

Supplementary Table 1: List of published variants in CACNA1C

c. mutation	p. mutation	Exon	Location	References
c.82G>A	A28T	2	Intracellular N-terminus	(Wemhöner et al. 2015)
c.116C>T	A39V	2	Intracellular N-terminus	(Antzelevitch et al. 2007)(Stockner 2013)
Deletion of exon 3		3	Transmembrane D1, S1	(Levy et al. 2022)
c.496T>C	F166L	4	Transmembrane/Intracellular D1, S2-S3	(Rodan et al. 2021)
c.512C>T	T171M	4	Transmembrane/Intracellular D1, S2-S3	(Narula et al. 2015)(Herold et al. 2023)
	K177R	4	Transmembrane/Intracellular D1, S2-S3	(Rodan et al. 2021)
c.620T>G	L207R	5	Transmembrane/Extracellular D1, S3-S4	(Levy et al. 2022)(Timothy et al. 2024)
c.898A>G	N300D	6	Intracellular/Transmembrane D1, S5	(Béziau et al. 2014)
c.911T>C	I304T	6	Intracellular/Transmembrane D1, S5	(Timothy et al. 2024)
c.970C>T	R324W	7	Extracellular D1, S5-S6 loop (P Loop)	(Rodan et al. 2021)
c.1141C>T	P381S	8/8A	Extracellular/Transmembrane D1, S6	(Wilkinson 2021)(Fukuyama et al. 2014)
c.1204G>A	G402S	8	Extracellular/Transmembrane D1, S6	(Splawski et al. 2005; Dufendach et al. 2018)
c.1207G>A	V403M	8/8A	Extracellular/Transmembrane D1, S6	(Rodan et al. 2021)
	S405R	8/8A	Extracellular/Transmembrane D1, S6	(Dufendach et al. 2018)
c.1216G>A	G406R	8	Extracellular/Transmembrane D1, S6	(Splawski et al. 2005; Walsh et al. 2018)
c.1216G>A	G406R	8a	Extracellular/Transmembrane D1, S6	(Splawski et al. 2004; Splawski et al. 2005; Walsh et al. 2018)
	E407G	9	Intracellular linker D1-D2	(Po' et al. 2019)
	E407A	9	Intracellular linker D1-D2	(Colson et al. 2019)
	R412M	9	Intracellular linker D1-D2	(Herold et al. 2023)
c.1255G>A	G419R	9	Intracellular linker D1-D2	(Bisabu et al. 2020)
	M456I	9	Intracellular linker D1-D2	(Wilkinson 2021)
c.1468G>A	G490R	10	Intracellular linker D1-D2	(Antzelevitch et al. 2007)
c.1552C>T	R518C	12	Intra-/Extracellular and Transmembrane D2, S1	(Seo et al. 2018)(Timothy et al. 2024)
c.1553G>A	R518H	12	Transmembrane (or membrane-adjacent) S0 helix of DII. This mutation is in close proximity to the CaVβ subunit binding site. It occurs just before S1.	(Boczek et al. 2015)
c.1745C>A	A582D	13	Intra-/Extracellular and Transmembrane D2, S2-S4	(Wilkinson 2021)
c.1768C>T	R590C	13	Intra-/Extracellular and Transmembrane D2, S2-S4	(Herold et al. 2023)
	L601R	13	Intra-/Extracellular and Transmembrane D2, S2-S4	(Rodan et al. 2021)
c.1832T>C	M611T	13	Intra-/Extracellular and Transmembrane D2, S2-S4	(Rodan et al. 2021)
c.1841T>G	L614R	13	Intra-/Extracellular and Transmembrane D2, S2-S4	(Rodan et al. 2021)
c.1841T>C	L614P	13	Intra-/Extracellular and Transmembrane D2, S2-S4	(Rodan et al. 2021)
c.1853T>G	V618G	14	Intracellular/Transmembrane D2, S4-S5 and Extracellular S5-S6 loop (P Loop)	(Timothy et al. 2024)
c.1896G>A	R632R	14	Intracellular/Transmembrane D2, S4-S5 and Extracellular S5-S6 loop (P Loop)	(Fukuyama et al. 2014)
c.1928C>T	S643F	14	Intracellular/Transmembrane D2, S4-S5 and Extracellular S5-S6 loop (P Loop)	(Ozawa et al. 2018)
c.1969C>T	L657F	14	Intracellular/Transmembrane D2, S4-S5 and Extracellular S5-S6 loop (P Loop)	(Rodan et al. 2021)
c.1973T>C	L658P	15	Extracellular D2, S5-S6 loop (P Loop) and Transmembrane D2 S6	(Levy et al. 2022)
c.1973T>C	L658P	15	Extracellular D2, S5-S6 loop (P Loop) and Transmembrane D2 S6	(Levy et al. 2022)
