

Supplementary Material

Table S1. Complete epilepsy-related mutations identified in NaV1.1 table

Variant	Location	Mutation	Disease	Alteration in biophysical properties and/or Clinical report	Reference
M1	N-terminal	Start codon mutation	SME	NR	(Depienne et al., 2008)
M1T	N-terminal	Start codon mutation	DS	NR	(Zuberi et al., 2011)
Q3X (De novo)	N-terminal	Nonsense	DS	First seizures Generalized tonic clonic seizures	(Claes et al., 2003; Lim et al., 2011)
L6P (Paternal)	N-termial	Nonsense	GEFS+	NR	(Cetica et al., 2017)
P8fsX12 (De novo)	N-terminal	FrameShift	DS	NR	(Wang et al., 2012)
P11Tfs*18	N-terminal	FrameShift	GEFS+	NR	(Cetica et al., 2017)
P11QfsX80 (De novo)	N-terminal	FrameShift	EE	NR	(Wei et al., 2018)

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P11LfsX81	N-terminal	FrameShift	DS	NR	(Ishii et al., 2017)
P14SfsX78 (De novo)	N-terminal	FrameShift	DS	NR	(Harkin et al., 2007)
P17del	N-terminal	In-Frame deletion	DS	NR	(Zuberi et al., 2011)
T18del	N-terminal	In-Frame deletion	DS	NR	(Djémié et al., 2016)
A19X	N-terminal	Nonsense	SME	NR	(Lee et al., 2014)
E20X (De novo)	N-terminal	Nonsense	SME DS	NR	(Ceulemans et al., 2004; Depienne et al., 2008; Wang et al., 2012)
A24GfsX4	N-terminal	FrameShift	DS	NR	(Zuberi et al., 2011)
A24T	N-terminal	Missense	SME	NR	(Xu et al., 2014)
E26X	N-terminal	Nonsense	DS	NR	(Zuberi et al., 2011)

A27T (Paternal)	N-terminal	Missense	GEFS+ SMEB	Diffuse spikes, prevailing in posterior regions (EEG)	(Nicita et al., 2010)
R28C (Paternal)	N-terminal	Missense	GEFS+	NR	(Lossin, 2009; Lal et al., 2016);
E32X	N-terminal	Nonsense	EP	NR	(Lindy et al., 2018)
L33A	N-terminal	Missense	GEFS+	NR	(Cetica et al., 2017)
L38fsX54 (De novo)	N-terminal	FrameShift	SME DS	NR	(Wallace et al., 2003; Depienne et al., 2008)
L41X	N-terminal	Nonsense	SME	NR	(Xu et al., 2014)
D43 MetfsX47	N-terminal	FrameShift	SME DS	Acute encephalopathy resulting in severe neurologic sequelae Generalized slow waves (EEG)	(Takayanagi et al., 2010; Wang et al., 2012)
D43MetfsX 49 (De novo)	N-terminal	FrameShift	DS	NR	(Depienne et al., 2008)
D45N (Paternal)	N -terminal	Missense	Epilepsy- Aphasia FS+	NR	(Zuberi et al., 2011; Carvill et al., 2013)

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D45E	N-terminal	Missense	DS	Multifocal discharges (EEG) Hippocampal atrophy (MRI)	(Zhou et al., 2018)
N47MfsX45	N-terminal	FrameShift	Epilepsy	NR	(Stosser et al., 2018)
N47LfsX45	N-terminal	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
G58X (De novo)	N-terminal	Nonsense	DS Focal Epilepsy	Moderate mental retardation Autistic characteristics Hyperactivity Periventricular nodular heterotopia (MRI)	(Barba et al., 2014)
G58R	N-terminal	Missense	FS+	Febrile and afebrile GTC Large amplitude and diffuse (EEG)	(Mina et al., 2015)
G58V	N-terminal	Missense	DS	NR	(Depienne et al., 2008)
L61F	N-terminal	Missense	DS	NR	(Depienne et al., 2008)
L61P (Paternal)	N-terminal	Missense	DS	Febrile seizures	(Halvorsen et al., 2016)

P62fsX30	N-terminal	FrameShift	SME	NR	(Xu et al., 2014)
F63L(Paternal)	N-terminal	Missense	DS	Severe developmental delay Spike and Waves in right fronto-temporal region with spreading (EEG)	(Nicita et al., 2010)
Y65X (De novo)	N-terminal	Nonsense	DS	Generalized tonic-clonic seizures	(Zucca et al., 2008)
I68T (Maternal)	N-terminal	Missense	SMEB	NR	(Zuberi et al., 2011)
Ser74Pro (De novo)	N-terminal	Missense	FS+	NR	(Marini et al., 2007)
E75D (De novo)	N-terminal	Missense	DS	Slow-spike-wave complexes (EEG)	(Arafat et al., 2017)
P76T (De novo)	N-terminal	Missense	DS	NR	(Ishii et al., 2017)
L77P (De novo)	N-terminal	Missense	DS	NR	(Kothur et al., 2018)
E78X	N-terminal	Nonsense	DS	NR	(Surovy et al., 2016)

E78GfsX7	N-terminal	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
E78D (De novo)	N-terminal	Missense	DS	NR	(Nabbout et al., 2003)
D79N(De novo)	N-terminal	Missense	DS	NR	(Depienne et al., 2008; Zuberi et al., 2011)
D79H (De novo)	N-terminal	Missense	SMEB	NR	(Harkin et al., 2007; Depienne et al., 2008)
L80_D81del (De novo)	N-terminal	In-frame deletion	DS	Pharmacoresistant	(Usluer et al., 2016)
D81N (De novo)	N-terminal	Missense	DS	Severe Motor and mental delay Severe Autistic Multi-focal spike-waves (EEG)	(Usluer et al., 2016)
D81E (De novo)	N-terminal	Missense	Epilepsy	NR	(Lindy et al., 2018)
Y83X (De novo)	N-terminal	Nonsense	SMEB	NR	(Zuberi et al., 2011)
Y84fsX4	N-terminal	FrameShift	DS	NR	(Ishii et al., 2017)

Y84C (De novo)	N-terminal	Missense	DS	NR	(Harkin et al., 2007; Wang et al., 2012)
N86SfsX7	N-terminal	FrameShift	DS	NR	(Ishii et al., 2017)
F90S(Paternal)	N-terminal	Missense	DS	Multifocal spikes, frontal-dominant spike-waves complex (EEG)	(Sun et al., 2008a; Wang et al., 2012; Xu et al., 2014; Butler et al., 2017b)
I91T (De novo)	N-terminal	Missense	DS	Frontal-dominant spike-waves complex (EEG)	(Sun et al., 2008a; Xu et al., 2014)
I91SfsX4	N-terminal	FrameShift	SMEB	NR	(Depienne et al., 2008; Villeneuve et al., 2014)
I91fs	N-terminal	FrameShift	SME	NR	(Lee et al., 2014)
L93EfsX2 (De novo)	N-terminal	FrameShift	DS	NR	(Riva et al., 2009)
L93S	N-terminal	Missense	SME	NR	(Lee et al., 2014)
L93X	N-terminal	Nonsense	DS	NR	(Cetica et al., 2017)
N94L (De novo)	N-terminal	Missense	DS	NR	(Ishii et al., 2017)

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G96EfsX24 (De novo)	N-terminal	FrameShift	NR	Genetic generalized epilepsy with intellectual disability	(Fry et al., 2016)
L97fsx14	N-terminal	FrameShift	SME	NR	(Xu et al., 2014)
A98P (De novo)	N-terminal	Missense	DS	NR	(Zuberi et al., 2011)
A98PfsX14	N-terminal	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
R101W (De novo; Paternal)	N-terminal	Missense	DS SMEB	NR	(Harkin et al., 2007; Depienne et al., 2008; Sun et al., 2010; Wang et al., 2012; Fry et al., 2016; Kothur et al., 2018)
R101Q(De novo; Maternal)	N-terminal	Missense	DS SMEB GEFS+ PEFS+	Psychomotor retardation	(Fukuma et al., 2004; Harkin et al., 2007; Marini et al., 2007; Depienne et al., 2008; Sun et al., 2010; Zuberi et al., 2011; Wang et al., 2012; Tonekaboni et al., 2013; Lee et al., 2014; Djémié et al., 2016)
S103G (Paternal)	N-terminal	Missense	SME DS	Severe mental decline Rare-spike wave complex (EEG)	(Fujiwara, 2003; Ebrahimi et al., 2010; Tonekaboni et al., 2013)
S103I	N-terminal	Missense	DS	NR	(Xu et al., 2015)

A104V (De novo)	N-terminal	Missense	DS	Epileptic discharges, slow spike and wave; sharp wave, sharp and slow wave complex (EEG)	(Kwong et al., 2012; Myers et al., 2017a)
T105I	N-terminal	Missense	DS	NR	(Wang et al., 2012; Lindy et al., 2018)
S106F (Paternal)	N-terminal	Missense	Focal epilepsy	Right temporal parietal occipital slow-wave and generalized spike-wave complex (EEG)	(Barba et al., 2014)
A107D (De novo)	N-terminal	Missense	DS	NR	(Ishii et al., 2017)
L108R	N-terminal	Missense	DS SMEB	Generalized tonic-clonic seizures	(Tang et al., 2011; Zuberi et al., 2011)
L108P	N-terminal	Missense	DS	NR	(Xu et al., 2015)
T112I	N-terminal	Missense	SME	Rare spike-wave complex and rare multifocal spikes (EEG)	(Fujiwara, 2003)
P113T	N-terminal	Missense	SMEB	NR	(Xu et al., 2014)
P113L	N-terminal	Missense	Epilepsy	NR	(Lindy et al., 2018)

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F114LfsX6 (De novo)	N-terminal	FrameShift	SME	NR	(Kodera et al., 2013)
L117QfsX6 (De novo)	N-terminal	FrameShift	DS	NR	(Depienne et al., 2008)
R118S (De novo)	N-terminal	Missense	DS	Generalized tonic- clonic seizures Severe mental retardation	(Zucca et al., 2008)
L123RfsX1 1	DIS1	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
I124N(Mate rnal)	DIS1	Missense	SME	NR	(Depienne et al., 2008)
H127N (De novo)	DIS1	Missense	SMEB DS	NR	(Zuberi et al., 2011; Cetica et al., 2017)
H127Y (De novo)	DIS1	Missense	GEFS+	NR	(Djémié et al., 2016)
H127L	DIS1	Missense	DS	NR	(Xu et al., 2015)
S128X (De novo)	DIS1	Nonsense	DS FS+ SME	NR	(Nabbout et al., 2003; Zuberi et al., 2011; Carvill et al., 2014)

L129del (De novo)	DIS1	In-frame deletion	DS	NR	(Riva et al., 2009)
S131R	DIS1	Missense	NR	NR	(Fry et al., 2016)
C136WfsX 14	DIS1	FrameShift	DS	NR	(Cho et al., 2018)
I138FfsX11 (Paternal)	DIS1	FrameShift	DS	NR	(Zuberi et al., 2011)
T140R (De novo)	DIS1	Missense	DS	NR	(Ishii et al., 2017)
Val143fsX1 6 (De novo)	DIS1	FrameShift	DS	NR	(Wang et al., 2012)
Phe144TyrfsX5 (De novo)	DIS1	Frameshift	SME DS	Moderate psychomotor retardation	(Fukuma et al., 2004; Zuberi et al., 2011; Wang et al., 2012; Villeneuve et al., 2014)
Met145AspfsX4 (De novo)	DIS1	Frameshift	PEFS+	Generalized tonic- clonic seizures without any provoked factors	(Yu et al., 2010)
Met145Val	DIS1	Missense	DS	NR	(Xu et al., 2015)
M145T (Paternal)	DIS1	Missense	Unidentified epilepsy	Decrease current density	(Mantegazza et al., 2005; Colosimo et al., 2007)

				Shift of steady-state inactivation to more positive values	
M145L	DIS1	Missense	DS	NR	(Lindy et al., 2018)
W153X	D1S1-S2	Nonsense	DS SMEB	NR	(Zuberi et al., 2011)
E158Q	DIS1-S2	Missense	Epilepsy	NR	(Lindy et al., 2018)
Y159SfsX1 3	DIS2	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
T162P (De novo)	DIS2	Missense	DS	NR	(Riva et al., 2009)
T162I	DIS2	Missense	SME	NR	(Cetica et al., 2017)
G163E	DIS2	Missense	SME	NR	(Hattori et al., 2008)
Y165X (De novo)	DIS2	Nonsense	DS	NR	(Nabbout et al., 2003)

T166VfsX5 (De novo)	DIS2	FrameShift	DS	NR	(Harkin et al., 2007)
S169IfsX10 8	DIS2	FrameShift	SME	Severe mental retardation Autistic features	(Le Gal et al., 2010; Barba et al., 2014)
S169P (Mosaic)	DIS2	Missense	DS	NR	(Yang et al., 2017)
I171L(De novo)	DIS2	Missense	SMEB	NR	(Harkin et al., 2007)
I171R (De novo)	DIS2	Missense	DS	NR	(Depienne et al., 2008)
A175T (De novo)	DIS2	Missense	SMEB	NR	(Harkin et al., 2007)
A175V (De novo)	DIS2	Missense	DS	NR	(Depienne et al., 2008)
G177R (De novo)	DIS2-S3	Missense	SME	NR	(Hattori et al., 2008; Reyes et al., 2011)
G177DfsX4	DIS2-S3	FrameShift	DS	Generalized tonic- clonic seizures	(Fujiwara, 2003)
G177E (De novo)	DIS2-S3	Missense	SME DS	Non-functional channel	(Nabbout et al., 2003; Ohmori et al., 2006; Usluer et al., 2016)

G177Val	DIS2-S3	Missense	DS	NR	(Cetica et al., 2017)
P178Ser	DIS2-S3	Missense	DS	NR	(Wang et al., 2012)
C179Arg	DIS2-S3	Missense	DS	NR	(Wang et al., 2012)
L180X (De novo)	DIS2-S3	Nonsense	DS	Focal spike wave (EEG)	(Liu et al., 2018)
E181X (Familial)	DIS2-S3	Nonsense	GEFS+	NR	(Orrico et al., 2009)
D182IfsX34 (De novo)	DIS2-S3	FrameShift	DS	NR	(Yang et al., 2017)
T184YfsX93	DIS2-S3	FrameShift	SMEB	NR	(Lindy et al., 2018)
D188V (Paternal)	DIS2-S3	Missense	GEFS+	Resistance to entry into closed state inactivation during high frequency stimulation	(Wallace et al., 2001; Cossette et al., 2003; Rilstone et al., 2012)
W190R (Maternal)	DIS3	Missense	DS	NR	(Fukuma et al., 2004; Wang et al., 2012)

W190X (De novo)	DIS3	Nonsense	DS	Febrile, partial and generalized tonic-clonic and myo-clonic seizures Severe intellectual disability.	(Marini et al., 2007; Kwong et al., 2012)
N191Y	DIS3	Missense	DS	NR	(Depienne et al., 2008)
N191T	DIS3	Missense	DS	NR	(Ishii et al., 2017)
N191L	DIS3	Missense	DS	NR	(Depienne et al., 2008)
W192X (De novo)	DIS3	Nonsense	DS	NR	(Depienne et al., 2008)
L193F(Paternal)	DIS3	Missense	GEFS+	Generalized tonic-clonic seizures	(Cui et al., 2011)
D194N(De novo)	DIS3	Missense	SME DS SMEB	NR	(Harkin et al., 2007; Riva et al., 2009; Azmanov et al., 2010; Zuberi et al., 2011; Kodera et al., 2013; Cho et al., 2018; Lindy et al., 2018)
D194H	DIS3	Missense	DS	NR	(Zuberi et al., 2011)
D194G	DIS3	Missense	DS	NR	(Depienne et al., 2008)

D194A	DIS3	Missense	SME	EEG reveals background slow	(Lee et al., 2014)
T199R (De novo)	DIS3	Missense	SMEB	NR	(Harkin et al., 2007)
T199SfsX15	DIS3	Frameshift	DS	NR	(Cho et al., 2018)
A201E	DIS3	Missense	DS	NR	(Do et al., 2017; Lindy et al., 2018)
Y202X (De novo)	DIS3	Nonsense	DS	NR	(Wang et al., 2012)
V207G	DIS3	Missense	EE	Early-onset multifocal seizures	(Daoud et al., 2016)
L209PfsX68	DIS3-S4	Frameshift	DS	NR	(Møller et al., 2016)
G210D	DIS3-S4	Missense	DS	NR	(Ishii et al., 2017)
V212A	DIS3-S4	Missense	SME	NR	(Hattori et al., 2008)

S213HfsX9	DIS3-S4	Frameshift	Epilepsy	NR	(Lindy et al., 2018)
S213W (De novo)	DIS3-S4	Missense	Epilepsy	Febrile and afebrile seizures Developmental delay	(Butler et al., 2017a)
L215_R219 delinsfsX	DIS3-S4	Frameshift	DS	NR	(Ko et al., 2018)
T217L (De novo)	DIS4	Missense	DS	NR	(Riva et al., 2009)
F218L (Paternal, Maternal)+	DIS4	Missense	GEFS+ PEFS+	Slow wave discharges in left posterior region with occasional generalization; A second EEG reveal multifocal spike and generalized slow wave-spike complex (EEG)	(Livingston et al., 2009; Catarino et al., 2011)
R219G (De novo)	DIS4	Missense	DS	NR	(Usluer et al., 2016)
R219T	DIS4	Missense	Epilepsy	NR	(Lindy et al., 2018)
R219SfsX57 (De novo)	DIS4	FrameShift	DS	Generalized tonic-clonic seizures	(Claes et al., 2001)
V220fsX4	DIS4	FrameShift	SME	NR	(Xu et al., 2014)

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V220D	DIS4	Missense	Malignat migrating partial seizures of infancy	NR	(Zhang et al., 2015)
L221P	DIS4	Missense	Epilepsy	NR	(Lindy et al., 2018)
R222X (De novo)	DIS4	Nonsense	DS SMEB	No measurable current	(Claes et al., 2001; Nabbout et al., 2003; Fukuma et al., 2004; Harkin et al., 2007; Depienne et al., 2008; Orrico et al., 2009; Zuberi et al., 2011; Wang et al., 2012; Xu et al., 2014; Esterhuizen et al., 2018)
A223E (De novo)	DIS4	Missense	DS	NR	(Depienne et al., 2008)
L224S	DIS4	Missense	Epilepsy	NR	(Lindy et al., 2018)
K225N	DIS4	Missense	SME	NR	(Lee et al., 2014; Xu et al., 2014; Lindy et al., 2018)
T226M (De novo)	DIS4	Missense	DS	NR	(Harkin et al., 2007; Mulley et al., 2013; Dhamija et al., 2014; Muona et al., 2015; Lindy et al., 2018)
T226K	DIS4	Missense	SME	NR	(Catarino et al., 2011)

T226R (De novo)	DIS4	Missense	DS	NR	(Wang et al., 2012; Lindy et al., 2018)
I227T (De novo)	DIS4	Missense	DS	NR	(Zuberi et al., 2011)
I227S (De novo)	DIS4	Missense	SME SMEB	Low current density (no detectable)	(Nabbout et al., 2003; Ohmori et al., 2006; Depienne et al., 2008; Riva et al., 2009; Mak et al., 2011; Wang et al., 2012; Lindy et al., 2018)
S228P	DIS4	Missense	DS		(Parrini et al., 2017)
G232S	DIS4	Missense	DS	NR	(Depienne et al., 2008; Zuberi et al., 2011)
L233EfsX43 (De novo)	DIS4	FrameShift	DS	NR	(Petrelli et al., 2012)
L233G	DIS4	Missense	Epilepsy	NR	(Lindy et al., 2018)
L233R (De novo)	DIS4	Missense	DS	NR	(Zuberi et al., 2011)
T235S	DIS4-S5	Missense	GEFS+	NR	(Cetica et al., 2017)

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I1236LfsX5	DIS4-S5	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
A239T (De novo, Paternal)	DIS4-S5	Missense	DS	NR	(Harkin et al., 2007; Sun et al., 2008a; Cetica et al., 2017)
A239V (De novo)	DIS4-S5	Missense	SME DS	Focal right fronto-temporal spikes with spreading (EEG)	(Iannetti et al., 2009; Nicita et al., 2010; Xu et al., 2014)
S243Y	DIS4-S5	Missense	SME	NR	(Depienne et al., 2008; Xu et al., 2014)
S243F	DIS4-S5	Missense	SME	Slow background, focal spikes and generalized epileptiform discharges (EEG)	(Lee et al., 2014)
V244L (Maternal)	DIS4-S5	Missense	DS	Myoclonic seizures and generalized spikes or spike-and-wave complexes in the interictal (EEG)	(Morimoto et al., 2006)
V244EfsX3 2 (De novo)	DIS4-S5	FrameShift	DS	NR	(Marini et al., 2007)
L247del	DIS4-S5	In-frame Deletion	Epilepsy	NR	(Lindy et al., 2018)
D249E	DIS4-S5	Missense	DS	Generalized tonic seizures; Absences Mental retardation	(Le Gal et al., 2014)

V250I	DIS4-S5	Missense	Epilepsy	NR	(Retterer et al., 2016; Lindy et al., 2018)
M251X	DIS5	Nonsense	SME	NR	(Xu et al., 2014)
I252N	DIS5	Missense	DS	NR	(Ceulemans et al., 2004)
I252M	DIS5	Missense	Epilepsy	NR	(Wang et al., 2012)
T254CfsX4	DIS5	FrameShift	DS	Moderate intellectual disability Slow speaking Spasticity Ataxia	(Martin et al., 2010)
T254I	DIS5	Missense	FS+	NR	(Zuberi et al., 2011)
F256LfsX2 0	DIS5	FrameShift	Epilepsy	NR	(Hesse et al., 2018)
C257R	DIS5	Missense	SME	NR	(Xu et al., 2014; Lindy et al., 2018)
S259R (De novo)	DIS5	Missense	DS	NR	(Sun et al., 2010; Wang et al., 2012)

