

SUPPLEMENTAL MATERIAL

Table S1. SNPs with significant difference in genotype and allele frequencies.

Gene	Region	mRNA	AA change	dbSNP	Type of variant	OR	Prior allele in SUNDS	Ref
SCN5A (NM_198056.2)	Intron 9	C1141-3>A	-	rs41312433	Intron	0.367	C	(1)
	Exon 18	C3269>T	P1090L	rs1805125	Missense	0.211	C	(1)
SCN10A (NM_006514)	Exon16	A2884>G	I962V	rs57326399	Missense	1.551	G	(2)
VCL (NM_014000.2)	Exon17	G2521>C	D841H	rs150385900	Missense	5.226	C	(3)
NOS1AP	5' UTR	-	-	rs12567209	-	0.656	G	(4)

AA = amino acid, OR = odds ratio. Ref = references

Table S2. Mutation/rare variants detected in SUNDS*:

Gene	Genomic region	mRNA	AA change	Protein region	Rate	dbSNP	Type of variant	Category†	ACMG definition	Ref
SCN5A (NM_198056.2)	Exon3	G283>A	V95I	N-terminus	1/123	rs199473054	Missense	RV	VUS	[1]
	Exon3	G362>A	R121Q	C-terminus	2/123	rs199473058	Missense	RV	LP	[1]
	Exon9	G1100>A	R367H	DIS5-S6	1/123	rs28937318	Missense	RV	LP	[1]
	Exon12	G1538>A	R513H	DI-DII	1/123	novel	Missense	Mutation	VUS	[1]
	Exon16	G2608>C	D870H	DIIS5-S6	1/123	novel	Missense	Mutation	VUS	[1]
	Exon18	G3292>T	V1098L	DII-DIII	1/123	rs199473191	Missense	RV	VUS	[1]
	Exon20	G3604>A	V1202M	DII-DIII	1/123	-	Missense	RV	VUS	[1]
	Exon23	G4018>A	V1340I	DIIS4	1/44	rs199473605	Missense	RV	VUS	[5]
	Exon26	C4534>T	R1512W	DIII-DIV	1/123	-	Missense	RV	VUS	[1].

	Exon28	T5291>A	V1764D	DIVS6	1/123	novel	Missense	Mutation	VUS	[1]
	Exon28	C5810>T	S1937F	C-terminus	1/123	novel	Missense	Mutation	VUS	[1]
SCN1B (NM_001037.4)	Exon3	G412>A	V138I	N-terminus	3/123	rs72558029	Missense	RV	VUS	[1]
	Exon4	C566>T	T189M	C-terminus	2/123	rs2305748	Missense	RV	VUS	[1]
SCN3B (NM_00104015 1.1)	Exon4	G583>A	A195T	C-terminus	1/123	rs375755770	Missense	RV	VUS	[1]
SCN10A (NM_006514)	Exon1	G 41>A	R14H	N-terminus	1/105	rs141207048	Missense	RV	VUS	[2]
	Exon9	T1157>G	F386C	DIS6	1/105	rs78555408	Missense	RV	VUS	[2]
	Exon15	G450>A	R817Q	DIIS5-S6	1/105	rs201068959	Missense	RV	VUS	[2]
	Exon20	C3542>T	T1181M	DIIS1-S2	1/105	rs150773437	Missense	RV	VUS	[2]
	Exon21	C3787>T	R1263*	DIIS4	1/105	novel	Nonsense	Mutation	LP	[2]

KCNQ1 (NM_000218.2)	Intron 8	1128+5G>A	-	-	1/44	rs76735093	Intron	RV	VUS	[5]
	Exon16	1876_1893del	G626_P631del	C-terminus	1/44	novel	Deletion	Mutation	LP	[5]
KCNH2 (NM_000238.3)	Intron 5	1128 + 6C > T	-	-	1/108	novel	Intron	Mutation	VUS	[6]
	Intron 11	2692 + 8G > A	-	-	1/104	novel	Intron	Mutation	VUS	[6]
	Exon 13	A3110>T	D1037V	C-terminus	1/44	novel	Missense	Mutation	VUS	[5]
KCNE1 (NM_000219.4)	Exon 3	T160 > G	F54V	Transmembrane	1/105	novel	Missense	Mutation	VUS	[6]
KCNE2 (NM_172201.1)	Exon 2	T370 > C	*124R	C-terminus	1/104	Novel	Terminator codon mutation	Mutation	LP	[6]
KCNJ5 (NM_000890.3)	Exon 3	A536>G	N179S	-	1/44	rs147070381	Missense	RV	VUS	[5]
CACNA1C (NM_000719.6)	Exon 37	T4393>C	F1465L	DIVS5-S6	1/44	rs886038809	Missense	RV	VUS	[5]
	Exon 44	C5329>T	R1777C	C-terminus	1/44	rs775251529	Missense	RV	VUS	[5]

