

Comprehensive Epilepsy Panel, Sequencing and Deletion/Duplication

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Epilepsy is a neurological disorder that causes recurrent unprovoked seizures and affects approximately 1% of the population.¹ It can be subclassified by seizure type (ie, focal, generalized, generalized and focal, or unknown) and can take idiopathic or syndromic forms. An estimated 30% of epilepsy cases are believed to have a genetic contribution,² and there is high genetic heterogeneity and significant phenotypic overlap between conditions. In addition to clinical evaluation and nonlaboratory testing, genetic testing can be useful to identify the basis of a patient's epilepsy and to inform prognosis, optimal treatment and management, recurrence risk, and testing of at-risk relatives.³

Disease Overview

According to guidelines from the National Society of Genetic Counselors, patients with unexplained epilepsy, regardless of age of onset, should be offered genetic testing.

Both focal and generalized epilepsy can have a genetic cause. Factors that increase the likelihood of a genetic cause include^{4,5}:

- Earlier age of seizure onset
- Presence of neurodevelopmental comorbidities such as intellectual disability, developmental delay, autism spectrum disorder, and/or encephalopathy
- Drug-resistant epilepsy
- A family history of epilepsy

Genetics

Genes

This panel includes genes associated with Mendelian forms of idiopathic epilepsy and syndromic epilepsy in which seizures are a major or presenting feature.

Refer to [Genes Tested](#) for additional details.

Etiology

Epilepsy may have infectious, structural, genetic, metabolic, immune, or unknown causes. An estimated 30% of epilepsy has a genetic cause.² Pathogenic germline variants in numerous genes have been associated with epilepsy.

Inheritance

Epilepsy may occur sporadically or as a familial trait with autosomal dominant, autosomal recessive, or X-linked inheritance. De novo variation is a common cause of sporadic epileptic encephalopathy.

Penetrance

Variable; influenced by gene and variant.

Featured ARUP Testing

[Comprehensive Epilepsy Panel, Sequencing and Deletion/Duplication 3001591](#)

Method: Massively Parallel Sequencing

Recommended test to establish a diagnosis or determine the genetic etiology of an epilepsy or seizure disorder

If a familial sequence variant has been previously identified, targeted sequencing for that variant may be appropriate; refer to the [Laboratory Test Directory](#) for additional information.

Test Interpretation

Methodology

This test is performed using the following sequence of steps:

- Selected genomic regions, primarily coding exons and exon-intron boundaries, from the targeted genes are isolated from extracted genomic DNA using a probe-based hybrid capture enrichment workflow.
- Enriched DNA is sequenced by massively parallel sequencing (MPS; also known as next generation sequencing, or NGS), followed by paired-end read alignment and variant calling using a custom bioinformatics pipeline. The pipeline includes an algorithm for detection of large deletions and duplications.
- Sanger sequencing is performed as necessary to fill in regions of low coverage and, in certain situations, to confirm variant calls.
- Large deletion/duplication calls made using MPS are confirmed by an orthogonal exon-level microarray when sample quality and technical conditions allow.

Clinical Sensitivity

Dependent on clinical phenotype.

Analytic Sensitivity/Specificity

Variant Class	Analytic Sensitivity (PPA) Estimate ^a (%) and 95% Credibility Region	Analytic Specificity (NPA) Estimate (%)
SNVs	>99 (96.9-99.4)	>99.9
Deletions 1-10 bp ^b	93.8 (84.3-98.2)	>99.9
Insertions 1-10 bp ^b	94.8 (86.8-98.5)	>99.9
Exon-level ^c deletions	97.8 (90.3-99.8) [2 exons or larger] 62.5 (38.3-82.6) [Single exon]	>99.9
Exon-level ^c duplications	83.3 (56.4-96.4) [3 exons or larger]	>99.9

^aPPA values are derived from larger methods-based MPS and/or Sanger validations. These values do not apply to testing performed by multiplex ligation-dependent probe amplification (MLPA) unless otherwise indicated.

^bVariants greater than 10 bp may be detected, but the analytic sensitivity may be reduced.

