

SUPPLEMENTAL MATERIAL

Appendix

LVNC Study Collaborators

Akiko Komori, Arata Sashinami, Atsuko Ishihara, Atsushi Kuwahara, Chisato Akita, Dai Miura, Daichi Fukumi, Etsuko Tsuda, Eizo Akagawa, Heima Sakaguchi, Hideaki Ueda, Hidenori Iwasaki, Hideshi Tomita, Hiroaki Kise, Hirohiko Shiraishi, Hirohumi Tomimatsu, Hirokazu Taniguchi, Hiroki Kajino, Hiroki Nagamine, Hiromi Katayama, Hiromichi Hamada, Hiroo Ooki, Hiroshi Mito, Hiroshi Miura, Hiroshi Ono, Hirotaka Ooki, Hiroyuki Yoshizawa, Hitoshi Horigome, Hitoshi Tonegawa, Joji Hayashi, Jun Matsushita, Jun Yanai, Jun Yoshimoto, Junichi Ohata, Junichi Takagi, Junichi Yoshikawa, Kazuhiro Takahashi, Kazuki Kouno, Kazuo Eguchi, Keitaro Arima, Kenji Kuroe, Kenji Yasuda, Kenzo Aoki, Kiyotaka Takefuta, Koichi Nihei, Kotaro Inaguma, Kotaro Oyama, Kouichi Nihei, Maki Osaki, Makoto Nakazawa, Makoto Shinohara, Masahiro Kamada, Masahiro Kojo, Masahumi Seguchi, Masaki Arai, Masaki Nakagawa, Masaki Tsukashita, Masaki Yamamoto, Masako Harada, Masato Kimura, Mio Sugiyama, Mitsuhiro Fujino, Mitsuo Takeda, Mitsuya Kudo, Motoyoshi Kawataki, Muneo Yoshibayashi, Naoyuki Shiraishi, Naoyuki Shirovani, Noboru Inamura, Nobuo Momoi, Norihide Fukushima, Norio Sakai, Noriyuki Haneda, Osamu Hirose, Osamu Matsuo, Reizo Baba, Sadataka Kawachi, Satoshi Hasegawa, Satoshi Takenaka, Satoshi Yasukochi, Sawako Kido, Seiichi Sato, Shigeyuki Echigo, Shingo Sakamoto, Shinichi Tsubata, Shinji Nakamura, Shio Suzuki, Shiro Ishikawa, Shunji Kurotobi, Shunji Miyake, Susumu Urata, Tadaaki Abe, Tadaro Abe, Tadashi Sakano, Taichi Kato, Takahiro Shindo, Takako Toda, Takamichi Ishikawa, Takamichi Uchiyama, Takaomi

Minami, Takashi Higaki, Takashi Honda, Takashi Kumamoto, Takashi Urashima, Takehiko Ishida, Takeo Mukai, Takeshi Isobe, Takeshi Kondo, Tamaki Hayashi, Taro Matsuoka, Tasuku Doi, Teiji Akagi, Tohru Matsushita, Tomoaki Murakami, Tomotaka Nakayama, Tomoyasu Ozaki, Tohru Hioka, Tohru Matsushita, Tohru Tsuji, Toshie Kadono, Toshihiro Mitomori, Yasuhiko Tanaka, Yasuhiro Morikami, Yasunobu Hayabuchi, Yasunobu Wakabayashi, Yasuo Murakami, Yasuo Ono, Yo Arita, Yoko Okada, Yoshimi Hiraumi, Yosuke Haneda, Yuichi Nomura, Yuko Kittaka, Yumiko Ikemoto, Yuriko Abe, Yusuke Seino, Yutaka Fukuda, Yutaka Odanaka.

Table S1. List of 73 analyzed genes of NGS.

