MNG STAT™ Actionable Epilepsy Panel (NGS418)

List of Genes & Potential Therapies

Please note that any potential therapies are for reference use only and are not to be used as a treatment guide. MNG does not endorse these therapies for clinical use.

GENE	ACTION/TREATMENT
ABCC8	Hypoglycemia, leucine and oral protein induced. Responsive to diazoxide therapy. Insulin treatment for (transient) neonatal diabetes. [1, 2]
ACADM	Episodes of illness associated with fasting, Frequent feedings, avoid fasting, supplementation of carnitine and riboflavin, low fat diet, and cornstarch slurry at bedtime.[3, 4]
ACSF3	Diet high in carbohydrates, avoid high protein content. L-Carnitine suplementation.[5, 6]
AKT2	Episode of illness associated with fasting.
ALDH7A1	Seizures are responsive to pyridoxine supplementation treatment.[7-9]
ALDOB	Fructose intolerance. Symptoms can be prevented by strict dietary restriction. Persistent exposure to fructose leads to chronic liver and kidney complications. http://www.bu.edu/aldolase/HFI/treatment/
ARX	Infantile spasms treated with systemic corticosteroid, monitoring during steroid therapy to prevent ocular damage and visual impairment.[10]
ATP1A2	Response to flunarizine, a calcium-entry blocker, with a greater than 70% decrease in migraine attack frequency. Episodes may be triggered by exercise, emotional stress, head trauma, angiography, lack of sleep, heat. [11, 12]
BCKDHA	Treatment consists of dietary leucine restriction, BCAA-free medical foods, judicious supplementation with isoleucine and valine, and frequent clinical and biochemical monitoring. [13, 14]
BCKDHB	Treatment consists of dietary leucine restriction, BCAA-free medical foods, judicious supplementation with isoleucine and valine, and frequent clinical and biochemical monitoring. [13, 14]Thiamine supplementation is recommended when BCKDHB variants are identified.[15, 16]
CAD	Affected children can have a favorable response to treatment with oral uridine.[17]
CBS	Management of homocystinuria includes low methionine, cystine supplemented diet for pyridoxine non-responders, and pyridoxine supplementation (Vitamin B6) for pyridoxine responders (50% responsive). Treatment with betaine, especially for pyridoxine non-responders.[18]
CDKL5	Management includes a ketogenic diet and steroid treatment for infantile spasms.[19-21]
COQ2	CoQ10 oral supplementation. In cases of multiple system atrophy 1, poor response to L-Dopa.[22]
CPT2	Triggered by exercise, fasting, or other metabolic stresses. Frequent feedings, medium-chain-fatty-acid triheptanoin appears to be effective for adult onset CPT II, restriction of lipid intake, supplementation with L-carnitine. [23]
DBT	Treatment consists of dietary leucine restriction, BCAA-free medical foods, judicious supplementation with isoleucine and valine, and frequent clinical and biochemical monitoring.[13, 14]
DHFR	Treatment with folinic acid offers some benefit for anemia and seizure control.[24, 25]
FBP1	Episodes triggered by fasting, illness, and fever. Patients show sorbitol and glycerol intolerance. Treatment restriction of fructose intake, high carbohydrate diet, and folic acid.[26]
FOLR1	Treatment with folinic acid therapy.[27]
FTL	Some response has been recorded with levodopa, tetrabenazine, orphenadrine, benzhexol, sulpiride, diazepam, clonazepam, and deanol in standard doses. Botulinum toxin is helpful for painful focal dystonia.[28, 29]