^cIn most cases, a single exon deletion or duplication is less than 450 bp and 3 exons span a genomic region larger than 700 bp.

bp, base pairs; NPA, negative percent agreement; PPA, positive percent agreement; SNVs, single nucleotide variants

Limitations

- A negative result does not exclude a heritable form of epilepsy.
- Diagnostic errors can occur due to rare sequence variations.
- Interpretation of this test result may be impacted if the patient has had an allogeneic stem cell transplantation.
- The following will not be evaluated:
 - Variants outside the coding regions and intron-exon boundaries of the targeted gene(s)
 - Variants in the mitochondrial genome
 - Regulatory region and deep intronic variants
 - Deletions/duplications in the *DYNC1H1*, *EMP2A*, *FARS2*, *SLC19A3*, and *WWOX* genes
 - Breakpoints of large deletions/duplications
 - Gene conversion events, complex inversions, and translocations
 - Repeat expansions (including common expansions in *ATN1* exon 5, *ARX*, and *CSTB* 5'UTR)
 - This assay does not assess for *PMM2*-associated hyperinsulinemic hypoglycemia and polycystic kidney disease (HIPKD)
 - SNVs and small deletions/insertions will not be called in the following exons due to technical limitations of the assay:

- *ABAT* (NM_001386615) 6
- *ABAT* (NM_001386616) partial exon 16(Chr16:8875107-8875145)
- *ADSL* (NM_001363840) 14
- *ALG13* (NM_001099922, NM_001257231) partial exon 24(ChrX:110987954-110988035)
- *ALG9* (NM_001352420, NM_001352421) 15
- *ALG9* (NM_001352415, NM_001352416, NM_001352419) 16
- *ALG9* (NM_001352417) 17
- *ANKRD11* (NM_013275, NM_001256183) partial exon 9(Chr16:89345816-89346020)
- *ANKRD11* (NM_001256182) partial exon 10(Chr16:89345816-89346020)
- *ANKRD11* (NM_013275, NM_001256183) 13
- *ANKRD11* (NM_001256182) 14
- *AP3B2* (NM_001348440) 5
- *ARHGEF9* (NM_001353923) 1
- *ARV1* (NM_001346992) 4
- *ARX* (NM_139058) partial exon 2(ChrX:25031469-25031834)
- *BRAT1* (NM_001350626) partial exon 14(Chr7:2578419-2578578)
- *BTD* (NM_001370752) 5
- *BTD* (NM_001370753) 4
- *CARS2* (NM_001352253) 9
- *CLN5* (NM_001366624) 4
- *CUL4B* (NM_001369145) 1
- *DMXL2* (NM_001378459) 32
- *DMXL2* (NM_001378463) partial exon 32(Chr15:51755500-51755555)
- *DMXL2* (NM_001378457, NM_001378458) 34
- *DNM1* (NM_001374269) 22
- *EHMT1* (NM_024757, NM_001145527, NM_001354263, NM_001354611) 1
- *EHMT1* (NM_001354259) 16
- *EHMT1* (NM_001354612) partial exon 9(Chr9:140657293-140657296)
- *EHMT1* (NM_001354611) partial exon 10(Chr9:140657293-140657296)
- *EPM2A* (NM_001368129, NM_001368132) 3
- *EPM2A* (NM_001368130) partial exon 3(Chr6:145956295-145956360)
- *FKTN* (NM_001351497) 6
- *FKTN* (NM_001351498) partial exon 9(Chr9:108382363-108382373)
- *FOXP1* (NM_005249) partial exon 1(Chr14:29236682-29236856)
- *GABBR2* (NM_005458, NM_001375347) 1
- *GABRG2* (NM_001375344) 7
- *GPHN* (NM_001377519, NM_001377514) 5
- *GPHN* (NM_001377515, NM_001377516, NM_001377517, NM_001377518) 9
- *GPHN* (NM_001377514, NM_001377515, NM_001377516) 10
- *GPHN* (NM_001377514) 11
- *KCNQ2* (NM_001382235) 15
- *KCTD7* (NM_001167961) 5
- *KDM5C* (NM_001353979, NM_001353981, NM_001353982, NM_001353984) 26
- *KIF1A* (NM_001379636) 36
- *KIF1A* (NM_001379639) 37
- *KIF1A* (NM_001379635, NM_001379638, NM_001379646) 38
- *MBD5* (NM_001378120) partial exon 9(Chr2:149241026-149241704)
- *NR2F1* (NM_005654) partial exon 1(Chr5:92920778-92920891)
- *NTRK2* (NM_001369547) 13
- *PLPBP* (NM_001349349) partial exon 1(Chr8:37620073-37620157)
- *PLPBP* (NM_001349349) 5
- *PLPBP* (NM_001349346) partial exon 6(Chr8:37632827-37632836)
- *RORB* (NM_001365023) 1
- *SAMHD1* (NM_001363733) 16
- *SLC19A3* (NM_001371413, NM_001371414) 3
- *SLC9A6* (NM_001379110) 14
- *SMARCA2* (NM_003070, NM_001289396, NM_001289397, NM_139045) 5