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F261IfsX16 (De novo)	DIS5	FrameShift	DS	NR	(Yang et al., 2017)
L263V (Paternal)	DIS5	Missense	FHM	Shift steady-state activation to more negative values Slightly resists to entry into the fast inactivation state and slow inactivated state Accelerated recovery from inactivation	(Kahlig et al., 2008; Castro et al., 2009; Barros et al., 2014)
K263X (De novo)	DIS5	Nonsense	DS	NR	(Zuberi et al., 2011)
I264fs	DIS5	FrameShift	SME	NR	(Lee et al., 2014)
I264T	DIS5	Missense	Epilepsy	NR	(Lindy et al., 2018)
G265W (De novo)	DIS5	Missense	DS	NR	(Depienne et al., 2008)
Q267X (De novo)	DIS5	Nonsense	DS	NR	(Wang et al., 2012)
G271R	DIS5	Missense	DS	NR	(Cetica et al., 2017)

L273Q	DIS5	Missense	DS	NR	(Cho et al., 2018)
L273P	DIS5	Missense	Epilepsy	NR	(Lindy et al., 2018)
N275K	DIS5	Missense	PEFS+	Hippocampa volume loss (MRI)	(Kim et al., 2014)
K276VfsX2	DIS5	FrameShift	DS	NR	(Xu et al., 2015)
K276Q	DIS5	Missense	DS	NR	(Xu et al., 2015)
K276I	DIS5	Missense	Epilepsy	NR	(Lindy et al., 2018)
C277R (De novo)	DIS5	Missense	DS	NR	(Depienne et al., 2008)
C277G	DIS5-S6	Missense	DS	NR	(Pérez Delgado et al., 2010)
Q279X (De novo)	DIS5-S6	Nonsense	SMEB	NR	(Zuberi et al., 2011)
W280R (De novo)	DIS5-S6	Missense	DS	Febrile seizures Status epilepticus Myoclonic	(Nabbout et al., 2003; Wang et al., 2012; Liu et al., 2018)

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				Multifocal discharges (EEG)	
W280C	DIS5-S6	Missense	DS	Sporadic, diffuse, irregular spike-wave complex (EEG)	(Miyama et al., 2008; Villeneuve et al., 2014)
W281R (De novo)	DIS5-S6	Missense	SME	NR	(Xu et al., 2014)
P281S	DIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
P281A	DIS5-S6	Missense	DS	NR	(Wang et al., 2012)
P281L (De novo)	DIS5-S6	Missense	DS	Moderate mental retardation	(Depienne et al., 2008; Gokben et al., 2017; Lindy et al., 2018)
S286WfsX6 (De novo)	DIS5-S6	FrameShift	DS	NR	(Nabbout et al., 2003; Riva et al., 2009)
E289X (De novo, Maternal)	DIS5-S6	Nonsense	DS	NR	(Nabbout et al., 2003; Orrico et al., 2009)
E289V	DIS5-S6	Missense	DS	Generalized tonic-clonic seizures Developmental delay	(Lemke et al., 2012)

H290R	DIS5-S6	Missense	DS	NR	(Wang et al., 2012)
S291G	DIS5-S6	Missense	GEFS+	NR	(Zuberi et al., 2011)
T297I (Maternal)	DIS5-S6	Missense	DS	In association with R1525Q provokes shift in steady state activation to more positive values	(Nabbout et al., 2003; Binini et al., 2017)
V298EfsX3	DIS5-S6	FrameShift	SME DS	Haploinsufficiency	(Zuberi et al., 2011; Petrelli et al., 2012)
N299fsX3	DIS5-S6	FrameShift	SME	NR	(Xu et al., 2014)
N306Metfs X26	DIS5-S6	FrameShift	DS	NR	(Wang et al., 2012)
F310fsX1	DIS5-S6	FrameShift	SME	NR	(Xu et al., 2014)
E311ValfsX 22	DIS5-S6	FrameShift	DS	NR	(Xu et al., 2015)
E311X (De novo)	DIS5-S6	Nonsense	DS	Haploinsufficiency	(Orrico et al., 2009)

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F312S	DIS5-S6	Missense	DS	NR	(Ishii et al., 2017)
D313fs	DIS5-S6	FrameShift	SME	NR	(Lee et al., 2014)
W314R (Maternal)	DIS5-S6	Missense	Myoclonic- atonic epilepsy	NR	(Zuberi et al., 2011)
W314G	DIS5-S6	Missense	GEFS+	NR	(Afawi et al., 2016)
W314X	DIS5-S6	Nonsense	Epilepsy	NR	(Lindy et al., 2018)
Y317H	DIS5-S6	Missense	SME	NR	(Lee et al., 2014)
Y317C	DIS5-S6	Missense	DS	NR	(Cetica et al., 2017)
D320_R322 delinsG (De novo)	DIS5-S6	Slice donor site	DS	NR	(Depienne et al., 2008)
S321X (De novo)	DIS5-S6	Nonsense	DS	NR	(Depienne et al., 2008)

R322I	DIS5-S6	Missense	DS	NR	(Marini et al., 2007; Depienne et al., 2008)
Y323X (De novo)	DIS5-S6	Nonsense	DS	NR	(Riva et al., 2009; Nicita et al., 2010)
H324N	DIS5-S6	Missense	DS	NR	(Ishii et al., 2017)
H324P (Mosaic, Maternal)	DIS5-S6	Missense	DS	NR	(Yang et al., 2017)
Y325C (De novo)	DIS5-S6	Missense	SME	NR	(Liu et al., 2013)
Y325del	DIS5-S6	In-Frame Deletion	DS	NR	(Wu et al., 2015)
Y325X	DIS5-S6	Nonsense	SME	NR	(Liu et al., 2013)
L327R (Mosaic)	DIS5-S6	Missense	DS	Generalized tonic-clonic seizures	(de Lange et al., 2018)
E328GfsX1 2	DIS5-S6	FrameShift	DS	Generalized tonic-clonic seizures Hemicconvulsion Absences.	(de Lange et al., 2018)

Supplementary Material

G329C	DIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
G329A (De novo)	DIS5-S6	Missense	GEFS+	Generalized tonic-clonic	(Myers et al., 2017a)
L331fsX (De novo)	DIS5-S6	FrameShift	SME SMEB	NR	(Zuberi et al., 2011; Verbeek et al., 2013)
L331FefsX9 (De novo)	DIS5-S6	FrameShift	DS	NR	(Riva et al., 2009)
D332G	DIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
C336Y	DIS5-S6	Missense	SME DS	NR	(Xu et al., 2014)
G337E	DIS5-S6	Missense	DS	NR	(Ishii et al., 2017)
S340F	DIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
A342S	DIS5-S6	Missense	DS	NR	(Xu et al., 2015)

A342V (De novo)	DIS5-S6	Missense	DS SME	NR	(Zuberi et al., 2011; Xu et al., 2014)
G343R	DIS5-S6	Missense	DS	NR	(Ishii et al., 2017)
G343C	DIS5-S6	Missense	DS	NR	(Ishii et al., 2017)
G343E (De novo)	DIS5-S6	Missense	SMEB SME DS	Spike-wave complex and multifocal spikes (EEG) Photo and pattern sensitivity	(Fujiwara, 2003; Depienne et al., 2008; Zuberi et al., 2011)
C345VfsX8	DIS5-S6	FrameShift	DS	NR	(Harkin et al., 2007; Depienne et al., 2008)
C345R (De novo)	DIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
C345Y	DIS5-S6	Missense	DS	Moderate intellectual disability Slow speaking Dysarthrophonia Bradykinesia Ataxia	(Martin et al., 2010)
C345X (De novo)	DIS5-S6	Nonsense	DS	NR	(Zuberi et al., 2011)
C345W (De novo)	DIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)

G348X (De novo)	DIS5-S6	Nonsense	DS	NR	(Riva et al., 2009)
M350VfsX6 (De novo)	DIS5-S6	FrameShift	DS	NR	(Harkin et al., 2007)
M350V	DIS5-S6	Missense	DS	NR	(Xu et al., 2015)
C351R	DIS5-S6	Missense	DS	NR	(Doccini et al., 2015)
C351W (De novo)	DIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
C351X	DIS5-S6	Nonsense	DS	NR	(Kwong et al., 2012)
V352CfsX5	DIS5-S6	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
K353fsX (De novo)	DIS5-S6	FrameShift	DS	NR	(Zuberi et al., 2011)
V352EfsX4 (De novo)	DIS5-S6	FrameShift	SME DS	NR	(Harkin et al., 2007; Xu et al., 2014)

G355D (De novo)	DIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
R356G	DIS5-S6	Missense	SMEB	NR	(Marini et al., 2007)
R356X	DIS5-S6	Nonsense	DS	NR	(Ishii et al., 2017)
N357Y	DIS5-S6	Missense	DS	NR	(Cho et al., 2018)
N357I (De novo)	DIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
P358T	DIS5-S6	Missense	SMEB SME	NR	(Marini et al., 2007; Xu et al., 2014)
P358S	DIS5-S6	Missense	DS	NR	(Xu et al., 2014)
N359S (De novo)	DIS5-S6	Missense	DS	NR	(Zuberi et al., 2011; Dhamija et al., 2014; Xu et al., 2014; Butler et al., 2017a)
N359IfsX20	DIS5-S6	FrameShift	DS	NR	(Wang et al., 2012)
N359I	DIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)

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N359K (De novo)	DIS5-S6	Missense	DS	NR	(Yang et al., 2017)
T363P	DIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
Thr363Arg	DIS5-S6	Missense	DS	Generalized tonic-clonic seizures	(Zuberi et al., 2011; Le Gal et al., 2014)
S364AfsX15 (De novo)	DIS5-S6	FrameShift	DS	NR	(Zuberi et al., 2011)
F365LfsX14 (De novo)	DIS5-S6	Missense	DS	NR	(Yang et al., 2017)
D366X (De novo)	DIS5-S6	Nonsense	DS	NR	(Depienne et al., 2008)
D366fsX76	DIS5-S6	FrameShift	SME	NR	(Xu et al., 2014)
D366E (De novo)	DIS5-S6	Missense	DS	Generalized tonic-clonic seizures	(Zucca et al., 2008)
A371V	DIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)

L373FfsX6	DIS5-S6	FrameShift	PEFS+	Mild ventricular dilatation (MRI) Developmental delay	(Kim et al., 2014)
S374fsX5 (De novo)	DIS5-S6	FrameShift	DS	NR	(Nabbout et al., 2003)
S374Y (De novo)	DIS5-S6	Missense	DS	NR	(Djémié et al., 2016)
L375F (De novo)	DIS5-S6	Missense	DS	NR	(Wei et al., 2018)
R377X (De novo)	DIS5-S6	Nonsense	DS	NR	(Depienne et al., 2008; Riva et al., 2009; Zuberi et al., 2011; Wang et al., 2012; Gaily et al., 2013; Xu et al., 2014; Djémié et al., 2016; Esterhuizen et al., 2018)
R377L	DIS5-S6	Missense	SME	NR	(Hattori et al., 2008)
R377Q (Maternal)	DIS5-S6	Missense	GEFS+	Generalized tonic-clonic seizures	(Zucca et al., 2008; Xu et al., 2015; Cetica et al., 2017)
L378Q	DIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
M379R	DIS5-S6	Missense	DS	Generalized tonic-clonic seizures Partial seizures Developmental delay	(Lemke et al., 2012)

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M379K	DIS5-S6	Missense	DS	NR	(Xu et al., 2015)
T380IfsX11	DIS5-S6	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
D382N (De novo)	DIS5-S6	Missense	SME	NR	(Zuberi et al., 2011)
D382R	DIS5-S6	Missense	DS	NR	(Xu et al., 2014)
F383D (De novo)	DIS5-S6	Missense	DS	NR	(Riva et al., 2009)
W384R (De novo)	DIS5-S6	Missense	DS SMEB SME	Generalized tonic-clonic seizures Partial seizures	(Zuberi et al., 2011; Wang et al., 2012; Verbeek et al., 2013)
W384X	DIS5-S6	Nonsense	DS	Complex partial seizures with generalization Tonic seizures	(Surovy et al., 2016)
E385K	DIS5-S6	Missense	SMEB	NR	(Harkin et al., 2007)
E385G(De novo)	DIS5-S6	Missense	DS	NR	(Petrelli et al., 2012; Ko et al., 2018)

E385V	DIS5-S6	Missense	DS	NR	(Doccini et al., 2015)
E385D (De novo)	DIS5-S6	Missense	DS	NR	(Wu et al., 2015)
N386KfsX64 (De novo)	DIS5-S6	FrameShift	DS	NR	(Wang et al., 2012)
Y388H (Paternal)	DIS5-S6	Missense	DS GEFS+	NR	(Mahoney et al., 2009; Bennett et al., 2017)
Q389X	DIS5-S6	Nonsense	DS	NR	(Nabbout et al., 2003)
T391P (De novo)	DIS5-S6	Missense	DS	Generalized tonic-clonic seizures Partial Seizures	(Reyes et al., 2011)
R393TfsX57	DIS5-S6	FrameShift	DS	NR	(Zuberi et al., 2011)
L392F	DIS5-S6	Missense	DS	NR	(Ishii et al., 2017)
R393C (De novo)	DIS5-S6	Missense	DS LGS SMEB	NR	(Harkin et al., 2007; Marini et al., 2007; Riva et al., 2009; Lim et al., 2011; Zuberi et al., 2011; Kwong et al., 2012; Allen et al., 2013; Villeneuve et al., 2014)

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R393S (De novo)	DIS5-S6	Missense	DS Myoclonic astatic epilepsy	NR	(Harkin et al., 2007; Marini et al., 2007; Depienne et al., 2008; Riva et al., 2009)
R393H (De novo)	DIS5-S6	Missense	DS SMEB	Generalized tonic-clonic seizures Myoclonus Febrile seizures Developmental delay	(Claes et al., 2003; Marini et al., 2007; Sun et al., 2010; Zuberi et al., 2011; Lemke et al., 2012; Rilstone et al., 2012; Wang et al., 2012; Xu et al., 2014; Djémié et al., 2016; Haginoya et al., 2018)
R393L	DIS5-S6	Missense	DS	NR	(Cetica et al., 2017)
A394D	DIS5-S6	Missense	GEFS+	Mild proeminence of lateral ventricles (MRI) Developmental delay Generalized tonic-clonic seizures	(Myers et al., 2017a)
A395SfsX5 5	DIS5-S6	FrameShift	DS	NR	(Xu et al., 2015)
A395P (De novo)	DIS5-S6	Missense	Cryptogenic focal epilepsy	NR	(Harkin et al., 2007)
A395MfsX6 (De novo)	DIS5-S6	FrameShift	DS	NR	(Sun et al., 2010)
G396E (De novo)	DIS5-S6	Missense	DS	NR	(Lim et al., 2011)

T398RfsX3	DIS5-S6	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
Y399D	DIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
Y399F	DIS5-S6	Missense	GEFS+	Focal seizures with secondary generalization arising from hemispheres (EEG)	(Gauthier et al., 2017)
Y399X (De novo)	DIS5-S6	Nonsense	DS	NR	(Harkin et al., 2007)
M400DfsX49	DIS5-S6	Missense	DS	NR	(Xu et al., 2015)
M400del (De novo)	DIS6	In-frame Deletion	SME DS SMEB	NR	(Ceulemans et al., 2004; Depienne et al., 2008; Wang et al., 2012)
M400K	DIS6	Missense	DS	NR	(Xu et al., 2015)
M400V	DIS6	Missense	GEFS+	NR	(Brunklau et al., 2015)
F402L (Mosaic)	DIS6	Missense	Epilepsy	NR	(Stosser et al., 2018)

F403L (De novo)	DIS6	Missense	DS	NR	(Harkin et al., 2007)
V406F	DIS6	Missense	DS	NR	(Zuberi et al., 2011)
V404CfsX4 6	DIS6	FrameShift	DS	NR	(Ream and Mikati, 2014; Mahdich et al., 2018)
F408L	DIS6	Missense	Epilepsy	NR	(Klassen et al., 2011)
L409W(Maternal)	DIS6	Missense	DS	NR	(Wang et al., 2012)
G408WfsX 6	DIS6	FrameShift	DS	NR	(Cetica et al., 2017)
F412I (Paternal)	DIS6	Missense	SMEB GEFS+	Febrile seizure	(Ebrahimi et al., 2010; Tonekaboni et al., 2013)
Y413N (De novo)	DIS6	Missense	DS	NR	(Harkin et al., 2007; Mulley et al., 2013)
I415K (De novo)	DIS6	Missense	Epilepsy	NR	(Staněk et al., 2018)

N416IfsX2	DIS6	FrameShift	DS	NR	(Zuberi et al., 2011)
N416KfsX2	DIS6	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
N416I	DIS6	Missense	DS	Focal spike-wave (EEG)	(Zhou et al., 2018)
L417X	DIS6	Nonsense	DS	NR	(Ishii et al., 2017)
A420WfsX 27	DIS6	FrameShift	DS	NR	(Zuberi et al., 2011)
A420V (De novo)	DIS6	Missense	GEFS+	NR	(Xu et al., 2015)
A420D	DIS6	Missense	Epilepsy	NR	(Butler et al., 2017a)
V421M	DIS6	Missense	DS	NR	(Trujillano et al., 2017)
V422M(De novo)	DIS6	Missense	DS	NR	(Kwong et al., 2012; Butler et al., 2017a)
V422Le(De novo)	DIS6	Missense	EE	Psychomotor developmental delay	(Ohashi et al., 2014)

				Theta activities with right predominance (EEG)	
V422E(De novo)	DIS6	Missense	Cryptogenic generalized epilepsy	NR	(Harkin et al., 2007)
V422A	DIS6	Missense	DS	NR	(Xu et al., 2015)
Y426N(De novo)	DI-DII	Missense	DS	Reduced current density Shift steady state inactivation to more negative values Larger time constant for the slow component of recovery from fast inactivation	(Nabbout et al., 2003; Ohmori et al., 2006; Allen et al., 2016)
Y426C (De novo)	DI-DII	Missense	DS	NR	(Depienne et al., 2008; Wang et al., 2012)
Y426X	DI-DII	Nonsense	DS	NR	(Hesse et al., 2018)
E427K	DI-DII	Missense	DS	NR	(Cho et al., 2018)
E431X	DI-DII	Nonsense	DS	NR	(Zuberi et al., 2011)
A432S	DI-DII	Missense	DS	NR	(Usluer et al., 2016)

L433fsX16 (De novo)	DI-DII	FrameShift	Myoclonic astatic epilepsy	Severe idiopathic generalized epilepsy of infancy with generalized tonic-clonic seizures	(Ebach et al., 2005)
L434WfsX1 4	DI-DII	FrameShift	DS	NR	(Xu et al., 2015)
E435X (De novo)	DI-DII	Nonsense	DS	Mild psychomotor retardation Myoclonic seizures Atypical absence	(Fukuma et al., 2004; Wang et al., 2012)
Q439X (De novo)	DI-DII	Nonsense	DS	NR	(Depienne et al., 2008; Wang et al., 2012)
E443X	DI-DII	Nonsense	DS	Multifocal Discharges Generalized polyspike- wave (EEG)	(Liu et al., 2018)
Q445X	DI-DII	Nonsene	DS	NR	(Surovy et al., 2016)
I448X (De novo)	DI-DII	Nonsense	DS	NR	(Wallace et al., 2003)
E449X	DI-DII	Nonsense	DS	NR	(Xu et al., 2015)
E449DfsX4 1 (De novo)	DI-DII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)

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Q450X (De novo)	DI-DII	Nonsense	DS	NR	(Depienne et al., 2008; Kwong et al., 2012; Mercimek-Mahmutoglu et al., 2015)
E450GfsX10 (De novo)	DI-DII	FrameShift	DS	NR	(Orrico et al., 2009)
Q459R(De novo)	DI-DII	Missense	DS GEFS+	NR	(Møller et al., 2016)
Q460X	DI-DII	Nonsense	DS	NR	(Zuberi et al., 2011)
S470FfsX17 (De novo)	DI-DII	FrameShift	DS	NR	(Depienne et al., 2008)
S470fsX15 (De novo)	DI-DII	FrameShift	DS	NR	(Sun et al., 2010)
G477AfsX13	DI-DII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
D481AfsX8	DI-DII	FrameShift	SME	NR	(Xu et al., 2015)
S487EfsX6 (Mosaic)	DI-DII	FrameShift	DS	Generalized tonic-clonic seizure Focal seizures with secondary generalization Mild motor and cognitive delay	(Sharkia et al., 2016)

K488EfsX6 (Maternal)	DI-DII	FrameShift	DS	NR	(Yang et al., 2017)
R498X (De novo)	DI-DII	Nonsense	DS	NR	(Depienne et al., 2008)
R500EfsX10 (De novo)	DI-DII	FrameShift	DS	NR	(Wang et al., 2012)
R500EfsX (De novo)	DI-DII	FrameShift	DS	NR	(Wang et al., 2012)
R500Q	DI-DII	Missense	DS	NR	(Zhou et al., 2018)
R501fsX43 (De novo)	DI-DII	FrameShift	SMEB	NR	(Ohmori et al., 2002)
R504TfsX12	DI-DII	FrameShift	SME	NR	(Villeneuve et al., 2014)
K505X (De novo)	DI-DII	Nonsense	DS	NR	(Liu et al., 2018)
Q506X	DI-DII	Nonsense	SME DS	NR	(Cantarín Extremera et al., 2011)
K507AfsX9	DI-DII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)

