

## SUPPLEMENTAL MATERIAL

### Supplemental Tables

**Supplemental Table 1.** Selected polymorphisms

Gene	rs number	References	Minor allele frequency in European (1000Genomes)	Minor allele frequency in East Asian (1000Genomes)	Minor allele frequency in European (Hapmap)	Minor allele frequency in Japanese (Hapmap)
<i>ADRA2C</i>	rs61767072	1	-	-	-	-
<i>ADRB1</i>	rs1801252	2	0.216	0.273	-	0
<i>ADRB1</i>	rs1801253	1, 2	0.227	0.168	0.308	0.151
<i>ADRB2</i>	rs28365031	3	-	-	-	-
<i>ATP1B1</i>	rs10919071	4, 5	0.125	0.023	0.129	-
<i>KCNE1</i>	rs1805128	5-9	0.009	0.003	0.023	0.011
<i>KCNH2</i>	rs1805123	5, 7, 9-12	0.177	0.031	0.239	0.035
<i>KCNH2</i>	rs3778873	4	0.170	0.302	0.162	0.284
<i>KCNH2</i>	rs3807375	4, 9, 12, 13	0.359	0.762	0.376	0.805
<i>KCNH2</i>	rs3815459	4, 11, 14	0.223	0.736	-	0.807
<i>KCNJ2</i>	rs17779747	4	0.340	0.077	0.310	0.088
<i>KCNQ1</i>	rs12296050	4, 13	0.244	0.374	0.186	0.372
<i>KCNQ1</i>	rs2074238	5, 6	0.065	0.033	0.065	0.045
<i>KCNQ1</i>	rs757092	11, 14	0.405	0.369	0.346	0.367
<i>NOS1AP</i>	rs10494366	4, 9, 13, 15-22	0.361	0.647	0.350	0.686
<i>NOS1AP</i>	rs12029454	6, 13	0.177	0.358	0.146	0.367
<i>NOS1AP</i>	rs12143842	4-6, 13, 18, 23, 24	0.244	0.318	0.188	0.363
<i>NOS1AP</i>	rs16857031	6	0.119	0.205	0.141	0.136
<i>NOS1AP</i>	rs4657139	9, 15, 16, 19, 25	0.344	0.696	0.292	0.750
<i>NOS1AP</i>	rs4657178	4	0.284	0.517	0.257	0.500
<i>CNOT3</i>	rs36643	26	0.380	0.220	0.350	0.181
<i>PLN</i>	rs11970286	4	0.460	0.217	0.491	0.155
<i>PLN</i>	rs12210810	4, 5	0.049	0.000	0.081	0
<i>SCN5A</i>	rs12053903	5, 6	0.372	0.556	0.301	0.522
<i>SCN5A</i>	rs1805124	7, 9, 27	0.183	0.103	0.179	0.129

Minor alleles were defined according to alleles frequencies in Europeans.

**Supplemental Table 2.** Methods and primers used for genotyping

**A. FRET**

<b>Gene</b>	<b>rs number</b>	<b>Forward primer</b>	<b>Reverse primer</b>	<b>Anchor probe (Red640)</b>	<b>Sensor probe</b>
<i>KCNH2</i>	rs1805123	CCCGGCAGTACGGAGTTA	AAGGTCTGAGGCCTGGGTA	CGCCTGCGGAAGGACAACCTTGC	GCCTCACCCGTGTCCGT
<i>NOS1AP</i>	rs12029454*	TATTTATTCATTTAAACACGGGGTG	GTATTGGCTCAAAAAGGGAAGT	GACAGTTCTAATCATTCCATCACACGCT	TTGATTGTTTCCTTTGACTGAGA

SNP allelic variants are bolded

\* in the discovery cohort

**B. HRM with an unlabeled probe**

<b>Gene</b>	<b>rs number</b>	<b>Forward primer</b>	<b>Reverse primer</b>	<b>Probe</b>
<i>KCNQ1</i>	rs12296050	GTGCTTAGACTGTGCCCG	GGGAGACCCTGTCTCGAA	CTCCTGGGCTCCTAACCTTTCACAG-3'P
<i>SCN5A</i>	rs12053903	GGTCCTCAAACCACACTTTGAATA	CCATCTTCTACATCTTGGGTTCTC	GCTGGGTGGGCAAGATACTAAGCAG-3'P

SNP allelic variants are bolded

**C. Sequencing**

<b>Gene</b>	<b>rs number</b>	<b>Forward primer</b>	<b>Reverse primer</b>
<i>ADRA2C</i>	rs61767072	AGCCGGACGAGAGCAGCGCA	AGGCCTCGCGGCAGATGCCGTACA
<i>ADRB2</i>	rs28365031	AACGGACACTCGAAGTCCAC	GCTGAAGAAGAAGGGGAACC