- *SPTAN1* (NM_001375318, NM_001375312) 2
- *SPTAN1* (NM_001375310) 50
- *SPTAN1* (NM_001363759) 52
- *SPTAN1* (NM_001375318) 53
- *ST3GAL3* (NM_001350619, NM_001350620) 12
- *ST3GAL3* (NM_001350621) 6,13
- *STXBP1* (NM_001374313, NM_001374314) 19
- *SYNGAP1* (NM_006772) partial exon 19(Chr6:33419581-33419683)
- *SZT2* (NM_001365999) 22
- *TPK1* (NM_001350884) 3
- *TPK1* (NM_001350883) 4
- *TPK1* (NM_001350882) 5
- *TPK1* (NM_001350895) 7
- *TPK1* (NM_001350881) 9
- *TSEN54* (NM_207346) 1
- *UBE3A* (NM_001354523) 5
- *UNC80* (NM_001371986) 27

- The following may not be detected:
 - Deletions/duplications/insertions of any size by MPS
 - Large duplications less than 3 exons in size
 - Noncoding transcripts
 - Some variants due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions
 - Low-level somatic or mosaic variants

Genes Tested

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>AARS1</i> (601065)	Developmental and epileptic encephalopathy 29 Hereditary diffuse leukoencephalopathy with spheroids 2	AR AD
<i>ABAT</i> (137150)	GABA-transaminase deficiency	AR
<i>ADGRG1</i> (604110)	Bilateral frontoparietal polymicrogyria; bilateral perisylvian polymicrogyria	AR
<i>ADSL</i> (608222)	Adenylosuccinase deficiency	AR
<i>ALDH5A1</i> (610045)	Succinic semialdehyde dehydrogenase deficiency	AR
<i>ALDH7A1</i> (107323)	Pyridoxine-dependent epilepsy	AR
<i>ALG1</i> (605907)	Congenital disorder of glycosylation type I κ	AR
<i>ALG13</i> (300776)	Developmental and epileptic encephalopathy 36	XL
<i>ALG3</i> (608750)	Congenital disorder of glycosylation type I δ	AR
<i>ALG6</i> (604566)	Congenital disorder of glycosylation type I ϵ	AR
<i>ALG8</i> (608103)	Congenital disorder of glycosylation type I η	AR
<i>ALG9</i> (606941)	Congenital disorder of glycosylation type II; Gillessen-Kaesbach-Nishimura syndrome	AR

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>AMACR</i> (604489)	Alpha-methylacyl-CoA racemase deficiency	AR
<i>AMT</i> (238310)	Glycine encephalopathy	AR
<i>ANKRD11</i> (611192)	KBG syndrome	AD
<i>AP3B2</i> (602166)	Developmental and epileptic encephalopathy 48	AR
<i>ARFGEF2</i> (605371)	Periventricular heterotopia with microcephaly	AR
<i>ARG1</i> (608313)	Argininemia	AR
<i>ARHGEF9</i> (300429)	Developmental and epileptic encephalopathy 8	XL
<i>ARV1</i> (611647)	Developmental and epileptic encephalopathy 38	AR
<i>ARX</i> (300382)	Developmental and epileptic encephalopathy 1; Proud syndrome; XL lissencephaly 2 with ambiguous genitalia; XL intellectual developmental disorder 29	XL
<i>ASAHI</i> (613468)	Spinal muscular atrophy with progressive myoclonic epilepsy	AR
<i>ASNS</i> (108370)	Asparagine synthetase deficiency	AR
<i>ATN1</i> (607462)	Congenital hypotonia, epilepsy, developmental delay, and digital anomalies	AD
<i>ATP1A1</i> (182310)	Hypomagnesemia, seizures, and impaired intellectual development 2	AD
<i>ATP1A3</i> (182350)	Alternating hemiplegia of childhood 2; developmental and epileptic encephalopathy 99	AD
<i>ATP6AP2</i> (300556)	Syndromic intellectual developmental disorder Hedera type	XL
<i>ATP7A</i> (300011)	Menkes disease	XL
<i>ATRX</i> (300032)	Alpha-thalassemia/mental retardation syndrome; XL intellectual disability-hypotonic facies syndrome	XL
<i>BCKDK</i> (614901)	Branched-chain keto acid dehydrogenase kinase deficiency	AR
<i>BRAT1</i> (614506)	Neurodevelopmental disorder with cerebellar atrophy and with or without seizures; rigidity and multifocal seizure syndrome, lethal neonatal	AR
<i>BTD</i> (609019)	Biotinidase deficiency	AR
<i>C12orf57</i> (615140)	Temptamy syndrome	AR
<i>CACNA1A</i> (601011)	Developmental and epileptic encephalopathy 42; episodic ataxia type 2; familial hemiplegic migraine 1	AD
<i>CACNA1D</i> (114206)	Primary aldosteronism, seizures, and neurologic abnormalities	AD
<i>CACNA1E</i> (601013)	Developmental and epileptic encephalopathy 69	AD
<i>CACNA2D2</i> (607082)	Cerebellar atrophy with seizures and variable developmental delay	AR

