Table S1 Pathogenic potential of the nonsynonymous variants of the DCM-associated genes in the sporadic DCM cohort

Gene	dbSNP ID	Change in AA	Pattern	PP2 Prediction (score)	Chrs.	Position (B37)	cDNA substitution	Orientation	SIFT Prediction (score)	Predicted damaging[a]	Predicted tolerated[b]
ABCC9	rs149319186	K976I	2	Benign (0.36)	12	21998706	A/T	-	Damaging (0.04)		
ABCC9		R1197C	1	Probably damaging (0.93)	12	21981972	C/T	-	Damaging (0.04)	X	
ACTN2		K96R	1	Probably damaging (0.98)	1	236882239	A/G	+	Tolerated (0.06)		
ACTN2		M316T	1	Probably damaging (0.96)	1	236902672	T/C	+	Tolerated (0.12)		
ACTN2	rs80257412	D475N	2	Probably damaging (0.99)	1	236910983	G/A	+	Tolerated (0.24)		
DES		R78L	1	Benign (0.00)	2	220283417	G/T	+	Tolerated (0.54)		X
LAMA4		A41V	1	Benign (0.00)	6	112575231	C/T	-	Tolerated (0.15)		X
LAMA4		C91S	1	Probably damaging (1.00)	6	112537595	T/A	-	Damaging (0.00)	X	
LAMA4	rs71543223	A283D	2	Benign (0.00)	6	112508769	CA/AC	-			
LAMA4	rs1050348	Y498H	2	Benign (0.00)	6	112493872	T/C	-	Tolerated (0.34)		X
LAMA4	rs2032567	G1117S	2	Benign (0.00)	6	112457390	G/A	-	Tolerated (1.00)		X
LAMA4	rs1050349	P1119R	2	Probably damaging (0.99)	6	112457383	C/G	-	Tolerated (0.13)		
LAMA4	rs70940811	V1315I	2	Benign (0.00)	6	112452195	G/A	-	Tolerated (0.43)		X
LAMA4		G1356R	1	Probably damaging (1.00)	6	112451145	G/C	-	Damaging (0.00)	X	
LAMA4	rs201094782	Y1391H	2	Probably damaging (1.00)	6	112450240	T/C	-	Tolerated (0.19)		
LAMA4	rs3734292	V1815I	2	Probably damaging (0.98)	6	112430669	G/A	-	Tolerated (0.18)		
LDB3		T28K	1	Probably damaging (1.00)	10	88428531	CA/AG	+			
LDB3	rs3740343	V55I	2	Benign (0.02)	10	88439193	G/A	+	Tolerated (0.42)		X
LDB3		E139K	1		10	88446896	G/A	+	Tolerated (0.79)		
LDB3	rs45521338	R218C	2	Benign (0.05)	10	88451756	C/T	+	Tolerated (0.07)		X
LDB3		S330P	1	Benign (0.20)	10	88476170	T/C	+	Tolerated (0.26)		X
LDB3	rs113817827	V426I	2	Benign (0.15)	10	88476458	G/A	+	Tolerated (0.28)		X
LDB3		M456R	1	Probably damaging (0.97)	10	88477741	T/G	+	Damaging (0.00)	X	
LDB3	rs145983824	P498L	1	Probably damaging (1.00)	10	88477867	C/T	+	Damaging (0.00)	X	
LMNA		R220H	1	Benign (0.37)	1	156104615	G/A	+	Damaging (0.01)		
MYBPC3	rs3729989	S236G	2	Benign (0.00)	11	47370041	A/G	-	Tolerated (1.00)		X
MYBPC3		E334K	1	Benign (0.33)	11	47367848	G/A	-	Damaging (0.00)		

