Updated complete list of hereditary myoclonus

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| **Designation** | **Alternate name** | **Clinical Clues** | **OMIM** | **MOI** |
| **Prominent myoclonus syndromes** |
| MYC-*CARS2812* | Combined oxidative phosphorylation deficiency 27 | Severe myoclonus, seizures, and cognitive problems, tetraparesis, visual and hearing impairment, areflexia, hypotonia813 | 612800 | AR |
| MYC-*CLN3814* | Neuronal ceroid lipofuscinosis 3 (CLN3)  | Mild myoclonus, severe epilepsy and cognitive problems, ataxia can be present, juvenile onset, parkinsonian signs, retinal degeneration, neuropsychiatric symptoms | 607042 | AR |
| MYC-*CLN5705* | Neuronal ceroid lipofuscinosis 5 (CLN5) | Severe myoclonus, epilepsy, and cognitive problems, late-infantile onset, ataxia can be present, blindness | 608102 | AR |
| MYC-*CLN6706, 815* | Neuronal ceroid lipofuscinosis 6 (CLN6)  | Severe myoclonus, epilepsy, and cognitive problems, early juvenile or adult onset, ataxia, visual failure | 606725 | AR |
| MYC-*CLN8816* | Neuronal ceroid lipofuscinosis 8 (CLN8)  | Severe myoclonus, epilepsy, and cognitive problems, late infantile onset, ataxia, retinopathy | 607837 | AR |
| MYC-*DHDDS520, 817* | Developmental delay and seizures with or without movement abnormalities (DEDSM) | Global developmental delay, variable intellectual disability, early-onset seizures and myoclonic component (can be prominent), variable ataxia, dystonia, and tremor | 617836 | AD |
| MYC-*DNAJC5818* | Neuronal ceroid lipofuscinosis 4 (CLN4)  | Severe myoclonus, epilepsy, and cognitive problems, adult-onset, ataxia | 611203 | AD |
| MYC-*GLRA1819*;MYC-*SLC6A5820*;MYC-*GLRB821* | Hyperekplexia | Mild myoclonus, generalized stiffness at birth and following startle, neonatal tonic cyanotic attacks, periodic limb movement during sleep and hypnagogic myoclonus  | 138491604159138492 | AD, ARAD, ARAR |
| MYC-*GRIA3250, 822, 823* | Syndromic intellectual disability disorder (MRXSW) | Broad phenotypic spectrum including mental retardation and seizures, myoclonus, and variable motor and behavioral impairment, prominent chorea needs to be confirmed | 300699 | XLR |
| MYC-*MFSD8824, 825* | Neuronal ceroid lipofuscinosis 7 (CLN7) | Neurodegenerative disease with variable phenotypic features including seizures, myoclonus, mental regression, speech impairment, loss of vision, and personality disorder | 610951 | AR |
| MYC-mt-*MTTK826* | Myoclonic epilepsy associated with ragged-red fibers (MERRF)A | Severe myoclonus, epilepsy and cognitive problems can be present, additional features including muscle weakness, hearing loss, peripheral neuropathy, optic atrophy, axial lipomas and variable other neurological manifestations (heterogeneous disease, multiple genes associated with phenotype)827  | 590060 | Mt |
| MYC-*SAMD12;*MYC-*RAPGEF2B, 828, 829* | Familial cortical myoclonic tremor associated with epilepsy (FCMTE) | Mild myoclonus, epilepsy, adult-onset, anxiety and depression, cognitive problems can be present | 601068, 618075 | AD |
| MYC-*SCARB2707* | Progressive myoclonic epilepsy-4 (EPM4), also known as action myoclonus-renal failure syndrome (AMRF) | Severe myoclonus, epilepsy, and ataxia, cognitive problems can be present, tremor, renal failure, peripheral neuropathy | 602257 | AR |