**D. Taqman**

<b>Gene</b>	<b>rs number</b>	<b>Applied Biosystems Taqman Assay</b>
<i>ADRB1</i>	rs1801252	C__8898508_10
<i>ADRB1</i>	rs1801253	C__8898494_10
<i>ATP1B1</i>	rs10919071	C__1264222_10
<i>KCNH2</i>	rs3815459	C__3219498_10

Gene	rs number	Applied Biosystems Taqman Assay
<i>KCNQ1</i>	rs2074238 <sup>†</sup>	C__15862454_10
<i>KCNQ1</i>	rs757092	C__2990605_10
<i>NOS1AP</i>	rs4657139	C__1777005_10
<i>NOS1AP</i>	rs4657178	C__133678_10
<i>NOS1AP</i>	rs12029454 <sup>‡</sup>	C__31087211_10
<i>SCN5A</i>	rs1805124	C__11987864_10

<sup>†</sup> in the discovery and the replication populations

<sup>‡</sup> in the replication populations

#### E. T<sub>m</sub> shift primers

Gene	rs number	Allele-specific primers		Common primer
<i>KCNE1</i>	rs1805128	<u>GCGGGCAGGGCGGGC</u> TCCTTCTCTTGCCAGGCcTC	<u>GCGGGCGTCCTTCTCTTGCCAGGCcTT</u>	CTGAGCTACATCCGCTCCAAGAA
<i>KCNH2</i>	rs3778873	<u>GCGGGCAGGGCGGGC</u> CACCTAATCCAACCCATcCG	<u>GCGGGCCACCTAATCCAACCCATcCC</u>	ACTGGTCATCAGACCTCTGCTTCT
<i>KCNH2</i>	rs3807375	<u>GCGGGCAGGGCGGGC</u> TAGAGAACTTCTGCGTTTAAaAG	<u>GCGGGCTAGAGAACTTCTGCGTTTAAaAA</u>	CTCTATACTGGGAGGGGGCAATG
<i>KCNJ2</i>	rs17779747	<u>GCGGGCAGGGCGGGC</u> CAAAGACAGAATTCTGGCcAC	<u>GCGGGCCAAAGACAGAATTCTGGCcAA</u>	CACTCACAGTTCCAGGATTTCTT
<i>NOS1AP</i>	rs10494366	<u>GCGGGCAGGGCGGGC</u> ATATTTATGGGAGGTATGCgGG	<u>GCGGGCATATTTATGGGAGGTATGCgGT</u>	GAGATGTGTCTAGATAGAGACCAGTA
<i>NOS1AP</i>	rs12143842	<u>GCGGGCAGGGCGGGC</u> CCAGGGTCACATCCCAGcTC	<u>GCGGGCCAGGGTCACATCCCAGcTT</u>	TGGGAACAGAGTCAGGAGACAGC
<i>NOS1AP</i>	rs16857031	<u>GCGGGCAGGGCGGGC</u> CTAACTATGACACTGCTCAtAG	<u>GCGGGCCTAACTATGACACTGCTCAtAC</u>	GCAAATGTGACAGGGTGTTTACC
<i>CNOT3</i>	rs36643	<u>GCGGGCAGGGCGGGC</u> AGAGGAGAATGACTGTaCC	<u>GCGGGCAGAGGAGAATGACTGTaCT</u>	CGTGCATAGCAGAATTGGTTGG
<i>PLN</i>	rs11970286	<u>GCGGGCAGGGCGGGC</u> CCAAAGGCATGAGAACTcGC	<u>GCGGGCCAAAGGCATGAGAACTcGT</u>	GGCTCATAACCCCTCACCTACCTT
<i>PLN</i>	rs12210810	<u>GCGGGCAGGGCGGGC</u> CACTGTCCTGTGTTACACAAaAG	<u>GCGGGCCACTGTCCTGTGTTACACAAaAC</u>	CTGACATCAGTCTTATTCTGATTACA