K507SfsX3 6	DI-DII	FrameShift	SME	NR	(Villeneuve et al., 2014)
Q509X (De novo)	DI-DII	Nonsense	Epilepsy	NR	(Staněk et al., 2018)
E511fsX54 3	DI-DII	FrameShift	DS	NR	(Wang et al., 2012)
E513KfsX3 1 (Paternal, Mosaic)	DI-DII	FrameShift	DS	NR	(Verbeek et al., 2011)
E513X	DI-DII	Nonsense	DS	NR	(Depienne et al., 2008)
E513GfsX5	DI-DII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
E524X	DI-DII	Nonsense	Epilepsy	NR	(Lindy et al., 2018)
S525F(De novo)	DI-DII	Missense	DS	NR	(Depienne et al., 2008)
Y525LfsX2	DI-DII	FrameShift	DS	NR	(Cetica et al., 2017)

I529SfsX15	DI-DII	FrameShift	DS	NR	(Ishii et al., 2017)
I529NfsX11	DI-DII	FrameShift	DS	NR	(Cetica et al., 2017)
R530KfsX10	DI-DII	FrameShift	DS	NR	(Haginoya et al., 2018)
G533VfsX11	DI-DII	FrameShift	DS	NR	(Ishii et al., 2017)
R542X (De novo)	DI-DII	Nonsense	SME DS	NR	(Marini et al., 2007; Depienne et al., 2008; Riva et al., 2009; Sun et al., 2010; Zuberi et al., 2011)
R542Q(Paternal)	DI-DII	Missense	GEFS+ SME	NR	(Escayg et al., 2001; Weiss et al., 2003; Combi et al., 2009; Orrico et al., 2009; Wang et al., 2012; Lee et al., 2014; Lal et al., 2016)
L543X	DI-DII	Nonsense	DS	NR	(Cetica et al., 2017)
T544HfsX14 (De novo)	DI-DII	FrameShift	SMEB	NR	(Lim et al., 2011)
Y545LfsX12	DI-DII	FrameShift	DS	NR	(Ishii et al., 2017)

E546X	DI-DII	Nonsense	DS	NR	(Liu et al., 2018)
Y549GfsX1 0	DI-DII	FrameShift	DS	NR	(Zuberi et al., 2011)
K547EfsX2 3	DI-DII	FrameShift	DS	NR	(Harkin et al., 2007; Depienne et al., 2008)
R548EsX23 (De novo)	DI-DII	FrameShift	SMEB	NR	(Ohmori et al., 2002)
Q554fsX17	DI-DII	FrameShift	DS	NR	(Sun et al., 2010)
E554R	DI-DII	Missense	SME	NR	(Xu et al., 2014)
Q554H (De novo)	DI-DII	Missense	DS	Genelized tonic-clonic seizure, atonic and myoclonic seizures	(Skjei et al., 2015)
S555FfsX6 (De novo)	DI-DII	FrameShift	DS	NR	(Zuberi et al., 2011)
L556CfsX2 (De novo)	DI-DII	FrameShift	DS	NR	(Sun et al., 2008a)

R560VfsX6 3	DI-DII	FrameShift	Epilepsy	Generalized epilepsy Developmental delay	(Hesse et al., 2018)
R560PfsX8 (De novo)	DI-DII	FrameShift	DS	NR	(Zuberi et al., 2011)
L563YfsX6 0 (De novo)	DI-DII	FrameShift	DS	NR	(Harkin et al., 2007)
L563Q	DI-DII	Missense	Episodic ataxia	NR	(Choi et al., 2017)
P566S	DI-DII	Missense	DS	NR	(Usluer et al., 2016)
R568X (De novo)	DI-DII	Nonsense	DS	NR	(Ohmori et al., 2002; Marini et al., 2007; Zuberi et al., 2011; Okumura et al., 2012; Villeneuve et al., 2014; Kothur et al., 2018)
R568Q	DI-DII	Missense	NR	Seizures	(Butler et al., 2017a)
S570N	DI-DII	Missense	EE	NR	(Posey et al., 2017)
S570I (Familial)	DI-DII	Missense	GEFS+	NR	(Cetica et al., 2017)

Supplementary Material

F575SfsX4 8 (De novo)	DI-DII	FrameShift	Cryptogenic focal epilepsy PEFS+	NR	(Harkin et al., 2007; Kim et al., 2014)
R580X (Familial)	DI-DII	Nonsense	DS	NR	(Depienne et al., 2008; Arlier et al., 2010; Zuberi et al., 2011)
K582SfsX7	DI-DII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
E602X	DI-DII	Nonsense	DS	NR	(Depienne et al., 2008)
R604H (Paternal)	DI-DII	Missense	DS Juvenile myoclonic epilepsy	Generalized tonic-clonic seizures and Febrile Seizures	(Escayg et al., 2001; Harkin et al., 2007; Fendri-Kriaa et al., 2009; Wang et al., 2012; Lal et al., 2016)
S607PfsX1 6	DI-DII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
L608CfsX1 5	DI-DII	FrameShift	SME SMEB	NR	(Ohmori et al., 2002; Depienne et al., 2008)
R612X (De novo)	DI-DII	Nonsense	DS	NR	(Sun et al., 2008a; Xu et al., 2014)
R613X (De novo)	DI-DII	Nonsense	SME DS	NR	(Kearney et al., 2006; Depienne et al., 2008; Riva et al., 2009; Zuberi et al., 2011; Rodda et al., 2012; Wang et al., 2012; Moehring et al., 2013; Lee et al., 2014; Xu et al., 2014)

E616RfsX7	DI-DII	FrameShift	DS	NR	(Cetica et al., 2017)
E616D	DI-DII	Missense	Epilepsy	NR	(Parrini et al., 2017)
R617TfsX10 (Paternal)	DI-DII	FrameShift	DS	NR	(Yang et al., 2017)
R618C (Paternal)	DI-DII	Missense	PEFS+	Generalized tonic-clonic seizures Multifocal epilepsy (EEG) Bilateral bursts of 3-4 Hz spike and wave (EEG)	(Brunklau et al., 2015)
R618AfsX5 (Paternal)	DI-DII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
S620AfsX5 (De novo)	DI-DII	FrameShift	SMEB	NR	(Marini et al., 2007)
T625PfsX47 (De novo)	DI-DII	FrameShift	DS	NR	(Depienne et al., 2008)
S626G	DI-DII	Missense	SME SMEB Cryptogenic generalized epilepsy	NR	(Harkin et al., 2007; Depienne et al., 2008; Xu et al., 2014; Lee et al., 2017)

R627K	DI-DII	Missense	GEFS+	NR	(Cetica et al., 2017)
H642TfsX30 (De novo)	DI-DII	FrameShift	DS	NR	(Ishii et al., 2017)
V645GfsX30 (De novo)	DI-DII	FrameShift	DS	NR	(Yang et al., 2017; Liu et al., 2018)
N648Lys	DI-DII	Missense	EE	NR	(Zhu et al., 2017)
P657L	DI-DII	Missense	DS	NR	(Xu et al., 2015)
S662X (De novo)	DI-DII	Nonsense	PEFS+	Generalized tonic-clonic seizures	(Yu et al., 2010)
D674G (De novo)	DI-DII	Missense	DS	NR	(Harkin et al., 2007)
T685LfsX5	DI-DII	FrameShift	SMEB	NR	(Zuberi et al., 2011)
K691X	DI-DII	Nonsense	SME	NR	(Xu et al., 2014)

S695TfsX7 (De novo)	DI-DII	FrameShift	DS	NR	(Depienne et al., 2008)
S696SfsX8 (De novo)	DI-DII	FrameShift	SME	NR	(Lim et al., 2011)
H698Y	DI-DII	Missense	SME	NR	(Villeneuve et al., 2014)
S700fsX4	DI-DII	FrameShift	SME	NR	(Xu et al., 2014)
D702AfsX2 5 (De novo)	DI-DII	FrameShift	EE	NR	(de Kovel et al., 2016)
P707NfsX9 (De novo)	DI-DII	FrameShift	DS	NR	(Kearney et al., 2006)
Q711X	DI-DII	Nonsense	SME	Slow background, generalized spikes (EEG) Generalized tonic- clonic seizures	(Lee et al., 2014)
Q711HfsX4 (De novo)	DI-DII	FrameShift	DS	NR	(Depienne et al., 2008)
R712X (De novo; Maternal)	DI-DII	Nonsense	SME DS	Focal epilepsy frontal right, beta activity (EEG) Reduced current density, low protein expression	(Ohmori et al., 2002; Sugawara et al., 2002, 2003; Fukuma et al., 2004; Depienne et al., 2008; Zuberi et al., 2011; Okumura et al., 2012; Wang et al., 2012; Moehring et al., 2013)

Supplementary Material

W737X	DI-DII	Nonsense	DS	NR	(Ko et al., 2018)
W738X (De novo)	DI-DII	Nonsense	SME	Febrile seizures Partial, generalized tonic-clonic, myoclonic Severe intellectual disability	(Kwong et al., 2012; Xu et al., 2014)
W738L	DI-DII	Missense	SME	NR	(Xu et al., 2014)
W738CfsX ₉	DI-DII	FrameShift	SME	NR	(Hattori et al., 2008)
I747TfsX9	DI-DII	FrameShift	DS	NR	(Ishii et al., 2017)
W748X	DI-DII	Nonsense	DS	NR	(Wang et al., 2012)
Y753X	DI-DII	Nonsense	DS	NR	(Do et al., 2017)
W754X	DI-DII	Nonsense	DS	NR	(Ishii et al., 2017)
W754L	DI-DII	Missense	DS	NR	(Xu et al., 2015)

H759fsX14 (De novo)	DI-DII	FrameShift	SME	NR	(Lin et al., 2013)
N762D (Paternal)	DI-DII	Missense	DS	NR	(Zuberi et al., 2011)
P768L	DIIS1	Missense	SME DS	NR	(Sun et al., 2010; Xu et al., 2014)
P768fsX5	DIIS1	FrameShift	DS	NR	(Sun et al., 2010)
F769Y	DIIS1	Missense	GEFS+	NR	(Cetica et al., 2017)
A773TfsX3 1 (De novo)	DIIS1	FrameShift	EE	NR	(Wei et al., 2018)
I774HfsX25	DIIS1	FrameShift	DS	NR	(Xu et al., 2015)
L780delins FI	DIIS1	In-frame Deletion	Epilepsy	NR	(Lindy et al., 2018)
L783P (De novo)	DIIS1	Missense	DS	NR	(Harkin et al., 2007)
M785V	DIIS1-S2	Missense	DS	NR	(Xu et al., 2015)

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M785T (De novo)	DIIS1-S2	Missense	DS	NR	(Zuberi et al., 2011; Lindy et al., 2018)
A786T	DIIS1-S2	Missense	DS	NR	(Cetica et al., 2017)
E788K	DIIS1-S2	Missense	SME	NR	(Hattori et al., 2008)
Y790C (Paternal)	DIIS1-S2	Missense	GEFS+	Reduced current density (91%) associated with reduction of cell surface expression (91%)	(Annesi et al., 2003; Orrico et al., 2009; Bechi et al., 2015; Bennett et al., 2017)
Y790F	DIIS1-S2	Missense	GEFS+ Panayiotopoulos Syndrome	NR	(Grosso et al., 2007; Cetica et al., 2017)
Y790X (De novo)	DIIS1-S2	Nonsense	DS	NR	(Depienne et al., 2008)
Q791X (De novo)	DIIS1-S2	Nonsense	DS	NR	(Esterhuizen et al., 2018)
N804K	DIIS2	Missense	DS	NR	(Cetica et al., 2017)
F807LfsX11 (De novo)	DIIS2	FrameShift	DS	NR	(Zuberi et al., 2011)

T808S (De novo)	DIIS2	Missense	ICEGTC	Rare sharp waves in left temporal (EEG) Moderate mental decline Increase current density Delayed recovery from inactivation	(Fujiwara, 2003; Rhodes et al., 2005)
T812I	DIIS2	Missense	SMEB	NR	(Zuberi et al., 2011)
T812R (De novo)	DIIS2	Missense	DS	NR	(Claes et al., 2009; Riva et al., 2009)
Y825fs	DIIS2	FrameShift	DS	NR	(Martin et al., 2010)
Y827D	DIIS2	Missense	DS	NR	(Xu et al., 2015)
E830X (De novo)	DIIS2	Nonsense	DS	NR	(Zhang et al., 2015)
W832X	DIIS3	Nonsense	DS	NR	(Depienne et al., 2008)
F835WfsX7 (De novo)	DIIS3	FrameShift	DS	NR	(Depienne et al., 2008)
D836X (De novo)	DIIS3	Nonsense	DS	NR	(Zuberi et al., 2011)

V841A	DIIS3	Missense	DS	NR	(Ko et al., 2018)
L842R	DIIS3	Missense	DS	NR	(Zuberi et al., 2011)
F843R	DIIS3	Missense	DS	NR	(Depienne et al., 2008)
S843X (De novo)	DIIS3	Nonsense	DS	EEG reveals focal spike activity, diffuse polyspike waves accompanied by myoclonic jerks	(Buoni et al., 2006)
S843R (De novo)	DIIS3	Missense	DS	NR	(Depienne et al., 2008)
L844X	DIIS3	Nonsense	SME	NR	(Dhamija et al., 2014)
E853K (De novo)	DIIS3	Missense	DS	NR	(Riva et al., 2009)
E846G	DIIS3	Missense	SME	NR	(Xu et al., 2014)
R846DfsX3 1	DIIS3	FrameShift	DS	NR	(Ishii et al., 2017)

G848DfsX2 9	DIIS3	FrameShift	DS	NR	(Depienne et al., 2008)
L849TfsX6 6	DIIS3	FrameShift	DS	NR	(Depienne et al., 2008)
L849P	DIIS3	Missense	DS	NR	(Cetica et al., 2017)
R851P (De novo)	DIIS3	Missense	DS	NR	(Esterhuizen et al., 2018)
E853K (De novo)	DIIS3-S4	Missense	DS	NR	(Riva et al., 2009)
G854_L855 del (De novo)	DIIS3-S4	In-frame Deletion	SMEB	NR	(Zuberi et al., 2011)
G854fsX23 (De novo)	DIIS3-S4	FrameShift	DS	NR	(Harkin et al., 2007)
V857FfsX2 0	DIIS3-S4	FrameShift	SME	NR	(Depienne et al., 2008; Lindy et al., 2018)
V857I	DIIS3-S4	Missense	Epilepsy	NR	(Lindy et al., 2018)
R859C (De novo, Paternal)	DIIS4	Missense	GEFS+ DS	Shift steady state activation to more positive values	(Barela et al., 2006; Depienne et al., 2008; Zuberi et al., 2011)

R859H (Paternal)	DIIS4	Missense	GEFS+	Shift steady state activation and inactivation to more negative values Increase Persistent current	(Volkers et al., 2011; Myers et al., 2017a; Lindy et al., 2018)
R862X (De novo, Familal)	DIIS4	Nonsense	GEFS+ SME SMEB	NR	(Orrico et al., 2009; Wang et al., 2012; Lee et al., 2014; Xu et al., 2014)
R862G (De novo)	DIIS4	Missense	MMPSI	Multifocal epilepsy Hemiclonic Severe intellectual disability	(Carranza Rojo et al., 2011; Barba et al., 2014)
R862Q	DIIS4	Missense	DS	NR	(Arlier et al., 2010; Zuberi et al., 2011)
L863W (De novo)	DIIS4	Missense	SME	NR	(Xu et al., 2014)
L864RfsX13 (De novo)	DIIS4	FrameShift	DS	NR	(Zuberi et al., 2011)
R865G	DIIS4	Missense	DS	Shift steady state activation to more negative values Increase Persistent current	(Volkers et al., 2011)
R865X (De novo)	DIIS4	Nonsense	DS	NR	(Ohmori et al., 2002; Depienne et al., 2008; Lim et al., 2011; Wang et al., 2012;

					Xu et al., 2014; Kothur et al., 2018)
K868del	DIIS4	In-frame Deletion	SME	NR	(Moehring et al., 2013)
K868fsX7	DIIS4	FrameShift	SME	NR	(Xu et al., 2014)
Ks868N (Maternal)	DIIS4	Missense	GEFS+	NR	(Cetica et al., 2017)
A870LfsX5 (De novo)	DIIS4	FrameShift	DS	NR	(Marini et al., 2007)
S872Y	DIIS4	Missense	SME	NR	(Xu et al., 2014)
W873X	DIIS4	Nonsense	SMEB	NR	(Villeneuve et al., 2014)
T875K (Paternal)	DIIS4	Missense	SME GEFS+	Self-limited focal epilepsy of childhood Atypical childhood epilepsy with centrotemporal spikes (EEG) Panayiotopoulos syndrome	(Depienne et al., 2008; Kivity et al., 2017)
T875M	DIIS4	Missense	PEFS+ SMEB	Enhance slow inactivation in the presence of beta1 subunity	(Escayg et al., 2000; Alekov et al., 2001; Spanpanato et al., 2001a; George, 2004; Wang et al., 2012)

				Increase persistent current Shift steady state activation to more positive values	
L876I	DIIS4	Missense	DS	NR	(Wang et al., 2012)
L879X	DIIS4-S5	Nonsense	DS	NR	(Depienne et al., 2008)
L879P	DIIS4-S5	Missense	DS GEFS+	NR	(Møller et al., 2016)
I880KfsX14	DIIS4-S5	FrameShift	SME	NR	(Depienne et al., 2008)
I882F (De novo)	DIIS4-S5	Missense	DS	NR	(Ishii et al., 2017)
S886F	DIIS4-S5	Missense	DS	NR	(Cetica et al., 2017)
Ala889LeufsX5 (De novo)	DIIS4-S5	FrameShift	DS	NR	(Zuberi et al., 2011)
Leu890Phe (De novo)	DIIS4-S5	Missense	DS	NR	(Zuberi et al., 2011; Tsai et al., 2018)

Asn892Ilefs X2 (De novo)	DIIS5	FrameShift	SME	NR	(Singh et al., 2009)
L893X (De novo)	DIIS5	Nonsense	DS	NR	(Riva et al., 2009)
T894S	DIIS5	Missense	Epilepsy	NR	(Lindy et al., 2018)
V896L (De novo)	DIIS5	Missense	DS	NR	(Depienne et al., 2008)
V896I	DIIS5	Missense	DS	Generalized tonic-clonic seizures	(Rilstone et al., 2012; Wang et al., 2012)
V896F	DIIS5	Missense	SMEB	NR	(Wang et al., 2012)
V896_A898 del	DIIS5	In-frame deletion	Epilepsy	NR	(Lindy et al., 2018)
L897S	DIIS5	Missense	DS	NR	(Xu et al., 2015)
I899T (De novo, Familial)	DIIS5	Missense	GEFS+ LGS	NR	(Orrico et al., 2009; Allen et al., 2013; Bennett et al., 2017)
F902C	DIIS5	Missense	DS	Not measurable current	(Ohmori et al., 2002; Rhodes et al., 2004)

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A905T	DIIS5	Missense	DS	NR	(Ishii et al., 2017)
A905P (De novo)	DIIS5	Missense	EE	NR	(Hamdan et al., 2017)
V906GfsX2 9	DIIS5	FrameShift	DS	NR	(Ishii et al., 2017)
V907F	DIIS5	Missense	Focal epilepsy	Bitemporal slow waves (EEG)	(Hildebrand et al., 2016)
G908R	DIIS5	Missense	Epilepsy	NR	(Lindy et al., 2018)
Q910K	DIIS5	Missense	SME	NR	(Xu et al., 2014)
Q910L	DIIS5	Missense	DS	NR	(Ishii et al., 2017)
S915AfsX20 (De novo)	DIIS5-S6	FrameShift	SMEB	NR	(Kearney et al., 2006)
D918IfsX17	DIIS5-S6	FrameShift	DS	NR	(Sun et al., 2010)

M923I (Paternal)	DIIS5-S6	Missense	DS	NR	(Liu et al., 2018)
S925VfsX10	DIIS5-S6	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
C927F (De novo)	DIIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
Q928X	DIIS5-S6	Nonsense	Epilepsy	NR	(Lindy et al., 2018)
L929SfsX6	DIIS5-S6	FrameShift	DS	Episode of status epilepticus followed by persistent lethargy afted 48 hours of acute febrile	(Tsuji et al., 2011)
R931C (De novo)	DIIS5-S6	Missense	DS SMEB	NR	(Ohmori et al., 2002; Depienne et al., 2008)
R931H	DIIS5-S6	Missense	SME DS	Fever vaccination Generalized tonic-clonic Dyscognitive Developmental regression after seizure onset	(Catarino et al., 2011; Zuberi et al., 2011; Rilstone et al., 2012; Xu et al., 2014)
R931P	DIIS5-S6	Missense	SME	NR	(Xu et al., 2014)
W932R (De novo)	DIIS5-S6	Missense	DS	NR	(Kothur et al., 2018)

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W932C	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
T932X (De novo)	DIIS5-S6	Nonsense	SME DS	Generalized tonic-clonic seizures Severe mental retardation	(Claes et al., 2003; Dhamija et al., 2014)
H933P	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
M934R	DIIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
M934I (De novo)	DIIS5-S6	Missense	DS	Moderate psychomotor retardation	(Fukuma et al., 2004; Depienne et al., 2008; Wang et al., 2012)
N935H (Paternal)	DIIS5-S6	Missense	PEFS+	Generalized tonic-clonic Hemiclonic seizure Multiple generalized slow waves with some spike discharges while awake, bilateral frontal spikes and spike waves during sleep (EEG)	(Sun et al., 2008b)
D936Y (De novo)	DIIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
D936V (De novo)	DIIS5-S6	Missense	SME	NR	(Lin et al., 2013)