Gene	Chromosome	NCBI Reference Sequence:	Sequence: (Start.End)	
ABCC9	12p12.1	NG_012819.1	NC_000012.11 (21950323..22094797, complement)	http://www.ncbi.nlm.nih.gov/gene/10060
ACTC1	15q14	NG_007553.1	NC_000015.9 (35080297..35087927, complement)	http://www.ncbi.nlm.nih.gov/gene/70
ACTN2	1q42-q43	NG_009081.1	NC_000001.10 (236849754..236927931)	http://www.ncbi.nlm.nih.gov/gene/88
AKAP9	7q21-q22	NG_011623.1	NC_000007.13 (91570181..91739987)	http://www.ncbi.nlm.nih.gov/gene/10142
ANK2	4q25-q27	NG_009006.2	NC_000004.11 (113739239..114304896)	http://www.ncbi.nlm.nih.gov/gene/287
BAG3	10q25.2-q26.2	NG_016125.1	NC_000010.10 (121410859..121437331)	http://www.ncbi.nlm.nih.gov/gene/9531
BMPR1A	10q22.3	NG_009362.1	NC_000010.10 (88516396..88684945)	http://www.ncbi.nlm.nih.gov/gene/657
CACNA1C	12p13.3	NG_008801.2	NC_000012.11 (2079952..2807115)	http://www.ncbi.nlm.nih.gov/gene/775
CACNB2	10p12	NG_016195.1	NC_000010.10 (18429373..18830688)	http://www.ncbi.nlm.nih.gov/gene/783

CALR3	19p13.11	NG_031959.2	NC_000019.9 (16589767..16607015, complement)	http://www.ncbi.nlm.nih.gov/gene/125972
CAPN3	15q15.1	NG_008660.1	NC_000015.9 (42646545..42704515)	http://www.ncbi.nlm.nih.gov/gene/825
CAV3	3p25	NG_008797.2	NC_000003.11 (8775486..8788451)	http://www.ncbi.nlm.nih.gov/gene/859
COL4A1	13q34	NG_011544.1	NC_000013.10 (110801310..110959496, complement)	http://www.ncbi.nlm.nih.gov/gene/1282
DES	2q35	NG_008043.1	NC_000002.11 (220283099..220291461)	http://www.ncbi.nlm.nih.gov/gene/1674
DMD	Xp21.2	NG_012232.1	NC_000023.10 (31137345..33357726, complement)	http://www.ncbi.nlm.nih.gov/gene/1756
DSC2	18q12.1	NG_008208.1	NC_000018.9 (28645938..28682388, complement)	http://www.ncbi.nlm.nih.gov/gene/1824
DSG2	18q12.1	NG_007072.3	NC_000018.9 (29078027..29128814)	http://www.ncbi.nlm.nih.gov/gene/1829
DSP	6p24	NG_008803.1	NC_000006.11 (7541808..7586946)	http://www.ncbi.nlm.nih.gov/gene/1832
ELN	7q11.23	NG_009261.1	NC_000007.13 (73442119..73484237)	http://www.ncbi.nlm.nih.gov/gene/2006
EMD	Xq28	NG_008677.1	NC_000023.10 (153607597..153609883)	http://www.ncbi.nlm.nih.gov/gene/2010
GAA	17q25.2-q25.3	NG_009822.1	NC_000017.10 (78075339..78093680)	http://www.ncbi.nlm.nih.gov/gene/2548

GATA4	8p23.1-p22	NG_008177.1	NC_000008.10 (11534433..11617510)	http://www.ncbi.nlm.nih.gov/gene/2626
GLA	Xq22	NG_007119.1	NC_000023.10 (100652779..100663001, complement)	http://www.ncbi.nlm.nih.gov/gene/2717
GPD1L	3p22.3	NG_023375.1	NC_000003.11 (32148003..32210207)	http://www.ncbi.nlm.nih.gov/gene/23171
HCN4	15q24.1	NG_009063.1	NC_000015.9 (73612200..73661605, complement)	http://www.ncbi.nlm.nih.gov/gene/10021
JUP	17q21	NG_009090.2	NC_000017.10 (39910859..39942964, complement)	http://www.ncbi.nlm.nih.gov/gene/3728
KCNE1	21q22.12	NG_009091.1	NC_000021.8 (35790910..35884573, complement)	http://www.ncbi.nlm.nih.gov/gene/3753
KCNE2	21q22.12	NG_008804.1	NC_000021.8 (35736323..35743440)	http://www.ncbi.nlm.nih.gov/gene/9992
KCNE3	11q13.4	NG_011833.1	NC_000011.9 (74165886..74178600, complement)	http://www.ncbi.nlm.nih.gov/gene/10008
KCNH2	7q36.1	NG_008916.1	NC_000007.13 (150642044..150675402, complement)	http://www.ncbi.nlm.nih.gov/gene/3757
KCNJ2	17q24.3	NG_008798.1	NC_000017.10 (68164757..68176189)	http://www.ncbi.nlm.nih.gov/gene/3759
KCNQ1	11p15.5	NG_008935.1	NC_000011.9 (2466221..2870340)	http://www.ncbi.nlm.nih.gov/gene/3784