The GC-rich tails are underlined

SNP allelic variants are bolded

Mismatched nucleotides are in lowercase

**Supplemental Table 3.** Sequencing primers used for validating other genotyping methods

<b>Gene</b>	<b>rs number</b>	<b>Forward primer</b>	<b>Reverse primer</b>
<i>ADRB1</i>	rs1801252	CCGGGCTTCTGGGGTGTTC	GGCGAGGTGATGGCGAGGTAGC
<i>ADRB1</i>	rs1801253	TTCAACCCCATCATCTACTGC	GGCCCTACACCTTGGATTC
<i>ATP1B1</i>	rs10919071	TGCTTTCAAGTATAAGTCTCAGTG	GGAGAACTGACATCAGTCTTATT
<i>KCNE1</i>	rs1805128	G TTCAGCAGGGTGGCAACAT	GCCAGATGGTTTTCAACGACA
<i>KCNH2</i>	rs1805123	CTGGGGCAAATCACATTG	AAGGGATGGGAAGGTCTGAG
<i>KCNH2</i>	rs3778873	GAGGAGTTATTGTGGGATCACCTA	GACAAGTTTGAACCTGGGCTG
<i>KCNH2</i>	rs3807375	CTATACTGGGAGGGGGCAAT	AGAGTTTGATGGTGGCCTTG
<i>KCNH2</i>	rs3815459	GGGCTAGGAATGGAAGAAGG	CTCACCCAGCTCTGCTCTCT
<i>KCNJ2</i>	rs17779747	CACCTCACAGTTCAGGATTTCTT	CACAGGCATTCACTGCAGAT
<i>KCNQ1</i>	rs12296050	GTGCTTAGACTGTGCCCG	GGGAGACCCTGTCTCGAA
<i>KCNQ1</i>	rs2074238	CTCAAGGAGCCTGGTACAGC	GCAATGTCTTGTGAGGAGCA
<i>KCNQ1</i>	rs757092	CACAGGGACACACCCATGTA	GTTCTGCTACCGAGGCTGTC
<i>NOS1AP</i>	rs10494366	GGTGAGGTCACTCTCTGAAC	CACCCAGAGAGATGTGTCCTA
<i>NOS1AP</i>	rs12029454	TATTTATTCATTTAAACACGGGGTG	GTATTGGCTCAAAAAGGGAAGT
<i>NOS1AP</i>	rs12143842	GGAGACAACACGAGGACGAT	GCTGGGAACAGAGTCAGGAG
<i>NOS1AP</i>	rs16857031	GTGGGGAACATGCCAGTTAT	AAGACGGAAGTGGTGAATGG
<i>NOS1AP</i>	rs4657139	CAGAGGTGGTGCAATTCCTT	TGCAGTCCTTCCCAGTTAC
<i>NOS1AP</i>	rs4657178	AACAACCCCAAGGGAAAGAT	CCCCACATAACTGCACACTG
<i>CNOT3</i>	rs36643	CCAGACAGGGAAACCGAATA	CCTCGTCTTTCTCCAAGTGC
<i>PLN</i>	rs11970286	GGTGGTGTAATTCAGTCTTGAGTTTG	GGCTCATACACCCTCACCTACCTT
<i>PLN</i>	rs12210810	AAGCAGGGATGGGAATCTTT	CCAGCAATCAACACACTATAGCACC
<i>SCN5A</i>	rs12053903	GGTCCTCAAACCACACTTTGAATA	CCATCTTCTACATCTTGGGTTCTC
<i>SCN5A</i>	rs1805124	GCCCTCAATGCTCTGAGAAG	TAATGAGACCACCCCATTC

**Supplemental Table 4.** Polymorphism allele frequencies in Caucasian and Japanese LQTS

patients from the discovery cohort

<b>Gene</b>	<b>rs number</b>		<b>Caucasian</b>		<b>Japanese</b>	
<i>ADRA2C</i>	rs61767072		Ins	Del	Ins	Del
		AS	0.92	0.08	0.95	0.05
		S	0.92	0.08	0.95	0.05
		All	0.92	0.08	0.95	0.05
<i>ADRB1</i>	rs1801252		A	G	A	G
		AS	0.89	0.11	0.90	0.10
		S	0.88	0.12	0.85	0.15
		All	0.89	0.11	0.88	0.12
<i>ADRB1</i>	rs1801253		C	G	C	G
		AS	0.73	0.27	0.77	0.23
		S	0.68	0.32	0.79	0.21
		All	0.71	0.29	0.78	0.22
<i>ADRB2</i>	rs28365031		Ins	Del	Ins	Del
		AS	0.76	0.24	0.67	0.33
		S	0.77	0.23	0.62	0.38
		All	0.76	0.24	0.65	0.35
<i>ATP1B1</i>	rs10919071		A	G	A	G
		AS	0.87	0.13	0.90	0.10
		S	0.87	0.13	0.94	0.06
		All	0.87	0.13	0.92	0.08
<i>KCNE1</i>	rs1805128		C	T	C	T
		AS	0.99	0.01	0.98	0.02
		S	0.95	0.05	1.00	0.00
		All	0.97	0.03	0.99	0.01
<i>KCNH2</i>	rs1805123		A	C	A	C
		AS	0.78	0.22	0.96	0.04
		S	0.81	0.19	0.99	0.01
		All	0.80	0.20	0.98	0.02
<i>KCNH2</i>	rs3778873		G	C	G	C
		AS	0.80	0.20	0.73	0.27
		S	0.80	0.20	0.66	0.34
		All	0.80	0.20	0.70	0.30
<i>KCNH2</i>	rs3807375		C	T	C	T
		AS	0.59	0.41	0.17	0.83
		S	0.61	0.39	0.18	0.82
		All	0.60	0.40	0.18	0.82