H939Y (De novo)	DIIS5-S6	Missense	DS	NR	(Sun et al., 2010)
H939P	DIIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
H939Q (De novo)	DIIS5-S6	Missense	DS	Status epilepticus Generalized tonic-clonic seizures Complex partial seizures Moderate mental retardation No measurable current	(Claes et al., 2003; Ohmori et al., 2006)
S940F	DIIS5-S6	Missense	DS	NR	(Wang et al., 2012)
L942V	DIIS5-S6	Missense	DS GEFS+	NR	(Møller et al., 2016)
L942P (De novo)	DIIS5-S6	Missense	DS	NR	(Riva et al., 2009)
I943CfsX10 (De novo)	DIIS5-S6	FrameShift	DS	NR	(Depienne et al., 2008)
I943D	DIIS5-S6	Missense	DS	NR	(Depienne et al., 2008)

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V944A (De novo)	DIIS5-S6	Missense	SMEB	NR	(Fukuma et al., 2004; Wang et al., 2012)
V944E (De novo)	DIIS5-S6	Missense	DS	NR	(Harkin et al., 2007; Rodda et al., 2012)
F945L (De novo)	DIIS5-S6	Missense	DS	NR	(Harkin et al., 2007)
R946fsX8 (De novo)	DIIS5-S6	FrameShift	DS	NR	(Fujiwara, 2003)
R946C (De novo)	DIIS5-S6	Missense	SME DS SMEB	Non-functional Channel	(Fukuma et al., 2004; Volkers et al., 2011; Zuberi et al., 2011; Wang et al., 2012; Lee et al., 2014; Xu et al., 2014)
R946S (De novo)	DIIS5-S6	Missense	Severe idiopathic generalized epilepsy of infancy	Short generalized tonic-clonic seizures at night Seizure onset left temporo-parietal (EEG) Tonic seizure right arm Seizure onset left frontal Seizure onset right frontocentral	(Ebach et al., 2005; Tiefes et al., 2019)
R946H (De novo)	DIIS5-S6	Missense	PEFS+ SMEB DS	Non-functional Channel	(Fukuma et al., 2004; Harkin et al., 2007; Depienne et al., 2008; Liao et al., 2010; Verbeek et al., 2011, 2013; Volkers et al., 2011; Zuberi et al., 2011; Wang et al., 2012)
R946P	DIIS5-S6	Missense	SME	NR	(Xu et al., 2014)

C949Y (De novo)	DIIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
C949S (De novo)	DIIS5-S6	Missense	SME	NR	(Depienne et al., 2008)
G950R (De novo)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
G950E (De novo)	DIIS5-S6	Missense	DS	NR	(Harkin et al., 2007; Rodda et al., 2012)
W952R (De novo)	DIIS5-S6	Missense	DS	NR	(Lim et al., 2011)
W952G (De novo)	DIIS5-S6	Missense	DS	NR	(Sun et al., 2008a; Xu et al., 2014)
W952X	DIIS5-S6	Nonsense	DS	Spikes in frontal-occipital; High voltage slow-waves (EEG)	(Fujiwara, 2003; Fukuma et al., 2004; Wang et al., 2012)
E954K	DIIS5-S6	Missense	DS	NR	(Arlier et al., 2010; Zuberi et al., 2011)
T955I	DIIS5-S6	Missense	DS	NR	(Ishii et al., 2017)
M956K (De novo)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)

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M956T (Familial)	DIIS5-S6	Missense	FS+	Reduced current density (80%) associated with reduction of cell surface expression (74%)	(Bechi et al., 2015; Pippucci et al., 2015)
W957R	DIIS5-S6	Missense	DS	NR	(Cantarín Extremera et al., 2011)
W957L (De novo)	DIIS5-S6	Missense	DS	NR	(Marini et al., 2007; Zuberi et al., 2011)
D958TfsX1 6	DIIS5-S6	FrameShift	DS	NR	(Zuberi et al., 2011)
D958RfsX1 3	DIIS5-S6	FrameShift	DS	NR	(Xu et al., 2015)
C959VfsX1 5 (De novo)	DIIS5-S6	FrameShift	DS	NR	(Sugawara et al., 2002)
C959R (De novo)	DIIS5-S6	Missense	DS	Post trauma epilepsy lateralized tonic-clonic seizures Severe mental retardation Non-functional Channel	(Claes et al., 2003; Ohmori et al., 2006)
C959Y (De novo)	DIIS5-S6	Missense	LGS SME	NR	(Allen et al., 2013; Xu et al., 2014)
C959S (De novo)	DIIS5-S6	Missense	DS	NR	(Cetica et al., 2017; Wei et al., 2018)

C959X	DIIS5-S6	Nonsense	Epilepsy	NR	(Lindy et al., 2018)
M960V	DIIS5-S6	Missense	DS	Spike-waves complex, rare focal spikes (EEG) Severe mental retardation	(Fujiwara, 2003)
M960T	DIIS5-S6	Missense	GEFS+	NR	(Zuberi et al., 2011)
M960R	DIIS5-S6	Missense	DS	NR	(Xu et al., 2015)
Q965X	DIIS5-S6	Nonsense	DS	NR	(Harkin et al., 2007)
Q965fsX	DIIS5-S6	FrameShift	DS	Multifocal discharges (EEG)	(Liu et al., 2018)
M967I (Maternal)	DIIS6	Missense	GEFS+	NR	(Selmer et al., 2008)
C968G (De novo)	DIIS6	Missense	EE	NR	(de Kovel et al., 2016)
C968F	DIIS6	Missense	DS	NR	(Xu et al., 2015)

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C968X (De novo)	DIIS6	Nonsense	SME DS	NR	(Depienne et al., 2008; Wang et al., 2012)
L969P (De novo)	DIIS6	Missense	DS	NR	(Do et al., 2017)
T970DfsX9	DIIS6	FrameShift	DS	NR	(Zuberi et al., 2011)
T970fsX97 2 (De novo)	DIIS6	FrameShift	DS	NR	(Riva et al., 2009)
V971I	DIIS6	Missense	DS	NR	(Cetica et al., 2017)
V971L (De novo)	DIIS6	Missense	DS	Generalized and unilateral tonic-clonic seizures Myoclonic seizures Apneic spells	(Poryo et al., 2017)
M973V (Paternal)	DIIS6	Missense	Cryptogenic generalized epilepsy	NR	(Harkin et al., 2007)
M973K (De novo)	DIIS6	Missense	DS	NR	(Depienne et al., 2008)
V975L	DIIS6	Missense	NR	Seizures and developmental delay	(Butler et al., 2017b)

M976RfsX1	DIIS6	FrameShift	DS	Myoclonic, atonic, focal or motor seizures	(Skjei et al., 2015)
M976I (De novo, Paternal)	DIIS6	Missense	GEFS+ DS	Generalized tonic-clonic seizures Focal Seizures Hemiconvulsions	(Orrico et al., 2009; Zuberi et al., 2011; Petrelli et al., 2012; Bennett et al., 2017)
V977M	DIIS6	Missense	DS	NR	(Xu et al., 2015)
G979R	DIIS6	Missense	ICEGTC	Bilateral frontal sharp wave, Spike-slow (EEG)	(Fujiwara, 2003; Rhodes et al., 2005)
G979V	DIIS6	Missense	SMEB	NR	(Zuberi et al., 2011)
G979E	DIIS6	Missense	DS	NR	(Xu et al., 2015)
N980S	DIIS6	Missense	Epilepsy	NR	(Lindy et al., 2018)
L981P	DIIS6	Missense	DS	NR	(Ishii et al., 2017)
V982L (De novo)	DIIS6	Missense	SMEB Acute encephalopathy with biphasic seizures and	Focal epilepsy Spastic quadriplegia Severe mental retardation	(Singh et al., 2009; Saitoh et al., 2012, 2015b, 2015a)

			late reduced diffusion		
V983F	DIIS6	Missense	DS	NR	(Martin et al., 2010)
V983A (De novo)	DIIS6	Missense	ICEGTC	Multifocal spikes, high voltage slow-waves (EEG) Reduced current density Shift steady state activation to ore positive values Acelerrated recovery from inactivation	(Fujiwara, 2003; Rhodes et al., 2005)
V983AfsX2 (De novo)	DIIS6	FrameShift	DS	Enlarged extracerebral gap (MRI)	(Wang et al., 2017)
N985I	DIIS6	Missense	DS	Spike waves complex, spike wave in bilateral-frontal (EEG)	(Fujiwara, 2003; Sugawara et al., 2003)
N985S	DIIS6	Missense	DS	NR	(Cetica et al., 2017)
L986F (De novo)	DIIS6	Missense	DS	Gereneralized tonic-clonic seizures Moderate mental retardation Non-fuctional channel	(Claes et al., 2001; Lossin et al., 2003)
L988WfsX5	DIIS6	FrameShift	DS	NR	(Ishii et al., 2017)

F987L (De novo)	DIIS6	Missense	DS	NR	(Wang et al., 2012)
A989V	DIIS6	Missense	Epilepsy	NR	(Lindy et al., 2018)
L990F	DIIS6	Missense	DS	NR	(Hattori et al., 2008)
L991VfsX2 (De novo)	DIIS6	FrameShift	DS	Febrile, partial, generalized tonic-clonic Myoclonic seizures Moderate intellectual disability	(Kwong et al., 2012)
S993R	DII-DIII	Missense	SMEB	NR	(Zuberi et al., 2011)
S994ifsX2	DII-DIII	FrameShift	DS	NR	(Xu et al., 2015)
S994fsX16	DII-DIII	FrameShift	SME	NR	(Xu et al., 2014)
F995L	DII-DIII	Missense	DS	NR	(Xu et al., 2014; Ishii et al., 2017; Lindy et al., 2018)
D998G	DII-DIII	Missense	DS	NR	(Depienne et al., 2008)

D998E	DII-DIII	Missense	Epilepsy	NR	(Lindy et al., 2018)
D998EfsX1 2	DII-DIII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
N999_Leu1 000del	DII-DIII	In-frame Deletion	DS	NR	(Zuberi et al., 2011)
A1002fsX8 (De novo)	DII-DIII	FrameShift	SMEB	NR	(Ohmori et al., 2002)
I1003fsX	DII-DIII	FrameShift	DS	NR	(Esterhuizen et al., 2018)
D1006fsX4	DII-DIII	FrameShift	SME	NR	(Xu et al., 2014)
E1008X (De novo)	DII-DIII	Nonsense	SMEB	NR	(Harkin et al., 2007; Rodda et al., 2012)
N1011I (De novo)	DII-DIII	Missense	ICEGTC	Rare sharp waves in lateral-temporal (EEG) Moderate mental retardation Reduced current density Shift steady state inactivation to more negative values	(Fujiwara, 2003; Rhodes et al., 2005)

L1012delins 9 (De novo)	DII-DIII	In-frame Deletion	DS	NR	(Wu et al., 2015)
H1020TfsX 4	DII-DIII	FrameShift	Intractable epilepsy	NR	(Wang et al., 2012)
E1021X (De novo)	DII-DIII	Nonsense	DS	NR	(Nicita et al., 2010)
K1021fsX1 0	DII-DIII	FrameShift	DS	NR	(Xu et al., 2014)
Y1025X	DII-DIII	Nonsense	Intractable epilepsy	NR	(Wang et al., 2012)
K1027X (De novo)	DII-DIII	Nonsense	DS	NR	(Ohmori et al., 2002)
E1032X	DII-DIII	Nonsense	DS	NR	(Lin et al., 2010; Rocca et al., 2010)
E1032DfsX 14 (De novo)	DII-DIII	FrameShift	DS	NR	(Harkin et al., 2007)
Q1035X	DII-DIII	Nonsense	DS	NR	(Ishii et al., 2017)
Q1035HfsX 11	DII-DIII	FrameShift	DS	NR	(Ishii et al., 2017)

Q1036X	DII-DIII	Nonsense	SME	NR	(Xu et al., 2014)
Q1042X	DII-DIII	Nonsense	Intractable epilepsy	NR	(Wang et al., 2012)
D1046MfsX9 (De novo)	DII-DIII	FrameShift	DS	Diffuse cerebral edema (Computed tomography)	(Myers et al., 2017b)
E1047X (De novo)	DII-DIII	Nonsense	DS	NR	(Zuberi et al., 2011)
N1056D (De novo)	DII-DIII	Missense	DS	NR	(Lim et al., 2011; Xu et al., 2014)
K1058TfsX21 (De novo)	DII-DIII	FrameShift	DS	NR	(Riva et al., 2009)
D1059Y	DII-DIII	Missense	DS	NR	(Zhou et al., 2018)
C1061X (De novo)	DII-DIII	Nonsense	DS	NR	(Depienne et al., 2008)
N1064IfsX14	DII-DIII	FrameShift	DS	NR	(Orrico et al., 2009)

T1065SfsX 8 (De novo)	DII-DIII	FrameShift	DS	NR	(Nabbout et al., 2003)
T1066A	DII-DIII	Missense	DS	NR	(Ishii et al., 2017)
E1068K	DII-DIII	Missense	DS	NR	(Depienne et al., 2008)
D1078Mfs X2 (De novo)	DII-DIII	FrameShift	SMEB	NR	(Harkin et al., 2007)
G1081R	DII-DIII	Missense	Juvenile abscente epilepsy	NR	(Escayg et al., 2001)
S1084C (Paternal)	DII-DIII	Missense	Juvenile myoclonic epilepsy DS	Paroxysmal generalised polyspike-and- wavecomplexeswithmy oclonic seizures (EEG)	(Jingami et al., 2014)
G1087E	DII-DIII	Missense	GEFS+	NR	(Cetica et al., 2017)
S1090KfsX 4	DII-DIII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
K1094NfsX 13	DII-DIII	FrameShift	DS	NR	(Cetica et al., 2017)

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E1099X (De novo)	DII-DIII	Missense	DS	Isolated diffuse spikes-waves; prominent generalized polyspike-wave paroxysms and multifocal spikes involving the frontal or temporo-parietal regions (EEG)	(Depienne et al., 2008; Riva et al., 2009)
S1100KfsX 8 (De novo)	DII-DIII	FrameShift	DS	Generalized clonic seizures Severe mental retardation	(Claes et al., 2001)
Y1102X (De novo)	DII-DIII	Nonsense	DS	NR	(Wang et al., 2012)
M1103Vfs X20	DII-DIII	FrameShift	DS	NR	(Wang et al., 2012)
S1104X (De novo)	DII-DIII	Missense	DS	Febrile seizures	(Depienne et al., 2008; Hernández Chávez et al., 2014)
L1111YfsX 12	DII-DIII	FrameShift	DS	NR	(Ishii et al., 2017)
P1116QfsX 4 (De novo)	DII-DIII	FrameShift	DS	NR	(Marini et al., 2007; Xu et al., 2014)
E1121X	DII-DIII	Nonsense	Epilepsy	NR	(Lindy et al., 2018)
F1124LfsX 4	DII-DIII	FrameShift	DS	NR	(Zhang et al., 2015)

E1125X (De novo)	DII-DIII	Missense	DS	NR	(Wang et al., 2012)
N1128KfsX 18 (De novo)	DII-DIII	FrameShift	SMEB	NR	(Lim et al., 2011)
E1130KfsX 16	DII-DIII	FrameShift	DS	NR	(Ishii et al., 2017)
D1137IfsX9	DII-DIII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
K1142X	DII-DIII	Nonsense	DS	NR	(Cetica et al., 2017)
L1145QfsX 2	DII-DIII	FrameShift	DS	NR	(Yang et al., 2017)
N1146KfsX 17 (De novo)	DII-DIII	FrameShift	DS	NR	(Wang et al., 2012)
E1147X (De novo)	DII-DIII	Nonsense	SME	NR	(Xu et al., 2014; Djémié et al., 2016)
E1147CfsX 4	DII-DIII	FrameShift	DS	NR	(Møller et al., 2016)
S1150LfsX 5	DII-DIII	FrameShift	DS	NR	(Zuberi et al., 2011)

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S1151X (De novo)	DII-DIII	Nonsense	SME DS	Neurologic sequelae with severe regressions of all skills MRI reveals focal hyperintensity in the left frontal lobe	(Depienne et al., 2008; Gaily et al., 2013)
S1152X	DII-DIII	Nonsense	DS	NR	(Xu et al., 2015)
E1153X (De novo)	DII-DIII	Nonsense	DS	Focal epilepsy with frontal-lateral activity (EEG)	(Hernández Chávez et al., 2014)
S1155AfsX9 (De novo)	DII-DIII	FrameShift	DS	NR	(Harkin et al., 2007)
S1155X (De novo)	DII-DIII	Nonsense	DS	NR	(Sun et al., 2010)
I1159fsX5	DII-DIII	FrameShift	DS	NR	(Xu et al., 2014)
P1162KfsX5	DII-DIII	FrameShift	DS	NR	(Zuberi et al., 2011)
P1162LfsX2	DII-DIII	FrameShift	SME	NR	(Wang et al., 2012)
V1163X	DII-DIII	Nonsense	DS	NR	(Sun et al., 2010)

Q1166X	DII-DIII	Nonsense	DS	NR	(Ishii et al., 2017)
Q1166RfsX 3	DII-DIII	FrameShift	DS	NR	(Ishii et al., 2017)
Q1172A	DII-DIII	Missense	DS	NR	(Cho et al., 2018)
T1174S (Maternal)	DII-DIII	Missense	FHM FS	Shifty steady state activation to more positive values Delayed fast inactivation Enhanced persistent current	(Escayg et al., 2001; Gargus and Tournay, 2007; Yordanova et al., 2011; Rilstone et al., 2012; Cestèle et al., 2013; Lal et al., 2016)
L1175RfsX 8 (De novo)	DII-DIII	FrameShift	DS	NR	(Fukuma et al., 2004; Wang et al., 2012)
E1176NfsX 32 (De novo)	DII-DIII	FrameShift	DS	Severe intellectual disability Intractable seizures despite multiple anti-epileptic drugs High hypermetropia and a substantial astigmatism	(Willemsen et al., 2012)
C1180SfsX 27	DII-DIII	FrameShift	DS	NR	(Zuberi et al., 2011)
E1183KfsX 25 (De novo)	DII-DIII	FrameShift	DS	NR	(Yang et al., 2017)

C1185VfsX 23	DII-DIII	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
C1185X (De novo)	DII-DIII	Nonsense	DS	NR	(Zuberi et al., 2011)
Q1187fsX2 9 (De novo)	DII-DIII	FrameShift	DS	NR	(Harkin et al., 2007)
K1190SfsX 18	DII-DIII	FrameShift	DS	NR	(Cetica et al., 2017)
C1192TfsX 29	DII-DIII	FrameShift	DS	NR	(Ishii et al., 2017)
I1194SfsX1 4 (De novo)	DII-DIII	FrameShift	EE	NR	(Veeramah et al., 2013)
I1194CfsX2 1	DII-DIII	FrameShift	DS	NR	(Cho et al., 2018)
G1201X	DII-DIII	Nonsense	SMEB	NR	(Zuberi et al., 2011)
Q1203X	DII-DIII	Nonsense	Epilepsy	NR	(Lindy et al., 2018)

Gln1203His fsX5	DII-DIII	FrameShift	DS	NR	(McArdle et al., 2008)
W1204R (Paternal)	DII-DIII	Missense	GEFS+	Enhanced persistent current Shift steady state activation and inactivation to more negative values	(Escayg et al., 2001; Lossin et al., 2003; Spampinato et al., 2003; Marini et al., 2007)
W1204S (Maternal)	DII-DIII	Missense	GEFS+	NR	(Zuberi et al., 2011)
W1204X	DII-DIII	Nonsense	DS	NR	(Sugawara et al., 2002)
W1205X	DII-DIII	Nonsense	SME	NR	(Xu et al., 2014)
L1207P	DII-DIII	Missense	DS	Hemiclonic seizures Absence seizures	(Zucca et al., 2008)
R1208K (Maternal)	DII-DIII	FrameShift	SMEB	NR	(Zuberi et al., 2011)
T1210K (De novo)	DII-DIII	Missense	DS	NR	(Sun et al., 2010; Xu et al., 2014)
T1210M (Paternal)	DII-DIII	Missense	GEFS+	NR	(Cetica et al., 2017)

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C1211X	DII-DIII	Nonsense	DS	NR	(Cho et al., 2018)
R1213X (De novo)	DII-DIII	Nonsense	SME DS LGS	Rare spikes, multifocal spikes and spike-wave complex (EEG) Severe mental delay	(Fujiwara, 2003; Depienne et al., 2008; Zuberi et al., 2011; Wang et al., 2012; Allen et al., 2013; Xu et al., 2014)
I1214R (De novo)	DIIS1	Missense	DS	Febrile Seizures, Partial and generalized tonic- clonic seizures Absence seizure Mild Intellectual disability	(Kwong et al., 2012)
V1215X	DIIS1	Nonsense	DS	NR	(Nabbout et al., 2003)
R1216K	DIIS1	Missense	DS	NR	(Ishii et al., 2017)
E1216X (De novo)	DIIS1	Nonsense	DS	NR	(Yang et al., 2017)
W1219IfsX 42 (De novo) (De novo)	DIIS1	FrameShift	SME	Neurologic sequel Left-side hemiparesis	(Gaily et al., 2013)
W1219X	DIIS1	Nonsense	DS	NR	(Depienne et al., 2008)
E1221K	DIIS1	Missense	DS	NR	(Zuberi et al., 2011)