KRAS	12p12.1	NG_007524.1	NC_000012.11 (25358180..25403870, complement)	http://www.ncbi.nlm.nih.gov/gene/3845
LAMP2	Xq24	NG_007995.1	NC_000023.10 (119560003..119603204, complement)	http://www.ncbi.nlm.nih.gov/gene/3920
LDB3	10q22.3-q23.2	NG_008876.1	NC_000010.10 (88426542..88495829)	http://www.ncbi.nlm.nih.gov/gene/11155
LMNA	1q22	NG_008692.2	NC_000001.10 (156052369..156109880)	http://www.ncbi.nlm.nih.gov/gene/4000
MYBPC3	11p11.2	NG_007667.1	NC_000011.9 (47352957..47374253, complement)	http://www.ncbi.nlm.nih.gov/gene/4607
MYH11	16p13.11	NG_009299.1	NC_000016.9 (15796992..15950887, complement)	http://www.ncbi.nlm.nih.gov/gene/4629
MYH6	14q12	NG_023444.1	NC_000014.8 (23849942..23878836, complement)	http://www.ncbi.nlm.nih.gov/gene/4624
MYH7	14q12	NG_007884.1	NC_000014.8 (23881947..23904870, complement)	http://www.ncbi.nlm.nih.gov/gene/4625
MYL2	12q24.11	NG_007554.1	NC_000012.11 (111348623..111358404, complement)	http://www.ncbi.nlm.nih.gov/gene/4633
MYL3	3p21.3-p21.2	NG_007555.2	NC_000003.11 (46899357..46904973, complement)	http://www.ncbi.nlm.nih.gov/gene/4634

MYLK	3q21	NG_029111.1	NC_000003.11 (123331143..123603149, complement)	http://www.ncbi.nlm.nih.gov/gene/4638
MYOZ2	4q26-q27	NG_029747.1	NC_000004.11 (120056939..120108944)	http://www.ncbi.nlm.nih.gov/gene/51778
NKX2-5	5q34	NG_013340.1	NC_000005.9 (172659107..172662315, complement)	http://www.ncbi.nlm.nih.gov/gene/1482
NRAS	1p13.2	NG_007572.1	NC_000001.10 (115247085..115259515, complement)	http://www.ncbi.nlm.nih.gov/gene/4893
PKP2	12p11	NG_009000.1	NC_000012.11 (32943680..33049780, complement)	http://www.ncbi.nlm.nih.gov/gene/5318
PLN	6q22.1	NG_009082.1	NC_000006.11 (118869442..118881587)	http://www.ncbi.nlm.nih.gov/gene/5350
PRKAG2	7q36.1	NG_007486.1	NC_000007.13 (151253200..151574316, complement)	http://www.ncbi.nlm.nih.gov/gene/51422
PTPN11	12q24	NG_007459.1	NC_000012.11 (112856536..112947717)	http://www.ncbi.nlm.nih.gov/gene/5781
RAF1	3p25	NG_007467.1	NC_000003.11 (12625100..12705700, complement)	http://www.ncbi.nlm.nih.gov/gene/5894
RPS7	2p25	NG_011744.1	NC_000002.11 (3622853..3628509)	http://www.ncbi.nlm.nih.gov/gene/6201