<b>Gene</b>	<b>rs number</b>	<b>Caucasian</b>		<b>Japanese</b>		
<i>KCNH2</i>	rs3815459	C	T	C	T	
		AS	0.74	0.26	0.21	0.79
		S	0.73	0.27	0.13	0.87
		All	0.73	0.27	0.17	0.83
<i>KCNJ2</i>	rs17779747	G	T	G	T	
		AS	0.73	0.27	0.90	0.10
		S	0.67	0.33	0.90	0.10
		All	0.70	0.30	0.90	0.10
<i>KCNQ1</i>	rs12296050	C	T	C	T	
		AS	0.78	0.22	0.59	0.41
		S	0.75	0.25	0.56	0.44
		All	0.76	0.24	0.57	0.43
<i>KCNQ1</i>	rs2074238	C	T	C	T	
		AS	0.90	0.10	1.00	0.00
		S	0.96	0.04	1.00	0.00
		All	0.93	0.07	1.00	0.00
<i>KCNQ1</i>	rs757092	A	G	A	G	
		AS	0.64	0.36	0.59	0.41
		S	0.63	0.37	0.62	0.38
		All	0.63	0.37	0.60	0.40
<i>NOS1AP</i>	rs10494366	T	G	T	G	
		AS	0.65	0.35	0.27	0.73
		S	0.65	0.35	0.24	0.76
		All	0.65	0.35	0.26	0.74
<i>NOS1AP</i>	rs12029454	G	A	G	A	
		AS	0.84	0.16	0.60	0.40
		S	0.85	0.15	0.59	0.41
		All	0.84	0.16	0.59	0.41
<i>NOS1AP</i>	rs12143842	C	T	C	T	
		AS	0.74	0.26	0.61	0.39
		S	0.69	0.31	0.61	0.39
		All	0.71	0.29	0.61	0.39
<i>NOS1AP</i>	rs16857031	C	G	C	G	
		AS	0.85	0.15	0.87	0.13
		S	0.87	0.13	0.80	0.20
		All	0.86	0.14	0.84	0.16
<i>NOS1AP</i>	rs4657139	T	A	T	A	
		AS	0.67	0.33	0.23	0.77
		S	0.63	0.37	0.22	0.78
		All	0.65	0.35	0.23	0.77

<b>Gene</b>	<b>rs number</b>	<b>Caucasian</b>		<b>Japanese</b>		
<i>NOS1AP</i>	rs4657178	C	T	C	T	
		AS	0.70	0.30	0.46	0.54
		S	0.70	0.30	0.44	0.56
		All	0.70	0.30	0.45	0.55
<i>CNOT3</i>	rs36643	T	C	T	C	
		AS	0.58	0.42	0.70	0.30
		S	0.58	0.42	0.68	0.32
		All	0.58	0.42	0.69	0.31
<i>PLN</i>	rs11970286	C	T	C	T	
		AS	0.54	0.46	0.78	0.22
		S	0.53	0.47	0.77	0.23
<i>PLN</i>	rs12210810	All	0.54	0.46	0.77	0.23
		G	C	G	C	
		AS	0.95	0.05	1.00	0.00
<i>SCN5A</i>	rs12053903	S	0.99	0.01	1.00	0.00
		All	0.97	0.03	1.00	0.00
		A	G	A	G	
<i>SCN5A</i>	rs1805124	AS	0.70	0.30	0.45	0.55
		S	0.67	0.33	0.50	0.50
		All	0.69	0.31	0.48	0.52
<i>SCN5A</i>	rs1805124	A	G	A	G	
		AS	0.80	0.20	0.91	0.09
		S	0.79	0.21	0.94	0.06
<i>SCN5A</i>	rs1805124	All	0.79	0.21	0.93	0.07

Asymptomatic patients (AS)