E1221Q	DIIS1	Missense	DS	NR	(Xu et al., 2015)
I1228S	DIIS1	Missense	Epilepsy	NR	(Lindy et al., 2018)
L1230F (Maternal)	DIIS1	Missense	GEFS+ DS	NR	(Zuberi et al., 2011)
L1230P (De novo)	DIIS1	Missense	DS	Focal spike-wave complex (EEG) Febrile seizures Myoclonic seizures	(Liu et al., 2018)
S1231T (De novo)	DIIS1	Missense	DS	NR	(Kearney et al., 2006)
S1231R (De novo)	DIIS1	Missense	DS	polyspike-wave and multiple spikes (EEG) Moderate mental delay	(Fujiwara, 2003)
G1233R	DIIS1	Missense	DS	NR	(Nabbout et al., 2003)
L1235fs (De novo)	DIIS1	FrameShift	DS	NR	(Riva et al., 2009)
A1234VfsX 36	DIIS1	FrameShift	DS	NR	(Cetica et al., 2017)

A1236P	DIIS1	Missense	SME	NR	(Xu et al., 2014)
E1238D	DIIS1	Missense	DS	NR	(Harkin et al., 2007)
D1239Y (De novo)	DIIS1-S2	Missense	DS	NR	(Depienne et al., 2008)
D1239G (De novo)	DIIS1-S2	Missense	DS	NR	(Depienne et al., 2008)
I1240YfsX3 0	DIIS1-S2	FrameShift	SME	NR	(Wang et al., 2012)
Y1241Rfsx 30 (De novo)	DIIS1-S2	FrameShift	DS	NR	(Sun et al., 2010)
Y1241H	DIIS1-S2	Missense	DS	NR	(Ishii et al., 2017)
D1243LfsX 28 (De novo)	DIIS1-S2	FrameShift	DS	NR	(Marini et al., 2007; Wang et al., 2012)
Q1244X	DIIS1-S2	Nonsense	SME DS	NR	(Xu et al., 2014; Wei et al., 2018)

R1245X (De novo)	DIIS1-S2	Nonsense	SME DS	NR	(Nabbout et al., 2003; Harkin et al., 2007; Depienne et al., 2008; Arlier et al., 2010; Zuberi et al., 2011; Moehring et al., 2013; Xu et al., 2014)
R1245Q (De novo)	DIIS1-S2	Missense	DS	NR	(Riva et al., 2009; Craig et al., 2012; Cetica et al., 2017)
T1247KfsX 4 (De novo)	DIIS1-S2	FrameShift	DS	NR	(Depienne et al., 2008)
K1249N (Familial)	DIIS1-S2	Missense	GEFS+	NR	(Orrico et al., 2009)
T1250M (Familial)	DIIS1-S2	Missense	SME GEFS+	Generalized tonic-clonic seizures Developmental delay after seizure onset Behavioural problems	(Orrico et al., 2009; Catarino et al., 2011; Lal et al., 2016)
E1253X	DIIS2	Nonsense	SME	NR	(Xu et al., 2014)
Y1254Mfs X16	DIIS2	FrameShift	SME	NR	(Cetica et al., 2017)
Y1254C	DIIS2	Missense	Epilepsy	NR	(Wang et al., 2012)
A1255D (De novo)	DIIS2	Missense	DS	NR	(Depienne et al., 2008)

V1257fsX1 3 (De novo)	DIIS2	FrameShift	DS	NR	(Zucca et al., 2008)
T1260HfsX 34	DIIS2	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
F1259S	DIIS2	Missense	Epilepsy	NR	(Lindy et al., 2018)
T1260P (De novo)	DIIS2	Missense	DS	NR	(Sun et al., 2010)
Y1261X (De novo)	DIIS2	Nonsense	DS	NR	(Depienne et al., 2008)
F1263L (De novo)	DIIS2	Missense	SMEB	Rare spike-wave complex and poly spike-waves complex (EEG)	(Fujiwara, 2003)
L1265P (De novo)	DIIS2	Missense	DS	NR	(Ohmori et al., 2002)
E1266A	DIIS2	Missense	DS	NR	(Zuberi et al., 2011)
L1268GfsX 22	DIIS2	FrameShift	DS	NR	(Xu et al., 2015)

K1270T (Maternal)	DIIS2	Missense	PEFS+ GEFS+	Multiple febrile seizures Generalized tonic clonic seizures Partial becoming generalized tonic-clonic	(Abou-Khalil et al., 2001; Sun et al., 2012; Allen et al., 2017)
K1270NfsX 21 (De novo)	DIIS2	FrameShift	DS	NR	(Zucca et al., 2008)
W1271X	DIIS2	Nonsense	SMEB	NR	(Ohmori et al., 2002)
A1273V	DIIS2	Missense	DS	Shift steady state activation and inactivation to more positive values	(Xu et al., 2015; Peters et al., 2016)
Y1274N (Paternal)	DIIS2	Missense	GEFS+	NR	(Ebrahimi et al., 2010; Tonekaboni et al., 2013)
Tyr1274Ser	DIIS2	Missense	DS	NR	(Xu et al., 2015)
G1275A (De novo)	DIIS2	Missense	EE	Prolonged febrile Generalized tonic- clonic seizures Generalized spike-wave complex (EEG)	(Veeramah et al., 2013)
Y1276X	DIIS2	Nonsense	SME	NR	(Xu et al., 2014)
Q1277X	DIIS2-S3	Nonsense	SME	NR	(Hattori et al., 2008)

W1284R	DIIS3	Missense	Epilepsy	NR	(Lindy et al., 2018)
W1284S (De novo)	DIIS3-S4	Missense	DS	NR	(Depienne et al., 2008)
W1284X	DIIS3-S4	Nonsense	Development delay with seizures	NR	(Trump et al., 2016)
W1284Cfs X7 (De novo)	DIIS3-S4	FrameShift	DS	Epileptic discharges (EEG)	(Petrelli et al., 2012)
C1285LfsX 9	DIIS3-S4	FrameShift	DS	NR	(Lindy et al., 2018)
W1286X (De novo)	DIIS3-S4	Nonsense	DS	NR	(Sun et al., 2010)
L1287Pro (De novo)	DIIS3-S4	Missense	DS	NR	(Sun et al., 2010)
D1288N (De novo)	DIIS3-S4	Missense	DS	NR	(Zuberi et al., 2011)
D1288G	DIIS3-S4	Missense	Epilepsy	NR	(Lindy et al., 2018)

F1289del (De novo)	DIIS3-S4	In-frame Deletion	SMEB DS	Non-functional channel	(Ohmori et al., 2002, 2006; Margherita Mancardi et al., 2006; Depienne et al., 2008)
L1290X	DIIS3-S4	Nonsense	DS	NR	(Cetica et al., 2017)
D1293X	DIIS3-S4	Nonsense	DS	NR	(Cetica et al., 2017)
D1293VfsX 7 (Familial)	DIIS3-S4	FrameShift	DS	NR	(Marini et al., 2007; Depienne et al., 2008, 2010)
T1300R	DIIS3-S4	Missense	DS	NR	(Xu et al., 2014)
T1300KfsX 19	DIIS3-S4	FrameShift	DS	NR	(Ishii et al., 2017)
C1303MfsX 29 (De novo)	DIIS3-S4	FrameShift	LGS	NR	(Allen et al., 2013)
Y1306X	DIIS3-S4	Nonsense	Epilepsy	NR	(Lindy et al., 2018)
E1308D(Fa milial)	DIIS3-S4	Missense	DS	NR	(Orrico et al., 2009; Nicita et al., 2010; Zuberi et al., 2011; Lal et al., 2016; Maksemous et al., 2016)
L1309F (Paternal)	DIIS4	Missense	GEFS+	Generalized clonic seizures of changing lateralization	(Dimova et al., 2010; Allen et al., 2017)

				Myoclonic, atonic seizures Generalized polyspike-wave discharges EEG)	
L1309SfsX 10	DIIS4	FrameShift	DS	NR	(Ishii et al., 2017)
G1310EfsX 9	DIIS4	FrameShift	DS	NR	(Zuberi et al., 2011)
A1311PfsX 8 (De novo)	DIIS4	FrameShift	DS	NR	(Zuberi et al., 2011)
K1313I	DIIS4	Missense	SME	NR	(Lee et al., 2014)
R1316W (De novo)	DIIS4	Missense	SMEB	NR	(Lim et al., 2011)
R1316G	DIIS4	Missense	DS	NR	(Wang et al., 2012)
R1316S (De novo)	DIIS4	Missense	DS	NR	(Depienne et al., 2008; Kothur et al., 2018)
L1318R (De novo)	DIIS4	Missense	DS	Bifrontal sharp waves in right side (EEG)	(Mak et al., 2011)

R1319X	DIIS4	Nonsense	DS	NR	(Cetica et al., 2017)
R1319SfsX 12 (De novo)	DIIS4	FrameShift	DS	NR	(Depienne et al., 2008)
A1320V (De novo)	DIIS4	mISSENSE	DS	NR	(Zuberi et al., 2011)
R1322II	DIIS4	Missense	SME	NR	(Lee et al., 2014)
R1322SfsX 6	DIIS4	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
P1323LfsX 2	DIIS4	FrameShift	DS	NR	(Zuberi et al., 2011)
P1323R(De novo)	DIIS4	Missense	PEFS+	NR	(Lim et al., 2011)
L1324fsX1	DIIS4	FrameShift	SME	NR	(Xu et al., 2014)
L1324fsX8 (De novo)	DIIS4	FrameShift	DS SME	NR	(Rocca et al., 2010)
R1325T (De novo)	DIIS4	Missense	Intractable epilepsy	NR	(Wang et al., 2012)

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A1326P (De novo)	DIIS4	Missense	SME DS	NR	(Wallace et al., 2003; Zuberi et al., 2011; Rodda et al., 2012)
A1326D(De novo)	DIIS4	Missense	SMEB	NR	(Singh et al., 2009)
A1326V (De novo)	DIIS4	Missense	Epilepsy- aphasia	NR	(Carvill et al., 2013)
S1328P	DIIS4	Missense	DS	NR	(Depienne et al., 2008; Wang et al., 2012; Xiong et al., 2015)
R1329X (De novo; Maternal)	DIIS4	Nonsense	DS	Myoclonic seizures Generalized tonic-clonic seizures	(Depienne et al., 2008; Selmer et al., 2009; Zuberi et al., 2011; Lindy et al., 2018)
F1330LfsX 3	DIIS4	FrameShift	DS	Generalized tonic-clonic seizures Status epilepticus and absence	(Lemke et al., 2012)
G1332E	DIIS4	Missense	DS	NR	(Ishii et al., 2017)
M1333T	DIIS4	Missense	GEFS+	NR	(Cantarín Extremera et al., 2011)
R1334M	DIIS4	Missense	Epilepsy	NR	(Coll et al., 2017)

V1335M (De novo)	DIIS4-S5	Missense	DS	Generalized tonic-clonic seizures Absence seizures Multifocal and diffuse spike-waves (EEG)	(Sun et al., 2008a; Zucca et al., 2008)
N1338fsX1 338 (De novo)	DIIS4-S5	FrameShift	DS	NR	(Lindy et al., 2018)
A1339V (De novo)	DIIS4-S5	Missense	SME DS	NR	(Okumura et al., 2012; Wang et al., 2012; Xu et al., 2014)
A1339D (De novo)	DIIS4-S5	Missense	Epilepsy	NR	(Lindy et al., 2018)
V1339G (De novo)	DIIS4-S5	Missense	DS	NR	(Esterhuizen et al., 2018)
L1340FfsX 38	DIIS4-S5	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
L1341fsX8	DIIS4-S5	FrameShift	SME	Febrile generalized clonic seizure	(Sanchez-Carpintero et al., 2013)
L1341WfsX 37	DIIS4-S5	FrameShift	DS	NR	(Depienne et al., 2008)
A1343P	DIIS4-S5	Missense	Epilepsy	NR	(Lindy et al., 2018)

I1344FfsX5	DIIS4-S5	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
I1344M	DIIS4-S5	Missense	DS	NR	(Wang et al., 2012)
P1345S (De novo)	DIIS4-S5	Missense	EE	NR	(Carvill et al., 2013)
P1345L (De novo)	DIIS4-S5	Missense	Malignant migrating partial seizures of infancy	NR	(Trump et al., 2016)
I1347T (De novo)	DIIS4-S5	Missense	EE	NR	(de Kovel et al., 2016)
M1348I	DIIS4-S5	Missense	DS	NR	(Xu et al., 2015)
V1350G (De novo)	DIIS4-S5	Missense	DS	NR	(Zuberi et al., 2011)
V1350AfsX28 (De novo)	DIIS4-S5	FrameShift	DS	NR	(Wang et al., 2012)
L1352P	DIIS5	Missense	DS	NR	(Xu et al., 2015)

V1353L (Maternal)	DIIS5	Missense	PEFS+ GEFS+	Non-functional channel	(Wallace et al., 2001; Lossin et al., 2003; Bennett et al., 2017)
C1354R	DIIS5	Missense	Epilepsy	NR	(Lindy et al., 2018)
C1354Y	DIIS5	Missense	SME	Slow background, generalized spikes (EEG)	(Lee et al., 2014)
I1356TfsX4 (De novo)	DIIS5	FrameShift	SMEB	NR	(Harkin et al., 2007)
L1355P	DIIS5	Missense	SMEB	NR	(Wang et al., 2012)
F1357L	DIIS5	Missense	Intractable epilepsy	NR	(Wang et al., 2012)
W1358R(D e novo)	DIIS5	Missense	DS	NR	(Zuberi et al., 2011)
W1358X (De novo)	DIIS5	Nonsense	DS	NR	(Zuberi et al., 2011)
W1358S (De novo)	DIIS5	Missense	DS	Hemiclonic seizures Severe mental retardation	(Zucca et al., 2008; Petrelli et al., 2012)
L1359I	DIIS5	Missense	DS	NR	(Cetica et al., 2017)

L1359Q (De novo)	DIIS5	Missense	DS	NR	(Gokben et al., 2017)
S1362R	DIIS5	Missense	SME	NR	(Xu et al., 2014)
I1363N	DIIS5	Missense	SME	NR	(Xu et al., 2014)
I1363fsX4	DIIS5	FrameShift	SMEB	NR	(Wang et al., 2012)
M1364Lys	DIIS5	Missense	SME	NR	(Villeneuve et al., 2014)
V1366I	DIIS5	Missense	ICEGTC GEEFS+ FS+	4-5Hz diffuse irregular spikes and wave complex at a drowsy state; Diffuse bilateral spike-waves only when valproate was reduced, otherwise no paroxysmal discharges were recorded (EEG)	(Osaka et al., 2007)
V1366L	DIIS5	Missense	Epilepsy	NR	(Lindy et al., 2018)
N1367K	DIIS5	Missense	SME	NR	(Depienne et al., 2008)
F1369LfsX 21	DIIS5	FrameShift	Epilepsy	NR	(Lindy et al., 2018)

A1370P	DIIS5	Missense	SMEB	NR	(Lindy et al., 2018)
A1370V	DIIS5	Missense	DS GEFS+	NR	(Cetica et al., 2017)
G1371V (De novo)	DIIS5	Missense	SME DS	NR	(Dhamija et al., 2014; Liu et al., 2018)
K1372E	DIIS5	Missense	GEFS+	Tonic-clonic and myoclonic seizures without fever Slow spike waves from the left fronto-central region (EEG)	(Goldberg-Stern et al., 2014)
F1373S	DIIS5	Missense	DS	NR	(Cetica et al., 2017)
C1376R (De novo)	DIIS5	Missense	DS	NR	(Wang et al., 2012)
C1376YfsX 2 (De novo)	DIIS5	FrameShift	DS	NR	(Lim et al., 2011; Kim et al., 2013)
N1378H	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
N1378TfsX 13	DIIS5-S6	FrameShift	DS	NR	(Zuberi et al., 2011; Cho et al., 2018)

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V1379L	DIIS5-S6	Missense	PEFS+	Febrile and generalized seizures Focal seizures with secondary generalization	(Mhanni et al., 2011)
G1382V (De novo)	DIIS5-S6	Missense	DS	Diffuse spike-waves dominant in bilatereal frontal regions (EEG)	(Haginoya et al., 2018; Liu et al., 2018)
D1383GfsX 4	DIIS5-S6	FrameShift	DS	Complex partial seizures with generalization Tonic seizures Myoclonic astatic seizures	(Surovy et al., 2016)
F1385V	DIIS5-S6	Missense	DS	NR	(Wang et al., 2012)
D1389AfsX 2	DIIS5-S6	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
V1390M (De novo)	DIIS5-S6	Missense	SME SMEB DS	Generalized spikes, focal spikes and polyspikes (EEG)	(Ohmori et al., 2002; Harkin et al., 2007; Sun et al., 2008a; Rilstone et al., 2012; Verbeek et al., 2013; Lee et al., 2014; Cho et al., 2018)
N1391S	DIIS5-S6	Missense	Epilepsy	NR	(Depienne et al., 2008)
N1392K (De novo)	DIIS5-S6	Missense	EEIE	NR	(Arafat et al., 2017)
His1393Asp (De novo)	DIIS5-S6	Missense	GEFS+	FS+ with focal motor and absence	(Myers et al., 2017a)

H1393P (De novo)	DIIS5-S6	Missense	SMEB	Febrile generalized tonic-clonic seizures	(Stefanaki et al., 2006)
T1394I (De novo)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
D1396Y (De novo)	DIIS5-S6	Missense	DS	Prolonged febrile seizures Generalized tonic-clonic seizures Atonic seizures	(Specchio et al., 2010)
C1396G (De novo)	DIIS5-S6	Missense	SMEB	NR	(Harkin et al., 2007)
C1396Y (De novo)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
C1396X	DIIS5-S6	Nonsense	SME	NR	(Xu et al., 2014)
L1397X	DIIS5-S6	Nonsense	DS	NR	(Depienne et al., 2008)
E1401KfsX3	DIIS5-S6	FrameShift	DS	NR	(Depienne et al., 2008)
R1402fsX9 (De novo)	DIIS5-S6	FrameShift	DS	Generalized tonic-clonic seizures Left-sided frontal epileptiform activity with secondary generalization (EEG)	(Yordanova et al., 2011)

A1406T(Par ternal)	DIIS5-S6	Missense	DS	NR	(Lim et al., 2011)
A1406GfsX 11	DIIS5-S6	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
R1407X (De novo)	DIIS5-S6	Nonsense	DS	Non-functional channel	(Sugawara et al., 2002, 2003; Harkin et al., 2007; Wang et al., 2012)
W1408X (De novo)	DIIS5-S6	Nonsense	DS	Generalized tonic- clonic seizures Frontal-dominant spike-wave, poly spike- waves (EEG)	(Fujiwara, 2003)
N1410Mfs X2 (De novo)	DIIS5-S6	FrameShift	DS	Febrile Seizures Partial and generalised tonic-clonic seizures Absence seizure Mild Intellectual disability	(Kwong et al., 2012)
N1414D (De novo)	DIIS5-S6	Missense	GEFS+	NR	(Zuberi et al., 2011)
N1414Y(De novo)	DIIS5-S6	Missense	DS	NR	(Marini et al., 2007)
F1415I	DIIS5-S6	Missense	DS	Shift steady state inactivation to more positive values	(Jiao et al., 2013)
F1415LfsX 4	DIIS5-S6	FrameShift	DS	NR	(Ishii et al., 2017)

F1415X (De novo)	DIIS5-S6	Nonsense	DS	NR	(Depienne et al., 2008; Sun et al., 2010)
D1416H (De novo)	DIIS5-S6	Missense	SME	NR	(Mulley et al., 2013)
D1416G (De novo)	DIIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
N1417S (De novo)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
V1418G	DIIS5-S6	Missense	DS	NR	(Wang et al., 2012)
G1419DfsX 19 (De novo)	DIIS5-S6	FrameShift	DS	NR	(Depienne et al., 2008)
G1419X	DIIS5-S6	Nonsense	Epilepsy	NR	(Lindy et al., 2018)
G1421W	DIIS5-S6	Missense	DS	NR	(Cho et al., 2018)
G1421AfsX 18	DIIS5-S6	FrameShift	DS	Generalized tonic-clonic seizures Hemiconvulsion	(de Lange et al., 2018)
Y1422C (De novo)	DIIS5-S6	Missense	DS	NR	(Riva et al., 2009)

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Y1422X	DIIS5-S6	Nonsense	Intractable Epilepsy	NR	(Wang et al., 2012; Zhu et al., 2017)
L1423F (Maternal)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
L1426R (De novo)	DIIS5-S6	Missense	DS	NR	(Riva et al., 2009)
Q1427cfsX16	DIIS5-S6	FrameShift	SME	NR	(Verbeek et al., 2013)
Q1427X (De novo)	DIIS5-S6	Nonsense	SMEB	NR	(Harkin et al., 2007)
Q1427P (De novo)	DIIS5-S6	Missense	DS	NR	(Wang et al., 2012)
V1428A	DIIS5-S6	Missense	GEFS+	Febrile seizures Right-temporal spike-wave (EEG)	(Sugawara et al., 2002; Perucca et al., 2017)
A1429del (De novo)	DIIS5-S6	In-frame Deletion	DS	NR	(Zuberi et al., 2011)
A1429S (Paternal)	DIIS5-S6	Missense	Autosomal dominant nocturnal frontal lobe epilepsy	NR	(Sone et al., 2012)

A1429T	DIIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
A1429D	DIIS5-S6	Missense	Intractable epilepsy	NR	(Wang et al., 2012)
A1429DfsX 15	DIIS5-S6	FrameShift	SMEB	NR	(Ohmori et al., 2002)
A1429V (De novo)	DIIS5-S6	Missense	GEFS+	MRI reveals a Pineal cyst FS+ with focal motor seizures	(Myers et al., 2017a)
F1431I	DIIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
K1432R	DIIS5-S6	Missense	SME	Generalized spikes (Ictal EEG)	(Lee et al., 2014)
K1432KfsX 6 (De novo)	DIIS5-S6	FrameShift	DS	NR	(Lim et al., 2011)
G1433R (De novo)	DIIS5-S6	Missense	DS	NR	(Nicita et al., 2010)
G1433V (Paternal)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)

