Supplementary Table 1: Structural mapping of disease-related mutations identified in human RyR1 and RyR2

hRyR1 (rRyR1)	Disease	hRyR1 (rRyR1)	Disease
L13R (L14)	MHS1	D544Y (D545)	MHS1
L13V (L14)	CCD	R552W (R553)	MHS1
C35R (C36)	MHS1	R614C (R615)	CCD&MHS1
R44C (R45)	CCD&MHS1	R614L (R615)	MHS1
R109W (R110)	MMDO	R1043C (R1044)	MHS1
E160G (E161)	CCD	E1058K (E1059)	MHS1
R163C (R164)	CCD&MHS1	Y1088C (Y1089)	SM
R163L (R164)	MHS1	S1342G (G1343)	MHS1
G165R (G166)	MHS1	A1352G (A1353)	MHS1
D166N (D167)	MHS1	K1393R (K1394)	MHS1
R177C (R178)	MHS1	R1679H (R1680)	MHS1
Y178C (Y179)	MHS1	G1704S (G1705)	CCD
G215E (G216)	CCD	P1787L (P1787)	CCD&MHS1
M226K (M227)	MHS1	G1832A (G1832)	MHS1
D227V (D228)	MHS1	H2035L (H2035)	CFTD
G248R (G249)	MHS1	G2060C (S2060)	CCD&MHS1
R328W (R329)	MHS1	M2101K (M2101)	MHS1
G341R (G342)	MHS1	V2117L (V2117)	MHS1
R367L (R368)	MHS1	D2129E (D2129)	MHS1
H382N (H383)	MHS1	R2163C (R2163)	MHS1
R401C (R402)	MHS1	R2163H (R2163)	CCD&MHS1
R401H (R402)	MHS1	R2163P (R2163)	MHS1
R401S (R402)	MHS1	V2168M (V2168)	CCD&MHS1
M402T (M403)	CFTD	H2204Q (H2204)	CCD
I403M (I404)	CCD&MHS1	T2206M (T2206)	MHS1
R471C (R472)	MHS1	T2206R (T2206)	MHS1
M485V (L486)	MMDO	V2214I (V2214)	MHS1
Y522S (Y523)	CCD&MHS1	V2280I (V2280)	MHS1
R530H (R531)	MHS1	I2321V (I2321)	MHS1
R533C (R531)	MHS1	R2336H (R2336)	MHS1
R533H (R531)	MHS1	N2342S (N2342)	MHS1

hRyR1 (rRyR1)	Disease	hRyR1 (rRyR1)	Disease
E2344D (E2344)	MHS1	C3402G (C3402)	CFTD
V2346M (V2346)	MHS1	P3527S (P3527)	CCD
Δ2347 (E2347)	MHS1	R3539H (R3539)	CCD
E2348G (E2348)	MHS1	E3583Q (E3583)	MHS1
A2350T (A2350)	MHS1	**Q3756E (E3757)**	**MHS1**
R2355C (R2355)	MHS1	**R3772Q (R3773)**	**CCD**
A2367T (A2367)	MHS1	**R3772W (R3773)**	**MHS1**
E2404K (E2404)	MHS1	**G3806R (G3807)**	**MHS1**
A2421P (A2421)	CCD	**I3916M (I3917)**	**MHS1**
M2423K (M2423)	MMDO&CCD	**Y3933C (Y3934)**	**CCD**
A2428T (A2428)	MHS1	**R4136S (R4137)**	**MHS1**
D2431N (D2431)	MHS1	**Δ4214-4216 (4215-4217)**	**CCD**
G2434R (G2434)	MHS1	**V4234L (V4235)**	**MHS1**
R2435H (R2435)	CCD&MHS	P4493A (P4492)	CCD
R2435L (R2435)	MHS1	P4501L (P4498)	MHS1
A2437V (A2437)	MHS1	**R4558Q (R4557)**	**CCD**
R2452W (R2452)	MHS1	**T4637A (T4636)**	**CCD**
R2454C (R2454)	MHS1	**T4637I (T4636)**	**CRD**
R2454H (R2454)	CCD&MHS1	**G4638D (G4637)**	**CCD**
R2458C (R2458)	MHS1	**Δ4647-4648 (4646-4647)**	**CCD**
R2458H (R2458)	MHS1	**L4650P (L4649)**	**CCD**
R2508G (R2508)	CCD	**H4651P (H4650)**	**CCD**
L2550V (L2550)	MHS1	**P4668S (P4667)**	**MHS1**
R2676W (R2676)	MHS1	**F4684S (F4683)**	**MHS1**
D2730G (D2730)	MHS1	**K4724Q (K4723)**	**CCD**
T2787S (T2787)	**MHS1**	**R4737Q (R4736)**	**MHS1**
E2880K (E2880)	**MHS1**	**R4737W (R4736)**	**MHS1**
S3217P (S3217)	MHS1	**G4743D (G4742)**	**CCD**
E3290K (E3290)	MHS1	**L4793P (L4792)**	**CCD**
N3326K (N3326)	CFTD	**Y4796C (Y4795)**	**CCD**
R3366H (R3366)	CCD	**L4814F (L4813)**	**CCD**

