Supplement to: Multi-Gene Panel Testing in a Large Cohort of Adults with Epilepsy: Diagnostic Yield and Clinically Actionable Genetic Findings

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Supplemental Table 1. ICD-10 codes for identifying clinical features

Clinical feature	ICD-10 code	Description
ID/DD	F84.9	Pervasive developmental disorder, unspecified
	R62.50	Unspecified lack of expected normal physiological development in childhood
	F70	Mild intellectual disabilities
	F71	Moderate intellectual disabilities
	F72	Severe intellectual disabilities
	F73	Profound intellectual disabilities
	F78	Other intellectual disabilities
	F79	Unspecified intellectual disabilities
Autism	F84.0	Autistic disorder
Family history of neurological disorders	Z81.0	Family history of intellectual disabilities
	Z82.0	Family history of epilepsy and other diseases of the nervous system
Pharmacoreseistant seizures	G40.011	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, with status epilepticus
	G40.019	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, without status epilepticus
	G40.111	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, with status epilepticus
	G40.119	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable,

		without status epilepticus
	G40.211	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, with status epilepticus
	G40.219	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, without status epilepticus
	G40.31	Generalized idiopathic epilepsy and epileptic syndromes, intractable
	G40.311	Generalized idiopathic epilepsy and epileptic syndromes, intractable, with status epilepticus
	G40.319	Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus
	G40.411	Other generalized epilepsy and epileptic syndromes, intractable, with status epilepticus
	G40.419	Other generalized epilepsy and epileptic syndromes, intractable, without status epilepticus
	G40.803	Other epilepsy, intractable, with status epilepticus
	G40.804	Other epilepsy, intractable, without status epilepticus
	G40.813	Lennox-Gastaut syndrome, intractable, with status epilepticus
	G40.814	Lennox-Gastaut syndrome, intractable, without status epilepticus
	G40.824	Epileptic spasms, intractable, without status epilepticus
	G40.911	Epilepsy, unspecified, intractable, with status epilepticus
	G40.919	Epilepsy, unspecified, intractable, without status epilepticus
	G40.A11	Absence epileptic syndrome, intractable, with status epilepticus
	G40.A19	Absence epileptic syndrome, intractable, without status epilepticus

	G40.B11	Juvenile myoclonic epilepsy, intractable, with status epilepticus
	G40.B19	Juvenile myoclonic epilepsy, intractable, without status epilepticus

Abbreviations: DD, developmental delay; ID, intellectual disability; ICD-10, *International Classification of Diseases, Tenth Revision*.

Supplemental Table 2. Variants observed in individuals with diagnostic findings

Gene	Variant	Effect	Interpretation	Individuals (n)
ALDH7A1	NM_001182.4:c.364C>T	p.Arg122Trp	Pathogenic	1
ALDH7A1	NM_001182.4:c.1513G>C	p.Gly505Arg	Pathogenic	1
ARX	NM_139058.2:c.315_335dup	p.Ala109_Ala115dup	Pathogenic	2
ATP1A2	NM_000702.3:c.2564G>A	p.Gly855Glu	Likely Pathogenic	1
ATP1A3	NM_152296.4:c.2443G>A	p.Glu815Lys	Pathogenic	1
ATP6AP2	NM_005765.2:c.321C>T	Silent	Pathogenic	1
CACNA1A	NM_001127221.1:c.904G>A	p.Asp302Asn	Pathogenic	1
CDKL5	NM_003159.2:c.154G>T	p.Glu52*	Pathogenic	1
CDKL5	NM_003159.2:c.282+1G>T	Splice donor	Pathogenic	1
CHD2	NM_001271.3:c.1081G>T	p.Glu361*	Pathogenic	1
CHD2	NM_001271.3:c.1541dup	p.Thr516Aspfs*38	Pathogenic	1
CHD2	NM_001271.3:c.1719G>A	Silent	Pathogenic	1
CHD2	NM_001271.3:c.2425C>T	p.Arg809*	Pathogenic	1
CHD2	NM_001271.3:c.3787dupG	p.Val1263Glyfs*4	Pathogenic	1