Table S1 *(continued)*

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Table S1 *(continued)*

Gene	dbSNP ID	Change in AA	Pattern	PP2 Prediction (score)	Chrs.	Position (B37)	cDNA substitution	Orientation	SIFT Prediction (score)	Predicted damaging[a]	Predicted tolerated[b]
MYBPC3	rs113276889	R409G	1	Benign (0.10)	11	47364698	A/G	-	Damaging (0.00)		
MYBPC3		G416S	1	Probably damaging (0.98)	11	47364677	G/A	-	Damaging (0.01)	X	
MYBPC3		P459fs	1		11	47364464	delC	-		X	
MYBPC3	rs147359039	R835L	1	Probably damaging (0.93)	11	47359039	GC/TT	-			
MYBPC3		R895H	1	Benign (0.41)	11	47357481	G/A	-	Tolerated (0.19)		X
MYH6	rs28711516	G56R	2	Probably damaging (0.95)	14	23876267	G/A	-	Damaging (0.00)	X	
MYH6	rs365990	V1101A	2	Benign (0.00)	14	23861811	T/C	-	Tolerated (1.00)		X
MYH6	rs28730771	A1130T	3	Possibly damaging (0.71)	14	23859610	G/A	-	Tolerated (0.17)		
MYH6	rs34935550	E1295Q	2	Probably damaging (0.95)	14	23858697	G/C	-	Damaging (0.01)	X	
MYH6	rs45574136	Q1593L	3	Benign (0.00)	14	23855705	A/T	-	Tolerated (0.14)		X
MYH6	rs61742476	V1613A	3	Benign (0.00)	14	23855645	T/C	-	Tolerated (1.00)		X
MYH6		K1860R	1	Benign (0.00)	14	23852515	AA/GG	-			
MYH7	rs121913653	T441M	1	Benign (0.02)	14	23898249	C/T	-	Tolerated (0.07)		X
MYH7	rs121913625	R453C	1	Probably damaging (1.00)	14	23898214	C/T	-	Damaging (0.00)	X	
MYH7		I736T	1	Probably damaging (1.00)	14	23894983	T/C	-	Tolerated (0.13)		
MYH7	rs121913628	E924K	1	Probably damaging (1.00)	14	23893268	G/A	-	Damaging (0.02)	X	
MYH7		LS1139LD	1	Benign (0.44)	14	23889361	GTC/AGA	-			
MYH7		R1250W	1	Probably damaging (0.99)	14	23888797	C/T	-	Damaging (0.02)	X	
MYH7		G1520R	1	Benign (0.07)	14	23886163	G/A	-	Damaging (0.03)		
MYH7		R1897H	1	Probably damaging (1.00)	14	23883068	G/A	-	Damaging (0.00)	X	
MYPN		R482K	1	Probably damaging (0.99)	10	69918370	G/A	+	Tolerated (0.12)		
MYPN	rs10823148	F628L	2	Benign (0.00)	10	69926334	C/G	+	Tolerated (0.67)		X
MYPN	rs10997975	S691N	2	Benign (0.00)	10	69933921	G/A	+	Tolerated (0.66)		X
MYPN	rs7916821	S707N	2	Benign (0.03)	10	69933969	G/A	+	Tolerated (0.39)		X
MYPN	rs3814182	S803R	2	Benign (0.12)	10	69934258	C/G	+	Tolerated (0.46)		X
MYPN	rs181848049	G847V	2	Probably damaging (1.00)	10	69934389	G/T	+	Damaging (0.01)	X	
MYPN	rs151282801	R1042C	1	Probably damaging (1.00)	10	69955255	C/T	+	Damaging (0.00)	X	