| MYC- *SEMA6B830-834* | Progressive myoclonic epilepsy-11 (EPM11) | Neurodegenerative disease with infancy-onset of developmental regression and seizures, followed by additional neurological symptoms, e.g., spasticity, loss of independent ambulation, myoclonus, tremor, ataxia, and severe cognitive impairment in the first and second decade | 618876 | AD |
| MYC-*SERPINI1835, 836* | Familial encephalopathy with neuroserpin inclusion bodies (FENIB) | Mild myoclonus, severe epilepsy and cognitive problems, ataxia can be present | 602445 | AD |
| MYC/PxMD-*SCN8AC, 837-839* | Familial myoclonus  | Familial myoclonus with childhood-onset of isolated action-induced nonepileptic myoclonus affecting the upper limbs, nonprogressive; also epilepsy or developmental and epileptic encephalopathy phenotypes | 618364 | AD |
| ATX/HSP-*FOLR1643, 840* | Cerebral folate transport deficiency | Severe epilepsy, ataxia, and cognitive problems, myoclonus can be present, chorea, drop attacks | 136430 | AR |
| *CHD2841, 842* | CHD2 encephalopathy | Severe epilepsy and cognitive problems, multiple seizure types of which atonic-myoclonic-absence most commonly, photosensitivity | 602119 | AD |
| CUX2843 | (Myoclonic) Developmental and epileptic encephalopathy 67 (DEE67) | Severe epilepsy and cognitive problems, infantile-onset myoclonic and absence seizures, stereotypies and dyskinesias | 610648 | AD |
| *GLDC844*;*AMT845* | Classic non-ketotic hyperglycinemia | Severe epilepsy and cognitive problems, mild myoclonus, neonatal onset: progressive lethargy, hypotonia  | 238300238310 | AR |
| *PIGA846* | Multiple congenital anomalies-hypotonia-seizures syndrome 2 (MCAHS2) | Severe epilepsy and cognitive problems, myoclonus can be present, dysmorphic features, neonatal hypotonia | 311770 | XLR |
| *SCN1AD, 847* | Dravet syndrome | Severe epilepsy and cognitive problems, febrile and prolonged seizures with alternating pattern, myoclonus and ataxia can be present  | 607208 | AD |
| *SLC6A1229* | Doose syndrome | Severe epilepsy, mild cognitive problems, atonic drop attacks | 137165 | AD |
| *TBC1D24848, 849* | TBC1D24-related disorders | Epilepsy and cognitive problems, type of seizures are variable, myoclonus, ataxia, and dystonia can be present, muscle hypotonia, extrapyramidal signs, hearing and visual loss31 | 613577 | AR |
| **Combined myoclonus syndromes: where myoclonus coexists with (an)other movement disorder(s) as a prominent and consistent feature** |
| MYC/ATX-*CSTB*665 | Myoclonic epilepsy of Unverricht and Lundborg | Myoclonic epilepsy, stimulus sensitive segmental or generalized myoclonus, action myoclonus, generalized tonic-clonic or absence seizures, mental and motor deterioration | 254800 | AR |
| MYC/ATX-*EPM2A364, 365* | Progressive myoclonus epilepsy (Lafora disease) | Myoclonic or other types of seizures, focal visual seizures, drop attacks cognitive decline, psychosis, myoclonus | 607566 | AR |
| MYC/ATX-*GOSR2*666 |  | Myoclonic, absence and tonic-clonic seizures, drop attacks, action myoclonus, tremor, areflexia, scoliosis, pes cavus, syndactyly | 614018 | AR |
| MYC/ATX-*KCTD7*667 | Progressive myoclonic epilepsy type 3 with or without intracellular inclusions | Myoclonic epilepsy, secondary generalization seizures, neurologic regression following seizure onset, mental retardation, hyperreflexia, opsoclonus, optic atrophy, visual loss, microcephaly | 611726 | AR |
| MYC/ATX-*NEU1*668 | Neuraminidase deficiency or sialidosis type I and II | Myoclonus, mental retardation, seizures, hyperreflexia, muscle atrophy, skeletal malformations, hepatosplenomegaly, cardiomyopathy, progressive vision loss, cherry-red spots, cataracts, nystagmus, sensorineural hearing loss, short stature, dysmorphic features  | 256550 | AR |