CHD2	NM_001271.3:c.390C>T	Silent	Likely Pathogenic	1
CHD2	NM_001271.3:c.4771_4772del	p.Leu1591Aspfs*32	Pathogenic	1
CHD2	NM_001271.3:c.552-?_1153+?del	Deletion (Exons 7-10)	Pathogenic	1
CHRNA4	NM_000744.6:c.839C>T	p.Ser280Phe	Pathogenic	1
CHRNA4	NM_000744.6:c.851C>T	p.Ser284Leu	Pathogenic	1
CNTNAP2	NM_014141.5:c.-516-?_97+?del	Deletion (Exon 1)	Pathogenic	1
CNTNAP2	NM_014141.5:c.2497delT	p.Trp833Glyfs*18	Pathogenic	1
CNTNAP2	NM_014141.5:c.3046C>T	p.Arg1016*	Pathogenic	1
CNTNAP2	NM_014141.5:c.403-?_550+?del	Deletion (Exon 4)	Pathogenic	1
DEPDC5	NM_001242896.1:c.1081+2T>G	Splice donor	Likely Pathogenic	1
DEPDC5	NM_001242896.1:c.1385_1386del	p.Tyr462*	Pathogenic	1
DEPDC5	NM_001242896.1:c.677dup	p.Tyr226*	Pathogenic	1
DEPDC5	NM_001242896.1:c.1555C>T	p.Gln519*	Pathogenic	1
DEPDC5	NM_001242896.1:c.21C>G	p.Tyr7*	Pathogenic	1
DEPDC5	NM_001242896.1:c.2826G>A	p.Trp942*	Pathogenic	1
DEPDC5	NM_001242896.1:c.3095del	p.Pro1032Glnfs*47	Pathogenic	1

DEPDC5	NM_001242896.1:c.319C>T	p.Gln107*	Pathogenic	1
DEPDC5	NM_001242896.1:c.346C>T	p.Arg116*	Pathogenic	1
DEPDC5	NM_001242896.1:c.3994C>T	p.Arg1332*	Pathogenic	1
DEPDC5	NM_001242896.1:c.768-2A>G	Splice acceptor	Likely Pathogenic	1
DEPDC5	NM_001242896.1:c.865C>T	p.Gln289*	Pathogenic	1
DNAJC5	NM_025219.2:c.346_348delCTC	p.Leu116del	Pathogenic	1
EEF1A2	NM_001958.3:c.1141C>T	p.Arg381Trp	Likely Pathogenic	1
EEF1A2	NM_001958.3:c.364G>A	p.Glu122Lys	Pathogenic	1
EEF1A2	NM_001958.3:c.370G>A	p.Glu124Lys	Likely Pathogenic	1
EPM2A	NM_005670.3:c.721C>T	p.Arg241*	Pathogenic	1
FLNA	NM_001456.3:c.7848_7849delGG	p.Glu2617Valfs*124	Pathogenic	1
FOXG1	NM_005249.4:c.256dup	p.Gln86Profs*35	Pathogenic	1
GABRA1	NM_000806.5:c.335G>A	p.Arg112Gln	Pathogenic	1
GABRA1	NM_000806.5:c.825C>A	p.Asn275Lys	Likely Pathogenic	1
GABRB2	NM_021911.2:c.895A>T	p.Ile299Phe	Likely Pathogenic	1
GABRB3	NM_000814.5:c.-114-?_*4247+?del	Deletion (Entire sequence)	Pathogenic	3
GLRA1	NM_000171.3:c.1259G>A	p.Arg420His	Pathogenic	1

GRIN1	NM_007327.3:c.2530C>T	p.Arg844Cys	Pathogenic	1
GRIN2A	NM_000833.4:c.292C>T	p.Leu98Phe	Likely Pathogenic	1
GRIN2B	NM_000834.3:c.1847A>G	p.Asn616Ser	Likely Pathogenic	1
GRIN2B	NM_000834.3:c.2459G>A	p.Gly820Glu	Pathogenic	1
GRIN2B	NM_000834.3:c.1345G>T	p.Glu449*	Pathogenic	1
HNRNPU	NM_031844.2:c.-218-?_*4150+?del	Deletion (Entire coding sequence)	Pathogenic	3
HNRNPU	NM_031844.2:c.1491_1492dup	p.Glu498Valfs*4	Pathogenic	1
IQSEC2	NM_001111125.2:c.2983C>T	p.Arg995Trp	Likely Pathogenic	1
IQSEC2	NM_001111125.2:c.3875del	p.Pro1292Hisfs*105	Pathogenic	1
KCNA2	NM_004974.3:c.-163-?_*129+?del	Deletion (Entire coding sequence)	Pathogenic	1
KCNA2	NM_004974.3:c.889C>T	p.Arg297Trp	Pathogenic	1
KCNA2	NM_004974.3:c.890G>A	p.Arg297Gln	Pathogenic	2
KCNC1	NM_001112741.1:c.959G>A	p.Arg320His	Pathogenic	3
KCNH2	NM_000238.3:c.1096C>T	p.Arg366*	Pathogenic	1
KCNH2	NM_000238.3:c.2692_2692+1insACACGG	Splice donor	Likely Pathogenic	1
KCNQ2	NM_172107.2:c.1342C>T	p.Arg448*	Pathogenic	1
KCNQ2	NM_172107.2:c.1678C>T	p.Arg560Trp	Pathogenic	1