hRyR1 (rRyR1)	Disease	hRyR1 (rRyR1)	Disease
L4824P (L4823)	**MHS1**	**R4893W (R4892)**	**CCD**
R4825C (R4824)	**CCD**	**G4897V (G4896)**	**CCD**
T4826I (T4825)	**MHS1**	**I4898T (I4897)**	**CCD**
L4838V (L4837)	**MHS1**	**G4899E (G4898)**	**CCD**
V4842M (V4841)	**CCD**	**G4899R (G4898)**	**CCD**
A4846V (A4845)	**CCD**	**A4906V (A4905)**	**CCD**
V4849I (V4848)	**MHS1&CCD**	**R4914G (R4913)**	**CCD**
Δ4860 (F4859)	**CCD**	**R4914T (R4913)**	**CCD**
R4861C (R4860)	**CCD**	**Δ4927-4928 (4926-4927)**	**CCD**
R4861H (R4860)	**CCD**	**I4938M (I4937)**	**CCD**
FYNKSED4863-4869Y (4862-4868)	**CCD**	**I4938T (I4937)**	**MHS1**
Y4864C (Y4863)	**CCD**	**D4939E (D4938)**	**MHS1**
K4876R (K4875)	**MHS1**	**A4940T (A4939)**	**CCD**
T4882M (T4881)	**CCD**	**G4942V (G4941)**	**MHS1**
G4891R (G4890)	**CCD**	**P4973L (P4972)**	**MHS1**
R4893Q (R4892)	**CCD**		

hRyR2 (rRyR1)	Disease	hRyR2 (rRyR1)	Disease
P164S (P152)	CPVT1	**N4104K (N4149)**	**CPVT1**
R176Q (R164)	CPVT1	**E4146K (E4191)**	**CPVT1**
R414L (Q399)	CPVT1	**T4158P (A4203)**	**CPVT1**
I419F (I404)	CPVT1	**Q4201R (Q4246)**	**CPVT1**
R420W (H405)	CPVT1	R4497C (R4557)	CPVT1
L433P (L418)	CPVT1	F4499C (F4559)	CPVT1
S2246L (S2279)	CPVT1	M4504I (F4564)	CPVT1
V2306I (V2339)	CPVT1	A4510T (A4570)	CPVT1
E2311D (E2344)	CPVT1	A4607P (A4678)	CPVT1
P2328S (P2361)	CPVT1	V4653F (V4724)	CPVT1
N2386I (H2420)	CPVT1	G4671R (G4742)	CPVT1
A2387P (A2421)	CPVT1	V4771I (V4841)	CPVT1
Y2392C (Y2426)	CPVT1	I4848V (I4918)	CPVT1
A2403T (A2437)	CPVT1	A4860G (A4930)	CPVT1
R2474S (R2508)	CPVT1	I4867M (I4937)	CPVT1
T2504M (T2538)	CPVT1	V4880A (V4950)	CPVT1
Q2958R (Q2993)	CPVT1	N4895D (S4965)	CPVT1
L3778F (L3817)	**CPVT1**	P4902L (P4972)	CPVT1
G3946S (G3991)	**CPVT1**	E4950K (D5020)	CPVT1
N4097S (N4142)	**CPVT1**	R4959Q (R5029)	CPVT1

CCD: central core disease;
CFTD: congenital fiber type disproportion;
CRD: core/rod disease;
MHS1: malignant hyperthermia susceptibility;
MMDO: minicore myopathy with ophthalmoplegia;
SM: samaritan myopathy;
CPVT1: catecholaminergic polymorphic ventricular tachycardia type 1.

The summary of mutations is extracted from the UNIPROT websites for human RyR1 and RyR2:
http://www.uniprot.org/uniprot/P21817
http://www.uniprot.org/uniprot/Q92736

The mutations are shaded with colors according to the domains where they are located: yellow for NTD, salmon for SPRY2, cyan for the Handle domain, green for the Helical domain, brown for the P2 domain, purple for the Central domain, and pale blue for the channel domain. The residues whose positions or side chains cannot be resolved in the structure are shaded grey.