RYR2	1q43	NG_008799.2	NC_000001.10 (237205510..237997288)	http://www.ncbi.nlm.nih.gov/gene/6262
SCN1B	9q13.1	NG_013359.1	NC_000019.9 (35521555..35531353)	http://www.ncbi.nlm.nih.gov/gene/6324
SCN3B	11q23.3	NG_016283.1	NC_000011.9 (123499895..123525315, complement)	http://www.ncbi.nlm.nih.gov/gene/55800
SCN4B	11q23.3	NG_011710.1	NC_000011.9 (118004092..118023630, complement)	http://www.ncbi.nlm.nih.gov/gene/6330
SCN5A	3p21	NG_008934.1	NC_000003.11 (38589553..38691164, complement)	http://www.ncbi.nlm.nih.gov/gene/6331
SGCD	5q33-q34	NG_008693.2	NC_000005.9 (155462147..156194799)	http://www.ncbi.nlm.nih.gov/gene/6444
SLC25A4	4q35	NG_013001.1	NC_000004.11 (186064417..186071538)	http://www.ncbi.nlm.nih.gov/gene/291
SMAD3	15q22.33	NG_011990.1	NC_000015.9 (67358036..67487533)	http://www.ncbi.nlm.nih.gov/gene/4088
SNTA1	20q11.2	NG_011622.1	NC_000020.10 (31995763..32031698, complement)	http://www.ncbi.nlm.nih.gov/gene/6640
SOS1	2p21	NG_007530.1	NC_000002.11 (39208690..39347686, complement)	http://www.ncbi.nlm.nih.gov/gene/6654
STARD3	17q11-q12		NC_000017.10 (37793333..37820454)	http://www.ncbi.nlm.nih.gov/gene/10948
TAZ	Xq28	NG_009634.1	NC_000023.10 (153639877..153650065)	http://www.ncbi.nlm.nih.gov/gene/6901

TBX5	12q24.1	NG_007373.1	NC_000012.11 (114791735..114846247, complement)	http://www.ncbi.nlm.nih.gov/gene/6910
TGFBR1	9q22	NG_007461.1	NC_000009.11 (101867412..101916474)	http://www.ncbi.nlm.nih.gov/gene/7046
TGFBR2	3p22	NG_007490.1	NC_000003.11 (30647994..30735634)	http://www.ncbi.nlm.nih.gov/gene/7048
TMEM43	3p25.1	NG_008975.1	NC_000003.11 (14166440..14185180)	http://www.ncbi.nlm.nih.gov/gene/79188
TNNC1	3p21.1	NG_008963.1	NC_000003.11 (52485107..52488057, complement)	http://www.ncbi.nlm.nih.gov/gene/7134
TNNI3	19q13.4	NG_007866.2	NC_000019.9 (55663135..55669100, complement)	http://www.ncbi.nlm.nih.gov/gene/7137
TNNT2	1q32	NG_007556.1	NC_000001.10 (201328136..201346836, complement)	http://www.ncbi.nlm.nih.gov/gene/7139
TPM1	15q22.1	NG_007557.1	NC_000015.9 (63334838..63364114)	http://www.ncbi.nlm.nih.gov/gene/7168
VCL	10q22.2	NG_008868.1	NC_000010.10 (75757836..75879918)	http://www.ncbi.nlm.nih.gov/gene/7414

Table S2. Silico predictive algorithms used in the study.

Category	Basis	Name	Website	Prediction Threshold
Missense prediction	Evolutionary conservation	FATHMM	http://fathmm.biocompute.org.uk	<-1.5 Damaging >-1.5 Tolerated
		SIFT	http://sift.jcvi.org	<0.05 Deleterious >0.05 Tolerated
Missense prediction	Protein structure/function and evolutionary conservation	Align GVGD	http://agvgd.iarc.fr/agvgd_input.php	\cong C15 Probably Damaging
		Mutation Taster	http://www.mutationtaster.org	Disease causing
		Polyphen-2	http://genetics.bwh.harvard.edu/pph2	\cong 0.432 Possibly Damaging \cong 0.85 Probably Damaging

Missense and insertion/deletions prediction	Alignment and measurement of similarity between variant sequence and protein sequence homolog	PROVEAN	http://provean.jcvi.org/index.php	<-2.5 Deleterious >-2.5 Neutral
Missense and insertion/deletions prediction	Contrasts annotations of fixed/nearly fixed derived alleles in humans with simulated variants	CADD	http://cadd.gs.washington.edu	$\cong 20$ 1% most deleterious $\cong 30$ 0.1% most deleterious

Reference

1. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, Grody WW, Hegde M, Lyon E, Spector E, Voelkerding K, Rehm HL. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the association for molecular autopsy. *Genet Med* 2015; 17:405–423.

Table S3. Frequency of MYH7 and MYBPC3 in LVNC, HCM and DCM patients.