KCNQ2	NM_172107.2:c.593G>A	p.Arg198Gln	Pathogenic	1
KCNQ2	NM_172107.2:c.817-?_1301+?del	Deletion (Exons 6-12)	Pathogenic	1
KCNQ2	NM_172107.2:c.821C>T	p.Thr274Met	Pathogenic	1
KCNT1	NM_020822.2:c.1193G>A	p.Arg398Gln	Pathogenic	2
KCNT1	NM_020822.2:c.1421G>A	p.Arg474His	Pathogenic	1
LGI1	NM_005097.2:c.1256T>G	p.Leu419*	Pathogenic	1
MECP2	Alternate transcript NM_001110792.1: c.47_57del	p.Gly16Glufs*22	Pathogenic	1
MECP2	NM_004992.3:c.1054_1271delins36	p.Lys352Profs*23	Pathogenic	1
MECP2	NM_004992.3:c.-226-?_*8554+?dup	Gain (Entire coding sequence)	Pathogenic	3
MECP2	NM_004992.3:c.1164_1207del	p.Pro389*	Pathogenic	1
MECP2	NM_004992.3:c.1216C>T	p.Gln406*	Pathogenic	1
MECP2	NM_004992.3:c.380C>T	p.Pro127Leu	Pathogenic	1
MECP2	NM_004992.3:c.454C>G	p.Pro152Ala	Pathogenic	1
MECP2	NM_004992.3:c.473C>T	p.Thr158Met	Pathogenic	1
MECP2	NM_004992.3:c.674C>G	p.Pro225Arg	Pathogenic	1
MECP2	NM_004992.3:c.808C>T	p.Arg270*	Pathogenic	1
MECP2	NM_004992.3:c.925C>T	p.Arg309Trp	Pathogenic	1

MECP2	NM_004992.3:c.983_1197del	p.Leu328Hisfs*5	Pathogenic	1
MEF2C	NM_002397.4:c.-654-?_258+?del	Deletion (Exons 1-3)	Pathogenic	1
NEXMIF	NM_001008537.3:c.3458dupA	p.Asn1153Lysfs*8	Pathogenic	1
NEXMIF	NM_001008537.3:c.652C>T	p.Arg218*	Pathogenic	1
NHLRC1	NM_198586.2:c.1091C>A	p.Ser364*	Pathogenic	1
NPRL3	NM_001077350.2:c.925-1G>C	Splice acceptor	Likely Pathogenic	1
NPRL3	NM_001077350.2:c.1025dup	p.Cys343Metfs*18	Pathogenic	1
NPRL3	NM_001077350.2:c.1270C>T	p.Arg424*	Pathogenic	1
NPRL3	NM_001077350.2:c.349del	p.Glu117Lysfs*5	Pathogenic	1
NPRL3	NM_001077350.2:c.630-?_767+?del	Deletion (Exon 8)	Pathogenic	2
PACS1	NM_018026.3:c.607C>T	p.Arg203Trp	Pathogenic	1
PCDH19	NM_001184880.1:c.-1676-?_*4633+?del	Deletion (Entire coding sequence)	Pathogenic	2
PCDH19	NM_001184880.1:c.1091dup	p.Tyr366Leufs*10	Pathogenic	1
PCDH19	NM_001184880.1:c.1479_1483del	p.Pro494Alafs*27	Pathogenic	1
PCDH19	NM_001184880.1:c.1681C>T	p.Pro561Ser	Pathogenic	1
PCDH19	NM_001184880.1:c.2656C>T	p.Arg886*	Pathogenic	1
PCDH19	NM_001184880.1:c.659del	p.Gly220Alafs*9	Pathogenic	1