CACNB2 (NM_201590.2)	Exon 14	C1354>T	R452C	-	1/44	rs111250176	Missense	RV	VUS	[5]
PKP2 (NM_004572.3)	Exon 3	G475>A	A159T	-	1/100	novel	Missense	Mutation	VUS	[7]
	Exon 3	G794>A	G265E	-		novel	Missense	Mutation	VUS	[7]
DSP (NM_004415.2)	Exon 2	A269>G	Q90R	-	1/40	rs188516326	Missense	RV	VUS	[8]
	Exon 3	A373>T	I125F	-	1/40	novel	Missense	Mutation	VUS	[8]
	Exon 12	A1562>C	D521A	-	1/40	rs748790273	Missense	RV	VUS	[8]
	Exon 23	G4071>C	E1357D	-	1/40	rs569786610	Missense	RV	VUS	[8]
	Exon 24	G7735>C	D2579H	-	1/40	rs750744914	Missense	RV	VUS	[8]
GJA1 (NM_000165.4)	Exon 2	C169>T	Q57*	-	1/124	novel	Nonsense	Mutation	LP	[9]
VCL (NM_014000.2)	Exon 3	G282>A	M94I	-	1/44	rs774870551	Missense	RV	VUS	[10]

LRRC10 (NM_201550.3)	5' UTR	-2G>T	Noncoding	-	1/88	rs762951776	Noncoding	Mutation	VUS	[11]
	Exon 1	C206>T	P69L	-	1/88	rs140389574	Missense	RV	VUS	[11]
	Exon 1	G385>A	E129K	-	1/113	rs762144273	Missense	Mutation	VUS	[11]
ABCC9 (NM_020297.2)	Exon 29	C3589>T	R197C	-	1/44	rs778849288	Missense	RV	VUS	[5]
ACTN2 (NM_001103.2)	Exon 13	T1162>A	W388R	-	2/44	-	Missense	RV	VUS	[5]
AKAP9 (NM_005751.4)	Exon 46	G11135>A	R3712Q	-	1/44	rs186148498	Missense	RV	VUS	[5]
	Exon 9	A1642>G	R548G	-	1/44	rs147247719	Missense	RV	VUS	[5]
ANKRD (NM_014391.2)	Exon5	G545>A	R182H	-	1/44	rs530739375	Missense	RV	VUS	[5]
DMPK (NM_004409.3)	Exon15	C1868>T	P623L	-	1/44	rs200199039	Missense	RV	VUS	[5]
EYA4 (NM_004100.4)	Exon 18	A1622>T	N541I	-	1/44	-	Missense	Mutation	VUS	[5]

GATA4 (NM_002052.3)	Exon 4	G544>C	G182R	-	2/44	-	Missense	Mutation	VUS	[5]
JUP (NM_002230.2)	Exon 6	C958>T	R320C	-	1/44	rs200740462	Missense	RV	VUS	[5]
LDB3 (NM_001171610.1)	Exon 10	T1333>C	S445P	-	1/44	rs868594949	Missense	RV	VUS	[5]
	Exon 10	C1457>G	P486R	-	1/44	rs12761754	Missense	RV	VUS	[5]
LMNA (NM_170707.3)	Exon 12	C1718>T	S573L	-	1/44	rs60890628	Missense	RV	VUS	[5]
MYBPC3 (NM_000256.3)	Exon 2	G104>A	R35Q	-	1/44	rs397515885	Missense	RV	VUS	[5]
	Exon 7	G787>A	G263R	-	1/44	rs373730381	Missense	RV	VUS	[5]
	Exon 32	C3579>G	I1193M	-	1/44	novel	Missense	Mutation	VUS	[5]
MYH6 (NM_002471.3)	Exon 13	C1154>T	S385L	-	1/44	rs778319108	Missense	RV	VUS	[5]
	Exon 30	G4207>A	E1403K	-	1/44	rs769398160	Missense	RV	VUS	[5]