Symptomatic patients (S)

**Supplemental Table 5.** Polymorphism genotypes in Caucasian and Japanese LQTS patients

from the discovery cohort

Gene	rs number	Caucasian			Japanese			
<i>ADRA2C</i>	rs61767072	II	ID+DD	OR [95% CI]	II	ID+DD	OR [95% CI]	
		AS	60	11	1.11 [0.60-2.05]	37	4	1.00 [0.37-2.72]
		S	59	12		37	4	
<i>ADRB1</i>	rs1801252	AA	AG+GG	OR [95% CI]	AA	AG+GG	OR [95% CI]	
		AS	57	14	1.28 [0.68-2.41]	33	8	1.51 [0.75-3.04]
		S	54	17		30	11	
<i>ADRB1</i>	rs1801253	CC	CG+GG	OR [95% CI]	CC	CG+GG	OR [95% CI]	
		AS	39	32	1.33 [0.80-2.21]	25	16	1.00 [0.56-1.78]
		S	34	37		25	16	
<i>ADRB2</i>	rs28365031	II	ID+DD	OR [95% CI]	II	ID+DD	OR [95% CI]	
		AS	39	32	0.75 [0.43-1.30]	19	22	1.50 [0.75-2.98]
		S	44	27		15	26	
<i>ATP1B1</i>	rs10919071	AA	AG+GG	OR [95% CI]	AA	AG+GG	OR [95% CI]	
		AS	52	19	0.86 [0.46-1.61]	35	6	0.81 [0.40-1.66]
		S	54	17		36	5	
<i>KCNE1</i>	rs1805128	CC	CT+TT	OR [95% CI]	CC	CT+TT	OR [95% CI]	
		AS	70	1	7.66 [1.21-48.31]	39	2	-
		S	64	7		41	0	
<i>KCNH2</i>	rs1805123	AA	AC+CC	OR [95% CI]	AA	AC+CC	OR [95% CI]	
		AS	43	28	0.78 [0.49-1.27]	38	3	0.32 [0.05-2.15]
		S	47	24		40	1	
<i>KCNH2</i>	rs3778873	GG	GC+CC	OR [95% CI]	GG	GC+CC	OR [95% CI]	
		AS	46	25	1.13 [0.69-1.86]	19	22	1.35 [0.74-2.46]
		S	44	27		16	25	
<i>KCNH2</i>	rs3807375	CC	CT+TT	OR [95% CI]	CC	CT+TT	OR [95% CI]	
		AS	27	44	0.94 [0.53-1.68]	0	41	-
		S	28	43		2	39	
<i>KCNH2</i>	rs3815459	CC	CT+TT	OR [95% CI]	CC	CT+TT	OR [95% CI]	
		AS	40	31	1.12 [0.67-1.88]	1	40	1.00 [0.06-17.17]
		S	38	33		1	40	
<i>KCNJ2</i>	rs17779747	GG	GT+TT	OR [95% CI]	GG	GT+TT	OR [95% CI]	
		AS	37	34	1.18 [0.69-2.03]	35	6	1.41 [0.62-3.25]
		S	34	37		33	8	
<i>KCNQ1</i>	rs12296050	CC	CT+TT	OR [95% CI]	CC	CT+TT	OR [95% CI]	
		AS	45	26	1.50 [0.85-2.66]	15	26	1.00 [0.55-1.81]
		S	38	33		15	26	
<i>KCNQ1</i>	rs2074238	CC	CT+TT	OR [95% CI]	CC	CT+TT	OR [95% CI]	
		AS	57	14	0.38 [0.19-0.73]	41	0	-
		S	65	6		41	0	
<i>KCNQ1</i>	rs757092	AA	AG+GG	OR [95% CI]	AA	AG+GG	OR [95% CI]	
		AS	27	44	0.94 [0.51-1.75]	12	29	0.65 [0.33-1.27]
		S	28	43		16	25	