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>CAD</i> (114010)	Developmental and epileptic encephalopathy 50	AR
<i>CARS2</i> (612800)	Combined oxidative phosphorylation deficiency 27	AR
<i>CASK</i> (300172)	FG syndrome 4; intellectual developmental disorder and microcephaly with pontine and cerebellar hypoplasia	XL
<i>CDKL5</i> (300203)	Developmental and epileptic encephalopathy 2	XL
<i>CHD2</i> (602119)	Developmental and epileptic encephalopathy 94	AD
<i>CHRNA4</i> (118504)	Nocturnal frontal lobe epilepsy 1	AD
<i>CHRNB2</i> (118507)	Nocturnal frontal lobe epilepsy 3	AD
<i>CLCN4</i> (302910)	Raynaud-Claes syndrome	XL
<i>CLN3</i> (607042)	Neuronal ceroid lipofuscinosis 3	AR
<i>CLN5</i> (608102)	Neuronal ceroid lipofuscinosis 5	AR
<i>CLN6</i> (606725)	Neuronal ceroid lipofuscinosis types 6A and 6B (Kufs type)	AR
<i>CLN8</i> (607837)	Neuronal ceroid lipofuscinosis 8; northern epilepsy variant	AR
<i>CLTC</i> (118955)	Intellectual developmental disorder 56	AD
<i>CNKS2</i> (300724)	XL syndromic intellectual developmental disorder (Houge type)	XL
<i>CNTNAP2</i> (604569)	Pitt-Hopkins like syndrome 1	AR
<i>COL4A1</i> (120130)	Brain small vessel disease with or without ocular anomalies	AD
<i>CPT2</i> (600650)	CPT II deficiency (infantile or neonatal lethal)	AR
	Susceptibility to acute infection-induced encephalopathy 4	AD/AR
<i>CSTB</i> (601145)	Progressive myoclonic epilepsy 1A (Unverricht and Lundborg)	AR
<i>CTSD</i> (116840)	Neuronal ceroid lipofuscinosis 10	AR
<i>CTSF</i> (603539)	Neuronal ceroid lipofuscinosis13 (Kufs type)	AR
<i>CUL4B</i> (300304)	XL syndromic intellectual developmental disorder, Cabezas type	XL
<i>DCX</i> (300121)	XL lissencephaly or subcortical laminar heterotopia	XL
<i>DDX3X</i> (300160)	XL syndromic intellectual developmental disorder, Snijders Blok type	XL
<i>DEAF1</i> (602635)	Neurodevelopmental disorder with hypotonia, impaired expressive language, and with or without seizures Vulto-van Silfout-de Vries syndrome	AR
		AD

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>DEPDC5</i> (614191)	Familial focal epilepsy with variable foci 1	AD
<i>DHDDS</i> (608172)	Developmental delay and seizures with or without movement abnormalities	AD
	Congenital disorder of glycosylation type 1bb/retinitis pigmentosa 59	AR
<i>DIAPH1</i> (602121)	Seizures, cortical blindness, microcephaly syndrome	AR
<i>DMXL2</i> (612186)	Developmental and epileptic encephalopathy 81	AR
<i>DNAJC5</i> (611203)	Neuronal ceroid lipofuscinosis 4 (Kufs type)	AD
<i>DNM1</i> (602377)	Developmental and epileptic encephalopathy 31	AD
<i>DNM1L</i> (603850)	Lethal encephalopathy due to defective mitochondrial peroxisomal fission 1	AR/AD
<i>DOCK7</i> (615730)	Developmental and epileptic encephalopathy 23	AR
<i>DPAGT1</i> (191350)	Congenital disorder of glycosylation type Ij	AR
<i>DPM1</i> (603503)	Congenital disorder of glycosylation type Ie	AR
<i>DPYD</i> (612779)	Dihydropyrimidine dehydrogenase deficiency	AR
<i>DYNC1H1</i> (600112)	Complex cortical dysplasia with other brain malformations	AD
<i>DYRK1A</i> (600855)	Intellectual developmental disorder 7	AD
<i>EEF1A2</i> (602959)	Developmental and epileptic encephalopathy 33; intellectual developmental disorder 38	AD
<i>EHMT1</i> (607001)	Kleefstra syndrome 1	AD
<i>EPM2A</i> (607566)	Progressive myoclonic epilepsy 2A (Lafora)	AR
<i>FARS2</i> (611592)	Combined oxidative phosphorylation deficiency 14	AR
<i>FGF12</i> (601513)	Developmental and epileptic encephalopathy 47	AD
<i>FKTN</i> (607440)	Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies) type A4	AR
<i>FLNA</i> (300017)	Neuronal intestinal pseudoobstruction; periventricular heterotopia 1	XL
<i>FOLR1</i> (136430)	Neurodegeneration due to cerebral folate transport deficiency	AR
<i>FOXP1</i> (164874)	Congenital variant Rett syndrome	AD
<i>FRRS1L</i> (604574)	Developmental and epileptic encephalopathy 37	AR
<i>GABBR2</i> (607340)	Developmental and epileptic encephalopathy 59; neurodevelopmental disorder with poor language and loss of hand skills	AD