c.2114G>A	G705E	15	Extracellular D2, S5-S6 loop (P Loop) and Transmembrane D2 S6	(Timothy et al. 2024)
c.2227_2229delATC 1743del		16	Transmembrane D2, S6 and intracellular linker D2-D3	(Rodan et al. 2021)
c.2284C>T	L762F	16	Transmembrane D2, S6 and intracellular linker D2-D3	(Landstrom et al. 2016) (Wilkinson 2021)
	E771K	16	Transmembrane D2, S6 and intracellular linker D2-D3	(Timothy et al. 2024)
c.2399A>C	K800T	17	Intracellular linker D2-D3	(Endres et al. 2020)
c.2500A>G	K834E	19	Intracellular linker D2-D3	(Boczek et al. 2013)
c.2548_2550delGAT 1850del		19	Intracellular linker D2-D3	(Burashnikov et al. 2010) (Sutphin et al. 2016)
c.2570C>T	P857R	19	Intracellular linker D2-D3	(Wemhöner et al. 2015), (Boczek et al. 2013)
c.2570C>T	P857L	19	Intracellular linker D2-D3	(Boczek et al. 2013)
c.2573G>A	R858H	19	Intracellular linker D2-D3	(Fukuyama et al. 2013)(Timothy et al. 2024)
c.2578C>G	R860G	19	Intracellular linker D2-D3	(Wemhöner et al. 2015)
	T941I	19?	Intracellular linker D2-D3	(Levy et al. 2022)
	A1012V	24	Transmembrane D3, S4	(Timothy et al. 2024)
c.3061T>C	C1021R	19	Intracellular linker D2-D3	(Dufendach et al. 2018; Nugud et al. 2021)
	R1024G	24	Transmembrane D3, S4	(Kosaki et al. 2018)
c.3139G>A	G1047R	25	Intracellular/Transmembrane D3, S5	(Timothy et al. 2024)
c.3343G>A	E1115K	27	Extracellular D3, S5-S6 loop (P Loop)	(Burashnikov et al. 2010) (Ye et al. 2019)
c.3416G>A	R1139H	28?	Extracellular D3, S5-S6 loop (P Loop) and Transmembrane D3 S6	(D'Gama et al. 2015)
c.3497T>C	I1166T	27	Extracellular D3, S5-S6 loop (P Loop) and Transmembrane D3 S6	(Boczek et al. 2015; Wemhöner et al. 2015)(Colson et al. 2019)
	I1166V	28	Extracellular D3, S5-S6 loop (P Loop) and Transmembrane D3 S6	(Wemhöner et al. 2015)
c.3700T>C	V1167A	28	Extracellular D3, S5-S6 loop (P Loop) and Transmembrane D3 S6	(Levy et al. 2022)
c.3518_3526del	G1173_Q1175del	28	Extracellular D3, S5-S6 loop (P Loop) and Transmembrane D3 S6	(Levy et al. 2022)
c.3560T>C	V1187A	28	Extracellular D3, S5-S6 loop (P Loop) and Transmembrane D3 S6	(Rodan et al. 2021)
c.3995G>A	R1332Q	32	Intracellular/Transmembrane D4 S3	(Levy et al. 2022)
c.4087G>A	V1363M	33	Extracellular D4 S3-S4 linker	(Levy et al. 2022)
c.4087G>T/C	V1363L	33	Extracellular D4 S3-S4 linker	(Levy et al. 2022)
c.4222C>G	L1408V	35	Transmembrane D4, S5	(Rodan et al. 2021)
c.4231G>C	V1411L	35	Transmembrane D4, S5	(Rodan et al. 2021)
c.4418C>G	A1473G	38	Transmembrane D4, S6	(Gillis et al. 2012)
c.4425C>G	I1475M	38	Intracellular C-terminus	(Wemhöner et al. 2015)
c.4486G>A	E1496K	38	Intracellular C-terminus	(Wemhöner et al. 2015)**
c.4567G>C	A1521P	39	Intracellular C-terminus	(Levy et al. 2022)
	K1580T	40	Intracellular C-terminus	(Kojima et al. 2017)
c.4870_4871delins 11624A		42	Intracellular C-terminus	(Barrett and Tsien 2008)
c.5347G>T	G1783C	44	Intracellular C-terminus	(Wilkinson 2021)
c.5717G>A	R1906Q	47	Intracellular C-terminus	(Boczek et al. 2013)
c.5729G>A	R1910Q	48	Intracellular C-terminus	(Fukuyama et al. 2013)
c.5731G>A/C	G1911R	47	Intracellular C-terminus	(Hennessey et al. 2014)
c.5747A>G	Q1916R	48	Intracellular C-terminus	(Liu et al., 2017)
	N2019S	50	Intracellular C-terminus	(Sutphin et al. 2016)
	E2062X	49	Intracellular C-terminus	(Levy et al. 2022)