	Exon 31	C4504>T	R1502W	-	1/44	-	Missense	RV	VUS	[5]
MYH7 (NM_000257.2)	Exon 25	C3235>T	R1079W	-	1/44	rs192722540	Missense	RV	VUS	[5]
	Exon 27	G3341>A	R1114H	-	1/44	rs730880773	Missense	Mutation	VUS	[5]
NUP155 (NM_153485.1)	Exon 13	C1507>T	L503F	-	1/44	rs758699546	Missense	RV	VUS	[5]
SGCD (NM_000337.5)	Exon 8	A848>G	Q283R	-	1//44	rs397516338	Missense	RV	VUS	[5]
TNNT2 (NM_000364.2)	Exon 16	C877>T	R293C	-	1/44	-	Missense	RV	VUS	[5]

*Only nonsynonymous and splice site rare variants with a MAF <0.01 in the East Asian (EAS, 4327 and 9345 individuals respectively) in Exome Aggregation Consortium (ExAC) and Genome Aggregation Database (gnomAD).

† Category: mutation: absent in controls and public database; RV = Rare variants.

LP = likely pathogenic, VUS = uncertain significance. Ref = references.

Supplemental References:

1. Liu C, Tester DJ, Hou Y, Wang W, Lv G, Ackerman MJ, Makielski JC, Cheng J. Is sudden unexplained nocturnal death syndrome in Southern China a cardiac sodium channel dysfunction disorder? *Forensic Sci Int.* 2014; 236:38-45.
2. Zhang L, Zhou F, Huang L, Wu Q, Zheng J, Wu Y, Yin K, Cheng J. Association of common and rare variants of SCN10A gene with sudden unexplained nocturnal death syndrome in Chinese Han population. *Int J Legal Med.* 2017; 131: 53-60.
3. Cheng J, Kyle JW, Lang D, Wiedmeyer B, Guo J, Yin K, Huang L, Vaidyanathan R, Su T, Makielski JC. An East Asian Common Variant Vinculin P.Asp841His Was Associated With Sudden Unexplained Nocturnal Death Syndrome in the Chinese Han Population. *J Am Heart Assoc.* 2017; 6:005330. doi:10.1161/JAHA.116.005330.
4. Huang L, Yu Y, Chen Y, Tester DJ, Tang S, Ackerman MJ, Yuan Z, Cheng J. Association of common variants in NOS1AP gene with sudden unexplained nocturnal death syndrome in the southern Chinese Han population. *Int J Legal Med.* 2014; 128: 933-8.
5. Zhang L, Tester DJ, Lang D, Chen Y, Zheng J, Gao R, Corliss RF, Tang S, Kyle JW, Liu C, Ackerman MJ, Makielski JC, Cheng J. Does Sudden Unexplained Nocturnal Death Syndrome Remain the Autopsy-Negative Disorder: A Gross, Microscopic, and Molecular Autopsy Investigation in Southern China. *Mayo Clin Proc.* 2016;91:1503-1514.
6. Liu C, Zhao Q, Su T, Tang S, Lv G, Liu H, Quan L, Cheng J. Postmortem molecular analysis of KCNQ1, KCNH2, KCNE1 and KCNE2 genes in sudden unexplained nocturnal death syndrome in the Chinese Han population. *Forensic Sci Int.* 2013;231:82-7.
7. Huang L, Tang S, Peng L, Chen Y, Cheng J. Molecular Autopsy of Desmosomal Protein Plakophilin-2 in Sudden Unexplained Nocturnal Death Syndrome. *J Forensic Sci.* 2016;61:687-91.

8. Zhao Q, Chen Y, Peng L, Gao R, Liu N, Jiang P, Liu C, Tang S, Quan L, Makielski JC, Cheng J. Identification of rare variants of DSP gene in sudden unexplained nocturnal death syndrome in the southern Chinese Han population. *Int J Legal Med.* 2016; 130: 317-22.
9. Wu Q, Wu Y, Zhang L, Zheng J, Tang S, Cheng J. GJA1 gene variations in sudden unexplained nocturnal death syndrome in the Chinese Han population. *Forensic Sci Int.* 2017;270: 178-182.
10. Cheng J, Kyle J, Wiedmeyer B, Lang D, Vaidyanathan R, Makielski J. Vinculin variant M94I identified in sudden unexplained nocturnal death syndrome decreases cardiac sodium current. *Sci Rep.* 2017;7:42953.
11. Huang L, Tang S, Chen Y, Zhang L, Yin K, Wu Y, Zheng J, Wu Q, Makielski JC, Cheng J. Molecular pathological study on LRRC10 in sudden unexplained nocturnal death syndrome in the Chinese Han population. *Int J Legal Med.* 2017;131:621-628.