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>GABRA1</i> (137160)	Developmental and epileptic encephalopathy 19; susceptibility to childhood absence or juvenile myoclonic epilepsy	AD
<i>GABRB2</i> (600232)	Developmental and epileptic encephalopathy 92	AD
<i>GABRB3</i> (137192)	Developmental and epileptic encephalopathy 43; susceptibility to childhood absence epilepsy	AD
<i>GABRD</i> (137163)	Idiopathic generalized epilepsy 10; susceptibility to juvenile myoclonic epilepsy; susceptibility to generalized epilepsy with febrile seizures type 5	AD
<i>GABRG2</i> (137164)	Developmental and epileptic encephalopathy 74; familial febrile seizures 8; generalized epilepsy with febrile seizures plus type 3	AD
<i>GALC</i> (606890)	Krabbe disease	AR
<i>GAMT</i> (601240)	Cerebral creatine deficiency syndrome 2	AR
<i>GATM</i> (602360)	Cerebral creatine deficiency syndrome 3	AR
<i>GFAP</i> (137780)	Alexander disease	AD
<i>GNAO1</i> (139311)	Developmental and epileptic encephalopathy 17; neurodevelopmental disorder with involuntary movements	AD
<i>GNB1</i> (139380)	Intellectual developmental disorder 42	AD
<i>GOSR2</i> (604027)	Congenital muscular dystrophy with or without seizures; progressive myoclonic epilepsy 6	AR
<i>GPHN</i> (603930)	Molybdenum cofactor deficiency C	AR
<i>GRIA3</i> (305915)	XL syndromic intellectual developmental disorder (Wu type)	XL
<i>GRIN1</i> (138249)	Developmental and epileptic encephalopathy 101	AR
	Neurodevelopmental disorder with or without hyperkinetic movements and seizures	AR/AD
<i>GRIN2A</i> (138253)	Epilepsy, focal, with speech disorder and with or without impaired intellectual development	AD
<i>GRIN2B</i> (138252)	Developmental and epileptic encephalopathy 27; intellectual developmental disorder 6 with or without seizures	AD
<i>HACE1</i> (610876)	Spastic paraparesis and psychomotor retardation with or without seizures	AR
<i>HCN1</i> (602780)	Developmental and epileptic encephalopathy 24; generalized epilepsy with febrile seizures plus type 10	AD
<i>HECW2</i> (617245)	Neurodevelopmental disorder with hypotonia, seizures, and absent language	AD
<i>HNRNPU</i> (602869)	Developmental and epileptic encephalopathy 54	AD
<i>HSD17B10</i> (300256)	HSD10 mitochondrial disease	XL
<i>IQSEC2</i> (300522)	XL intellectual developmental disorder 1	XL
<i>ITPA</i> (147520)	Developmental and epileptic encephalopathy 35	AR

