

Supplementary Material

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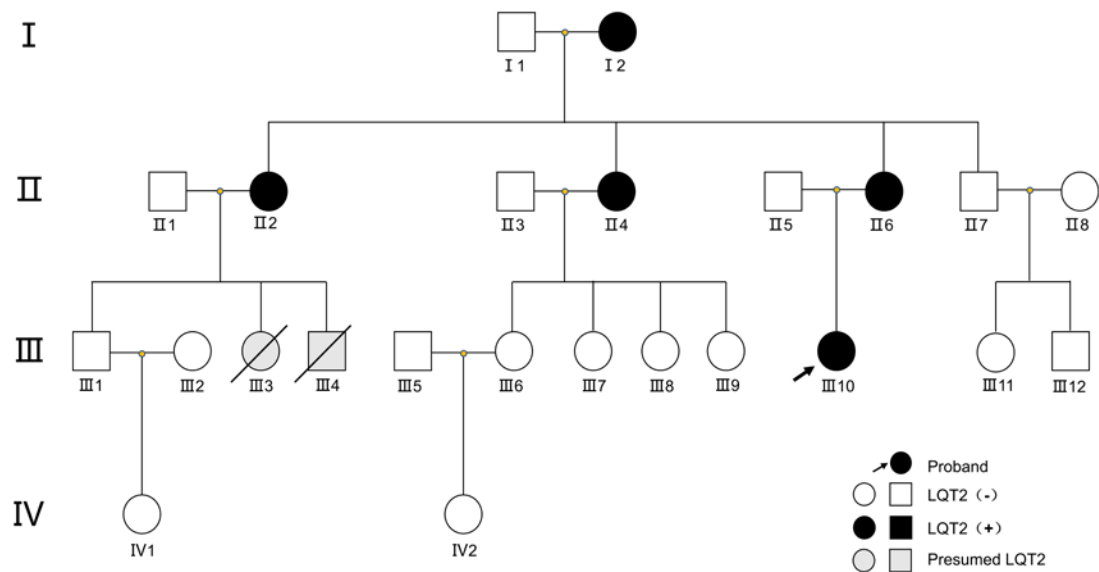
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Supplementary Figure 1: Pedigree chart

Note: Pedigree of a family with long QT syndrome type 2 (LQT2). I, II, III, IV denote four generations (I: grandparents, II: parents, III: children, IV: grandchildren).

Supplementary Table 1: Pedigree screening

Family Member	Sex	Age at Diagnosis	Schwartz Score	QTc Interval	Cardiac Events
I2	Female	81 years	5.5	500ms	None
II2	Female	52 years	5.5	554ms	None
II4	Female	47 years	5.5	556ms	None
II6	Female	42 years	5.5	583ms	None
III3	Female	17 years*	/	Presumed LQT2	Sudden Death
III4	Male	17 years*	/	Presumed LQT2	Sudden Death
III10	Female	18 years	7.5	592ms	Syncope / Malignant Arrhythmia

Note: * Indicates sudden death at 17 years old, with no relevant assessment performed, presumed to be LQT2.

Supplementary Table 2: Action potential characteristics of iPSC-CMs

	Father iPSC-CMs (n = 15)	Proband iPSC-CMs (n = 15)	Mother iPSC-CMs (n = 15)
0.5-Hz			
APA (mV)	100.99 ± 1.42	101.65 ± 1.16	99.16 ± 1.41
RMP (mV)	-55.56 ± 0.82	-55.30 ± 0.88	-55.97 ± 1.09
APD ₉₀ (ms)	306.89 ± 5.96	746.15 ± 26.28 ^{ac}	485.70 ± 9.38 ^b
APD ₅₀ (ms)	258.13 ± 5.00	637.83 ± 23.31 ^{ac}	398.48 ± 9.96 ^b
1-Hz			
APA (mV)	103.44 ± 5.97	102.74 ± 1.89	101.07 ± 1.49
RMP (mV)	-55.34 ± 0.85	-56.29 ± 0.93	-54.39 ± 1.62
APD ₉₀ (ms)	247.25 ± 6.02	592.35 ± 10.76 ^{ac}	452.21 ± 7.05 ^b
APD ₅₀ (ms)	209.73 ± 5.41	484.86 ± 9.86 ^{ac}	376.09 ± 4.21 ^b

Note: APA: Action potential amplitude; RMP: Resting membrane potential; APD₉₀: Action potential duration at 90% repolarization; APD₅₀: Action potential duration at 50% repolarization. a indicates $P < 0.05$ for proband iPSC-CMs compared with father iPSC-CMs; b indicates $P < 0.05$ for mother iPSC-CMs compared with father iPSC-CMs; c indicates $P < 0.05$ for proband iPSC-CMs compared with mother iPSC-CMs.