| MYC/ATX-*NHLRC1*669  | Lafora disease | Myoclonic or other types of seizures, focal visual seizures, drop attacks cognitive decline, psychosis, myoclonus | 608072 | AR |
| ATX/MYC-*NUS1520, 834* | Mental retardation 55 with seizures (MRD55) | Broad phenotypic spectrum including developmental delay, intellectual disability, ataxia, myoclonus, (myoclonic) seizures, resting and intention tremor, and rarely parkinsonism | 617831 | AD |
| ATX/MYC-*TPP1*663,664  | Spinocerebellar ataxia, Neuronal ceroid lipofuscinosis type 2 (CLN2) | Myoclonus, developmental regression, speech and language difficulties, nystagmus, diplopia, hypermetric saccades, progressive vision loss, retinopathy, postural tremor, pyramidal signs, spastic paraparesis, decreased vibration sense, fasciculations, seizures | 609270, 204500 | AR |
| MYC/DYT-*KCTD17398-401* |  | Onset of mild myoclonic symptoms in the first or second decade of life, followed by later onset of progressive dystonia with predominant involvement of the cranial and laryngeal muscles; dystonia dominates the clinical picture | 616398 | AD |
| MYC/DYT-*SGCE402* | Myoclonus-dystonia | Myoclonus-dystonia predominantly in upper body, psychiatric disorders | 604149 | AD |
| **Disorders that usually present with other phenotypes but can manifest as a prominent myoclonus syndrome** |
| ATX-*ATM*551 | Ataxia-telangiectasia (including variant ataxia-telangiectasia) | Telangiectasias and other skin alterations, oculomotor apraxia, dystonia, chorea, myoclonus, tremor, seizures, peripheral neuropathy, distal muscular atrophy, short stature, hypogonadism, respiratory dysfunction, immunodeficiency, predisposition to neoplasia, glucose intolerance | 208900 | AR |
| ATX-*ATN1*487 | Dentatorubropallidoluysian atrophy (DRPLA) | Dentatorubropallidoluysian atrophy (DRPLA): ataxia, myoclonus, chorea, parkinsonism, dementia, supranuclear gaze palsy, seizures (particularly in young patients)  | 607462 | AD |
| ATX-*MT-ATP6695, 850* | MT-ATP6-mitochondrial disease: neuropathy, ataxia, and retinitis pigmentosa (NARP); Leigh syndrome; mitochondrial encephalomyopathy | Variable phenotype including ataxia, less commonly myoclonus, cognitive dysfunction, neuropathy, seizures, and retinopathy | 551500 | mt |
| ATX-*NPC1*590 | Niemann-Pick disease type C1 | Developmental regression, cognitive impairment, psychiatric symptoms, loss of speech, vertical supranuclear gaze palsy, dystonia, intention tremor, spasticity, seizures, hepatosplenomegaly, cholestatic jaundice, gelastic cataplexy | 257220 | AR |
| ATX-*PRKCG*482 |  | Relatively pure ataxia; sometimes other movement disorders (dystonia, myoclonus)  | 605361 | AD |
| ATX/HSP-*SACS*648 | Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) or autosomal recessive spastic ataxia type 6 | Spastic paraparesis, delayed walking development, retinal striation, nystagmus, impaired smooth pursuit, pes cavus, hammertoes, finger deformities, hyperreflexia, ankle areflexia, spasticity, extensor plantar responses, scoliosis, distal muscle weakness and atrophy, peripheral neuropathy, dystonia, erectile dysfunction  | 270550 (SPAX6) | AR |
| ATX/PxMD-*CACNA1A851, 852* | Episodic ataxia type 2 (EA2) | Gene associated with EA2, but recent publications report phenotypes including progressive myoclonus epilepsy | 108500 | AD |