Gene	% Frequency of mutations in LVNC patients in this study (n=102)	% Frequency of mutations in HCM in Japanese cohort* (n=127)	% Frequency of mutations in HCM in French cohort† (n=172)	% Frequency of mutations in HCM in US cohort study‡ (n=389)	% Frequency of mutations in DCM in Finnish cohort study§ (n=145)
MYH7	19.6	24.4	26.2	15.2	0.7
MYBPC3	0.98	15	26.2	18	0

* *Heart Vessels*. (2016). doi:10.1007/s00380-016-0920-0. † *Circulation* 2003; 107: 2227–2232. ‡ *J Am Coll Cardiol* 2004; 44: 1903–1910.

§ *Eur Heart J*. 2015;36(34):2327-2337.

Table S4. Novel mutations, absent in Exome Aggregation Consortium and Human Genetic Variation Database (HGVD).

Gene	variant	Prediction						
		FATHMM	SIFT	Polyphen2	Align	Mutation Taster	Provean	CADD
GVGD								
MYH7	R941C	Damaging	Deleterious	Probably Damaging	C65	Disease causing	Deleterious	34
		Score: -2.13	Score:0	Score:1			Score: -6.13	
	Q315R	Damaging	Deleterious	Possibly Damaging	C0	Disease causing	Deleterious	23.8
		Score: -2.33	Score:0.011	Score:0.51			Score: -3.16	
	F230S	Damaging	Deleterious	Probably Damaging	C0	Disease causing	Deleterious	27.7
		Score: -4.96	Score:0	Score:0.984			Score: -6.07	
	K542N	Damaging	Deleterious	Probably Damaging	C65	Disease causing	Deleterious	31
		Score: -2.47	Score:0	Score:1			Score: -4.4	

A223V	Damaging	Deleterious	Probably Damaging	C0	Disease causing	Deleterious	25.1
	Score: -3.17	Score:0.08	Score:0.854			Score: -2.75	
M362R	Damaging	Deleterious	Benign	C0	Disease causing	Deleterious	26.9
	Score: -3.64	Score:0	Score:0.001			Score: -5.15	
K542T	Damaging	Deleterious	Possibly Damaging	C65	Disease causing	Deleterious	27.4
	Score: -2.48	Score:0	Score:0.517			Score: -4.4	
E667V	Damaging	Tolerated	Probably Damaging	C65	Disease causing	Deleterious	26.1
	Score: --2.46	Score:0.113	Score:0.994			Score: -5.14	
E448K	Damaging	Deleterious	Possibly Damaging	C0	Disease causing	Deleterious	32
	Score: -2.22	Score:0.002	Score:0.798			Score: -2.61	
L693R	Damaging	Deleterious	Probably Damaging	C65	Disease causing	Deleterious	28.3
	Score: -4.85	Score:0	Score:0.997			Score: -5.29	
R712H	Damaging	Deleterious	Probably Damaging	C25	Disease causing	Deleterious	35

		Score: -4.54	Score:0	Score:0.988			Score: -4.35	
	c.896-1 G>A	NA	NA	NA	NA	NA	NA	24.9
TAZ	Q159P	Damaging	Deleterious	Probably Damaging	C0	Disease causing	Deleterious	23.4
		Score: -4.39	Score:0.001	Score:0.993			Score: -5.73	
	M185V	Damaging	Deleterious	Probably Damaging	C0	Disease causing	NA	26.6
		Score: -3.16	Score:0.03	Score:0.932				
	L169F	Damaging	Deleterious	Probably Damaging	C0	Disease causing	Deleterious	31
		Score: -4.78	Score:0.01	Score:0.886			Score: -3.33	
	H176Y	Damaging	Deleterious	Probably Damaging	C0	Disease causing	NA	16.57
		Score: -3.15	Score:0	Score:0.999				
ACTC1	T231R	Damaging	NA	Probably Damaging	C65	Disease causing	Deleterious	24.9
		Score: -4.39		Score:0.908			Score: -2.65	
	Y93H	Damaging	NA	Possibly Damaging	C65	Disease causing	Deleterious	24