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>KANSL1</i> (612452)	Koolen-De Vries syndrome	AD
<i>KCNA1</i> (176260)	Episodic ataxia/myokymia syndrome	AD
<i>KCNA2</i> (176262)	Developmental and epileptic encephalopathy 32	AD
<i>KCNB1</i> (600397)	Developmental and epileptic encephalopathy 26	AD
<i>KCNC1</i> (176258)	Progressive myoclonic epilepsy 7	AD
<i>KCNH1</i> (603305)	Temple-Baraitser syndrome; Zimmermann-Laband syndrome 1	AD
<i>KCNJ10</i> (602208)	SESAME syndrome	AR
<i>KCNJ11</i> (600937)	Permanent neonatal diabetes 2 with or without neurologic features	AD
<i>KCNMA1</i> (600150)	Cerebellar atrophy, developmental delay, and seizures	AR
	Liang-Wang syndrome paroxysmal nonkinesigenic dyskinesia 3 with or without generalized epilepsy; susceptibility to idiopathic generalized epilepsy 16	AD
<i>KCNQ2</i> (602235)	Benign neonatal seizures 1; developmental and epileptic encephalopathy 7	AD
<i>KCNQ3</i> (602232)	Benign neonatal seizures 2	AD
<i>KCNT1</i> (608167)	Developmental and epileptic encephalopathy 14; nocturnal frontal lobe epilepsy 5	AD
<i>KCTD7</i> (611725)	Progressive myoclonic epilepsy 3 with or without intracellular inclusions	AR
<i>KDM5C</i> (314690)	XL syndromic intellectual developmental disorder (Claes-Jensen type)	XL
<i>KIF1A</i> (601255)	NESCAV syndrome	AD
<i>LGII</i> (604619)	Familial temporal lobe epilepsy 1	AD
<i>MBD5</i> (611472)	Intellectual developmental disorder 1	AD
<i>MDH2</i> (154100)	Developmental and epileptic encephalopathy 51	AR
<i>MECP2</i> (300005)	Rett syndrome; severe neonatal encephalopathy; XL autism susceptibility 3; XL syndromic intellectual developmental disorder (Lubs type or 13)	XL
<i>MED17</i> (603810)	Postnatal progressive microcephaly with seizures and brain atrophy	AR
<i>MEF2C</i> (600662)	Neurodevelopmental disorder with hypotonia, stereotypic hand movements, and impaired language	AD
<i>MFSD8</i> (611124)	Neuronal ceroid lipofuscinosis 7	AR
<i>MOCS2</i> (603708)	Molybdenum cofactor deficiency B	AR
<i>MOGS</i> (601336)	Congenital disorder of glycosylation type IIb	AR

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>MPDU1</i> (604041)	Congenital disorder of glycosylation type If	AR
<i>MTHFR</i> (607093)	Homocystinuria due to MTHFR deficiency	AR
<i>MTOR</i> (601231)	Smith-Kingsmore syndrome	AD
<i>NDE1</i> (609449)	Lissencephaly 4 with microcephaly	AR
<i>NECAP1</i> (611623)	Developmental and epileptic encephalopathy 21	AR
<i>NEDD4L</i> (606384)	Periventricular nodular heterotopia 7	AD
<i>NEU1</i> (608272)	Sialidosis type I or II	AR
<i>NEXMIF</i> (300524)	XL intellectual developmental disorder 98	XL
<i>NGLY1</i> (610661)	Congenital disorder of deglycosylation 1	AR
<i>NHLRC1</i> (608072)	Progressive myoclonic epilepsy 2B (Lafora)	AR
<i>NPRL2</i> (607072)	Familial focal epilepsy with variable foci 2	AD
<i>NPRL3</i> (600928)	Familial focal epilepsy with variable foci 3	AD
<i>NR2F1</i> (132890)	Bosch-Boonstra-Schaaf optic atrophy syndrome	AD
<i>NRXN1</i> (600565)	Pitt-Hopkins-like syndrome 2	AR
<i>NSD1</i> (606681)	Sotos syndrome	AD
<i>NTRK2</i> (600456)	Developmental and epileptic encephalopathy 58; obesity, hyperphagia, and developmental delay	AD
<i>OPHN1</i> (300127)	XL syndromic intellectual developmental disorder (Billuart type)	XL
<i>PACS1</i> (607492)	Schuurs-Hoeijmakers syndrome	AD
<i>PAFAH1B1</i> (601545)	Lissencephaly 1	AD
<i>PCDH19</i> (300460)	Developmental and epileptic encephalopathy 9	XL
<i>PEX1</i> (602136)	Peroxisome biogenesis disorder 1A (Zellweger) or 1B (NALD/IRD)	AR
<i>PEX12</i> (601758)	Peroxisome biogenesis disorder 3A (Zellweger)	AR
<i>PEX2</i> (170993)	Peroxisome biogenesis disorder 5A (Zellweger)	AR
<i>PEX3</i> (603164)	Peroxisome biogenesis disorder 10A (Zellweger) or 10B	AR
<i>PEX6</i> (601498)	Peroxisome biogenesis disorder 4A (Zellweger) or 4B	AR
<i>PHF6</i> (300414)	Borjeson-Forssman-Lehmann syndrome	XL