Table S1 *(continued)*

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Table S1 *(continued)*

Gene	dbSNP ID	Change in AA	Pattern	PP2 Prediction (score)	Chrs.	Position (B37)	cDNA substitution	Orientation	SIFT Prediction (score)	Predicted damaging[a]	Predicted tolerated[b]
MYPN	rs7079481	P1135T	2	Probably damaging (1.00)	10	69959242	C/A	+	Damaging (0.00)	X	
MYPN	rs138313730	L1161I	1	Probably damaging (1.00)	10	69959320	C/A	+	Damaging (0.00)	X	
MYPN	rs199585352	S1296T	1	Probably damaging (0.99)	10	69970135	T/A	+	Damaging (0.02)	X	
RBM20		G40W	1	Probably damaging (1.00)	10	112404330	G/T	+	Damaging (0.00)	X	
RBM20		P48delinsPP	1		10	112404356	insGCC	+			
RBM20	rs143785916	R641Q	2	Probably damaging (0.92)	10	112572077	G/A	+	Tolerated (0.08)		
RBM20	rs138926584	R673Q	3	Probably damaging (1.00)	10	112572173	G/A	+	Damaging (0.02)	X	
RBM20	rs1417635	W768S	3	Benign (0.00)	10	112572458	G/C	+	Tolerated (0.80)		X
RBM20		Q856X	1		10	112579845	C/T	+		X	
RBM20	rs188054898	R1057Q	2	Benign (0.00)	10	112581547	G/A	+	Tolerated (0.85)		X
RBM20		R1182H	1	Probably damaging (1.00)	10	112590912	G/A	+	Damaging (0.02)	X	
RBM20	rs942077	E1223Q	2	Benign (0.32)	10	112595719	G/C	+	Tolerated (0.12)		X
SCN5A	rs199473071	R225Q	1	Possibly damaging (0.88)	3	38655263	G/A	-	Damaging (0.00)	X	
SCN5A	rs199473561	A226V	1	Probably damaging (0.95)	3	38655260	C/T	-	Damaging (0.03)	X	
SCN5A	rs1805124	H558R	2	Benign (0.00)	3	38645420	A/G	-	Tolerated (1.00)		X
SCN5A	rs45600438	R568C	1	Possibly damaging (0.64)	3	38645391	C/T	-	Damaging (0.01)	X	
SCN5A		R659W	1	Probably damaging (0.98)	3	38640457	C/T	-	Damaging (0.00)	X	
SCN5A	rs1805125	P1090L	2	Benign (0.03)	3	38620946	C/T	-	Tolerated (0.65)		X
SCN5A	rs41310765	A1180V	1	Benign (0.02)	3	38616915	C/T	-	Tolerated (0.33)		X
SCN5A	rs41261344	R1193Q	2	Benign (0.01)	3	38616876	G/A	-	Tolerated (0.12)		X
SCN5A	rs199473251	I1448N	1	Possibly damaging (0.76)	3	38598026	T/A	-	Damaging (0.00)	X	
SCN5A		P1619T	1	Probably damaging (0.93)	3	38593008	C/A	-	Damaging (0.00)	X	
SGCD		C34G	1	Probably damaging (1.00)	5	155771595	T/G	+	Damaging (0.01)	X	
SGCD		P253fs	1		5	156186287	insC	+		X	
SGCD		Q283R	1	Probably damaging (0.97)	5	156186376	A/G	+	Tolerated (0.10)		
TAZ		H111N	1	Benign (0.08)	X	153641865	C/A	+	Tolerated (0.29)		X

Table S1 *(continued)*

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Table S1 *(continued)*

Gene	dbSNP ID	Change in AA	Pattern	PP2 Prediction (score)	Chrs.	Position (B37)	cDNA substitution	Orientation	SIFT Prediction (score)	Predicted damaging[a]	Predicted tolerated[b]
TNNT2		R151Q	1	Probably damaging (1.00)	1	201333463	G/A	-	Damaging (0.04)	X	
TNNT2	rs3730238	K260R	3	Benign (0.01)	1	201330429	A/G	-	Tolerated (0.27)		X
TPM1		D34E	1	Benign (0.00)	15	63335130	C/A	+	Tolerated (1.00)		X
VCL	rs144683137	M209L	2	Benign (0.01)	10	75834503	A/T	+	Tolerated (1.00)		X
VCL	rs201528612	P398S	2	Benign (0.29)	10	75849796	C/T	+	Tolerated (0.09)		X

