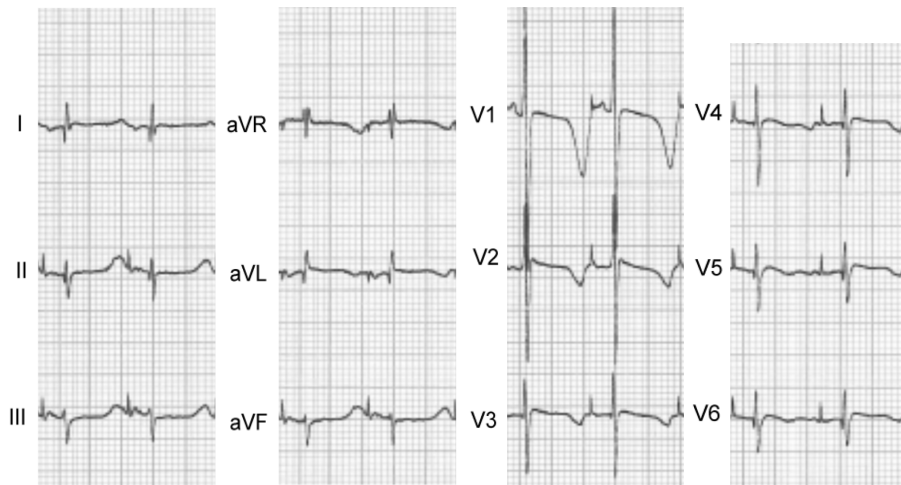


# Novel Calmodulin Mutations Associated with Congenital Long QT Syndrome Affect Calcium Current in Human Cardiomyocytes

## Syndrome Affect Calcium Current in Human Cardiomyocytes

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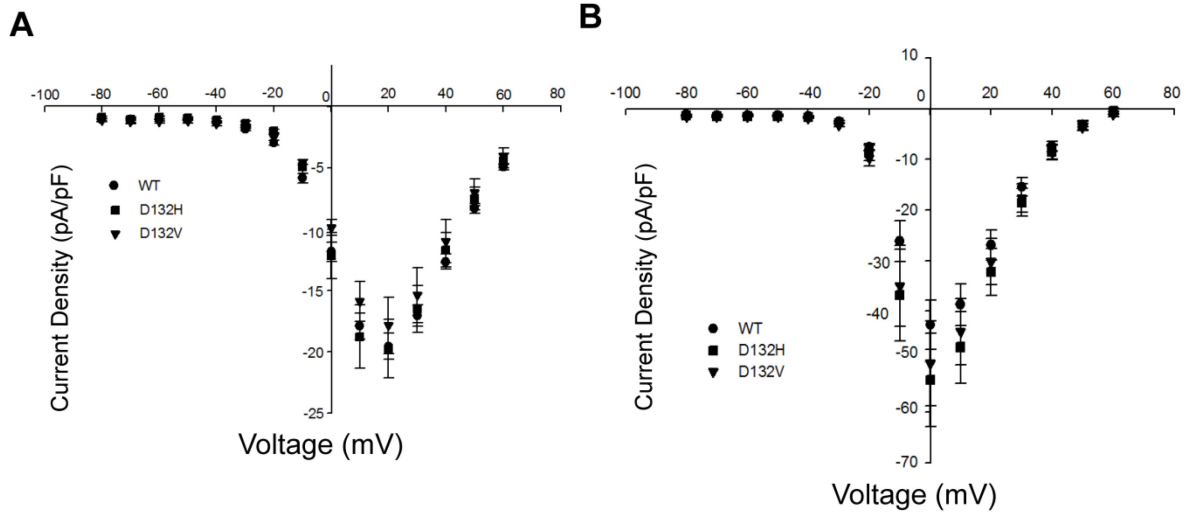
### SUPPLEMENTAL INFORMATION



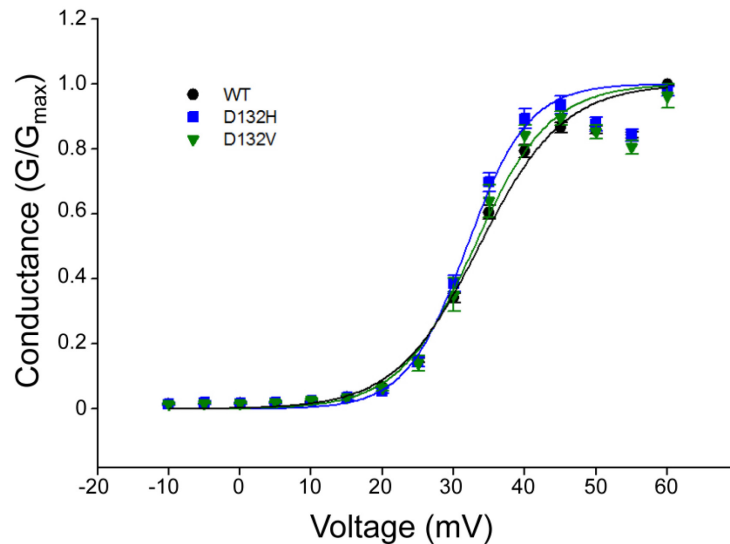
**Figure S1. Standard 12-lead ECG obtained from the subject described as Case 1 after recovery from cardiogenic shock. A paced atrial rhythm is shown. Rate corrected QT interval by Bazett's formula is 535 msec.**