		Score: - 3.43		Score:0.531			Score: -3.59	
TPM1	R238Q	Damaging	Deleterious	Probably Damaging	C35	Disease causing	Deleterious	35
		Score: -6.36	Score:0.001	Score:0.999			Score: -3.22	
	D14G	Damaging	Deleterious	Probably Damaging	C0	Disease causing	Deleterious	29.9
		Score: -2.38	Score:0.001	Score:1			Score: -3.21	
MYL2	E88K	Tolerated	Deleterious	Probably Damaging	C15	Disease causing	Deleterious	34
		Score: -1.15	Score:0.017	Score:0.995			Score: -3.62	
TNNC1	E94A	Damaging	Deleterious	Benign	C65	Disease causing	Deleterious	24.2
		Score: -3.74	Score:0	Score:0.012			Score: -5.36	
MYBPC3	G758D	Tolerated	Deleterious	Probably Damaging	C65	Disease causing	Deleterious	32
		Score: -1.64	Score:0.001	Score:0.926			Score: -5.96	
LMNA	A244V	Damaging	Deleterious	Probably Damaging	C65	Disease causing	Deleterious	34
		Score: -2.5	Score:0.001	Score:1			Score: -3.76	

SGCD	N99H*	Damaging	Deleterious	Possibly Damaging	C0	Disease causing	Neutral	23.4
		Score: -3.45	Score:0.05	Score:0.744			Score: -0.69	
BMPR1A	R284L	Damaging	Deleterious	Probably Damaging	C65	Disease causing	Deleterious	35
		Score: -3.32	Score:0	Score:0.988			Score: -6.74	
HCN4	G480S	Damaging	Deleterious	Probably Damaging	C55	Disease causing	Deleterious	25.9
		Score: -7.52	Score:0.024	Score:1			Score: -5.74	
TBX5 [†]	p. Arg279Ter	NA	NA	NA	C25	Disease causing	NA	40

The classification of novel variants is all likely pathogenic except TBX5 p. Arg279Ter. * Two patients have this variant. † Nonsense mutation and classification is pathogenic.

Table S5. Gene collapsing test of rare variants.

Rank	Gene	Frequency		Qualifying	Frequency		Fisher's
		Qualifying	Qualifying	Controls	Qualifying	Exact	
		Cases	Cases (N=102)	Cases	Controls	Test p-value	
					(N=4327)		
1	MYH7	19	0.1862	41	0.0095	1.29 E-17	
2	TAZ	6	0.0588	2	0.0005	3.48 E-9	
3	MYL2	2	0.0196	5	0.0012	0.01	
4	ACTC1	2	0.0196	2	0.0005	0.003	
5	TPM1	2	0.0196	2	0.0005	0.003	
6	SGCD	2	0.0196	5	0.0012	0.01	
7	ANK2	1	0.0098	4	0.0009	0.251	
8	TNNC1	1	0.0098	5	0.0012	0.131	
9	BMPRI1A	1	0.0098	5	0.0012	0.131	
10	KCNE3	1	0.0098	6	0.0014	0.151	
11	TBX5	1	0.0098	7	0.0016	0.170	
12	HCN4	1	0.0098	8	0.0018	0.193	
13	LMNA	1	0.0098	9	0.0021	0.208	
14	KCNH2	1	0.0098	20	0.0046	0.388	
15	MYBPC3	1	0.0098	35	0.0081	0.569	
16	JUP	1	0.0098	37	0.0086	0.589	

Table S6. Specific variants found in subjects with systolic dysfunction versus those without dysfunction

with systolic dysfunction			without systolic dysfunction		
ID	Gene	variant	ID	Gene	variant
132	MYL2	E88K	250	MYH7	E677V
133	ACTC1	Y93H	298	MYH7	R904C
143	MYH7	E1801K	401	HCN4	G480S
153	MYH7	E448K			
159	TAZ	c.109+1G>C			
233	KCNH2	A561T			
247	MYH7	R712H			
260	SGCD	N99H			
309	MYH7	M362R			
312	ACTC1	T231R			
313	TAZ	M185V			
315	MYBPC3	G758D			
321	TNN1C	E94A			
327	TAZ	L169F			
333	MYH7	A223V			
341	ANK2	R321W			
350	TPM1	R238Q			
361	MYH7	c.896-1 G>A			
362	MYH7	F230S			
365	MYL2	P144fs			
377	MYH7	L693R			
378	MYH7	L620P			
386	TBX5	p. Arg279Ter			

390	MYH7	E1914K
391	MYH7	E1801K
392	MYH7	Q315R
415	TAZ	Q159P
427	MYH7	R941C
403	TAZ	G197R
404	MYH7	R23W
405	LMNA	A244V
342	MYH7	P838L
	BMPR1A	R284L
280	MYH7	K542N
	JUP	E146K
274	KCNE3	R99H
	TAZ	H176Y
339	ANK2	W3620R
	MYH7	K542N
234	SGCD	N99H
	TPM1	D14G

Table S7. Details for each subject.