| DYT-*ANO3132, 853* | Tremorous cervical dystonia | Typically isolated dystonia, sometimes myoclonus-dystonia phenotype predominantly in upper body, tremor | 610110 | AD |
| CHOR-*HTT*792 | Huntington’s disease (HD) | Predominant chorea and dementia, young onset may have predominant parkinsonism (Westphal variant), additional clinical signs including myoclonus, ataxia, epilepsy, cognitive problems, and behavioral abnormalities | 143100 | AD |
| CHOR-*NKX2*-1794 | Isolated benign hereditary chorea, Brain–lung–thyroid syndrome, Brain and thyroid disease | Phenotypes: 1. Isolated benign hereditary chorea (13%)795
2. Brain–lung–thyroid syndrome (50%): infantile onset global developmental delay, childhood onset chorea-athetosis, hypothyroidism and pulmonary dysfunction
3. Brain and thyroid disease (30%): infantile onset global developmental delay childhood onset chorea-athetosis, hypothyroidism
 | 600635 | AD |
| HSP-*KIF5A854, 855* | Neonatal intractable myoclonus | Severe myoclonus and cognitive problems, neonatal onset, eye movement abnormalities, apnea, ptosis, optic nerve pallor, hypotonia, epilepsy, leukoencephalopathy may be seen58  | 617235 | AD |
| PARK-*GBA709* | Gaucher’s disease | Myoclonus, developmental delay, dementia, psychiatric symptoms, spastic paraparesis, horizontal supranuclear gaze palsy, abnormal saccade eye movements, strabismus, seizures, short stature, hepatosplenomegaly, pancytopenia | multiple | AR |
| *APP856* | Familial Alzheimer’s disease | Prominent cognitive problems, myoclonus and epilepsy | 104760 | AD |
| *ASAH1857* | Spinal muscular atrophy | Severe myoclonus and epilepsy, progressive lower motor neuron disease manifestations, cognitive problems may be present | 613468 | AR |
| *CSNK2B858* | *CSNK2B*-related disorders | Severe epilepsy, infantile onset of myoclonic seizures, speech and language disorder, mild cognitive problems | 115441 | AD |
| *CTSA859* | Galactosialidosis | Severe myoclonus, epilepsy, ataxia, and cognitive problems, coarse facies, vertebral changes, cherry-red spots, corneal clouding, absence of visceromegaly, angiokeratoma | 613111 | AR |
| *EEF1A2860-862* | Developmental and epileptic encephalopathy 33 (DEE33), Mental retardation (MRD38) | Epilepsy phenotype with various types of seizures in the first month of life and severe global developmental delay with impaired intellectual development and poor or absent speech, sometimes prominent myoclonic epilepsy | 616409, 616393 | AD |
| *FARS2863* | *FARS2-*related disorders | Early infantile onset of myoclonic seizures, severe cognitive problems, GTCS and infantile spasms | 611592 | AR |
| *PRNP864, 865* | Familial Creutzfeldt-Jakob disease | Severe myoclonus, epilepsy, and cognitive problems, epilepsy can be present, chorea, visual impairment, akinetic mutism, sleep disturbances, psychiatric disorders, peripheral neuropathy | 176640 | AD |
| *PSEN1765, 866* | Familial Alzheimer’s disease | Severe cognitive problems, mild myoclonus and/or epilepsy, spastic paraparesis, rigidity, behavioral symptoms, language and dysexecutive deficits, ataxia can be present | 104311 | AD |
| *RORB867, 868* | Susceptibility to idiopathic generalized epilepsy 15 (EIG15) | Epilepsy phenotype with various types of seizures in the first decade (most commonly absence seizures), majority with developmental delay with impaired intellectual development, predominant eyelid myoclonus  | 618357 | AD |