AA, Amino Acid; Chrs., chromosome; PP2, PolyPhen 2; PP2 scores range from 0 to 1, with three levels of pathogenic potential (probably damaging, possibly damaging, and benign); PP2 scores were obtained by using a web-based tool, HumVar model, at http://genetics.bwh.harvard.edu/pph2/index.shtml. SIFT, Sorts Intolerant From Tolerant; SIFT scores range from 0 to 1 (damaging or tolerated) with 0.05 as the threshold value; SIFT scores were obtained by using a web-based tool at http://siftdna.org/www/Extended_SIFT_chr_coords_submit.html. a, b: A variant is predicted to be damaging when both PP2 and SIFT scores fall in the damaging ranges, while it is predicted to be tolerated when both scores are in the benign or tolerated ranges.

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Table S2 Comparison of symptoms between the sporadic DCM patients with and without risk variants

Patient ID	Gender (female=0 male=1)	Age (years)	Drinking (no=0 yes=1)	Smoking (no=0 yes=1)	Hypertension (no=0 yes=1)	Diabetes (no=0 yes=1)	Symptoms to diagnosis (months)	Diagnosis to inclusion (months)	Arrhythmias[1]	NYHA class	Number of risky variants
DCM patients without risk variants											
1398	1	17	0	0	0	0	(N.A.)	180	N	4	0
1400	1	22	0	1	0	0	4	0	3	3	0
1403	1	40	0	0	0	0	(N.A.)	48	1; 3; 4	3	0
1408	0	56	0	0	1	1	6	0	N	4	0
1409	1	61	0	1	0	0	(N.A.)	240	3; 4	3	0
1412	0	60	0	0	0	0	304	120	3; 5	3	0
1421	0	66	0	0	0	1	(N.A.)	96	N	3	0
1424	1	36	(N.A.)	(N.A.)	0	0	(N.A.)	NA	N	4	0
1426	0	62	0	0	0	0	240	0	7	3	0
1432	1	58	0	1	1	0	6	0	3; 4	4	0
1433	1	36	0	1	0	0	2	0	N	2	0
1437	0	42	0	1	0	0	49	11	N	4	0
1446	1	59	1	1	0	1	0	26	N	4	0
1447	0	46	0	0	1	0	0	22	N	1	0
1448	1	49	1	0	0	0	0	11	N	0	0
1454	1	48	0	0	0	0	60	36	N	1	0
1455	1	28	0	0	0	0	0	0	N	3	0
1459	1	51	0	0	0	0	0	60	N	4	0
1462	1	63	1	0	0	1	0	0	N	3	0
1463	1	41	0	1	1	1	7	7	N	4	0
1468	1	77	0	0	0	0	5	5	N	2	0
1471	1	65	1	0	0	0	60	0	N	4	0
1472	1	20	0	0	0	0	0	2	N	2	0
1473	1	81	0	0	0	0	0	60	N	3	0
1475	1	40	0	0	0	0	12	0	N	2	0
1479	1	45	0	0	0	0	0	84	N	4	0
Mean ± SD		48.8±16.6					36.0±81.5	40.3±62.0		3±1	
DCM patients with risk variants											
1401	1	36	1	1	0	0	12	24	0	3	2
1402	1	38	0	0	0	0	(N.A.)	36	4	4	1
1404	1	43	0	1	1	0	(N.A.)	36	N	3	2
1405	0	51	0	0	0	0	1	0	N	3	2
1406	0	51	0	0	0	0	(N.A.)	96	7	4	1
1410	1	77	0	1	1	0	1	0	N	4	4
1411	1	65	0	0	0	1	1	0	5	3	2
1414	1	52	0	0	0	0	0	9	3	3	1