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G1433E (De novo)	DIIS5-S6	Missense	DS SME	Rare multifocal spikes (EEG) Hemiclonic seizures	(Sun et al., 2008a; Verbeek et al., 2013; Xu et al., 2014)
W1434R (De novo)	DIIS5-S6	Missense	DS SME	Myoclonic seizures Severe regression of all skills after seizures Severe psychomotor disability	(Claes et al., 2003; Gaily et al., 2013)
W1434X (De novo)	DIIS5-S6	Nonsense	DS	Hemiclonic seizures	(Zucca et al., 2008) (Xu et al., 2015)
M1435K	DIIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
M1435R	DIIS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
I1437M (De novo)	DIIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
M1438 (De novo)	DIIS5-S6	Missense	DS	NR	(Do et al., 2017)
A1440QfsX 36	DIIS5-S6	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
A1440E (De novo)	DIIS5-S6	Missense	SME	NR	(Gaily et al., 2013)

A1440G	DIIS5-S6	Missense	Juvenile myoclonic epilepsy	NR	(Lee et al., 2018)
A1440V	DIIS5-S6	Missense	Autism spectrum disorder	Tonic-clonic and potentially myoclonic seizures	(D’Gama et al., 2015)
A1441T	DIIS5-S6	Missense	SME	Focal spikes; generalized epileptiform discharges (EEG)	(Lee et al., 2014)
A1441P (De novo)	DIIS5-S6	Missense	DS	NR	(Harkin et al., 2007; Mulley et al., 2013)
Q1450K (De novo)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
Q1450P (De novo)	DIIS5-S6	Missense	SME	Slow background (EEG)	(Lin et al., 2013; Lee et al., 2014)
Q1450R (De novo)	DIIS5-S6	Missense	SMEB	NR	(Ohmori et al., 2002)
P1451S (De novo)	DIIS5-S6	Missense	DS	NR	(Zuberi et al., 2011)
P1451L (De novo)	DIIS5-S6	Missense	DS	NR	(Riva et al., 2009)
Y1451CfsX 22 (De novo)	DIIS5-S6	FraneShift	DS	Multifocal discharges (EEG)	(Liu et al., 2018)

Y1453C	DIIS5-S6	Missense	SMEB	NR	(Wang et al., 2012)
Y1453X (De novo)	DIIS5-S6	Nonsense	DS	NR	(Zuberi et al., 2011)
E1454K(De novo)	DIIS5-S6	Missense	DS	NR	(Depienne et al., 2008)
Leu1461Ile (Paternal)	DIIS6	Missense	DS	NR	(Nabbout et al., 2003)
Y1462H (De novo)	DIIS6	Missense	DS SMEB	NR	(Zuberi et al., 2011; Wang et al., 2012)
Y1462LfsX 24 (De novo)	DIIS6	FrameShift	Epilepsy	NR	(Staněk et al., 2018)
Y1462C	DIIS6	Missense	DS	Absence and hemiplegic seizures	(Zucca et al., 2008)
Y1462CfsX 22 (De novo)	DIIS6	FrameShift	DS	NR	(Depienne et al., 2008)
F1463L (De novo)	DIIS6	Missense	DS	Afebrile unilateral clonic seizure Generalized tonic- clonic Generalized and focal epileptic discharges (EEG)	(Reyes et al., 2011)

F1463S (De novo)	DIIS6	Missense	DS	NR	(Nabbout et al., 2003) (Lindy et al., 2018)
I1467L	DIIS6	Missense	DS	NR	(Cetica et al., 2017)
G1470W (De novo)	DIIS6	Missense	DS	NR	(Marini et al., 2007)
S1471F	DIIS6	Missense	DS	NR	(Xu et al., 2015)
F1472S (De novo)	DIIS6	Missense	SMEB	NR	(Wang et al., 2012)
F1473del (De novo)	DIIS6	In-frame Deletion	DS	NR	(Depienne et al., 2008)
L1475S (De novo)	DIIS6	Missense	DS	NR	(Riva et al., 2009)
N1476K (De novo)	DIIS6	Missense	SMEB	NR	(Zuberi et al., 2011)
F1478C	DIIS6	Missense	Epilepsy	NR	(Lindy et al., 2018)
G1480C	DIIS6	Missense	Epilepsy	NR	(Lindy et al., 2018)

G1480V (De novo)	DIIS6	Missense	Myoclonic astatic epilepsy	NR	(Harkin et al., 2007)
I1483del	DIIS6	In-frame Deletion	DS	NR	(Depienne et al., 2008)
D1484IfsX1 6 (De novo)	DIII-DIV	FrameShift	Intractable epilepsy	NR	(Wang et al., 2012)
D1484G	DIII-DIV	Missense	SMEB	NR	(Depienne et al., 2008)
N1485D (De novo)	DIII-DIV	Missense	SME	NR	(Carvill et al., 2013)
N1485Y	DIII-DIV	Missense	DS	NR	(Wang et al., 2012)
Q1489K (Maternal)	DIII-DIV	Missense	FHM	Shift steady state activation to more negative values Faster recovery from inactivation at negative voltages	(Dichgans et al., 2005)
K1491X	DIII-DIV	Nonsense	DS	NR	(Zuberi et al., 2011; Wang et al., 2012)
K1492EfsX 18	DIII-DIV	FrameShift	DS	NR	(Ishii et al., 2017)

K1492N(De novo)	DIII-DIV	Missense	DS	NR	(Yang et al., 2017)
G1495Dfs7	DIII-DIV	FrameShift	DS	Afebrile seizures	(Haginoya et al., 2018)
G1495VfsX 6 (De novo)	DIII-DIV	FrameShift	DS	NR	(Yang et al., 2017)
Q1496KfsX 5 (De novo)	DIII-DIV	FrameShift	DS	NR	(Riva et al., 2009)
I1498N	DIII-DIV	Missense	Epilepsy	NR	(Lindy et al., 2018)
I1498M (Parternal)	DIII-DIV	Missense	FHM	Hemiplegic attacks were usually preceded by flashing lights or scotoma, speech problems and/or unilateral sensory symptoms	(Weller et al., 2014)
F1499LfsX 2	DIII-DIV	FrameShift	SME	Generalized tonic-clonic convulsion; Epileptic attack after photic stimulation with associated ictal discharges and temporal spikes waves (EEG)	(Lam et al., 2015)
F1499LfsX 2	DIII-DIV	FrameShift	DS	NR	(Zuberi et al., 2011)
T1501fs	DIII-DIV	FrameShift	DS	NR	(Do et al., 2017)

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E1503K (De novo)	DIII-DIV	Missense	SMEB	NR	(Shi et al., 2009; Zuberi et al., 2011; Wang et al., 2012)
E1503del (De novo)	DIII-DIV	In-frame Deletion	SMEB	NR	(Wang et al., 2012)
E1503G	DIII-DIV	Missense	SME	Background with theta activity and focal left-frontal focal discharges (EEG)	(Moehring et al., 2013)
Q1504L	DIII-DIV	Missense	Epilepsy	NR	(Lindy et al., 2018)
K1506NfsX 9 (De novo)	DIII-DIV	FrameShift	DS	NR	(Depienne et al., 2008)
Y1507D	DIII-DIV	Missense	DS	NR	(Ishii et al., 2017)
Y1507X	DIII-DIV	Nonsense	DS	NR	(Farwell et al., 2015; Helbig et al., 2016)
Y1508X	DIII-DIV	Nonsense	DS	NR	(Zuberi et al., 2011)
D1509Mfs X3 (De novo)	DIII-DIV	FrameShift	DS	NR	(Harkin et al., 2007)

Me511K	DIII-DIV	Missense	Intractable epilepsy	NR	(Wang et al., 2012)
M1511R	DIII-DIV	Missense	Epilepsy	NR	(Lindy et al., 2018)
K1513NfsX 2	DIII-DIV	FrameShift	DS	NR	(Wang et al., 2012)
L1514IfsX2 3 (De novo)	DIII-DIV	FrameShift	DS	NR	(Depienne et al., 2008)
L1514S(Ma ternal)	DIII-DIV	Missense	DS	NR	(Depienne et al., 2008)
G1515R	DIII-DIV	Missense	Epilepsy	NR	(Lindy et al., 2018)
S1516X (De novo)	DIII-DIV	Nonsense	DS	NR	(Sugawara et al., 2002; Harkin et al., 2007; Depienne et al., 2008; Riva et al., 2009; Zuberi et al., 2011)
S1516W	DIII-DIV	Missense	DS	NR	(Xu et al., 2015)
S1516L	DIII-DIV	Missense	Epilepsy	NR	(Lindy et al., 2018)
K1518NfsX 21	DIII-DIV	FrameShift	Epilepsy	NR	(Depienne et al., 2008)

K1517X	DIII-DIV	Nonsense	DS	NR	(Xu et al., 2015)
K1518NfsX 21 (De novo)	DIII-DIV	FrameShift	DS	NR	(Depienne et al., 2008)
P1519TfsX 18	DIII-DIV	FrameShift	DS	NR	(Hesse et al., 2018)
P1519T	DIII-DIV	Missense	SME	Bilateral deactivation in the posterior cingulate cortex associated with the interictal epileptiform discharges together with deactivated areas in both parietal lobes (EEG)	(Moehring et al., 2013; Lindy et al., 2018)
P1519S	DIII-DIV	Missense	Epilepsy	NR	(Hesse et al., 2018)
P1519L	DIII-DIV	Missense	Epilepsy	NR	(Lindy et al., 2018)
Q1520KfsX 19 (De novo)	DIII-DIV	FrameShift	DS	Febrile Seizures Partial Seizures	(Kwong et al., 2012)
K1521SfsX 18	DIII-DIV	FrameShift	Epilepsy	NR	(Hesse et al., 2018)
I1523T	DIII-DIV	Missense	SME	Generalized tonic-clonic seizures Febrile seizures	(Catarino et al., 2011)

				Austistic features Behavioural problems	
R1525X (De novo)	DIII-DIV	Nonsense	DS SMEB Myoclonic astatic epilepsy	Febrile seizures Tonic-clonic seizures	(Kearney et al., 2006; Harkin et al., 2007; Depienne et al., 2008; Orrico et al., 2009; Vadlamudi et al., 2010; Zuberi et al., 2011; Djémié et al., 2016)
R1525Q	DIII-DIV	Missense	DS	Shift steady state activation to more negative values	(Binini et al., 2017; Cetica et al., 2017)
P1526QfsX 13	DIII-DIV	FrameShift	DS	NR	(Zuberi et al., 2011)
N1528K	DIII-DIV	Missense	DS	NR	(Ishii et al., 2017)
K1529NfsX 9	DIII-DIV	FrameShift	DS	Generalized tonic-clonic seizures Mental retardation; Obsessive-compulsive disorder	(Skjei et al., 2015)
F1535fs	DIII-DIV	FrameShift	SME	NR	(Marini et al., 2007)
V1538I	DIVS1	Missense	SME Acute encephalopathy	NR	(Depienne et al., 2008)
T1539P	DIVS1	Missense	SME	NR	(Verbeek et al., 2013)

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F1543S(Ma ternal)	DIVS1	Missense	Cyptogenic focal epilepsy PEFS+	NR	(Harkin et al., 2007; Kim et al., 2014)
F1543fsX2	DIVS1	FrameShift	DS	NR	(Zuberi et al., 2011)
D1544H	DIVS1	Missense	Epilepsy	NR	(Lindy et al., 2018)
D1544G (De novo)	DIVS1	Missense	DS	NR	(Zuberi et al., 2011)
D1544A (De novo)	DIVS1	Missense	DS	NR	(Depienne et al., 2008)
I1545V (De novo)	DIVS1	Missense	DS	NR	(Harkin et al., 2007; Wang et al., 2012; Cetica et al., 2017)
S1546fsX15 48	DIVS1	FrameShift	Intractable epilepsy	NR	(Wang et al., 2012)
M1548K	DIVS1	Missense	DS	NR	(Cetica et al., 2017)
C1552Y	DIVS1	Misesense	DS	NR	(Wu et al., 2015)

L1553HfsX 8	DIVS1	FrameShift	DS	NR	(Zuberi et al., 2011)
L1553_N15 54delinsHis Ile	DIVS1	In-frame Deletion	DS	NR	(Cetica et al., 2017)
N1554KfsX 4	DIVS1	FrameShift	DS	NR	(Lim et al., 2011)
M1555R	DIVS1	Missense	DS	NR	(Wang et al., 2012)
M1558del	DIVS1	In-frame Deletion	DS	NR	(Wang et al., 2012)
M1558I	DIVS1	Missense	Epilepsy	NR	(Lindy et al., 2018)
M1559K	DIVS1	Missense	DS	Hemiclonic and generalized tonic clonic seizures	(Kumar et al., 2018)
V1560EfsX 5	DIVS1	FrameShift	DS	NR	(Wang et al., 2012)
E1561K	DIVS2	Missense	DS	NR	(Depienne et al., 2008)
E1561X	DIVS2	Nonsense	Epilepsy	NR	(Lindy et al., 2018)

Q1565X	DIVS2	Nonsense	Epilepsy	NR	(Lindy et al., 2018)
T1571TfsX 20	DIVS2	FrameShift	SMEB	NR	(Wang et al., 2012)
S1574HfsX 17	DIVS2	FrameShift	DS	NR	(Depienne et al., 2008)
R1575C (De novo; Maternal; Paternal)	DIVS2	Missense	DS	Focal seizures Mental deterioration Enhanced persistent current	(Depienne et al., 2008; Ohmori et al., 2008; Lim et al., 2011; Saitoh et al., 2012, 2015a)
I1576T	DIVS2	Missense	DS	NR	(Tuncer et al., 2015)
V1579E	DIVS2	Missense	DS	NR	(Depienne et al., 2008)
H1583R	DIVS2	Missense	GEFS+	Generalized tonic- clonic seizures	(Hattori et al., 2008) (Tan et al., 2012)
T1585fsX6	DIVS2	FrameShift	DS	NR	(Wang et al., 2012)
G1586E (De novo)	DIVS2	Missense	DS	NR	(Depienne et al., 2008; Sun et al., 2010; Zuberi et al., 2011)

C1588R (De novo)	DIVS2	Missense	DS	NR	(Marini et al., 2007; Zuberi et al., 2011; Mercimek-Mahmutoglu et al., 2015)
C1588LfsX 21 (De novo)	DIVS2	FrameShift	DS	NR	(Orrico et al., 2009)
C1588X	DIVS2	Nonsense	DS	NR	(Cetica et al., 2017)
Val1589Gly	DIVS2	Missense	DS	NR	(Xu et al., 2015)
Leu1590Pro	DIVS2	Missense	EE	NR	(Ostrander et al., 2018)
Lys1591X	DIVS2	Nonsense	DS	NR	(Wang et al., 2012)
Leu1592His	DIVS2	Missense	SMEB	NR	(Zuberi et al., 2011)
Leu1592Pro	DIVS2	Missense	DS	NR	(Zuberi et al., 2011)
Ile1593LeufsX15	DIVS2	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
Ile1593Asn	DIVS2	Missense	DS	NR	(Cho et al., 2018)

Ser1594Tyr fsX14	DIVS2	FrameShift	DS	NR	(Wang et al., 2012)
Leu1595Thr fsX13	DIVS2	FrameShift	DS	NR	(Wang et al., 2012)
Arg1596Cys (De novo; Paternal)	DIVS2-S3	Missense	FS+ DS	Myoclonic seizures Generalized tonic-clonic seizures	(Dlugos et al., 2007; Hoffman-Zacharska et al., 2015)
Arg1596His (Paternal)	DIVS2-S3	Missense	GEFS+	NR	(Hoffman-Zacharska et al., 2015)
R1596L	DIVS2-S3	Missense	DS	NR	(Depienne et al., 2008)
Y1598F	DIVS2-S3	Missense	GEFS+	NR	(Lindy et al., 2018)
Y1598X	DIVS2-S3	Nonsense	DS	NR	(Harkin et al., 2007)
I1602LfsX16 (De novo)	DIVS2-S3	FrameShift	DS	NR	(Yang et al., 2017)
W1604X	DIVS3	Nonsense	DS	NR	(Xu et al., 2015)

N1605S (De novo)	DIVS3	Missense	SMEB	NR	(Zuberi et al., 2011)
N1605I	DIVS3	Missense	DS	NR	(Parrini et al., 2017)
F1607X	DIVS3	Nonsense	DS	NR	(Harkin et al., 2007; Parrini et al., 2017)
F1607LfsX 11	DIVS3	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
D1608Y (De novo)	DIVS3	Missense	DS	NR	(Marini et al., 2007; Xu et al., 2014)
D1608VfsX 10 (De novo)	DIVS3	FrameShift	DS	NR	(Sun et al., 2010)
D1608G (De novo)	DIVS3	Missense	DS	NR	(Wang et al., 2012)
F1609LfsX 1610 (De novo)	DIVS3	FrameShift	DS	NR	(Depienne et al., 2008)
V1610fsX3 3	DIVS3	FrameShift	DS	NR	(Xu et al., 2014)
11611WfsX 8	DIVS3	FrameShift	DS	NR	(Xu et al., 2015)

V1611F (Maternal)	DIVS3	Missense	GEFS+ ICEGTC	Generalized tonic-clonic seizure Enhanced persistent current Shift steady state activation and inactivation to more negative values	(Fujiwara, 2003; Rhodes et al., 2005)
V1612I (Paternal; Maternal)	DIVS3	Missense	DS	Febrile Seizures Partial and generalized tonic-clonic seizures Absence seizure Moderate Intellectual disability Focal sharp waves; spike-wave discharges (EEG)	(Depienne et al., 2008; Kwong et al., 2012; Lee et al., 2014)
L1614PfsX4 (De novo)	DIVS3	FrameShift	DS	NR	(Zuberi et al., 2011)
S1615fs	DIVS3	FrameShift	SME	Focal spikes (EEG)	(Lee et al., 2014)
I1616T (Paternal)	DIVS3	Missense	PEFS+	NR	(Hattori et al., 2008; Shi et al., 2012)
M1619V (Maternal)	DIVS3	Missense	Intractable Epilepsy	NR	(Wang et al., 2012)
F1620V	DIVS3	Missense	GEFS+	NR	(Cetica et al., 2017)

L1624Q(Maternal)	DIVS3	Missense	Focal Family Epilepsy	NR	(Oates et al., 2018)
L1624P (Maternal)	DIVS3	Missense	FHM	Enhanced persistent current Delayed fast inactivation Faster recovery from inactivation Shift steady state inactivation to more positive values	(Fan et al., 2016)
T1628X (De novo)	DIVS3	Nonsense	DS	NR	(Sun et al., 2010)
V1630M (Familial)	DIVS3-S4	Missense	DS	NR	(Marini et al., 2007)
V1630L (Maternal)	DIVS3-S4	Missense	SMEB	Acute encephalopathy Moderate neurologic sequelae	(Okumura et al., 2012; Wang et al., 2012)
V1630G	DIVS3-S4	Missense	DS	NR	(Djémié et al., 2016)
S1631C	DIVS3-S4	Missense	DS	Multifocal spikes (EEG)	(Haginoya et al., 2018)
P1632S	DIVS3-S4	Missense	ICEGTC	Generalizes tonic-clonic Severe mental delay	(Fujiwara, 2003)

T1633YfsX 10	DIVS3-S4	FrameShift	Epilepsy	NR	(Lindy et al., 2018)
L1634CfsX 4	DIVS3-S4	FrameShift	DS	Generalized tonic-clonic seizures Focal tonic and myoclonic seizures	(Rilstone et al., 2012)
F1635L (Maternal)	DIVS4	Missense	GEFS+	NR	(Zhang et al., 2015)
R1636X (De novo)	DIVS4	Nonsense	SMEB DS	NR	(Lim et al., 2011; Zuberi et al., 2011; Cetica et al., 2017; Tsai et al., 2018)
R1636Q(De novo)	DIVS4	Missense	DS LGS	Epileptic encephalopathy Myoclonic seizures Dystonia, and spasticity	(Harkin et al., 2007; Butler et al., 2017b)
R1636P (De novo)	DIVS4	Missense	Malignant migrating partial seizures of infancy	NR	(Gokben et al., 2017)
V1637E (De novo)	DIVS4	Missense	DS	Episodes of status epilepticus triggered by fever- unresponsive to medications	(Nishri et al., 2010; Zuberi et al., 2011)
I1638VfsX1 1	DIVS4	FrameShift	DS	NR	(Depienne et al., 2008)

I1638T (De novo)	DIVS4	Missense	DS	NR	(Zuberi et al., 2011)
I1638N (De novo)	DIVS4	Missense	DS	NR	(Wang et al., 2012)
R1639G	DIVS4	Missense	DS	NR	(Depienne et al., 2008)
R1639VfsX11	DIVS4	FrameShift	DS	NR	(Kumar et al., 2018)
R1639P	DIVS4	Missense	Epilepsy	NR	(Lindy et al., 2018)
A1641T (Mosaic)	DIVS4	Missense	DS	NR	(Yang et al., 2017)
R1642M	DIVS4	Missense	SME	Generalized tonic-clonic seizures	(Lee et al., 2014)
R1642S (De novo)	DIVS4	Missense	DS	NR	(Wang et al., 2012)
I1643LfsX7 (De novo)	DIVS4	FrameShift	SME	NR	(Gaily et al., 2013)
R1642S	DIVS4	Missense	Epilepsy	NR	(Lindy et al., 2018)