GAMT	Creatine monohydrate and ornithine supplementation, and protein- or arginine-restricted diet decrease GAA accumulation by competitive inhibition of AGAT enzyme activity. [30-32]
GATM	Oral creatine monohydrate and ornithine supplementation, and arginine restriction.[30-32]
GBA	Enzyme replacement therapy (ERT), or substrate reduction therapy (SRT), bone marrow transplant. Symptomatic treatment includes partial or total splenectomy for massive splenomegaly and thrombocytopenia. [33-36]
GCH1	Treatment with levodopa/decarboxylase inhibitor (DCI), GTPCH1-deficient DRD may respond to trihexyphenidyl and bromocriptine.[37, 38]
GCK	Diet and diazoxide therapy, Insulin, hypoglycemia is corrected with intravenous glucose to normalize plasma glucose concentration and prevent brain damage.[39, 40]
GLRA1	Clonazepam appears to be the most effective treatment, other drugs with variable results include carbamazepine, phenytoin, diazepam, valproate, 5-hydroxytryptophan, piracetam, and phenobarbital. [41-43]
GLUD1	Diet of frequent and high-carbohydrate feedings, medical treatment with: diazoxide, somatostatin analogs, nifedipine, glucagon, recombinant IGF-1, or glucocorticoids.[1, 44]
GYS2	Diet of frequent and high-carbohydrate feedings, and nighttime feedings of suspensions of uncooked corn starch. [45]
HADH	Triggered by periods of fasting or by illnesses such as viral infections. The drugs Glycerol and Heparin have been mentioned in the context of this disorder to consider.[1, 46]
KCNJ1	Treatment options include insulin, a high caloric diet, and indomethacin, a nonselective cyclooxygenase (COX) inhibitor, but this drug has a broad range of side effects and therefore requires extensive monitoring. Pancreatic enzyme replacement therapy is required for those with exocrine pancreatic insufficiency.[47]
KCNJ11	Hypoglycemia is treated with intravenous glucose to normalize plasma glucose concentration and prevent brain damage. Long-term medical management includes the use of diazoxide, somatostatin analogs, nifedipine, glucagon, recombinant IGF-I, glucocorticoids, human growth hormone, dietary intervention, or combinations of these therapies. [1, 2]
KCNQ2	Antiepileptic treatment usually start with phenobarbital, beta-adrenergic blockers for long QT interval or sodium channel blockers.[48-50]
KCNQ3	Generally controlled with conventional antiepileptics such as phenobarbital, carbamazepine, or valproate. [48, 51]
KCNT1	Carbamazepine is associated with remission in about 70% of individuals, and treatment with quinidine is described.[52, 53]
MECP2	Treatment includes Topiramate, and avoidance of drugs known to prolong the QT interval like Type 1A, and Type 1C antiarrhythmics, antipsychotics: Haloperidol, Droperidol, Quetiapine, Thioridazine, and Ziprasidone, antimicrobials: Levofloxacin, Ciprofliocacin, and Erythtomycin.[54-56]
MEF2C	Treatment with antiepileptic medication is helpful. Promising results with the drug NitroSynapsin in mice.[57, 58]
MMAA	A low-protein, high-calorie diet is recommended. When vitamin B12 responsive, use hydroxocobalamin injections, carnitine supplementation, and in some patients rotating oral antibiotics to reduce the production of propionate from gut flora.[59-61]
MMACHC	Avoid fasting, dietary protein intake below or above the recommended dietary allowance, and the anesthetic nitrous oxide. Parenteral hydroxocobalamin (OHCbl) is the mainstay of therapy, Patients with elevated tHcy should also receive betaine and folate or folinic acid. Other considerations: methionine supplementation, pyridoxine, and levocarnitine.[59-62]
MMADHC	Avoid fasting, dietary protein intake below or above the recommended dietary allowance, and the anesthetic nitrous oxide. Parenteral hydroxocobalamin (OHCbl) is the mainstay of therapy, Patients