PCDH19	NM_001184880.1:c.687del	p.Asp230Thrfs*16	Pathogenic	1
PRRT2	NM_145239.2:c.-65-?_*1243+?del	Deletion (Entire coding sequence)	Pathogenic	1
PRRT2	NM_145239.2:c.649dup	p.Arg217Profs*8	Pathogenic	7
PRRT2	NM_145239.2:c.653_660dup	p.Gln221Cysfs*11	Pathogenic	1
PRRT2	NM_145239.2:c.971del	p.Gly324Glufs*13	Likely Pathogenic	1
PURA	NM_005859.4:c.175C>T	p.Gln59*	Pathogenic	1
PURA	NM_005859.4:c.697_699delTTC	p.Phe233del	Pathogenic	1
ROGDI	NM_024589.2:c.665dup	p.Ala223Argfs*5	Pathogenic	1
SCN1A	NM_001165963.1:c.1931_1939delinsA	p.Thr644Lysfs*29	Pathogenic	1
SCN1A	NM_001165963.1:c.-18-?_*2085+?del	Deletion (Entire coding sequence)	Pathogenic	3
SCN1A	NM_001165963.1:c.1028+1G>T	Splice donor	Pathogenic	1
SCN1A	NM_001165963.1:c.1028G>C	p.Gly343Ala	Likely Pathogenic	1
SCN1A	NM_001165963.1:c.1178G>C	p.Arg393Pro	Pathogenic	1
SCN1A	NM_001165963.1:c.1663-?_2176+?del	Deletion (Exons 11-12)	Pathogenic	1
SCN1A	NM_001165963.1:c.2134C>T	p.Arg712*	Pathogenic	1
SCN1A	NM_001165963.1:c.2495G>A	p.Trp832*	Pathogenic	1
SCN1A	NM_001165963.1:c.2589+3A>T	Intronic	Pathogenic	2

SCN1A	NM_001165963.1:c.2729A>G	p.Gln910Arg	Likely Pathogenic	1
SCN1A	NM_001165963.1:c.2836C>T	p.Arg946Cys	Pathogenic	1
SCN1A	NM_001165963.1:c.2837G>A	p.Arg946His	Pathogenic	1
SCN1A	NM_001165963.1:c.2860G>C	p.Glu954Gln	Likely Pathogenic	1
SCN1A	NM_001165963.1:c.2947G>T	p.Val983Phe	Likely Pathogenic	1
SCN1A	NM_001165963.1:c.295_301delATCTTCC	p.Ile99Glyfs*11	Pathogenic	1
SCN1A	NM_001165963.1:c.2961del	p.Leu988Trpfs*5	Pathogenic	1
SCN1A	NM_001165963.1:c.3343_3344delGT	p.Val1115Thrfs*8	Pathogenic	1
SCN1A	NM_001165963.1:c.337C>A	p.Pro113Thr	Pathogenic	1
SCN1A	NM_001165963.1:c.3637C>T	p.Arg1213*	Pathogenic	1
SCN1A	NM_001165963.1:c.3726del	p.Ile1242Metfs*28	Pathogenic	1
SCN1A	NM_001165963.1:c.4269_4272delCTCT	p.Ser1424Cysfs*13	Pathogenic	1
SCN1A	NM_001165963.1:c.4372del	p.Tyr1458Thrfs*18	Pathogenic	1
SCN1A	NM_001165963.1:c.4507G>A	p.Glu1503Lys	Pathogenic	1
SCN1A	NM_001165963.1:c.4822G>T	p.Asp1608Tyr	Pathogenic	1
SCN1A	NM_001165963.1:c.4907G>A	p.Arg1636Gln	Pathogenic	1
SCN1A	NM_001165963.1:c.4943G>A	p.Arg1648His	Pathogenic	1