ID	Gene	variant	Sex (1M 2F)	age on set	Heart failure	family history (0 no)	LVEF%	LVDD-Z SCORE	Arrhythmia (0 normal)	Prognosis (0: alive)
132	MYL2	E88K	1	0.083	1	father DCM	39	1.2	0	0
133	ACTC1	Y93H	2	0	1	Mother LVNC	36	1.88	0	0
143	MYH7	E1801K	1	0	1	0	42	1	0	0
153	MYH7	E448K	2	0.083	0	Sister LVNC	46	0.795	0	0
159	TAZ	c.109+1G>C	1	0.167	1	Mother LVNC	20	2.888	0	death
233	KCNH2	A561T	1	0	1	0	31	1.1116	non-specific change	death
247	MYH7	R712H	2	0	1	0	36	-0.244	0	Heart transplantation

250	MYH7	E677V	1	0.04	1	0	60	1.6326	0	0
260	SGCD	N99H	1	0.083	0	0	45	1.5	0	0
298	MYH7	R904C	2	6	0	0	65	2.1	0	0
309	MYH7	M362R	2	0.01	0	Father and brother LVNC	39	1.08	0	0
312	ACTC1	T231R	1	4	1	0	49.4	1.8727	Supraventricular tachycardia	ICD
313	TAZ	M185V	1	0.083	1	Mother LVNC	40	3.3333	0	Heart transplantation
315	MYBPC3	G758D	2	3	0	0	38.5	1.25	0	0
321	TNN1C	E94A	2	0.333	0	0	32.5	2.22	0	Heart transplantation
327	TAZ	L169F	1	0	1	brother LVNC	22	2.566	0	0

333	MYH7	A223V	1	0	1	0	10	-0.4	0	0
339	MYH7	K542N	2	0	1	0	48	1	non-specific change	0
341	ANK2	R321W	2	0.083	1	0	46.8	1.9166	non-specific change	0
350	TPM1	R238Q	2	0	1	0	38.4	1.33	0	0
361	MYH7	c.896-1 G>A	2	0	1	0	38	0.977	0	0
362	MYH7	F230S	2	0.0833	0	0	40	-0.823	0	0
365	MYL2	P144fs	2	0.0416	1	0	34	1.7391	0	0
377	MYH7	L693R	2	0.0833	1	0	30	1.3333	0	0
378	MYH7	L620P	2	0	1	Sister LVNC	20	0.1	AF	0
386	TBX5	p. Arg279Ter	1	0	1	0	31	1.88	non-specific change	0
390	MYH7	E1914K	1	0	0	0	43.5	3.3833	0	0
391	MYH7	E1801K	2	0.8333	1	0	38	2.6785	0	0

392	MYH7	Q315R	1	0.0833	1	0	29	2.1428	T wave	0
415	TAZ	Q159P	1	0.8333	1	Sister LVNC	14	2.4	0	0
427	MYH7	R941C	2	1.5	0	father DCM	44.1	1.3709	0	0
401	HCN4	G480S	2	0.0166	1	Mother LVNC	59.4	-0.833	0	0
403	TAZ	G197R	1	0.25	1	0	6	4.4523	0	0
404	MYH7	R23W	2	0.08333	0	0	48.9	0.0408	0	0
405	LMNA	A244V	2	0.08333	1	Sister LVNC	34	1.89	0	0
342	MYH7	P838L	2	0	1	0	38	1.72	ventricular fibrillation	death
342	BMPR1A	R284L								
280	MYH7	K542N	1	0	1	0	40	2.16	0	death
280	JUP	E146K								
274	KCNE3	R99H	1	0.005	1	0	45	2.03	left bundle branch	death

274	TAZ	H176Y							block	
234	SGCD	N99H	1	0	1	0	27	3.3095	0	death
234	TPM1	D14G								