**Figure S2. Standard 12-lead ECG obtained 12 months after the clinical event of the subject in Case 2.** Sinus rhythm and paced atrial rhythm alternate near the lower rate limit for the subject's device. Corrected QT interval is 480 msec.



**Figure S3. Current-voltage relationship for CaM mutants.** **A**, Current-voltage curve for  $\text{Ca}^{2+}$  currents measured in cells expressing WT or mutant CaM. Numeric data are presented in Table S1. Current amplitudes for cells expressing WT, D132H or D132V are not significantly different ( $p > 0.1$ ). **B**, Current-voltage curve for  $\text{Ba}^{2+}$  currents measured in cells expressing WT or mutant CaM. Numeric data are presented in Table S2. Current amplitudes for cells expressing WT, D132H or D132V are not significantly different. Number of replicates: WT ( $n = 10$ ), D132H ( $n = 8$ ) and D132V ( $n = 8$ ).



**Figure S4. Conductance-voltage relationships.** Normalized conductance was plotted against voltage and data were fit with a Boltzmann function.  $V_{1/2}$  values were calculated for individual cells in each group and then averaged: WT,  $-5.3 \pm 0.7$ ; D132H,  $-2.6 \pm 0.8$ ; D132V,  $-5.4 \pm 0.8$ ; ( $p > 0.1$ ).

**Table S1. Mean and standard deviation of current-voltage relationships for CaM mutants under Ca<sup>2+</sup> conditions from Figure S3A.**

V (mV)	WT (Ca <sup>2+</sup> , pA/pF)	$\sigma$	D132H (Ca <sup>2+</sup> , pA/pF)	$\sigma$	D132V (Ca <sup>2+</sup> , pA/pF)	$\sigma$
-80	-1.07	0.47	-0.89	0.36	-1.04	0.42
-70	-1.02	0.44	-1.06	0.61	-1.15	0.52
-60	-1.09	0.46	-0.88	0.31	-1.13	0.49
-50	-1.04	0.39	-0.94	0.35	-1.13	0.45
-40	-1.26	0.42	-1.08	0.44	-1.43	0.52
-30	-1.82	0.70	-1.36	0.56	-1.63	0.49
-20	-2.94	1.06	-2.00	0.44	-2.50	0.74
-10	-5.83	1.95	-4.89	1.68	-4.55	0.65
0	-11.84	3.97	-12.15	5.61	-10.18	1.77
10	-17.92	5.38	-18.78	7.76	-16.70	4.38
20	-19.56	5.24	-19.75	7.16	-18.87	6.39
30	-17.05	4.30	-16.50	5.72	-16.29	6.26
40	-12.67	3.09	-11.69	4.27	-11.76	4.84
50	-8.29	1.99	-7.49	2.76	-7.44	3.03
60	-4.92	1.19	-4.41	1.79	-4.45	1.72

**Table S2. Mean and standard deviation of current-voltage relationships for CaM mutants under Ba<sup>2+</sup> conditions from Figure S3B.**

V (mV)	WT (Ba <sup>2+</sup> , pA/pF)	$\sigma$	D132H (Ba <sup>2+</sup> , pA/pF)	$\sigma$	D132V (Ba <sup>2+</sup> , pA/pF)	$\sigma$
-80	-1.19	0.50	-0.89	0.32	-0.95	0.26
-70	-1.11	0.42	-0.99	0.29	-1.06	0.36
-60	-1.22	0.38	-0.98	0.35	-1.01	0.36
-50	-1.34	0.46	-0.95	0.29	-1.13	0.34
-40	-1.62	0.52	-1.08	0.28	-1.33	0.40
-30	-2.56	0.86	-1.77	0.52	-1.76	0.39
-20	-7.92	4.13	-5.64	3.11	-4.88	3.25
-10	-26.76	15.16	-23.07	17.34	-14.19	7.67
0	-42.83	16.88	-34.55	13.55	-25.91	8.00
10	-41.01	15.10	-32.65	9.54	-30.66	7.55
20	-29.97	11.05	-23.60	6.94	-26.31	11.04
30	-18.24	6.71	-14.31	4.78	-18.10	10.22
40	-9.82	3.40	-7.57	2.84	-10.30	7.52
50	-4.90	1.72	-3.71	1.76	-5.25	5.03
60	-2.07	1.16	-1.44	1.08	-2.23	3.10