



Fig. S1. Color ultrasound results of Patient 1. The patient had enlargement of heart.

Supplementary Table 1. The arrhythmia-related genes list.

<i>ABCC9</i>	<i>CACNA2D1</i>	<i>CMYA5</i>	<i>EYA4</i>	<i>HCN4</i>	<i>KCNJ8</i>	<i>MYL3</i>	<i>NOS1AP</i>	<i>PPP3R1</i>	<i>SLMAP</i>	<i>TNNI3</i>
<i>ABRA</i>	<i>CACNB2</i>	<i>COL3A1</i>	<i>FBN1</i>	<i>HDAC1</i>	<i>KCNQ1</i>	<i>MYL5</i>	<i>NOTCH1</i>	<i>PRKAG2</i>	<i>SMAD3</i>	<i>TNNT1</i>
<i>ACADVL</i>	<i>CACNB2B</i>	<i>COL5A1</i>	<i>FBN2</i>	<i>HDAC2</i>	<i>KRAS</i>	<i>MYL7</i>	<i>NPPA</i>	<i>PRKCE</i>	<i>SMYD1</i>	<i>TNNT2</i>
<i>ACTA1</i>	<i>CALM1</i>	<i>COL5A2</i>	<i>FBXL22</i>	<i>HEY2</i>	<i>LAMA4</i>	<i>MYLK</i>	<i>NRAP</i>	<i>PTPN11</i>	<i>SMYD2</i>	<i>TPM1</i>
<i>ACTA2</i>	<i>CALM2</i>	<i>COX15</i>	<i>FERMT2</i>	<i>HRAS</i>	<i>LAMP2</i>	<i>MYLK2</i>	<i>NRAS</i>	<i>RAF1</i>	<i>SNTA1</i>	<i>TPM2</i>
<i>ACTC1</i>	<i>CAML3</i>	<i>CRELD1</i>	<i>FHL1</i>	<i>ILK</i>	<i>LBD3</i>	<i>MYLK3</i>	<i>NRG1</i>	<i>RANGRF</i>	<i>SOS1</i>	<i>TPM3</i>
<i>ACTN1</i>	<i>CALR3</i>	<i>CRYAB</i>	<i>FHL2</i>	<i>ITGB1BP2</i>	<i>LEFTY2</i>	<i>MYO6</i>	<i>OBSCN</i>	<i>RBM20</i>	<i>SYNE1</i>	<i>TRDN</i>
<i>ACTN2</i>	<i>CAPN1</i>	<i>CSRP3</i>	<i>FKRP</i>	<i>JAG1</i>	<i>LIMS1</i>	<i>MYOM1</i>	<i>OBSL1</i>	<i>RYR1</i>	<i>SYNE2</i>	<i>TRIM54</i>
<i>ACVR2B</i>	<i>CAPN2</i>	<i>CTNNA3</i>	<i>FKTN</i>	<i>JPH2</i>	<i>LIMS2</i>	<i>MYOM2</i>	<i>PAK1</i>	<i>RYR2</i>	<i>SYNM</i>	<i>TRIM55</i>
<i>AKAP13</i>	<i>CAPN3</i>	<i>DES</i>	<i>FLNC</i>	<i>JUP</i>	<i>LMCD1</i>	<i>MYOT</i>	<i>PALLD</i>	<i>SCN1B</i>	<i>TAZ</i>	<i>TRIM63</i>
<i>AKAP9</i>	<i>CAPNS1</i>	<i>DICER1</i>	<i>FOXH1</i>	<i>KBTBD13</i>	<i>LMNA</i>	<i>MYOZ1</i>	<i>PARVB</i>	<i>SCN2B</i>	<i>TBX20</i>	<i>TRPM4</i>
<i>ALMS1</i>	<i>CAPZA1</i>	<i>DMD</i>	<i>GAA</i>	<i>KCNA5</i>	<i>MAP2K1</i>	<i>MYOZ2</i>	<i>PDE5A</i>	<i>SCN3B</i>	<i>TBX5</i>	<i>TTN</i>
<i>ANK2</i>	<i>CAPZA2</i>	<i>DNAJB6</i>	<i>GATA4</i>	<i>KCND3</i>	<i>MAP2K2</i>	<i>MYOZ3</i>	<i>PDLIM1</i>	<i>SCN4B</i>	<i>TCAP</i>	<i>TTR</i>
<i>ANKRD1</i>	<i>CAPZB</i>	<i>DNM1L</i>	<i>GATD1</i>	<i>KCNE1</i>	<i>MIB1</i>	<i>MYPN</i>	<i>PDLIM3</i>	<i>SCN5A</i>	<i>TGFB2</i>	<i>TXNRD2</i>
<i>ANKRD2</i>	<i>CASQ2</i>	<i>DPP6</i>	<i>GDF1</i>	<i>KCNE2</i>	<i>MIR208</i>	<i>MYZAP</i>	<i>PDLIM5</i>	<i>SCN10A</i>	<i>TGFB3</i>	<i>UNC45B</i>
<i>ATP2A2</i>	<i>CAV3</i>	<i>DSC2</i>	<i>GJA1</i>	<i>KCNE3</i>	<i>MYBPC3</i>	<i>NEB</i>	<i>PDLIM7</i>	<i>SDHA</i>	<i>TGFBRI</i>	<i>VCL</i>

