Table S1. *KCNA1* mutations associated with ataxia and epilepsy and with DEE

Mutation	Position	Clinical symptoms	Functional defects	Treatment	References
F184C	S1	Severe ataxia, severe neuromyotonia, epilepsy, visual disturbances	LoF, Reduced current density and positive shift of voltage-dependent activation	Phenytoin partially effective	[8]
T226R	S2	Moderate ataxia, severe neuromyotonia, epilepsy, cataplexy, sleep disturbances, skeletal deformities	LoF, Reduced current density	Acetazolamide and carbamazepine effective; phenytoin, valproic acid and phenobarbital partially effective	[7]
A242P	S2	Moderate ataxia, myokymia, epilepsy	LoF, Reduced current density	Lamotrigine effective; acetazolamide ineffective	[29]
A261T (de novo)	S3	Fever-induced seizures, ataxia, myokymia	GoF, Negative shift of voltage-dependent activation	Carbamazepine effective, valproate partially effective	[12, 18]
L319R	S4-S5	Paroxysmal kinesigenic dyskinesia without ataxia; in some carriers seizures	LoF, Reduced current density and dominant-negative effect, positive shift of voltage-dependent activation	Oxcarbazepine or carbamazepine effective	[9]
R324T	S4-S5	Moderate ataxia, severe neuromyotonia, epilepsy, suspected paroxysmal kinesigenic dyskinesia	LoF, Reduced current density	Carbamazepine effective	[10]
S342I	S5	Ataxia and seizures	NA	Phenytoin effective	[11]
V368L	S5-S6	DEE, ataxia, myokymia	LoF, Non-functional channels	Phenobarbital partially effective, valproic acid and oxcarbazepine effective	[15]
G376S	S5-S6	Seizures, mild cognitive and motor delay, ataxia, myokymia	NA	Valproic acid effective	[12]
P403S (de novo) In twins	PVP, S6	DEE; Twin A: early onset epilepsy, moderate cognitive and motor development delay; ataxia. Twin B: epilepsy, severe intellectual disability, ataxia and myokymia, language loss.	LoF, Non-functional channels	Twin A: lamotrigine partially effective. Twin B: drug-resistant seizures. Combinations of valproic acid, vigabatrin, lamotrigine, oxacarbazepine, phenytoin and clobazam poorly effective	[16]
P403A (de novo)	PVP, S6	Epilepsy, ataxia and intellectual disability	LoF, Reduced current density and dominant-negative effect, positive shift of voltage-	Lacosamide and acetazolamide effective	This study

			dependent activation, slower kinetics of activation		
P405S (de novo)	PVP, S6	DEE, cognitive impairment; fever-induced seizures.	LoF, Markedly reduced current density and marked depolarizing shift of voltage-dependent activation	Drug-resistant seizures. At last follow up treatment comprises: clobazam, carbamazepine, zonisamide and valproic acid poorly effective. Phenobarbital ineffective	[16]
P405L (de novo)	PVP, S6	DEE, neonatal onset epilepsy, developmental delay, status epilepticus during sleep (ESES)	LoF, Non-functional channels	Phenobarbital, carbamazepine, levetiracetam ineffective and phenitoin partially effective. At last follow up treatment comprises: acetazolamide, lamotrigine and valproic acid with seizures control. ESES responsive to ACTH	[16, 17]
V408L	S6	Global developmental delay, myokymia with postural abnormalities, mild ataxia, seizures	LoF, Faster inactivation	Carbamazepine or phenytoin effective	[13]
F414C	C-term	Moderate episodic ataxia, myokymia, neuromyotonia, isolated photosensitive generalized tonic-clonic seizure	LoF, Non-functional channels and dominant-negative effect	Clonazepam partially effective; acetazolamide and oxcarbazepine ineffective	[30]
R417Stop	C-term	Severe ataxia, dysarthria and slurred speech; periocular myokymia; epilepsy and tremor	LoF, Non-functional channels and dominant-negative effect	Carbamazepine and acetazolamide partially effective; lamotrigine, vigabatrin and clonazepam ineffective	[31]

NA = Not available; DEE = developmental and epileptic encephalopathy; LoF = loss-of-function