Table S2 *(continued)*

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Table S2 *(continued)*

Patient ID	Gender (female=0 male=1)	Age (years)	Drinking (no=0 yes=1)	Smoking (no=0 yes=1)	Hypertension (no=0 yes=1)	Diabetes (no=0 yes=1)	Symptoms to diagnosis (months)	Diagnosis to inclusion (months)	Arrhythmias[1]	NYHA class	Number of risky variants
1416	1	26	0	1	0	0	1	0	N	3	1
1417	0	51	0	0	0	0	(N.A.)	60	3; 4	4	2
1418	1	60	1	1	0	0	(N.A.)	48	7	3	2
1419	0	55	0	0	0	0	7	1	3	3	3
1428	1	36	0	0	1	0	1	0	N	3	1
1429	1	34	0	1	1	0	2	0	N	1	1
1430	1	61	(N.A.)	(N.A.)	0	0	(N.A.)	(N.A.)	N	3	1
1431	0	16	0	0	0	0	9	0	N	3	2
1435	1	82	0	1	0	0	24	0	5; 7	2	1
1436	0	62	0	0	0	0	31	5	1; 3	2	1
1438	1	19	0	1	0	0	0	0	11	3	1
1439	0	17	0	0	0	0	(N.A.)	(N.A.)	N		1
1440	1	53	0	0	0	0	60	0	N	3	1
1442	1	58	1	1	0	1	11	60	N	4	2
1443	1	50	1	0	0	1	0	0	N	4	1
1444	1	50	1	1	0	0	0	0	N	1	1
1449	1	47	0	0	0	0	0	33	N	3	1
1451	0	63	1	1	0	0	0	5	N	4	2
1452	0	62	0	1	0	0	7	57	N	1	2
1453	0	36	1	0	1	0	0	0	N	4	1
1456	1	69	0	0	0	0	0	18	N	4	1
1457	1	54	0	0	0	0	19	18	N	4	1
1461	1	66	0	0	0	0	2	18	N	4	1
1464	0	51	0	0	0	0	0	12	N	3	1
1465	1	56	1	1	1	0	26	0	N	3	1
1466	1	42	1	1	1	0	2	0	N	2	3
1467	1	48	0	0	1	0	2	2	N	4	1
1469	1	71	0	0	0	0	10	26	N	3	1
1470	1	36	1	1	0	0	1	0	N	4	1
1474	0	46	0	0	1	0	0	36	N	3	1
1478	1	29	0	0	0	0	0	6	N	3	1
1480	0	64	0	0	0	0	0	24	N	3	2
Mean ± SD		49.6±15.9					7.0±12.7	16.6±23.0		3±1	
P values[2]	0.579	0.854	0.537	0.431	0.543	0.247	(0.602)	(0.258)	0.778	(0.812)	

1: Arrhythmias: atrial fibrillation or flutter=0; atrial premature beat=1; atrial tachycardia=2; ventricular premature beat=3; ventricular tachycardia=4; first-degree AV block=5; third-degree AV block=6; complete left or right bundle branch block=7. 2: Compared with the corresponding parameter of the patients without risky variants. P values in the parentheses were obtained from the Mann-Whitney rank sum test. N, no symptom; N.A., data not available; SD, standard deviation.

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Table S3 Comparison of echocardiographic parameters between the sporadic DCM patients with and without risk variants