<i>BAG3</i>	<i>CBL</i>	<i>DSG2</i>	<i>GJA5</i>	<i>KCNE5</i>	<i>MYH11</i>	<i>NEBL</i>	<i>PKP2</i>	<i>SGCD</i>	<i>TGFBR2</i>	<i>XIRP1</i>
<i>BCAR1</i>	<i>CBS</i>	<i>DSP</i>	<i>GJC1</i>	<i>KCNH2</i>	<i>MYH6</i>	<i>NEURL2</i>	<i>PLN</i>	<i>SHOC2</i>	<i>TMEM43</i>	<i>XIRP2</i>
<i>BMP10</i>	<i>CFC1</i>	<i>DTNA</i>	<i>GLA</i>	<i>KCNJ2</i>	<i>MYH7</i>	<i>NEXN</i>	<i>POLR2M</i>	<i>SLC25A4</i>	<i>TMOD1</i>	<i>ZIC3</i>
<i>BRAF</i>	<i>CFL2</i>	<i>ELN</i>	<i>GLRX3</i>	<i>KCNJ5</i>	<i>MYH7B</i>	<i>NKX2-5</i>	<i>PPP3B</i>	<i>SLC2A10</i>	<i>TMPO</i>	
<i>CACNA1C</i>	<i>CHRM2</i>	<i>EMD</i>	<i>GPD1L</i>	<i>KCNJ5</i>	<i>MYL2</i>	<i>NODAL</i>	<i>PPP3CA</i>	<i>SLC8A1</i>	<i>TNNC1</i>	

Supplementary Table 2. Primers and sequences of Sanger sequencing.

Primer	Sequences	Primer	Sequences
RYR2 f	GCACTACACGCAGTCAGAAA	RYR2 r	TCAGGACGCTCTCTGCTAAT
KCNE1 f	GATCCTGTCTAACACCACAGC	KCNE1 r	CATAGGCCTTGTCTTCTCTTG
KCNQ1 f	TGGGACTCGCTGCCTTA	KCNQ1 r	CCTGGAAGTTTCCGACTTACC
KCNH2 f	AGTGACAGCCATGGACAAC	KCNH2 r	GCCTGGCAGCAGAAGAA
TRPM4 f	GGCAGTCTTCCTGTCTTTCTT	TRPM4 r	AAGTTGACCAGCAGGATGTT

Supplementary Table 3. The ultrasound scan data of Patient 1.

LVEDd	58 mm	LAS	39 mm	RVD	36 mm	RAS	43 mm
IVsd	8 mm	LVPWd	7 mm	AO	23 mm	PA	22 mm
AOV	150 cm/s	PAV	57 cm/s	E/A	Unimodality	EF	37%
FS	18%						

LVEDd, left ventricular end-diastolic dimension; LAD, left atrial diameter; RVD, right ventricular diameter; RAD, right atrial diameter; IVsd, interventricular septal defect; LVPWd, left ventricular posterior wall thickness; AO, aortic diameter; PA, pulmonary artery diameter; AOV, aortic velocity; PAV, pulmonary artery velocity; E/A, E peak/A peak; EF, ejection fraction; FS, fractional shortening.

