+	+	+	ND
23	*PKP2*	c.2146-1G->C	M	30	+	++	+	+	++	ND
24	*PKP2*	c.2146-1G->C	M	41	-	++	+	+	++	-
25	*PKP2*	c.2197_2202delinsG	F	32	+	+	+	+	+	-
26	*PKP2*	c.2197_2202delinsG	M	25	-	++	+	+	++	ND
27	*PKP2*	c.2197_2202delinsG	M	56	-	++	-	+	++	ND
28	*PKP2*	c.2359C>T	M	52	-	++	+	+	+	-
29	*PKP2*	c.2489+1G>A	M	22	++	++	+	+	+	ND
30	*PKP2*	c.2489+1G->A	F	38	-	++	+	+	++	-
31	*PKP2*	c.2489+1G->A	M	51	++	+	-	-	+	ND
32	*PKP2*	c.2489+1G->T	M	24	-	+	+	+	+	ND
33	*DSG2*	c.137G>A	M	11	-	-	+	+	++	+
34	*DSG2*	c.1520 G->A	M	38	-	+	+	+	++	ND
35	*DSG2*	c.2434G>T	F	23	++	-	+	-	+	ND
36	*DSP*	c.1331 A>G	F	24	-	-	+	+	+	++
37	*JUP*	c.56C>T	M	17	-	++	+	+	+	ND
38	*PKP2*	c.2484C->T (homozygous)	M	23	-	+	+	+	++	ND
39	*PKP2* *DSG2*	c.145_148delCAGA c.1003A>G	M	27	-	+	+	+	+	-
40	*PKP2* *DSG2*	c.1237C>T c.829 -1_835del	M	22	-	+	+	+	+	ND
41	*PKP2* *PKP2*	c.1759G>A c.2145+1G->C	M	64	-	++	+	+	++	ND
42	*DSG2* *DSG2*	c.146 G->A c.918 G->A	M	24	-	+	+	+	++	ND
43	*PKP2* *PKP2* *DSG2*	c.419C>T c.2146-1G->C c.166G>A	M	50	-	+	+	+	++	++
44			F	2	-	-	+	+	+	++
45			M	18	++	-	-	+	++	ND
46			M	14	-	++	+	+	++	ND
47			M	13	-	-	+	+	++	-
48			M	18	+	+	-	+	+	++
49			F	27	++	+	+	-	+	-
50			M	22	-	++	+	-	+	ND
51			M	35	-	++	+	+	+	ND

52			F	31	++	-	+	-	+	-
53			M	31	-	++	+	+	+	ND
54			F	29	-	+	+	+	++	ND
55			F	40	++	+	+	+	+	-
56			F	28	+	++	+	+	+	++
57			F	38	-	+	+	+	+	-
58			F	35	++	++	-	-	+	ND
59			M	43	++	+	-	-	+	-
60			F	36	-	++	-	+	+	-
61			M	42	-	++	+	-	++	++
62			M	41	-	++	+	-	+	-
63			M	40	-	++	+	+	++	++
64			F	41	-	+	+	+	+	ND
65			M	47	++	+	+	-	+	ND
66			F	41	-	+	+	+	++	ND
67			F	48	++	-	+	+	++	ND
68			F	41	-	-	+	+	++	ND
69			F	24	-	++	+	+	+	ND
70			F	43	-	-	+	-	+	++
71			F	43	++	+	+	-	+	ND
72			M	48	+	++	+	+	-	ND
73			F	53	++	-	+	-	+	ND
74			F	42	-	-	+	+	++	ND
75			F	41	-	+	+	+	+	ND
76			F	45	-	++	+	+	++	ND
77			M	46	-	++	+	-	++	ND
78			F	51	++	+	+	+	-	-
79			M	30	++	-	-	+	+	-
80			M	63	-	-	+	+	++	ND
81			M	57	-	++	+	+	++	++
82			M	76	-	-	-	-	++	++

Each individual is listed with a unique case number. Gene indicates the gene in which a mutation was identified. The six categories for criteria are shown as Family History, Depolarization abnormalities (Depol), Repolarization abnormalities (Repol), Arrhythmia (Arrhyth), Structural RV disease (Struct), and tissue. For these columns, '+' indicates meeting a minor criterion, '++' indicates meeting a major criterion, and '?' indicates that they were not adequately tested for that criterion.

Supplemental Figure 2

Non-conserved desmosome protein variants excluded due to presence in controls or lack of conservation:

PKP2	***DSP***	***DSC2***	***DSG2***	***JUP***
p.D26N	p.I305F	p.N11S	p.V158G	p.R142H
p.S70I	p.A1505V	p.Q638H	p.E713K	p.V648I
p.A195V	p.Y1512C	p.A596V	p.H790Y	p.M697L
p.P276S	p.N1526K	p.I776V	p.S883F	
p.P366L	p.R1537C	p.R798Q	p.S1098C	
p.A372P	p.R1738Q	p.A897fsX900		
p.T526M				
p.I531S				
p.A830P*				

* refers to a nucleotide alteration which may alter splicing though mRNA was not available to test further

Supplemental Table 3: Clinical and genetic characteristics of patients with probable ARVD/C

Case	Gene	Nucleotide change	Gender	Age first symptom	Family History	Depol	Repol	Arrhyth	Struct	Tissue	Minor criteria	Major criteria
1	*PKP2*	c.145_148delCAGA	F	38	-	-	+	+	+	ND	3	0
2	*PKP2*	c.216insG	M	46	++	+	-	-	-	ND	1	1
3	*PKP2*	c.2146-1G>C	F	16	-	-	+	+	+	ND	3	0
4	*PKP2*	c.2509delA	M	21	+	-	+	-	+	ND	3	0
5	*DSG2*	c.146G>A	M	38	-	-	+	+	+	ND	3	0
6			M	28	-	++	-	-	+	ND	1	1
7			F	26	-	-	+	+	+	ND	3	0
8			M	36	-	++	-	-	+	ND	1	1
9			M	29	++	+	-	-	-	ND	1	1
10			F	36	-	-	-	+	+	ND	2	0
11			M	33	-	+	-	+	-	ND	2	0
12			F	33	-	-	+	+	-	ND	2	0
13			F	39	-	-	-	+	++	-	1	1
14			F	37	-	+	-	+	-	ND	2	0
15			F	31	-	-	+	+	+	ND	3	0
16			F	18	+	-	-	+	-	ND	2	0
17			F	40	-	-	-	+	+	ND	2	0
18			F	13	++	-	-	-	+	ND	1	1

Each individual is listed with a unique case number. Gene indicates the gene in which a mutation was identified. The six categories for criteria are shown as Family History, Depolarization abnormalities (Depol), Repolarization abnormalities (Repol), Arrhythmia (Arrhyth), Structural RV disease (Struct), and tissue. For these columns, '+' indicates meeting a minor criterion, '++' indicates meeting a major criterion, and '?' indicates that they were not adequately tested for that criterion.