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G1644D	DIVS4	Missense	Epilepsy	NR	(Lindy et al., 2018)
R1645X (De novo)	DIVS4	Nonsense	DS	Generalized spike and wave, polyspike and wave discharges with photosensitivity (EEG)	(Fukuma et al., 2004; Harkin et al., 2007; Marini et al., 2007; Gökben et al., 2009; Zuberi et al., 2011; Wang et al., 2012; Cho et al., 2018)
R1645Q (De novo)	DIVS4	Missense	DS	NR	(Harkin et al., 2007; Oates et al., 2018)
R1645P	DIVS4	Missense	DS	NR	(Xu et al., 2015)
R1648C	DIVS4	Missense	DS	Increase current density Shift steady state activation to more positive values Shift steady state inactivation to more negative values	(Ohmori et al., 2002; Rhodes et al., 2005; Orrico et al., 2009; Zuberi et al., 2011)
R1648H (Paternal)	DIVS4	Missense	GEFS+	Enhanced persistent current Delayed inactivation	(Alekov et al., 2000; Escayg et al., 2000; Spampinato et al., 2001; Rhodes et al., 2004; Depienne et al., 2008)
R1648L	DIVS4	Missense	Epilepsy	NR	(Lindy et al., 2018)
L1649Q(Paternal)	DIVS4	Missense	FHM	NR	(Vanmolkot et al., 2007)

K1651QfsX 22 (De novo)	DIVS4	FrameShift	SMEB	NR	(Harkin et al., 2007)
G1652X	DIVS4	Nonsense	DS	NR	(Depienne et al., 2008)
A1653E	DIVS4	Missense	SMEB	NR	(Zuberi et al., 2011)
I1656S (De novo)	DIVS4	Missense	DS	NR	(Usluer et al., 2016)
I1656M (Maternal)	DIVS4	Missense	GEFS+	Shift steady state activation to more positive values	(Lossin et al., 2003)
R1657C (Maternal)	DIVS4	Missense	DS	Decrease current density Shift steady state activation to more positive values Faster recovery from slow inactivation	(Lossin et al., 2003)
R1657H	DIVS4	Missense	GEFS+	Febrile seizures Focal seizures Generalized tonic- clonic seizures	(Harkin et al., 2007; Catarino et al., 2011)
T1658R (De novo; Maternal)	DIVS4-S5	Missense	SMEB DS	NR	(Marini et al., 2007; Depienne et al., 2008)
T1658M (Maternal)	DIVS4-S5	Missense	DS SME	NR	(Depienne et al., 2008)

L1659M	DIVS4-S5	Missense	DS	NR	(Cetica et al., 2017)
L1660P	DIVS4-S5	Missense	SME DS	NR	(Zuberi et al., 2011; Rodda et al., 2012)
F1661L (Maternal)	DIVS4-S5	Missense	FHM	NR	(Weller et al., 2014)
F1661S (De novo)	DIVS4-S5	Missense	DS	Reduce current density Enhanced persistent current	(Claes et al., 2003; Rhodes et al., 2004)
A1662V	DIVS4-S5	Missense	SMEB	NR	(Wang et al., 2012)
L1663FfsX 10 (De novo)	DIVS4-S5	FrameShift	DS	NR	(Zuberi et al., 2011)
M1664K (Maternal)	DIVS4-S5	Missense	DS	Reduced current density (92%) associated with reduction of cell surface expression (95%)	(Depienne et al., 2008; Bechi et al., 2015)
S1666fsX7	DIVS4-S5	FrameShift	SME	NR	(Xu et al., 2014)
M1665_S1666insIle (De novo)	DIVS4-S5	In-frame Insertion	DS	NR	(Yang et al., 2017)

M1665I	DIVS4-S5	Missense	Epilepsy	NR	(Lindy et al., 2018)
S1666F	DIVS4-S5	Missense	DS	NR	(Xu et al., 2015)
L1667P (De novo)	DIVS4-S5	Missense	DS	NR	(Zuberi et al., 2011; Wang et al., 2012)
P1668A (Maternal)	DIVS4-S5	Missense	DS	NR	(Nabbout et al., 2003)
P1668R (Maternal)	DIVS4-S5	Missense	SME	NR	(Huang et al., 2014)
P1668fsX12	DIVS4-S5	FrameShift	SME	NR	(Xu et al., 2014)
P1668L	DIVS4-S5	Missense	SMEB	NR	(Zuberi et al., 2011)
A1669T	DIVS4-S5	Missense	NR	Moderate/Severe developmental delay Epilepsy with continuous spikes and waves during sleep (EEG)	(Fry et al., 2016)
A1669E	DIVS4-S5	Missense	Malignant migrating partial seizures of infancy	Left arm clonic activity Microcephaly (autopsy)	(Freilich et al., 2011)

L1670W (Maternal)	DIVS4-S5	Missense	FHM3	Reduced current density Shift steady state activation and inactivation to more positive values Incomplete inactivation faster recovery from fast inactivation Resistance to entry into closed state inactivation	(Zhang et al., 2017; Dhifallah et al., 2018; Bertelli et al., 2019)
F1671fsX8 (De novo)	DIVS4-S5	FrameShift	DS	Generalized tonic-clonic seizures Severe mental retardation	(Claes et al., 2001; Sugawara et al., 2002; Depienne et al., 2008; Riva et al., 2009)
N1672H	DIVS4-S5	Missense	SME	NR	(Xu et al., 2014)
N1672I	DIVS4-S5	Missense	DS	NR	(Zuberi et al., 2011)
I1673T	DIVS5	Missense	DS GEFS+	Generalized tonic-clonic seizure with fever	(Skjei et al., 2015)
I1673N	DIVS5	Missense	DS	NR	(Cetica et al., 2017)
G1674S (Maternal)	DIVS5	Missense	FS+ Hemiconvulsions hemiplegia epilepsy	Febrile seizure Hemiconvulsion	(Saitoh et al., 2015a)
G1674R(De novo)	DIVS5	Missense	DS	NR	(Ohmori et al., 2002; Depienne et al., 2008)

Leu1675P (De novo)	DIVS5	Missense	DS	NR	(Yang et al., 2017)
L1677F	DIVS5	Missense	DS	NR	(Depienne et al., 2008; Lim et al., 2011; Wang et al., 2012)
M1681CfsX 34	DIVS5	FrameShift	DS	NR	(Depienne et al., 2008)
M1681Kfs X35	DIVS5	Frame Shift	DS	NR	(Riva et al., 2009)
F1682S	DIVS5	Missense	DS	Severe psycomotor retardation	(Fukuma et al., 2004)
I1683T (De novo)	DIVS5	Missense	DS SMEB	NR	(Zuberi et al., 2011; Wang et al., 2012; Lee et al., 2014)
Y1684D	DIVS5	Missense	DS	NR	(Zuberi et al., 2011)
Y1684S	DIVS5	Missense	Intractable Epilepsy	NR	(Wang et al., 2012)
Y1684X (De novo)	DIVS5	Nonsense	SMEB	NR	(Zuberi et al., 2011)
A1685D(De novo)	DIVS5	Missense	DS	Spike-wave complex (EEG) Non-fuctional channel	(Fujiwara, 2003) (Sugiura et al., 2012)

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A1685V	DIVS5	Missense	PEFS+	Frequent seizures, both febrile and afebrile, during infancy and subsequently developed epilepsies Non functional channel	(Sugawara et al., 2001) (Sugiura et al., 2012)
F1687S (Familial)	DIVS5	Missense	Myoclonic astatic epilepsy GEFS+	NR	(Marini et al., 2007; Cetica et al., 2017)
G1688W (De novo)	DIVS5	Missense	DS	NR	(Zuberi et al., 2011)
G1688V	DIVS5	Missense	DS	NR	(Xu et al., 2015)
M1689R	DIVS5	Missense	DS	NR	(Ishii et al., 2017)
S1690AfsX 25	DIVS5	FrameShift	DS	NR	(Ream and Mikati, 2014)
F1692S (De novo)	DIVS5	Missense	DS	NR	(Wang et al., 2012)
Y1694YfsX 22 (De novo)	DIVS5	FrameShift	DS	NR	(Zuberi et al., 2011)
Y1694C (De novo)	DIVS5	Missense	DS	Myoclonic seizures Atypical absence	(Fukuma et al., 2004; Wang et al., 2012; Cetica et al., 2017)

				Severe psychomotor retardation	
Y1694X	DIVS5	Nonsense	DS	NR	(Xu et al., 2015)
V1695LfsX 20 (De novo)	DIVS5	FrameShift	DS	NR	(Depienne et al., 2008)
K1696EfsX 6 (De novo)	DIVS5	FrameShift	DS	NR	(Orrico et al., 2009)
I1701DfsX3 (De novo)	DIVS5-S6	FrameShift	DS	NR	(Wang et al., 2012)
D1702H	DIVS5-S6	Missense	DS	NR	(Cetica et al., 2017)
D1702Y	DIVS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
D1702E	DIVS5-S6	Missense	SME	NR	(Xu et al., 2014)
D1703Y	DIVS5-S6	Missense	DS	NR	(Ishii et al., 2017)
D1703V	DIVS5-S6	Missense	SME	NR	(Xu et al., 2014)

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F1707V	DIVS5-S6	Missense	DS	NR	(Harkin et al., 2007; Rodda et al., 2012)
F1707L	DIVS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
T1709P	DIVS5-S6	Missense	DS	NR	(Haginoya et al., 2018)
T1709I (Maternal)	DIVS5-S6	Missense	ICEGTC	Spike-wave complex and multifocal spikes (EEG) Non-functional channel	(Fujiwara, 2003) (Rhodes et al., 2005)
T1709N	DIVS5-S6	Missense	DS	NR	(Cetica et al., 2017)
G1711S	DIVS5-S6	Missense	Epilepsy	NR	(Lindy et al., 2018)
N1712K	DIVS5-S6	Missense	DS	NR	(Ishii et al., 2017)
S1713N	DIVS5-S6	Missense	DS	Focal spikes in the right parietal region; sharp waves over the left frontal region in the sleep record (EEG)	(Kimura et al., 2005)
A1713D (De novo)	DIVS5-S6	Missense	DS	Febrile seizures, Hemiclonic, generalized tonic clonic seizures Focal spike-waves complex (EEG)	(Liu et al., 2018)

M1714V (Maternal)	DIVS5-S6	Missense	GEFS+	NR	(Tsai et al., 2018)
M1714R (De novo)	DIVS5-S6	Missense	DS	NR	(Riva et al., 2009; Zuberi et al., 2011)
M1714K	DIVS5-S6	Missense	DS	NR	(Depienne et al., 2008)
C1716R (De novo)	DIVS5-S6	Missense	SMEB Epilepsy and/or NDD	Febril convulsions Afebril concussions Parcial seizures Generalized spikes- wave (EEG)	(Marini et al., 2007; Lindy et al., 2018)
L1717P (De novo)	DIVS5-S6	Missense	SME	Generalized tonic clonic seizure	(Verbeek et al., 2013)
T1721R (De novo)	DIVS5-S6	Missense	DS	NR	(Harkin et al., 2007)
T1721K	DIVS5-S6	Missense	Ep and/or NDD	Seizures	(Retterer et al., 2016; Lindy et al., 2018)
I1722FfsX4 6	DIVS5-S6	Frameshift	DS	Not reported	(Ko et al., 2018)
T1722A (De novo)	DIVS5-S6	Missense	DS	Myoclonic, hemiclonic Focal seizures	(Wu et al., 2015)

S1723F	DIVS5-S6	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
A1724P	DIVS5-S6	Missense	Intractable Epilepsy	NR	(Wang et al., 2012)
A1724T (De novo)	DIVS5-S6	Missense	DS	NR	(Ishii et al., 2017)
G1725C (De novo)	DIVS5-S6	Missense	DS	NR	(Depienne et al., 2008)
W1726R (De novo)	DIVS5-S6	Missense	DS	NR	(Harkin et al., 2007)
W1726X	DIVS5-S6	Nonsense	DS	NR	(Zuberi et al., 2011)
G1728S.fsX 4	DIVS5-S6	Frameshift	Ep and/or NDD	NR	(Lindy et al., 2018)
D1727G (De novo)	DIVS5-S6	Missense	DS	NR	(Wang et al., 2012)
L1729W (De novo)	DIVS5-S6	Missense	DS	NR	(Ishii et al., 2017)

L1730P	DIVS5-S6	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
A1731P (De novo)	DIVS5-S6	Missense	DS	NR	(Ishii et al., 2017)
I1733FfsX4 6	DIVS5-S6	Frameshift	DS	Generalized tonic clonic seizure Atonic, complex partial and absence seizures	(de Lange et al., 2018)
L1729FfsX 9 (De novo)	DIVS5-S6	Frameshift	DS	NR	(Depienne et al., 2008)
P1732L (De novo)	DIVS5-S6	Missense	DS	NR	(Djémié et al., 2016)
N1733D	DIVS5-S6	Missense	DS GEFS+	Generalized tonic clonic seizure	(Tan et al., 2012)
L1734P	DIVS5-S6	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
P1739L	DIVS5-S6	Missense	GEFS+ FS+	NR	(Zuberi et al., 2011)
D1740N	DIVS5-S6	Missense	FS+/FS+ and focal seizures Ep and/or NDD	NR	(Lindy et al., 2018)

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C1741R (De novo)	DIVS5-S6	Missense	DS	NR	(Wang et al., 2012)
C1741S (De novo)	DIVS5-S6	Missense	TLT-MTS	Febrile status epilepticus	(Tiefes et al., 2019)
C1741S (De novo)	DIVS5-S6	Missense	LGS	NR	(Allen et al., 2013)
C1741Y	DIVS5-S6	Missense	DS Ep and/or NDD	NR	(Xu et al., 2015; Lindy et al., 2018)
D1742G	DIVS5-S6	Missense	PEFS+	Myoclonic atstatic seizures Febrile seizures Generalized tonic-clonic seizure	(Pineda-Trujillo et al., 2005)
G1746W	DIVS5-S6	Missense	DS	NR	(Esterhuizen et al., 2018)
1747Nfs177 9X	DIVS5-S6	Frameshift	DS	NR	(Margherita Mancardi et al., 2006)
G1749E (De novo)	DIVS5-S6	Missense	DS	Generalized tonic-clonic seizures Complex partial seizures Reduced current density	(Claes et al., 2003; Rhodes et al., 2005)

S1750fsX17 78 (De novo)	DIVS5-S6	Deletion and insertion	DS	NR	(Sun et al., 2010)
S1751GfsX 29	DIVS5-S6	Frameshift	DS	NR	(Xu et al., 2015)
G1754V	DIVS5-S6	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
G1754R (De novo)	DIVS5-S6	Missense	DS	Focal seizures Hemiconvulsions	(Petrelli et al., 2012)
D1755G	DIVS5-S6	Missense	SME	NR	(Xu et al., 2014)
C1756G	DIVS5-S6	Missense	SMEB	Febrile seizures with generalized tonic clonic seizure	(Herini et al., 2010)
G1757R (De novo)	DIVS5-S6	Missense	DS	NR	(Djémié et al., 2016)
G1757E	DIVS5-S6	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
N1758IfsX3 5	DIVS5-S6	Frameshift	Ep and/or NDD	NR	(Lindy et al., 2018)

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F1764fsX17	DIVS6	Frameshift	SME	NR	(Xu et al., 2014)
G1762E (De novo)	DIVS6	Missense	DS	NR	(Margherita Mancardi et al., 2006)
I1763F De novo	DIVS6	Missense	DS	NR	(Zuberi et al., 2011)
I1763N De novo	DIVS6	Missense	DS	NR	(Zuberi et al., 2011)
F1764Y	DIVS6	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
F1765fsX17 94	DIVS6	Frameshift	DS	Generalized tonic-clonic seizures Multifocal spikes (EEG)	(Fujiwara, 2003)
F1765L De novo	DIVS6	Missense	PEFS+	Complete absence of sodium current	(Liao et al., 2010)
F1765delX1 777 De novo	DIVS6	Frameshift	DS	Febrile convulsions Generalized spike-wave (EEG)	(Marini et al., 2007)

F1756del	DIVS6	In-frame deletion	SMEB	NR	(Fukuma et al., 2004)
F1766CfsX28	DIVS6	Frameshift	DS	NR	(Xu et al., 2015)
S1768R De novo	DIVS6	Missense	DS	Absences and tonic-clonic seizures	(Willemsen et al., 2012)
I1770F	DIVS6	Missense	DS	NR	(Zuberi et al., 2011)
I1770HfsX24	DIVS6	Frameshift	Ep and/or NDD	NR	(Lindy et al., 2018)
I1770N	DIVS6	Missense	DS Secondary epilepsy	Encephalopathic Movement disorder Cognitive regression	(Tang et al., 2011)
I1770T	DIVS6	Missense	SMEB	NR	(Zuberi et al., 2011)
I1771N	DIVS6	Missense	DS	NR	(Depienne et al., 2008)
A1772T De novo	DIVS6	Missense	DS	Febrile seizures Focal to bilateral tonic-clonic Focal spike wave (EEG)	(Esterhuizen et al., 2018)

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S1773F De novo	DIVS6	Missense	DS	NR	(Margherita Mancardi et al., 2006)
F1774S	DIVS6	Missense	HM3	Enhanced persintet current	(Chastan et al., 2016; Bertelli et al., 2019)
L1775P	DIVS6	Missense	DS	NR	(Jiménez-Arredondo et al., 2017)
V1776F	DIVS6	Missense	DS	NR	(Ishii et al., 2017)
M1780T De novo	DIVS6	Missense	DS	NR	(Nabbout et al., 2003)
Y1781H De novo	DIVS6	Missense	DS	NR	(Depienne et al., 2008)
Y1771C	DIVS6	Missense	DS	NR	(Fukuma et al., 2004)
I1782S	DIVS6	Missense	DS	NR	(Depienne et al., 2008)

I1782M	DIVS6	Missense	DS SME	Febrile and hemiclonic seizures	(Villeneuve et al., 2014)
A1783T De novo	DIVS6	Missense	DS SME DS	Generalized tonic-clonic seizures Myoclonic seizures Complex partial seizures Clonic seizures	(Sun et al., 2010; Klassen et al., 2011; Petrelli et al., 2012; Moehring et al., 2013; Lindy et al., 2018)
A1783V De novo	DIVS6	Missense	DS Epilepsy and/or NDD	Febril convulsions Afebril convulsions Myoclonic seizures Parcial seizures Generalized spikes-wave and focal (EEG)	(Marini et al., 2007; Klassen et al., 2011; Petrelli et al., 2012; Wang et al., 2012; Butler et al., 2017a)
I1785fsX11	DIVS6	Frameshift	SME	NR	(Xu et al., 2014)
E1787K	DIVS6	Missense	DS	Febril convulsions Generalized spikes-wave and multifocal (EEG)	(Marini et al., 2007)
E1787D	DIVS6	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
N1788fsX1796	C-terminal	Frameshift	DS	NR	(Wallace et al., 2003)
N1788K(;)H939P	C-terminal	Missense Compound	DS	NR	(Depienne et al., 2008)

F1789LfsX 5	C-terminal	Frameshift	DS	NR	(Marini et al., 2007)
A1792T De novo	C-terminal	Missense	DS	NR	(Wang et al., 2012)
A1792D	C-terminal	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
E1795Q	C-terminal	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
E1795G De novo	C-terminal	Missense	Epilepsy	NR	(Staněk et al., 2018)
A1797P	C-terminal	Missense	Tonic- clonic + focal seizures	Tonic-clonic and focal seizures	(Butler et al., 2017a)
A1797EfsX 4	C-terminal	Frameshift	DS	NR	(Cho et al., 2018)
S1801RfsX 56	C-terminal	Frameshift	Ep and/or NDD	NR	(Lindy et al., 2018)

E1802X	C-terminal	Nonsense	DS	NR	(Xu et al., 2015)
F1805X De novo	C-terminal	Frameshift	DS	NR	(Nabbout et al., 2003)
E1806X	C-terminal	Nonsense	Ep and/or NDD	NR	(Lindy et al., 2018)
1807delMF YE	C-terminal	In-frame deletion	DS	Generalized tonic clonic seizures	(Fujiwara, 2003)
F1808L	C-terminal	Missense	ICEGTC	Reduced current density Shift steady state activation and inactivation to more negative values	(Fujiwara, 2003; Rhodes et al., 2005)
F1808I De novo	C-terminal	Missense	SME	NR	(Depienne et al., 2008)
W1812G De novo	C-terminal	Missense	DS Epilepsy and/or NDD	Generalized tonic clonic seizures Multifocal spikes (EEG)	(Fujiwara, 2003; Skjei et al., 2015; Lindy et al., 2018)
W1812R	C-terminal	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)

W1812S De novo	C-terminal	Missense	DS	NR	(Depienne et al., 2008)
W1812X De novo	C-terminal	Nonsense	GEFS+	NR	(Cetica et al., 2017)
W1812C (;) 1813– 1815EFK De novo	C-terminal	In-frame deletion	DS	NR	(Nabbout et al., 2003)
E1813_F18 15del De novo	C-terminal	In-frame deletion	SME	NR	(Depienne et al., 2008)
Q1815K De novo	C-terminal	Missense	EE	Febrile and afebrile seizures Generalized tonic clonic seizures Generalized spikes and waves (EEG)	(Mercimek-Mahmutoglu et al., 2015)
A1819S	C-terminal	Missense	GEFS+	NR	(Cetica et al., 2017)
Q1821X De novo	C-terminal	Nonsense	SME	NR	(Djémié et al., 2016)
M1823R (De novo)	C-terminal	Missense	DS	NR	(Ishii et al., 2017)