Patient ID	ARD (mm)	LVEDD (mm)	LVESD (mm)	LAD (mm)	IVST (mm)	LVPWT (mm)	FS (%)	LVEF (%)	RWT
DCM patients without risk variants									
1398	22	73	68	51	8	8	12	25	0.110
1400	23	84	76	50	8	6	15	30	0.071
1403	33	81	71	50	8	7	13	27	0.086
1408	35	60	51	56	10	10	25	50	0.167
1409	35	69	63	42	9	8	10	20	0.116
1412	30	85	78	46	8	8	13	26	0.094
1421	31	64	51	48	7	9	22	45	0.141
1424	37	76	67	67	9	8	18	36	0.105
1426	33	66	57	36	9	9	16	32	0.136
1432	41	72	56	45	10	9	16	32	0.125
1433	37	68	59	40	10	9	14	28	0.132
1437	25	75	65	51	8	8	13	25	0.107
1446	36	84	61	44	10	10	13	26	0.119
1447	30	65	53	37	8	8	20	40	0.123
1448	37	55	40	40	10	10	29	55	0.182
1454	23	54	45	49	8	8	18	35	0.148
1455	32	58	40	34	10	9	18	36	0.155
1459	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)
1462	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)
1463	33	44	37	39	10	10	31	59	0.256
1468	38	63	41	44	14	12	19	38	0.273
1471	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)
1472	31	64	44	35	9	10	25	52	0.286
1473	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)
1475	36	84	64	50	11	12	10	20	0.240
1479	30	71	64	49	9	8	12	24	0.163
Mean ± SD	32±5	69±11	57±12	46±8	9±1	8±1	17±6	35±11	0.152±0.061
DCM patients with risk variants									
1401	29	54	45	63	8	11	17	32	0.204
1402	26	74	56	66	7	7	17	34	0.095
1404	34	82	70	60	9	10	15	29	0.122
1405	30	59	42	45	8	8	29	56	0.136
1406	29	72	61	47	6	6	17	34	0.083
1410	34	74	55	52	12	13	20	39	0.176
1411	36	75	64	48	10	10	14	28	0.133
1414	35	64	56	52	10	10	20	40	0.156

Table S3 *(continued)*

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Table S3 *(continued)*

Patient ID	ARD (mm)	LVEDD (mm)	LVESD (mm)	LAD (mm)	IVST (mm)	LVPWT (mm)	FS (%)	LVEF (%)	RWT
1416	30	67	58	52	7	7	12	24	0.104
1417	26	74	62	54	10	10	15	30	0.135
1418	39	81	71	53	12	11	16	33	0.136
1419	32	59	44	39	9	8	24	48	0.136
1428	27	62	43	42	9	10	21	42	0.161
1429	33	74	62	50	7	8	15	30	0.108
1430	35	88	73	58	9	10	15	30	0.114
1431	25	70	60	38	7	7	13	26	0.100
1435	34	66	47	36	10	10	25	50	0.152
1436	30	61	43	48	10	9	23	45	0.148
1438	22	57	48	31	5	9	16	31	0.158
1439	24	67	54	42	9	8	17	35	0.119
1440	30	65	52	50	9	9	18	36	0.138
1442	30	75	60	48	8	8	9	17	0.107
1443	32	65	58	40	8	8	10	21	0.123
1444	28	78	69	44	8	8	12	24	0.103
1449	25	76	63	52	10	10	15	31	0.132
1451	33	68	61	39	8	9	12	23	0.132
1452	30	75	64	68	11	11	14	29	0.147
1453	31	72	59	57	8	8	17	34	0.111
1456	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)
1457	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	16	32	
1461	37	59	43	39	7	9	18	35	0.231
1464	34	63	51	43	8	8	19	38	0.186
1465	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	13	26	
1466	34	75	58	68	10	11	15	29	0.162
1467	27	79	68	50	8	9	14	28	0.180
1469	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)
1470	34	54	38	41	10	10	32	60	0.244
1474	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)
1478	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)
1480	30	77	65	53	8	8	14	28	0.151
Mean ± SD	31±4	69±8	57±9	49±9	9±2	9±1	17±5	34±9	0.142±0.037
P values	0.246	0.825	0.916	0.150	0.195	0.666	0.742	0.703	0.452

Compared with the corresponding parameter of the patients without risk variants; SD, standard deviation. ARD, aortic root diameter; FS, shortening fraction; LAD, left atrial diameter; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVPWT, left ventricule post wall thickness; IVST, interventricular septal thickness; N, no symptom; N.A., data not available; RWT, relative wall thickness.

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