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>PHGDH</i> (606879)	Phosphoglycerate dehydrogenase deficiency	AR
<i>PIGA</i> (311770)	Multiple congenital anomalies-hypotonia-seizures syndrome 2; neurodevelopmental disorder with epilepsy and hemochromatosis	XL
<i>PIGG</i> (616918)	Neurodevelopmental disorder with or without hypotonia, seizures, and cerebellar atrophy	AR
<i>PIGN</i> (606097)	Multiple congenital anomalies-hypotonia-seizures syndrome 1	AR
<i>PIGO</i> (614730)	Hyperphosphatasia with impaired intellectual development syndrome 2	AR
<i>PIGQ</i> (605754)	Multiple congenital anomalies-hypotonia-seizures syndrome 4	AR
<i>PIGT</i> (610272)	Multiple congenital anomalies-hypotonia-seizures syndrome 3	AR
<i>PIGV</i> (610274)	Hyperphosphatasia with impaired intellectual development syndrome 1	AR
<i>PLCB1</i> (607120)	Developmental and epileptic encephalopathy 12	AR
<i>PLPBP</i> (604436)	Early-onset vitamin B6-dependent epilepsy	AR
<i>PMM2</i> (601785)	Congenital disorder of glycosylation type Ia	AR
<i>PNKP</i> (605610)	Microcephaly, seizures, and developmental delay	AR
<i>PNPO</i> (603287)	Pyridoxamine 5'-phosphate oxidase deficiency	AR
<i>POLG</i> (174763)	Mitochondrial DNA depletion syndrome type 4A (Alpers type) or 4B (MNGIE type); mitochondrial recessive ataxia syndrome (includes SANDO and SCAE)	AR
<i>PPT1</i> (600722)	Neuronal ceroid lipofuscinosis 1	AR
<i>PRICKLE2</i> (608501)	Early-onset epilepsy	AD
<i>PRRT2</i> (614386)	Benign familial infantile seizures 2; episodic kinesigenic dyskinesia 1; familial infantile convulsions with paroxysmal choreoathetosis	AD
<i>PSAP</i> (176801)	Atypical Gaucher disease; atypical Krabbe disease; combined SAP deficiency, metachromatic leukodystrophy due to SAP-b deficiency	AR
<i>PTPN23</i> (606584)	Neurodevelopmental disorder and structural brain anomalies with or without seizures and spasticity	AR
<i>PURA</i> (600473)	Neurodevelopmental disorder with neonatal respiratory insufficiency, hypotonia, and feeding difficulties	AD
<i>QARS1</i> (603727)	Microcephaly, progressive, seizures, and cerebral and cerebellar atrophy	AR
<i>QDPR</i> (612676)	Hyperphenylalaninemia BH4-deficient C	AR
<i>RELN</i> (600514)	Familial temporal lobe epilepsy 7	AD
	Lissencephaly 2 (Norman-Roberts type)	AR
<i>RFT1</i> (611908)	Congenital disorder of glycosylation type IIn	AR

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>RNASEH2A</i> (606034)	Aicardi-Goutieres syndrome 4	AR
<i>RNASEH2B</i> (610326)	Aicardi-Goutieres syndrome 2	AR
<i>RNASEH2C</i> (610330)	Aicardi-Goutieres syndrome 3	AR
<i>ROGDI</i> (614574)	Kohlschutter-Tonz syndrome	AR
<i>RORB</i> (601972)	Susceptibility to idiopathic generalized epilepsy 15	AD
<i>SAMHD1</i> (606754)	Aicardi-Goutieres syndrome 5	AR
<i>SATB2</i> (608148)	Glass syndrome	AD
<i>SCARB2</i> (602257)	Progressive myoclonic epilepsy 4 with or without renal failure	AR
<i>SCN1A</i> (182389)	Dravet syndrome; developmental and epileptic encephalopathy 6B (non-Dravet); familial febrile seizures 3A; familial hemiplegic migraine 3; generalized epilepsy with febrile seizures plus type 2	AD
<i>SCN1B</i> (600235)	Developmental and epileptic encephalopathy 52	AR
	Generalized epilepsy with febrile seizures plus type 1	AD
<i>SCN2A</i> (182390)	Benign familial infantile seizures 3; developmental and epileptic encephalopathy 11; episodic ataxia type 9	AD
<i>SCN3A</i> (182391)	Developmental and epileptic encephalopathy 62; familial focal epilepsy with variable foci 4	AD
<i>SCN8A</i> (600702)	Benign familial infantile seizures 5; developmental and epileptic encephalopathy 13	AD
<i>SERPINI1</i> (602445)	Familial encephalopathy with neuroserpin inclusion bodies	AD
<i>SETBP1</i> (611060)	Intellectual developmental disorder 29; Schinzel-Giedion midface retraction syndrome	AD
<i>SLC12A5</i> (606726)	Developmental and epileptic encephalopathy 34	AR
	Susceptibility to idiopathic generalized epilepsy 14	AD
<i>SLC13A5</i> (608305)	Developmental and epileptic encephalopathy 25, with amelogenesis imperfecta	AR
<i>SLC19A3</i> (606152)	Thiamine metabolism dysfunction syndrome 2 (biotin- or thiamine-responsive encephalopathy type 2)	AR
<i>SLC1A2</i> (600300)	Developmental and epileptic encephalopathy 41	AD
<i>SLC25A12</i> (603667)	Developmental and epileptic encephalopathy 39	AR
<i>SLC25A22</i> (609302)	Developmental and epileptic encephalopathy 3	AR
<i>SLC2A1</i> (138140)	GLUT1 deficiency syndrome 1 infantile onset	AD/AR
	Dystonia 9; GLUT1 deficiency syndrome 2, childhood onset: stomatin-deficient cryohydrocytosis with neurologic defects; susceptibility to idiopathic generalized epilepsy 12	AD