Gene	rs number	Caucasian			Japanese			
		AS	S	OR [95% CI]	AS	S	OR [95% CI]	
<i>NOS1AP</i>	rs10494366	TT	TG+GG	OR [95% CI]	TT	TG+GG	OR [95% CI]	
		AS	25	46	0.59 [0.33-1.07]	3	38	1.00 [0.24-4.11]
		S	34	37		3	38	
<i>NOS1AP</i>	rs12029454	GG	GA+AA	OR [95% CI]	GG	GA+AA	OR [95% CI]	
		AS	50	21	1.00 [0.59-1.71]	14	27	1.00 [0.51-1.98]
		S	50	21		14	27	
<i>NOS1AP</i>	rs12143842	CC	CT+TT	OR [95% CI]	CC	CT+TT	OR [95% CI]	
		AS	37	34	1.00 [0.56-1.77]	15	26	0.90 [0.39-2.11]
		S	37	34		16	25	
<i>NOS1AP</i>	rs16857031	CC	CG+GG	OR [95% CI]	CC	CG+GG	OR [95% CI]	
		AS	52	19	0.86 [0.45-1.65]	31	10	1.98 [1.07-3.67]
		S	54	17		25	16	
<i>NOS1AP</i>	rs4657139	TT	TA+AA	OR [95% CI]	TT	TA+AA	OR [95% CI]	
		AS	29	42	0.84 [0.45-1.59]	0	41	-
		S	32	39		3	38	
<i>NOS1AP</i>	rs4657178	CC	CT+TT	OR [95% CI]	CC	CT+TT	OR [95% CI]	
		AS	35	36	1.00 [0.64-1.57]	9	32	1.16 [0.44-3.07]
		S	35	36		8	33	
<i>CNOT3</i>	rs36643	TT	TC+CC	OR [95% CI]	TT	TC+CC	OR [95% CI]	
		AS	22	49	0.94 [0.57-1.54]	20	21	0.91 [0.47-1.74]
		S	23	48		21	20	
<i>PLN</i>	rs11970286	CC	CT+TT	OR [95% CI]	CC	CT+TT	OR [95% CI]	
		AS	23	48	1.22 [0.72-2.08]	24	17	0.81 [0.50-1.34]
		S	20	51		26	15	
<i>PLN</i>	rs12210810	GG	GC+CC	OR [95% CI]	GG	GC+CC	OR [95% CI]	
		AS	64	7	0.27 [0.05-1.38]	41	0	-
		S	69	2		41	0	
<i>SCN5A</i>	rs12053903	AA	AG+GG	OR [95% CI]	AA	AG+GG	OR [95% CI]	
		AS	35	36	1.33 [0.73-2.42]	7	34	0.85 [0.41-1.74]
		S	30	41		8	33	
<i>SCN5A</i>	rs1805124	AA	AG+GG	OR [95% CI]	AA	AG+GG	OR [95% CI]	
		AS	43	28	0.84 [0.48-1.44]	36	5	1.00 [0.41-2.45]
		S	46	25		36	5	

Asymptomatic patients (AS)

Symptomatic patients (S)

Insertion (I)

Deletion (D)

**Supplemental Table 6.** QTc duration in Caucasian and Japanese LQTS patients from the discovery cohort presented by rs12029454 genotype

Gene	SNP		AA		Aa and aa	
			QTc (ms)	n	QTc (ms)	n
<i>NOS1AP</i>	rs12029454	Caucasian	474 ± 43	97	485 ± 43	41
		Japanese	463 ± 49	28	483 ± 54	54

**Supplemental Table 7.** Power to detect previously reported effect on cardiac events or QTc in LQTS patients or healthy populations in our discovery cohort

A. Power to detect previously reported effect on cardiac events in LQTS patients in our discovery cohort

SNP	Previously reported effect		Power <sup>‡</sup>
	OR	References	
rs10494366	1.42	Tomas et al., 2010	30%
rs12143842 <sup>*</sup>	1.40	Crotti et al., 2009	35 %
rs4657139	1.38	Tomas et al., 2010	27%
	1.80	Crotti et al., 2009	58%

B. Power to detect previously reported effect on QTc in LQTS patients in our discovery cohort

SNP	Previously reported effect		Power <sup>‡</sup>
	Effect size	References	
rs12143842 <sup>*</sup>	8 ms	Tomas et al., 2010	39%
rs4657139	7 ms	Tomas et al., 2010	27%

C. Power to detect previously reported effect on QTc in healthy populations in our discovery cohort

SNP	Power <sup>‡</sup>
rs10919071	9-12%
rs1805128	14-17%
rs1805123	9-12%
rs3778873	9%
rs3807375	7-13%
rs3815459	8%
rs17779747	7%
rs12296050	8-9%
rs2074238 <sup>§</sup>	14-19%
rs757092	9%
rs10494366	9-14%
rs12029454	15%
rs12143842	13-21%
rs16857031	13%

SNP	Power <sup>‡</sup>
rs4657139	15%
rs4657178	10%
rs36643	7%
rs11970286	8%
rs12210810 <sup>§</sup>	7-8%
rs12053903	8%
rs1805124	8%

\* Effect reported for rs16847548 which is in strong linkage disequilibrium with rs12143842 ( $r^2 > 0.8$  in Europeans)

<sup>†</sup> Using QUANTO program, we calculated the power to detect previously reported effect, at a significance level of 0.05, under a dominant model, with a prevalence of 35%, according to allele frequencies in our discovery population and for 112 duos constituting our matched case-control study.