SCN1A	NM_001165963.1:c.5081A>G	p.Tyr1694Cys	Pathogenic	1
SCN1A	NM_001165963.1:c.5179G>T	p.Asp1727Tyr	Pathogenic	1
SCN1A	NM_001165963.1:c.5288_5289delinsCCCATCTG	p.Ile1763delinsThrHisLeu	Likely Pathogenic	1
SCN1A	NM_001165963.1:c.5536_5539del	p.Lys1846Serfs*11	Pathogenic	2
SCN1A	NM_001165963.1:c.557T>C	p.Leu186Pro	Likely Pathogenic	1
SCN1A	NM_001165963.1:c.5656C>T	p.Arg1886*	Pathogenic	1
SCN1A	NM_001165963.1:c.5767C>A	p.Gln1923Lys	Likely Pathogenic	1
SCN1A	NM_001165963.1:c.680T>G	p.Ile227Ser	Pathogenic	1
SCN1B	NM_199037.3:c.363C>G	p.Cys121Trp	Pathogenic	1
SCN2A	NM_021007.2:c.-356-?_*2486+?del	Deletion (Entire sequence)	Pathogenic	1
SCN2A	NM_021007.2:c.1342C>T	p.Gln448*	Pathogenic	1
SCN2A	NM_021007.2:c.3400-?_*2486+?del	Deletion (Exons 18-27)	Pathogenic	1
SCN2A	NM_021007.2:c.3955C>T	p.Arg1319Trp	Likely Pathogenic	1
SCN2A	NM_021007.2:c.3956G>A	p.Arg1319Gln	Pathogenic	1
SCN2A	NM_021007.2:c.4350T>G	p.Tyr1450*	Pathogenic	1
SCN8A	NM_014191.3:c.3563G>A	p.Arg1188Gln	Likely Pathogenic	1
SCN8A	NM_014191.3:c.779T>C	p.Phe260Ser	Pathogenic	1

SLC2A1	NM_006516.2:c.418G>C	p.Val140Leu	Pathogenic	1
SLC6A1	NM_003042.3:c.1460T>C	p.Met487Thr	Likely Pathogenic	1
SLC6A8	NM_005629.3:c.-278-?_262+?del	Deletion (Exon 1)	Pathogenic	1
SLC6A8	NM_005629.3:c.418_421dup	p.Val141Aspfs*49	Pathogenic	1
SMC1A	NM_006306.3:c.2161C>T	p.Gln721*	Pathogenic	1
SMC1A	NM_006306.3:c.3249dup	p.Ile1084Aspfs*3	Pathogenic	1
SPATA5	NM_145207.2:c.2080-?_2213+?del	Deletion (Exons 12-13)	Pathogenic	2
SPATA5	NM_145207.2:c.1912A>G	p.Lys638Glu	Likely Pathogenic	2
STX1B	NM_052874.4:c.-242-?_*3565+?del	Deletion (Entire sequence)	Pathogenic	1
STXBP1	NM_003165.3:c.128_130del	p.Ser43del	Likely Pathogenic	1
STXBP1	NM_003165.3:c.170-?_246+?del	Deletion (Exon 4)	Pathogenic	1
STXBP1	NM_003165.3:c.847G>A	p.Glu283Lys	Pathogenic	1
STXBP1	NM_003165.3:c.875G>A	p.Arg292His	Pathogenic	1
STXBP1	NM_003165.3:c.964-?_1359+?del	Deletion (Exons 12-15)	Likely Pathogenic	1
SYNGAP1	NM_006772.2:c.1744del	p.Glu582Argfs*68	Pathogenic	1
SYNGAP1	NM_006772.2:c.2726delT	p.Met909Argfs*168	Pathogenic	1

SYNGAP1	NM_006772.2:c.663+1G>T	Splice donor	Likely Pathogenic	1
TBC1D24	NM_001199107.1:c.457G>A	p.Glu153Lys	Pathogenic	1
TBC1D24	NM_001199107.1:c.845C>G	p.Pro282Arg	Pathogenic	4
TBC1D24	NM_001199107.1:c.1153C>T	p.Gln385*	Pathogenic	1
TCF4	NM_001083962.1:c.1328C>G	p.Ser443*	Pathogenic	1
TCF4	NM_001083962.1:c.1481_1482insAA	p.Tyr494*	Pathogenic	1
TSC1	NM_000368.4:c.1271_1272delGA	p.Arg424Asnfs*17	Pathogenic	1
TSC1	NM_000368.4:c.2074C>T	p.Arg692*	Pathogenic	1
TSC1	NM_000368.4:c.211-1G>T	Splice acceptor	Likely Pathogenic	1
TSC1	NM_000368.4:c.2356C>T	p.Arg786*	Pathogenic	1
TSC1	NM_000368.4:c.2391+1G>C	Splice donor	Likely Pathogenic	1
TSC1	NM_000368.4:c.2509_2512del	p.Asn837Valfs*11	Pathogenic	1
TSC2	NM_000548.3:c.225+2T>C	Splice donor	Likely Pathogenic	1
TSC2	NM_000548.3:c.848+281C>T	Intronic	Pathogenic	1
UBE3A	NM_130838.1:c.-44-?_*1888+?del	Deletion (Entire sequence)	Pathogenic	3
UBE3A	NM_130838.1:c.-44-?_*1888+?dup	Gain (Entire sequence)	Pathogenic	12
UBE3A	Partial Deletion	Exon 3	Pathogenic	1