	with elevated tHcy should also receive betaine and folate or folinic acid. Other considerations: methionine supplementation, pyridoxine, and levocarnitine.[59-61]
NAGS	Can be effectively treated with N-carbamylglutamate.[63, 64]
PAH	A low-protein diet and use of a Phe-free medical formula. Avoid Aspartame, or artificial sweeteners containing phenylalanine. All affected individuals except those with two trans pathogenic null variants should consider sapropterin supplementation.[65, 66]
PC	Avoid fasting and avoid a ketogenic diet which aggravates metabolic acidosis. Citrate supplementation reduces the acidosis and provides substrate for the citric acid cycle. Aspartic acid supplementation allows the urea cycle to proceed and reduces the plasma and urine ammonia concentrations but has little effect on the neurologic disturbances as the aspartate does not enter the brain freely. Biotin supplementation is given to help optimize the residual PC enzyme activity but is usually of little use. [67]
PCDH19	Antiepileptic treatment, most effective drugs are clobazam and bromide.[68, 69]
PDHA1	Supportive treatment includes use of sodium bicarbonate or sodium citrate for acidosis and antiepileptic drugs for seizures. Dystonia is treated with benzhexol, baclofen, tetrabenazine, and gabapentin either alone or in combination, or by injections of botulinum toxin. A subset of patients improve with thiamine.[70-72]
PNKD	Clonazepam or diazepam may be effective. Alcohol, coffee, tea, chocolate, excitement, stress, and fatigue are all known to precipitate attacks and thus should be avoided.[73, 74]
PNPO	Treatment with activated vitamin B6 (pyridoxal 5-prime phosphate/PLP) has shown better results than with pyridoxine supplementation.[75]
POLG	Avoid valproic acid and sodium divalproate due to liver toxicity causing liver failure. Clinical management is largely supportive of a multi therapy approach.[76]
PROSC	Gene name is also PLPBP, response to treatment with activated vitamin B6 (pyridoxal 5-prime-phosphate; PLP) and/or pyridoxine. Multiple anticonvulsants are needed to control seizures.[77]
PRRT2	Treatment with anticonvulsants phenytoin or carbamazepine are typically given at at low doses. Other anticonvulsants proven to be effective include oxcarbazepine, ethosuximide, lamotrigine, and gabapentin.[78-81]
PTS	Treatment options include dietary intervention, and substitution with neurotransmitter precursors (levodopa, 5-hydroxytryptophan), monoamine oxidase inhibitors, and tetrahydrobiopterin.[82, 83]
QDPR	Treatment with BH4 is effective. Neurotransmitter treatment with L-dopa and serotonin or precursors is effective. [84-86]
SCN1A	Treatment with antiepileptic drugs: benzodiazepines (diazepam and clonazepam), stiripentol (used in Europe; not currently FDA approved for use in the US), topiramate, and valproic acid. Avoid sodium channel blockers (Carbamazepine, lamotrigine, vigabatrin, phenytoin, rufinamide, and acetaminophen). In general, vasoconstricting agents should be avoided because of the risk of stroke. Cerebral angiography is hazardous as it may precipitate a severe attack. A ketogenic diet is recommended.[87-94]
SCN1B	Generalized Epilepsy with Febrile Seizures type 9 are triggered by illness associated with a high temperature. Medical intervention is based on symptoms. [95, 96]
SCN2A	Medical intervention is based on clinical symptoms. Spontaneous resolution by 12 months of age with no recurrence later in life.[97, 98]
SCN8A	Seizures controlled with drug polytherapy. Several studies suggest that patients with SCN8A-related epilepsy with encephalopathy respond favorably to sodium channel blockers including phenytoin, valproate, carbamazepine, lacosamide, lamotrigine, rufinamide, and oxcarbazepine. Sleep deprivation and illness can exacerbate SCN8A-related seizures.[99-102]

SCN9A	In pain disorders, cooling the extremities reduces pain, but there is no consensus on pain management strategies. Generalized Epilepsy with Febrile Seizures type 7 are triggered by illness associated with a high temperature. Medical intervention is based on seizure type.[103]
SLC13A5	A ketogenic diet may be effective as seizures are poorly responsive to treatment.[104, 105]
SLC16A1	Triggered by fasting or infection, following a ketogenic diet is recommended.[106]
SLC19A2	Supplementation with pharmacologic doses of oral thiamine (vitamin B1) can improve the hematologic picture.[107, 108]
SLC19A3	Biotin and thiamine therapy are effective. [109, 110]
SLC25A20	Avoid fasting, supplement diet with Medium Chain Triglyceride (MCT) and L-carnitine, and high carbohydrate diet [23, 111]
SLC2A1	Treatment involves antiepileptic drugs such as ethosuximide, valproate, and lamotrigine. However, lack of response is common. A ketogenic diet may be helpful. An alternative choice for patients with childhood absence epilepsy and photosensitivity are levetiracetam or topiramate. [112-114]
SLC46A1	Folate replacement therapy, parenteral (intramuscular), high-dose oral 5-formyltetrahydrofolate (5-formylTHF, folinic acid, Leucovorin®) or the active isomer of 5-formylTHF (Isovorin® or Fusilev®) are common treatment options. [115-117]
SLC6A8	Oral creatine monohydrate and ornithine supplementation, and arginine restriction.[118-120]
SPR	Treatment with BH4 is effective. Neurotransmitter treatment with L-dopa and serotonin or precursors is effective. [121, 122]
STX1B	Treatment based on clinical presentation, seizures tend to remit later in childhood [123, 124]
STXBP1	Seizure management is symptomatic. The most commonly used AEDs were phenobarbital, valproic acid, and vigabatrin. Clobazam, zonisamide, lamotrigine, and oxcarbamazepine have also been used. [125, 126]
TPP1	Seizures associated with neuronal ceroid lipofuscinosis type 2 (CLN2) can be controlled with Cerliponase alfa (Brineura™) which is available through BioMarin Pharmaceutical Inc. [127]

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