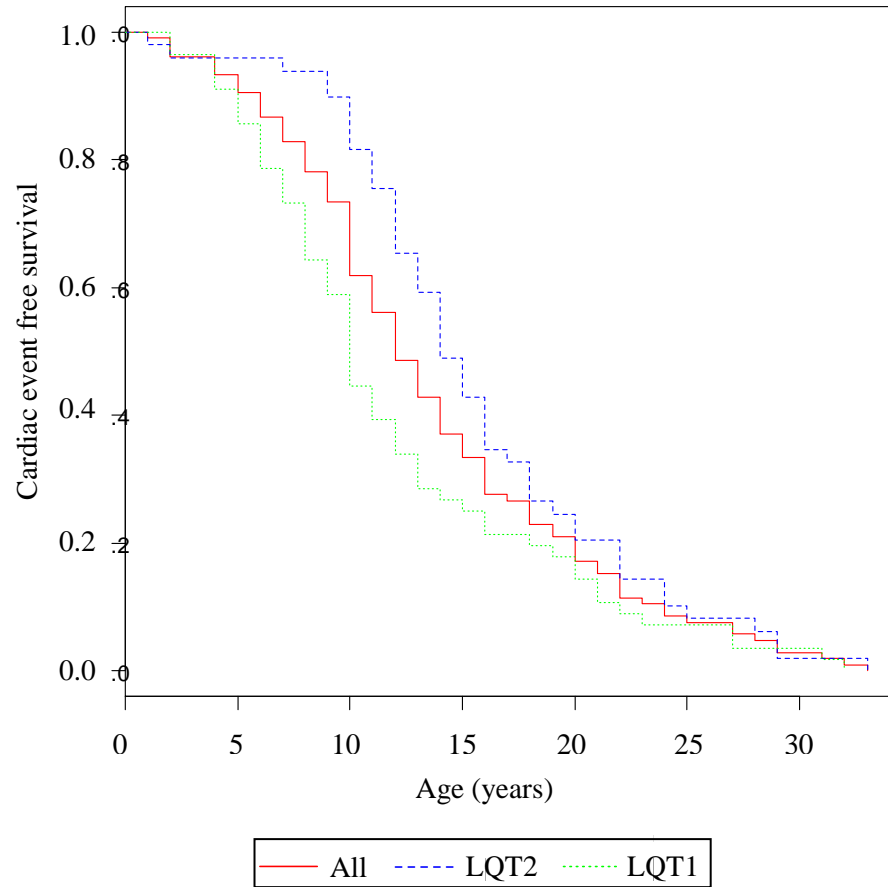
<sup>‡</sup> Using QUANTO program, we calculated the power to detect previously reported effect, at a significance level of 0.05, under a dominant model, with a prevalence of 35%, according to allele frequencies in our discovery population and for 224 individuals constituting our LQTS cohort

<sup>§</sup> Power was calculated according to allele frequencies in Caucasian discovery population and for 142 individuals constituting our Caucasian matched case-control study (SNPs non polymorphic in Japanese)