WDR45	NM_007075.3:c.10C>T	p.Gln4*	Pathogenic	1
WDR45	NM_007075.3:c.752_754del	p.Ser251del	Pathogenic	1
ZEB2	NM_014795.3:c.432dupT	p.Glu145*	Pathogenic	1
ZEB2	NM_014795.3:c.67A>T	p.Lys23*	Pathogenic	1

eTable 3. Genes associated with epilepsy that have clinically actionable implications

Gene	Associated syndrome or disorder	Inheritance	Clinical action	Potential clinical management options for daily maintenance of seizures[a]	Potential clinical management options for other manifestations	References (PMIDs)
ALDH7A1	Pyridoxine-dependent epilepsy; folinic acid-responsive seizures	AR	Metabolic treatment	Indicated: pyridoxine, folinic acid, lysine-restricted diet		24664145, 20301659, 19142996, 24748525
ATP1A3	Alternating hemiplegia of childhood type 2; dystonia 12; cerebellar ataxia, areflexia, pes cavus, optic atrophy and sensorineural hearing loss	AD	Other		Indicated for AHC episodes: flunarizine, TPM, KD Indicated for dystonia: high-dose BZD	20301294, 25447930, 24996492, 24532324
CACNA1A	Developmental and epileptic encephalopathy; episodic ataxia type 2 (EA2); familial hemiplegic migraine type 1 (FHM1)	AD	Other		Indicated for ataxia: acetazolamide, 4-aminopyridine (4-AP) therapy Indicated for migraine: acetazolamide	20301319, 21734179, 30142438
CDKL5	Developmental and epileptic encephalopathy; atypical Rett syndrome; Angelman-like syndrome	XLD	ASM indications	Indicated: oral ganaxolone (open-label, extended access program)		Pestana-Knight E et al. Abstract 419. Presented at AES. December 2020.
CHD2	Childhood-onset epileptic encephalopathy	AD	ASM indications	Indicated: LEV, VPA		31677157, 25672921

DEPDC5	Familial focal epilepsy with variable foci; autosomal dominant nocturnal frontal lobe epilepsy	AD	Surgical indications	Indicated: high resolution neuroimaging; epilepsy surgery for identifiable epileptogenic foci		26434565, 30782578, 27683934, 30093711
EPM2A	Progressive myoclonus epilepsy, Lafora type	AR	ASM indications; ASM contraindications	Indicated: VPA and BZDs-as first-line; LEV, ZNS, TPM, and PER as second-line; primidone, PB, piracetam, and ESM as third-line Contraindicated: PHT, LTG, CBZ, OXC		20301563, 27459034
GLRA1	Hyperekplexia 1	AD/AR	ASM indications	Indicated: clonazepam		20301437, 25356525
KCNH2	Long QT syndrome type 2; short QT syndrome	AD	Other		Indicated: pharmacotherapy; device therapy, surgery; lifestyle modifications Contraindicated: QT prolonging drugs	29097296, 24011539
KCNQ2	Benign familial neonatal seizures; developmental and epileptic encephalopathy	AD	ASM indications (subject to GoF/LoF considerations)[b]	Indicated: CBZ, PHT, PB		25880994, 20437616, 27602407

KCNT1	Autosomal dominant nocturnal frontal lobe epilepsy; developmental and epileptic encephalopathy	AD	ASM indications; Metabolic treatment	Indicated: quinidine, KD		26369628, 32167590, 31054119
LGI1	Autosomal dominant lateral temporal lobe epilepsy	AD	ASM indications	Indicated: PHT, CBZ, VPA		20301709, 7647791
NHLRC1	Progressive myoclonus epilepsy, Lafora type	AR	ASM indications; ASM contraindications	Indicated: VPA and BZDs as first-line; LEV, ZNS, TPM, and PER as second-line; primidone, PB, piracetam, and ESM as third-line Contraindicated: PHT, LTG, CBZ, OXC		20301563, 25667898
NPRL3	Familial focal epilepsy with variable foci	AD	Surgical intervention	Indicated: high resolution neuroimaging; epilepsy surgery for identifiable epileptogenic foci		26434565, 26285051
PCDH19	Developmental and epileptic encephalopathy	XLD	ASM indications; Metabolic treatment	Indicated: clobazam, potassium bromide, PHT, KD		26820223, 23712037
PRRT2	Episodic kinesigenic dyskinesia; benign familial infantile seizure 2; familial infantile convulsions with paroxysmal choreoathetosis	AD	ASM indications	Indicated: OXC, CBZ		28056630, 29334453, 32392383