Supplementary Table 4. The target sequencing results of 6 subjects in this study.

Patient	Gene	Mutation	Mutation Taster	PolyPhen-2	SIFT	1000G	ExAC	gnomAD	OMIM clinical phenotype	ACMG classification
1	<i>RYR2</i>	c.12269C>T, p.P4090L	D	D	D	-	-	-	AD, Arrhythmogenic right ventricular dysplasia 2; AD, Ventricular tachycardia, catecholaminergic polymorphic, 1	PS2, PM1, PM2, PP3
	<i>SYNE1</i>	c.18727G>C, p.E6243Q	D	D	D	0.00020	0.00001	0.00006	AR, Arthrogryposis multiplex congenita, myogenic type; AD, Emery-Dreifuss muscular dystrophy 4;	PP3, BS4, BP5
	<i>SYNE1</i>	c.5666A>C, p.Q1889P	D	P	T	-	0.00004	0.00002	AR, Spinocerebellar ataxia	BP4 BP5
	<i>COL5A1</i>	c.5335A>G, p.N1779D	D	B	D	-	0.00014	0.00006	AD, Ehlers-Danlos syndrome, classic type, 1	BS4, BP5
	<i>CTNNA3</i>	c.1853A>G, p.H618R	D	D	T	0.00020	0.00002	0.00003	AD, Arrhythmogenic right ventricular dysplasia, familial, 13	PS2, BP5
	<i>CAPN1</i>	c.169C>T, p.R57C	D	D	T	-	0.00005	0.00002	AR, Spastic paraplegia 76	BS4, BP5
	<i>FERMT2</i>	c.1538C>T, p.T513M	D	P	T	0.00200	0.00246	0.00201	-	BP4, BP5
<i>UNC45B</i>	c.1816G>A, p.E606K	D	D	D	0.00020	0.00001	0.00003	AD, Cataract 43	PP3, BS4, BP5	
2	<i>SLC8A1</i>	c.959A>G, p.E320G	D	D	D	-	-	-	-	PS2, PM2, PP3, BP5
	<i>XIRP2</i>	c.1985C>T, p.P662L	D	D	D	-	-	-	-	PM2, PP3, BS4, BP5
	<i>TTN</i>	c.82688G>A, p.R27563H	D	B	T	0.00060	0.00020	0.00022	AD, Cardiomyopathy, dilated, 1G; AD, Cardiomyopathy, familial hypertrophic, 9; AR, Muscular dystrophy, limb-girdle; AD, Myopathy, myofibrillar, 9, with early respiratory failure; AR, Salih myopathy; AD, Tibial muscular dystrophy, tardive	BS4, BP4, BP5
	<i>OBSL1</i>	c.3680G>A, p.R1227H	D	D	T	-	0.00005	0.00003	AR, 3-M syndrome 2	BS4, BP5
	<i>TNNC1</i>	c.304C>G,	D	B	D	-	-	-	AD, Cardiomyopathy, dilated, 1Z; AD,	PM2, BS4,