Supplementary Table 3: Calcium transient characteristics of iPSC-CMs

	Father iPSC-CMs (<i>n</i> = 15)	Proband iPSC-CMs (<i>n</i> = 15)	Mother iPSC-CMs (<i>n</i> = 15)
Amplitude ($\Delta F/F_0$)	0.66 ± 0.04	0.85 ± 0.04 ^{ac}	0.67 ± 0.02
Upstroke time (ms)	228.66 ± 17.63	469.72 ± 11.13 ^{ac}	284.63 ± 9.56 ^b
CaTD ₉₀ (ms)	688.00 ± 27.44	1072.40 ± 23.81 ^{ac}	909.16 ± 25.55 ^b
CaTD ₅₀ (ms)	239.67 ± 18.37	579.06 ± 15.93 ^{ac}	531.09 ± 8.24 ^b

Note: CaT: Calcium transients; CaTD₉₀: Calcium transient duration at 90% decay; CaTD₅₀: Calcium transient duration at 50% decay. a indicates $P < 0.05$ for proband iPSC-CMs compared with father iPSC-CMs; b indicates $P < 0.05$ for mother iPSC-CMs compared with father iPSC-CMs; c indicates $P < 0.05$ for proband iPSC-CMs compared with mother iPSC-CMs.

Supplementary Table 4: Field potential characteristics of iPSC-CMs

	Father iPSC-CMs (<i>n</i> = 15)	Proband iPSC-CMs (<i>n</i> = 15)	Mother iPSC-CMs (<i>n</i> = 15)
FPD (ms)	277.15 ± 5.20	830.60 ± 21.21 ^{ac}	618.85 ± 7.80 ^b
BR (bpm)	27.17 ± 0.83	24.70 ± 1.06	26.86 ± 0.89
AMP (μV)	281.73 ± 18.37	268.33 ± 15.19	266.73 ± 15.17
cFPD	92.66 ± 2.24	286.72 ± 8.09 ^{ac}	207.42 ± 3.64 ^b
EADs/TAs (%)	0	46.7(7/15) ^{ac}	6.7(1/15)

Note: FPD: Field potential duration; BR: Beats rate; AMP: Amplitude; cFPD: Corrected field potential duration; EADs: Early afterdepolarizations; TAs: Triggered arrhythmias. a indicates $P < 0.05$ for proband iPSC-CMs compared with father iPSC-CMs; b indicates $P < 0.05$ for mother iPSC-CMs compared with father iPSC-CMs; c indicates $P < 0.05$ for proband iPSC-CMs compared with mother iPSC-CMs.

Supplementary Table 5: Incidence of EADs/TAs

Arrhythmia Susceptibility	Father iPSC-CMs (<i>n</i> = 15)	Proband iPSC-CMs (<i>n</i> = 15)	Mother iPSC-CMs (<i>n</i> = 15)
0.5-Hz pacing rhythm	0/15	7/15	2/15
EADs (%)	0	46.7 ^a	13.3
1-Hz pacing rhythm	0/15	3/15	0/15
EADs (%)	0	20.0	0
Spontaneous rhythm	0/15	7/15	1/15
EADs (%)	0	46.7 ^{ac}	6.7
Spontaneous rhythm	0/15	3/15	0/15
“VT”-like TAs (%)	0	20.0	0

Note: EADs: Early afterdepolarizations; VT: Ventricular tachycardia; TAs: Triggered arrhythmias.

a indicates $P < 0.05$ for proband iPSC-CMs compared with father iPSC-CMs; b indicates $P < 0.05$

for mother iPSC-CMs compared with father iPSC-CMs; c indicates $P < 0.05$ for proband iPSC-CMs

compared with mother iPSC-CMs.