SCN1A	Seizure disorders ranging from simple febrile seizures and genetic epilepsy with febrile seizure plus to Dravet syndrome and intractable childhood epilepsy with generalized tonic-clonic seizures; familial hemiplegic migraine 3	AD	ASM indications; ASM contraindications; Metabolic treatment; Surgical contraindications (subject to GoF/LoF considerations)[b]	Indicated: clobazam and VPA are optimal first-line ASMs; CBD (aged >1 year) and fenfluramine (aged >2 years) for Dravet syndrome; KD Contraindicated: sodium channel blockers; resective surgical intervention		20301494, 26600876, 26339958, 28538134, 24902755, 30061856
SCN2A	Benign familial neonatal seizures; developmental and epileptic encephalopathy; episodic ataxia; intellectual disability, and autism spectrum disorder	AD	ASM indications ASM contraindications; (subject to GoF/LoF considerations)[b]	Indicated: sodium channel blockers for GoF/early infantile epilepsy, PHT most effective Contraindicated: sodium channel blockers for LoF/later onset seizures (aged >3 months)		28379373, 26291284
SCN8A	Developmental and epileptic encephalopathy; benign familial neonatal seizures	AD	ASM indications (subject to GoF/LoF considerations)[b]	Indicated: PHT, VPA, CBZ, OXC, LTG, TPM		26252990, 26029160, 27559564, 25568300, 30615093
SLC2A1	Glucose transporter type 1 deficiency syndrome	AD/AR	Metabolic treatment; ASM contraindications	Indicated: KD Contraindicated: PB, acetazolamide, TPM, ZNS		20301603, 32913944
SLC6A1	Myoclonic-atonic epilepsy	AD	Metabolic treatment	Indicated: KD		27600546, 25865495
SLC6A8	Creatine transporter deficiency	XLR	Metabolic treatment	Indicated: oral creatine consideration		24953403, 20301745

				of arginine and/or glycine supplementation		
STXBP1	Developmental and epileptic encephalopathy	AD	ASM indications; Other	Indicated: PB, VPA, VGB, LEV	Indicated for dystonia, dyskinesia, and choreoathetosis: monoamine depleters, dopaminergic agents	27905812, 26865513
TSC1	Tuberous sclerosis complex	AD	ASM indications; Surgical indications	Indicated: VGB as first-line treatment for IS; everolimus (mTOR inhibitor) for adjunctive treatment (aged >2 years); CBD (aged >1 year); consideration of epilepsy surgery		15563014, 10073425, 33346789, 24053983, 31335226, 32854808
TSC2	Tuberous sclerosis complex	AD	ASM indications; Surgical indications	Indicated: VGB as first-line treatment for IS; everolimus (mTOR inhibitor) for adjunctive treatment (aged >2 years); CBD (aged >1 year); consideration of epilepsy surgery		15563014, 10073425, 33346789, 24053983, 31335226, 32854808

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; ASM, antiseizure medication; AHC, alternating hemiplegia of childhood; BZD, benzodiazepine; CBD, cannabidiol; CBZ, carbamazepine; ESM, ethosuximide; GoF, gain of function; IS, infantile spasms; KD, ketogenic diet; LEV, levetiracetam; LoF, loss of function; LTG, lamotrigine; mTOR, mammalian target of rapamycin; OXC, oxcarbazepine; PB, phenobarbital; PER, perampanel; PHT, phenytoin; TPM, topiramate; VGB, vigabatrin; VPA, valproic acid; XLD, X-linked dominant; XLR, X-linked recessive; ZNS, zonisamide.

[a]These treatments may also be indicated based on clinical diagnosis and an individual's clinical presentation.

[b]This gene demonstrates both GoF and LoF mechanisms that may result in different clinical presentations. Drug therapy selection could be different depending on patient presentation and predicted variant effect.