	<i>CMYA5</i>	p.R102G c.10000G>A, p.Q3334K	D	B	D	-	-	-	Cardiomyopathy, hypertrophic, 13	BP5 PS2, PM2, BP5
	<i>MYH6</i>	c.2717G>A, p.R906H	D	D	D	0.00020	0.00000	0.00001	AD, Atrial septal defect 3; AD, Cardiomyopathy, dilated, 1EE; AD, Cardiomyopathy, hypertrophic, 14	PP3, BS4, BP5
	<i>FBN1</i>	c.79G>A, p.A27T	D	B	D	0.00120	0.00044	0.00041	AD, Acromicric dysplasia; AD, Ectopia lentis, familial; AD, Geleophysic dysplasia 2; AD, Marfan lipodystrophy syndrome; AD, Marfan syndrome; AD, MASS syndrome; AD, Stiff skin syndrome; AD, Weill-Marchesani syndrome 2	BS4, BP5
	<i>KCNE1</i>	c.169T>C, p.F57L	D	D	T	-	-	-	AD, Long QT syndrome 5; AR, Jervell and Lange- Nielsen syndrome 2	PM1, PM2, PP1, PP3
	<i>OBSCN</i>	c.3140C>T, p.A1047V	D	D	T	0.00180	0.00025	0.00013	-	PM6, BP5
	<i>FHL2</i>	c.62T>G, p.L21R	D	D	T	-	0.00001	0.00002	-	PM6, BP5
	<i>FBN2</i>	c.8674G>T, p.D2892Y	D	B	D	0.00060	0.00040	0.00043	AD, Contractural arachnodactyly, congenital; AD, Macular degeneration, early-onset	PM6, BP5
	<i>FBN2</i>	c.3626A>G, p.N1209S	D	B	T	0.00020	0.00003	0.00006		BP4, PM6, BP5
3	<i>RBM20</i>	c.1922G>A, p.R641Q	D	D	D	0.00100	0.00012	0.00022	AD, Cardiomyopathy, dilated, 1DD	PM6, PP3, BP5
	<i>KCNQ1</i>	c.853A>C, p.K285Q	D	D	D	-	-	-	AD, Atrial fibrillation, familial, 3; AD, Long QT syndrome 1; AD, Short QT syndrome 2; AR, Jervell and Lange-Nielsen syndrome	PM1, PM2, PP3
	<i>RYR1</i>	c.13089C>A, p.F4363L	D	B	T	-	0.00010	0.00003	AD, Malignant hyperthermia susceptibility 1; AD/AR, Central core disease; AD, King- Denborough syndrome; AR, Minicore myopathy with external ophthalmoplegia; AD/AR, Neuromuscular disease, congenital, with uniform type 1 fiber	PM6, BP4, BP5
4	<i>OBSL1</i>	c.4610-1G>C	D	-	-	-	-	-	AR, 3-M syndrome 2	PM2, PP3, BS4, BP5

<i>KCNH2</i>	c.793T>C, p.C265R	D	P	D	-	-	-	AD, Long QT syndrome 2; AD, Short QT syndrome 1	PS2, PM2, PP2
<i>TMOD1</i>	c.1028G>T, p.R343M	D	D	D	-	-	-	-	PM2, PP3, BS4, BP5
<i>MYH7B</i>	c.649A>G, p.I217V	D	B	D	-	-	-	-	PS2, PM2, BP5
<i>NEB</i>	c.24862A>G, p.I8288V	D	D	D	0.00080	0.00024	0.00026	AR, Nemaline myopathy 2	PM6, PP3, BS4, BP5
<i>TTN</i>	c.62723G>A, p.R20908Q	D	D	T	0.00020	0.00008	0.00003	AD, Cardiomyopathy, dilated, 1G; AD, Cardiomyopathy, familial hypertrophic, 9; AR, Muscular dystrophy, limb-girdle; AD, Myopathy, myofibrillar, 9, with early respiratory failure; AR, Salih myopathy; AD, Tibial muscular dystrophy, tardive	PM6, BP5
<i>TTN</i>	c.60928C>T, p.R20310C	D	D	D	0.00020	0.00008	0.00003	AD, Testicular anomalies with or without congenital heart disease; AD, Atrial septal defect 2; AD, Atrioventricular septal defect 4; AD, Tetralogy of Fallot; AD, Ventricular septal defect 1	PM6, PP3, BP5
<i>GATA4</i>	c.1075G>A, p.E359K	D	D	T	-	0.00005	0.00004	AD, Emery-Dreifuss muscular dystrophy 5	PS1, PM6, BP5
<i>SYNE2</i>	c.10556A>G, p.E3519G	D	D	T	-	0.00003	0.00013	AD, Erythrokeratoderma variabilis et progressiva	PM6, BP5
<i>TRPM4</i>	c.2985_3012del, p.E996Gfs*118	D	-	-	-	0.00021	0.00016	AD, Progressive familial heart block, type IB	PVS1, PM4, PPI1, PP3

5

Red words, mutations identified in this study; D, disease causing; T, tolerated; P, polymorphism; B, benign; AR, autosomal recessive; AD, autosomal dominant.