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
<i>SLC35A2</i> (314375)	Congenital disorder of glycosylation type IIb	XL
<i>SLC6A1</i> (137165)	Myoclonic-atonic epilepsy	AD
<i>SLC9A6</i> (300231)	XL syndromic intellectual developmental disorder (Christianson type)	XL
<i>SMARCA2</i> (600014)	Blepharophimosis-impaired intellectual development syndrome; Nicolaides-Baraitser syndrome	AD
<i>SMC1A</i> (300040)	Cornelia de Lange syndrome 2; developmental and epileptic encephalopathy 85 with or without midline brain defects	XL
<i>SMS</i> (300105)	XL syndromic intellectual developmental disorder (Snyder-Robinson type)	XL
<i>SNAP25</i> (600322)	Congenital myasthenic syndrome 18	AD
<i>SPATA5</i> (613940)	Neurodevelopmental disorder with hearing loss, seizures, and brain abnormalities	AR
<i>SPTAN1</i> (182810)	Developmental and epileptic encephalopathy 5	AD
<i>ST3GAL3</i> (606494)	Developmental and epileptic encephalopathy 15	AR
<i>ST3GAL5</i> (604402)	Salt and pepper developmental regression syndrome	AR
<i>STRADA</i> (608626)	Polyhydramnios, megalencephaly, and symptomatic epilepsy	AR
<i>STX1B</i> (601485)	Generalized epilepsy with febrile seizures plus type 9	AD
<i>STXBP1</i> (602926)	Developmental and epileptic encephalopathy 4	AD/AR
<i>SUOX</i> (606887)	Sulfite oxidase deficiency	AR
<i>SYN1</i> (313440)	XL epilepsy 1 with variable learning disabilities and behavior disorders	XL
<i>SYNGAP1</i> (603384)	Intellectual developmental disorder 5	AD
<i>SYNJ1</i> (604297)	Early-onset Parkinson disease 20; developmental and epileptic encephalopathy 53	AR
<i>SZT2</i> (615463)	Developmental and epileptic encephalopathy 18	AR
<i>TBC1D24</i> (613577)	Developmental and epileptic encephalopathy 16; DOORS syndrome; familial infantile myoclonic epilepsy; rolandic epilepsy with paroxysmal exercise-induce dystonia and writer's cramp	AR
<i>TBL1XR1</i> (608628)	Intellectual developmental disorder 41; Pierpont syndrome	AD
<i>TCF4</i> (602272)	Pitt-Hopkins syndrome	AD
<i>TPK1</i> (606370)	Thiamine metabolism dysfunction syndrome 5 (episodic encephalopathy type)	AR
<i>TPP1</i> (607998)	Neuronal ceroid lipofuscinosis 2	AR
<i>TREX1</i> (606609)	Aicardi-Goutieres syndrome 1	AR/AD

Gene Symbol (OMIM Number)	Associated Disorders	Inheritance
	Vasculopathy, retinal, with cerebral leukoencephalopathy and systemic manifestations	AD
TSC1 (605284)	Tuberous sclerosis-1	AD
TSC2 (191092)	Tuberous sclerosis-2	AD
TSEN54 (608755)	Pontocerebellar hypoplasia (types 2A, 4, 5)	AR
UBA5 (610552)	Developmental and epileptic encephalopathy 44	AR
UBE3A (601623)	Angelman syndrome	AD
UNC80 (612636)	Infantile hypotonia with psychomotor retardation and characteristic facies 2	AR
VPS13A (605978)	Choreoacanthocytosis	AR
WDR45 (300526)	Neurodegeneration with brain iron accumulation 5	XL
WWOX (605131)	Developmental and epileptic encephalopathy 28; spinocerebellar ataxia, 12	AR
ZEB2 (605802)	Mowat-Wilson syndrome	AD

AD, autosomal dominant; AR, autosomal recessive; XL, X-linked

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