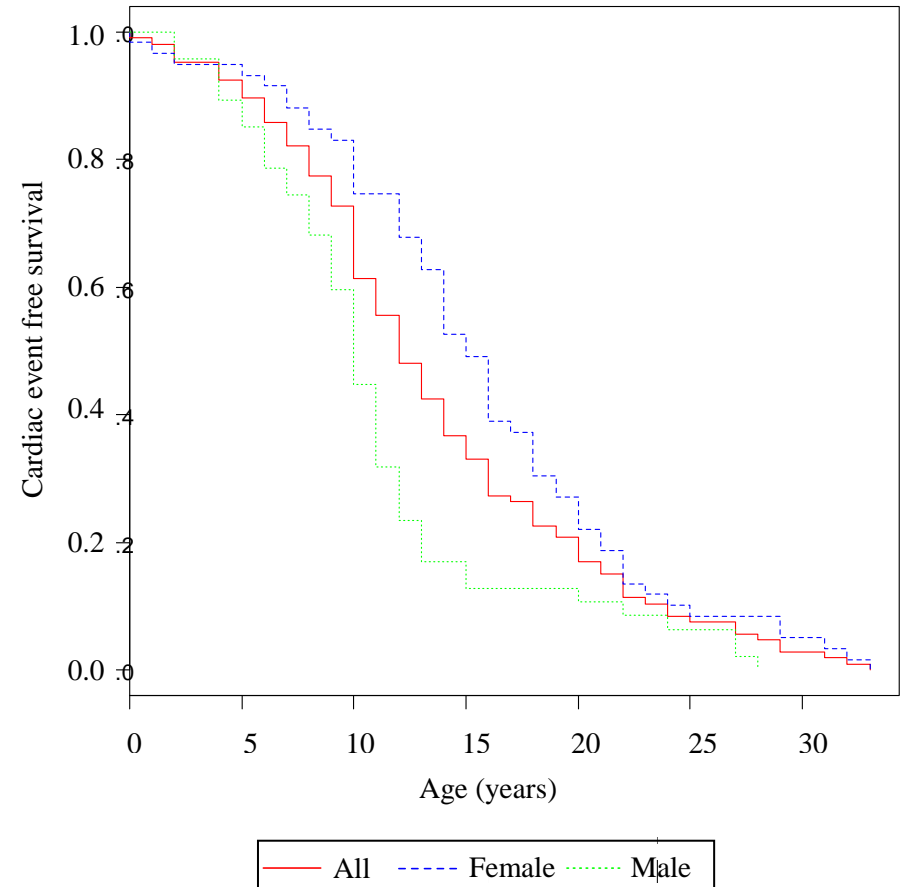
Supplemental Figures

Supplemental Figure 1.

A



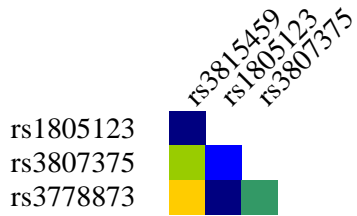
B



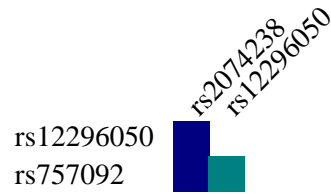
**Supplemental Figure 2.**

**A.**

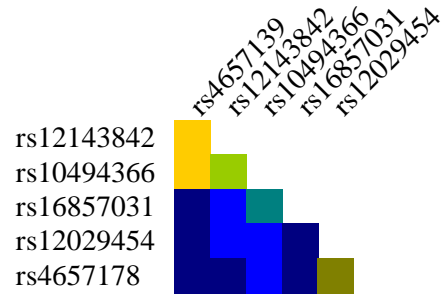
**KCNH2**



**KCNQ1**

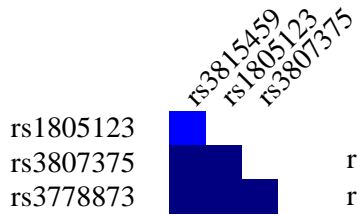


**NOS1AP**

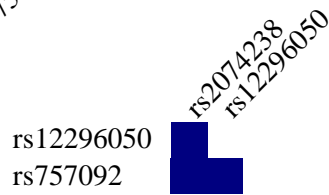


**B.**

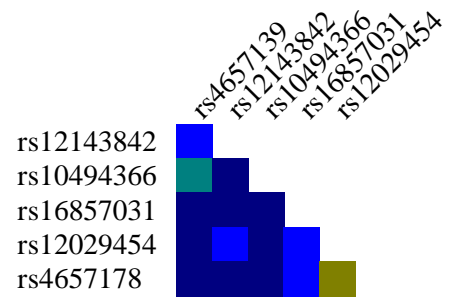
**KCNH2**



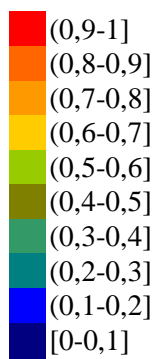
**KCNQ1**



**NOS1AP**



**r<sup>2</sup>**



## Supplemental Figures Legends

**Supplemental Figure 1.** Kaplan-Meier curves of survival free from cardiac events among the symptomatic group from the discovery cohort.

The age-related probability of not experiencing a first cardiac event, with birth used as time of origin, was plotted using the Kaplan-Meier method in the symptomatic population by genetic locus (A) or sex (B).

**Supplemental Figure 2.** Pairwise LD between polymorphisms in LQTS patients from the discovery cohort

A. Pairwise LD calculated from asymptomatic Caucasian patients

SNPs in *ADRB1*, *PLN* or *SCN5A* have  $r^2 < 0.1$

B. Pairwise LD calculated from asymptomatic Japanese patients

SNPs in *ADRB1*, *PLN* or *SCN5A* have  $r^2 < 0.1$

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