| *RPS6KA3869, 870* | Coffin-Lowry syndrome | Stimulus-induced drop episodes, myoclonus, mild cognitive problems, dysmorphism, progressive skeletal changes, hearing loss, mitral valve deformity | 300075 | XLD |
| *SCN2A270, 278, 871, 872* | Developmental and epileptic encephalopathy 11 (DEE11), Episodic ataxia type 9 (EA9), Benign familial infantile seizures 3  | Gene associated with multiple diseases and therefore with a broad and overlapping phenotypic spectrum including developmental delay, seizures and various movement disorders, myoclonus can be a dominant feature  | 613721, 618924, 607745 | AD |
| *SETD1B873* | Intellectual developmental disorder with seizures and language delay  | Global developmental delay with speech and language impairment and seizures, mostly myoclonic (absence) seizures as predominant feature, often accompanying behavioral abnormalities (autism spectrum disorder or anxiety), sometimes additional features like facial dysmorphism, tapering fingers, and pigmentary skin changes | 619000 | AD |
| *SLC2A1874-876* | Glucose transport type 1 deficiency | Myoclonic, myoclonic-astatic, GTC and absence seizures starting in early up to middle childhood, cognitive impairment, other phenotypes include paroxysmal exertion-induced dyskinesia, absence epilepsy or episodic choreoathetosis and spasticity | 138140 | AD |
| *SYNGAP1877* | *SYNGAP1*-associated intellectual disability and epilepsy | Early infantile onset of drop attacks, massive myoclonic jerks and (myoclonic)-absence seizures, cognitive problems, hypotonia, behavioral disorder, ASD, orthopedic problems  | 603384 | AD |
| *UBE3A878, 879* | Angelman syndrome | Myoclonic, myoclonic absence and myoclonic-tonic seizures in early childhood; non-epileptic myoclonus first presenting in adolescence, severe cognitive problems, sleep dysfunction, absent or limited expressive language  | 601623 | # |
| mUDPC7880 | Silver-Russell syndrome | Growth retardation, dysmorphism, Myoclonus-dystonia predominantly located in upper body  | 180860 | IC |

AD = autosomal dominant, AMRF, action myoclonus renal failure, AR = autosomal recessive, MOI = Mode of inheritance, OMIM = Online Mendelian Inheritance in Man (<https://www.omim.org/about>), XLD = x-linked dominant; XLR = x-linked recessive.

# Loss of the maternally inherited *UBE3A* gene.

A The following additional genetic mutations are able to cause MERRF: MYC-mt-MTTL1 (OMIM 590050), MYC-mt-MTTH (OMIM 590040), MYC-mt-MTTS1 (OMIM 590080), MYC-mt-MTTS2 (OMIM 590085), MYC-mt-MTTF (OMIM 590070), and MYC-mt-MTTW (OMIM 590095).

B Recently, authors have proven the pentanucleotide repeat TTTCA (and TTTTA) to be causative of FCMTE in the intron of MYC-*SAMD12* and MYC-*RAPGEF2*.828 Although the authors believe the intronic pentanucleotide repeat to be pathogenic irrespective of the gene, we have stated the two genes which have been confirmed in literature.

C Gene mutations can also cause Familial Myoclonus Type 2 (OMIM [**618364**](https://www.omim.org/entry/618364); Table 5), autosomal-dominant cognitive impairment with or without cerebellar ataxia (OMIM [**614306**](https://www.omim.org/entry/614306)), and/or autosomal-dominant developmental and epileptic encephalopathy 13 (DEE13, OMIM [**614558**](https://www.omim.org/entry/614558)).

D The following genes have been reported to cause a Dravet syndrome-like phenotype by at least two independent research groups: *SCN1B* (OMIM 600235), *PCDH19* (OMIM 300460), *GABRA1* (OMIM 615744).

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