E1824X	C-terminal	Nonsense	SME	NR	(Xu et al., 2014)
L1828S	C-terminal	Missense	Neurodevelopmental disorder, epilepsy-related	NR	(Stosser et al., 2018)
Q1830X De novo	C-terminal	Nonsense	DS	NR	(Zuberi et al., 2011)
F1831S De novo	C-terminal	Missense	DS	Generalized tonic clonic seizures Ataxia Severe mental decline Small current density reduction	(Sugawara et al., 2002; Fujiwara, 2003; Le Gal et al., 2014)
F1831Lfx2 7	C-terminal	Frameshift	DS	NR	(Depienne et al., 2008)
A1832P	C-terminal	Missense	DS	NR	(Zuberi et al., 2011)
L1835F De novo	C-terminal	Missense	DS	NR	(Depienne et al., 2008)
L1835_P18 37del	C-terminal	In-frame deletion	Ep and/or NDD	NR	(Lindy et al., 2018)

E1836GfsX 25	C-terminal	Frameshift	DS	NR	(Depienne et al., 2008)
Q1837X	C-terminal	Nonsense	DS	NR	(Wang et al., 2012)
L1839V	C-terminal	Missense	SME	NR	(Xu et al., 2014)
L1839P De novo	C-terminal	Missense	DS	Generalized tonic-clonic seizures Hemiclonic and focal seizures	(Wu et al., 2015)
L1841P	C-terminal	Missense	DS	Focal seizures	(Kumar et al., 2018)
M1845Hfs X5	C-terminal	Frameshift	DS	NR	(Ko et al., 2018)
K1846S.fsX 11 De novo	C-terminal	Frameshift	DS SMEB	Generalized tonic clonic seizures	(Wallace et al., 2003; Margherita Mancardi et al., 2006; Zucca et al., 2008; Nicita et al., 2010; Sun et al., 2010; Petrelli et al., 2012; Lee et al., 2014; Haginoya et al., 2018)
K1846X	C-terminal	Nonsense	DS	NR	(Sun et al., 2010)
Q1848X	C-terminal	Nonsense	DS	NR	(Ishii et al., 2017)

M1852K	C-terminal	Missense	DS	NR	(Zuberi et al., 2011)
M1852T	C-terminal	Missense	DS GEFS+	Reduced current density	(Xu et al., 2015)
M1852IfsX 9	C-terminal	Frameshift	Intractable Epilepsy	NR	(Wang et al., 2012)
P1855S	C-terminal	Missense	Epilepsy	NR	(Butler et al., 2017a)
P1855L De novo	C-terminal	Missense	DS	NR	(Zuberi et al., 2011)
M1856T	C-terminal	Missense	FS+ Epilepsy and/or NDD	NR	(Lindy et al., 2018)
M1856K	C-terminal	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
V1857L	C-terminal	Missense	GEFS+	Febrile seizures Generalized tonic- clonic convulsion	(Nagao et al., 2005)
G1859Wfs X2	C-terminal	Frameshift	DS	NR	(Depienne et al., 2008)

R1861W	C-terminal	Missense	Intractable Epilepsy	NR	(Wang et al., 2012)
R1861P	C-terminal	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
D1866Y	C-terminal	Missense	GEFS+	Shift steady state inactivation to more positive values Enhanced persistent current	(Spampanato, 2004)
D1866G (De novo)	C-terminal	Missense	DS	NR	(Ishii et al., 2017)
I1867NfsX7 8	C-terminal	Frameshift	DS	NR	(Depienne et al., 2008)
I1867T	C-terminal	Missense	GEFS+	Generalized tonic-clonic seizures	(Hindocha et al., 2008)
I1867TfsX1 0 De novo	C-terminal	Frameshift	DS	NR	(Depienne et al., 2008)
T1872fsX	C-terminal	Frameshift	DS	Secondary generalized tonic-clonic seizures Focal tonic seizures	(Rilstone et al., 2012)

L1876P	C-terminal	Missense	DS Epilepsy and/or NDD	NR	(Lindy et al., 2018)
D1876X	C-terminal	Frameshift	DS	NR	(Zuberi et al., 2011)
G1877V	C-terminal	Missense	GEFS+	Febrile convulsions with non-febrile seizures Psychomotor delay Generalize tonic clonic/complex seizures	(Kim and Lee, 2017)
S1879fsX31 De novo	C-terminal	Frameshift	SME	Febrile seizures Generalized tonic- clonic seizures	(Verbeek et al., 2013)
G1880E	C-terminal	Missense	DS	NR	(Zuberi et al., 2011)
E1881K	C-terminal	Missense	DS	Focal seizures	(Petrelli et al., 2012)
E1881X De novo	C-terminal	Nonsense	DS SMEB	Febrile and generalized seizures	(Villeneuve et al., 2014)
E1881D De novo	C-terminal	Missense	DS SME	NR	(Wallace et al., 2003; Rodda et al., 2012)

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R1886X De novo	C-terminal	Nonsense	DS	Febrile and hemiclonic seizures	(Margherita Mancardi et al., 2006; Villeneuve et al., 2014; Djémié et al., 2016)
R1886fsX1 910 De novo	C-terminal	Frameshift	DS	NR	(Nabbout et al., 2003)
R1886Q	C-terminal	Missense	SME	Generalized tonic-clonic seizures Atypic absences	(Moehring et al., 2013)
E1890fsX1 910 De novo	C-terminal	Frameshift	DS	NR	(Nabbout et al., 2003)
F1893AfsX 53	C-terminal	Frameshift	DS	Febrile and generalized seizures	(Villeneuve et al., 2014)
R1892X De novo	C-terminal	Nonsense	DS	Reduced current density	(Sugawara et al., 2002; Nicita et al., 2010)
R1892G	C-terminal	Missense	Epilepsy	NR	(Afawi et al., 2016)
P1894L De novo	C-terminal	Missense	EP+ASD	NR	(O’Roak et al., 2011)

P1898LfsX 13 De novo	C-terminal	Frameshift	DS	Febrile and myoclonic seizures Secondary generalized tonic-clonic seizures	(Zhou et al., 2018)
Q1904X	C-terminal	Nonsense	DS Epilepsy and/or NDD	NR	(Lindy et al., 2018)
Q1904fsX4 2	C-terminal	Frameshift	DS	NR	(Sugawara et al., 2002)
T1907fsX4	C-terminal	Frameshift	SME	NR	(Xu et al., 2014)
T1909I	C-terminal	Missense	DS	Reduced current density Enhanced persistent current	(Ohmori et al., 2006)
T1909del De novo	C-terminal	In-frame deletion	DS	NR	(Zuberi et al., 2011)
R1912KfsX 32 De novo	C-terminal	Frameshift	DS	NR	(Zuberi et al., 2011)
R1912X De novo	C-terminal	Nonsense	DS	Generalized tonic-clonic seizures Absence, myoclonic, partial and hemiclonic seizures	(Ozmen et al., 2011)

K1913X	C-terminal	Nonsense	Ep and/or NDD	NR	(Lindy et al., 2018)
p.1914_1914del De novo	C-terminal	In-frame deletion	DS	Febrile seizures Myoclonic seizures Focal to bilateral tonic-clonic Multifocal discharges (EEG)	(Liu et al., 2018)
Q1914del De novo	C-terminal	In-frame deletion	Pediatric refractory epilepsy	NR	(Liu et al., 2018)
Q1914RfsX 30 De novo	C-terminal	Frameshift	ICEGTC	NR	(Harkin et al., 2007)
E1915X	C-terminal	Frameshift	DS	Febrile and hemiclonic seizures	(Villeneuve et al., 2014)
E1915K	C-terminal	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
E1915G.fsX 28 De novo	C-terminal	Frameshift	DS	NR	(Ream and Mikati, 2014)
E1916KfsX 16	C-terminal	Frameshift	Ep and/or NDD	NR	(Lindy et al., 2018)

E1916X	C-terminal	Nonsense	Ep and/or NDD	NR	(Lindy et al., 2018)
S1918F	C-terminal	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
I1922T	C-terminal	Missense	DS	NR	(Harkin et al., 2007; Mulley et al., 2013; Lindy et al., 2018)
Q1923R	C-terminal	Missense	PEFS+	Secondarily generalized tonic-clonic and complex partial seizures Focal spike-waves and generalized spike-wave (EEG)	(Shi et al., 2012)
R1924LfsX 8 De novo	C-terminal	Frameshift	DS	NR	(Djémié et al., 2016)
A1925T	C-terminal	Missense	FS+	NR	(Møller et al., 2016)
Y1926X	C-terminal	Nonsense	DS	NR	(Zuberi et al., 2011)
R1927delin sIle,Ile,Gln De novo	C-terminal	Frameshift	DS	NR	(Zuberi et al., 2011)
R1927T	C-terminal	Missense	DS	NR	(Xu et al., 2015)

R1928G	C-terminal	Missense	DS	NR	(Zucca et al., 2008)
L1930FfsX 2 De novo	C-terminal	Frameshift	SMEB	NR	(Zuberi et al., 2011)
K1936E	C-terminal	Missense	Ep and/or NDD	NR	(Lindy et al., 2018)
A1951S	C-terminal	Missense	DS	NR	(Cetica et al., 2017)
E1957G	C-terminal	Missense	Infantile spasms DS	NR	(Wallace et al., 2003; Cherepanova et al., 2013)
M1977L	C-terminal	Missense	GEFS+	Generalized convulsions Afebrile seizures Bilateral frontal spike- waves (EEG)	(Saitoh et al., 2012)
R1988W	C-terminal	Missense	Epilepsy- aphasia with FS+	NR	(Carvill et al., 2013)
del SCN1A De novo	5'UTR	Partial gene deletion (73.8Kb)	DS	Generalized tonic clonic seizures Myoclonic seizures Atypical absences Focal seizures Status epilepticus	(Nakayama et al., 2010)

del SCN1A,7A,9A	5'UTR	Partial gene deletion	SMEB	Generalized tonic clonic seizures Focal seizures Status epilepticus Secondary generalization	(Nakayama et al., 2010)
del SCN1A	N-terminal	Partial gene deletion	DS	NR	(Zuberi et al., 2011)
del SCN1A	Chromosome	Partial gene deletion (Exon 12-14)	DS	Febrile convulsions Absence seizures Multifocal spike-waves (EEG)	(Altarescu et al., 2012)
del SCN1A	Chromosome	Partial gene deletion (Exon 1 a 20)	SMEB	NR	(Lim et al., 2011)
del SCN1A	Chromosome	Whole gene deletion (0.2 Mb)	DS	Tonic-clonic seizure Hemiclonic seizure	(Lim et al., 2015)
del SCN1A	Chromosome	Partial gene deletion (Exons 2-4)	DS FS+	Febrile seizures Febrile seizures plus Generalized clonic seizures Generalized tonic-clonic seizures	Guerrini R.2010
del SCN1A	Chromosome	Partial gene deletion (Exons 2-16)	SFE	Focal seizures Status epilepticus Secondary generalization	(Nakayama et al., 2010)
del SCN1A De novo	Chromosome	Partial gene deletion (exon 8-26)	DS	NR	(Wang et al., 2008)

del SCN1A	Chromosome	Partial gene deletion (Exons 7 - 9)	DS	NR	(Depienne et al., 2008)
del SCN1A	Chromosome	Partial gene deletion (Exon 9)	DS	NR	(Depienne et al., 2008)
del SCN1A	Chromosome	Partial gene deletion (Exons 14 – 20)	DS	NR	(Depienne et al., 2008)
del SCN1A	Chromosome	Partial gene deletion (Exons 22 - 26)	DS	NR	(Depienne et al., 2008)
del SCN1A	Chromosome	Partial gene deletion (Exons 24)	DS	NR	(Depienne et al., 2008)
dup SCN1A	Chromosome	Partial gene duplication (Exons 2- 21)	DS	NR	(Depienne et al., 2008)
del SCN1A	Chromosome DI-DII	Partial gene deletion	SME	NR	<u>(Hattori et al., 2008)</u>
del SCN1A	Chromosome	Partial gene deletion	DS	Generalized tonic– clonic seizures Absence, myoclonic and partial seizures	<u>(Ekici et al., 2011)</u>

del De novo	Chromosome	Partial gene deletion (exons 3 and 17–26)	DS	Tonic clonic seizures Myoclonic seizures Atypical absences Focal seizures Status epilepticus Seizures provoked by fever	(Nakayama et al., 2010)
del SCN1A	Chromosome	Partial gene deletion (Exons 17-20)	DS	Focal myoclonus seizures Generalized tonic–clonic seizures	(Skjei et al., 2015)
del SCN1A De novo	Chromosome	Partial gene deletion (Exons 14–16)	DS	Generalized tonic clonic seizures Myoclonic seizures Atypical absences Focal seizures Status epilepticus Seizures provoked by fever	(Nakayama et al., 2010)
del SCN1A	Chromosome	Partial gene deletion (Exon 20)	SMEB	Generalized tonicclonic seizures Focal seizures Status epilepticus Secondary generalization	(Nakayama et al., 2010)
del SCN1A De novo	Chromosome	Partial gene deletion (Exons 17-26)	DS	NR	(Wang et al., 2008)
del SCN1A De novo	Chromosome	Partial gene deletion (Exons 20-26)	DS	NR	(Wang et al., 2008)

del SCN1A De novo	Chromosome	Partial gene deletion	DS	NR	(Sun et al., 2010)
del SCN1A De novo	Chromosome	Whole gene deletion (607 kb)	DS	Febrile and afebrile myoclonic seizures Generalized spike-waves (EEG)	(Madia et al., 2006)
del SCN1A	Chromosome	Whole gene deletion (0.750 Mb)	DS	NR	(Wang et al., 2008)
del SCN1A	Chromosome	Whole gene deletion (1.139 Mb)	DS	NR	(Wang et al., 2008)
del SCN1A De novo	Chromosome	Whole gene deletion (1.277 Mb)	DS	NR	(Wang et al., 2008)
del SCN1A	Chromosome	Whole gene deletion (1.5 Mb)	MMPSI	Focal clonic seizure	(Lim et al., 2015)
del SCN1A	Chromosome	Whole gene deletion (1.549 Mb)	DS	NR	(Wang et al., 2008)
del SCN1A De novo	Chromosome	Whole gene deletion (3.1 Mb)	DS	Unilateral febrile clonic seizure Febrile and afebrile myoclonic seizures	(Madia et al., 2006)

				Generalized spike-waves (EEG)	
del SCN1A De novo	Chromosome	Whole gene deletion (4 Mb)	DS	Myoclonic seizure Light sensitivity	(Suls et al., 2006)
del SCN1A De novo	Chromosome	Whole gene deletion (4.5 Mb)	DS	Generalized tonic-clonic seizure	(Suls et al., 2006)
del SCN1A De novo	Chromosome	Whole gene deletion (4.7 Mb)	DS	Myoclonic or hemiclonic seizures Generalized spike-waves (EEG)	(Madia et al., 2006)
del SCN1A	Chromosome	Whole gene deletion (5 Mb)	DS and Leigh syndrome	Generalized tonic-clonic seizure	(Suls et al., 2006)
Del SCN1A, SCN2A, SCN1A, SCN3A, SCN9A and SCN7A	Chromosome	Deletion (10.29 - 10.58 Mb) (De novo interstitial deletion)	Severe epilepsy	Focal and generalized seizures Lack of eye contact Stereotypic and repetitive hand movements Slow background with high amplitude delta waves mixed with spikes and sharp waves on the temporo-occipital areas (EEG)	(Pescucci et al., 2007)

Del SCN1A, SCN2A, SCN3A, SCN7A and SCN9A	Chromosome	Deletion (10.4-Mb)	Severe epilepsy	Epileptic seizure with pale, atonic periods followed by a spas- m-like out-throwing of both arms Predominantly right- sided epileptiform activity (EEG)	(Davidsson et al., 2008)
del SCN1A (De novo)	Chromosome	Whole gene deletion (11.06 Mb)	MMPSI	Multifocal seizures Status epilepticus	(Carranza Rojo et al., 2011)
del SCN1A, 9A, ABCB11 and LRP2 (De novo)	Chromosome	partial gene deletion	DS	NR	(Ma et al., 2016)
del SCN1A, 9A	Chromosome	whole gene deletion (0.2 Mb)	DS	Tonic-clonic seizure Hemiclonic seizure	(Lim et al., 2015)
del SCN1A, 2A, 3A, 7A, 9A	Chromosome	partial gene deletion (8.4 Mb)	MMPSI	Tonic—clonic seizure Multifocal seizures	(Lim et al., 2015)
del SCN1A De novo	Chromosome	partial gene deletion (Exon 7)	DS	>10 seizures/month	(Do et al., 2017)
del SCN1A, 2A, 3A, 7A, 9A	Chromosome	whole gene deletion (4.3 Mb)	MMPSI	Multifocal seizures Hemiclonic seizure	(Lim et al., 2015)

del SCN1A (De novo)	Chromosome	partial gene deletion (Exon 8 – 26)	DS	NR	(Ishii et al., 2017)
del SCN1A (De novo)	Chromosome	partial gene deletion (Exon 17 – 26)	DS	NR	(Ishii et al., 2017)
del SCN1A (De novo)	Chromosome	partial gene deletion (Exon 20 – 26)	DS	NR	(Ishii et al., 2017)
del SCN1A (De novo)	Chromosome	partial gene deletion (Exon 1)	DS	NR	(Ishii et al., 2017)
del SCN1A De novo	Chromosome	partial gene deletion (Exon 5-8)	DS	NR	(Esterhuizen et al., 2018)
del SCN1A (De novo)	Chromosome	partial gene deletion (Exon 2-3)	DS	NR	(Ishii et al., 2017)
del SCN1A (De novo)	Chromosome	partial gene deletion (Exon 1-26)	DS	NR	(Ishii et al., 2017)
del SCN1A (De novo)	Chromosome	partial gene deletion (Exon 7)	DS	NR	(Ishii et al., 2017)
del SCN1A	Chromosome	partial gene deletion (Exon 1 a 13)	DS	NR	(Cetica et al., 2017)

del SCN1A	Chromosome	partial gene deletion (Exon 2 a 4)	DS FS	NR	(Cetica et al., 2017)
del SCN1A	Chromosome	partial gene deletion (Exon 1 a 26)	DS	NR	(Cetica et al., 2017)
del SCN1A	Chromosome	partial gene deletion (Exon 17 e 18)	DS	NR	(Cetica et al., 2017)
del SCN1A	Chromosome	partial gene deletion (Exons 2-23)	DS	Generalized tonic clonic seizure Focal, complex partial and tonic seizures	(de Lange et al., 2018)
dup SCN1A	Chromosome	Partial gene duplication	SME	NR	(Xu et al., 2014)
dup SCN1A	Chromosome	Partial gene duplication (Exons 2–16)	DS	Tonic clonic seizures Myoclonic seizures Atypical absences Focal seizures Status epilepticus Seizures provoked by fever	(Nakayama et al., 2010)
dup SCN1A De novo	Chromosome	Partial gene duplication	DS	NR	(Sun et al., 2010)

dup SCN1A	Chromosome	Partial gene duplication	SME	Generalized tonic clonic seizures	(Petrelli et al., 2012)
dup SCN1A De novo	Chromosome	Partial gene duplication (Exon 17 a 20)	DS	Afebrile seizures Generalized tonic clonic seizures	(Verbeek et al., 2013)
Del SCN1A and SCN2A	Chromosome	whole gene deletion	IEE	NR	(Kwong et al., 2015)
dup SCN1A De novo	Chromosome	Whole gene duplication	Neonatal seizure	Abnormal back- ground activities with spiky transients (EEG)	(Okumura et al., 2011)
dup SCN1A De novo	Chromosome	Whole gene duplication (6.7 Mb)	Epilepsy	Focal tonic seizures	(Goeggel Simonetti et al., 2012)
dup SCN1A De novo	Chromosome	Whole gene duplication (10.1 Mb)	Epilepsy	Multifocal clonic seizures	(Goeggel Simonetti et al., 2012)
dup SCN1A	Chromosome	Whole gene duplication	NIE	Facial flushing Focal tonic seizures Generalized tonic clonic seizures	(Raymond et al., 2011; Goeggel Simonetti et al., 2012)
dup SCN1A De novo	Chromosome	Whole gene duplication (11.19 Mb)	Epilepsy with cognitive impairment /ASD	NR	(Nicholl et al., 2013)

dup SCN1A	Chromosome	Partial gene duplication	GEFS+	NR	(Cetica et al., 2017)
translocation De novo	Chromosome	t(2;5)(q24.3,q34)	DS	Afebrile epileptic seizure Generalized convulsive seizure	(Møller et al., 2008)
unbalanced translocation De novo	Chromosome	t(2;15)	Epilepsy, apnoea, mental retardation & dysmorphic features	Epileptic seizures accompanied by severe central apnea	(Langer et al., 2006)

Epilepsy (Ep); Generalized epilepsy with febrile seizures plus (GEFS+); Febrile seizures (FS); Febrile seizures plus (FS+); Lennox-Gastaut syndrome (LGS); Dravet syndrome (DS); Epileptic encephalopathy (EE); Borderline severe myoclonic epilepsy (SMEB); Severe myoclonic epilepsy (SME); Familial hemiplegic migraine (FHM); Partial epilepsy with antecedent FS (PEFS+); neurodevelopmental disorders (NDD); Intractable childhood epilepsy with generalized tonic-clonic seizures (ICE-GTC); Malignant migrating partial seizures of infancy (MMPSI); Temporal lobe epilepsy (TLE); Mesial temporal sclerosis (MTS); Neonatal- infantile epilepsy (NIE); Symptomatic focal epilepsy (SFE); Autism spectrum disorders (ASD); Not Reported (NR); Electroencephalography (EEG); Magnetic resonance imaging (MRI).

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