Supplementary Table S1 - Clinical data and genetic findings for each patient for which a positive diagnosis was established using the INT MET panel.

Cases	Age	Sex	HPO	Gene	Variants	Phenomizer	Disorder MIM	Changes in medication and/or diet*	Parents/Inheritance
1	2 m	M	Focal myoclonic seizures EEG with burst suppression Lethargy Nonketotic hyperglycinemia Intellectual disability	*AMT*	c.2T>C/ c.878-1G>A	p=0.0040	Glycine encephalopathy #605899	Yes	Carriers Autosomal recessive
2	9 y	M	Cerebral palsy Epileptic encephalopathy Epileptic spasms	*PCCA*	c.469-4A>G/ c.929C>G	p=0.4157	Propionic acidemia #606054	Yes	Carriers Autosomal recessive
3	-	M	Focal myoclonic seizures EEG with burst suppression Lethargy Nonketotic hyperglycinemia	*GLDC*	c.2714T>G	p=0.0221	Glycine encephalopathy #605899	Yes	*De novo* Autosomal dominant
4	3 m	F	Seizures Xanthine nephrolithiasis Encephalopathy Microcephalia Hypouricemia Growth delay	*MOCS2*	c.244A>T/ c.244A>T	p=0.0481	Molybdenum cofactor deficiency B #252160	Yes	Carriers Autosomal recessive
5	7 m	F	Anemia Leukopenia Thrombocytopenia Gingivitis Abnormality of homocysteine metabolism Sepsis	*TCN2*	g.(?_31018929)_(31019095_?)del/ g.(?_31018929)_(31019095_?)del	p=0.0326	Transcobalamin II deficiency #275350	Yes	Carriers Autosomal recessive
6	1 y	F	Hyperphenylalaninemia Abnormality tyrosine metabolism	*PAH*	c.842C>T/ c.490A>G	p=0.0018	Hyperphenylalaninemia #261600	No	Carriers Autosomal recessive
7	3 y	M	Hyperphenylalaninemia Abnormality tyrosine metabolism	*PAH*	c.782G>A/ c.136G>A	p=0.0018	Hyperphenylalaninemia #261600	No	Carriers Autosomal recessive
8	7 m	M	Hypocalcemia Vitamin D deficiency Organic aciduria	*MCCC2*	c.1015G>A/ c.1423G>A	p=0.0458	3-Methylcrotonyl-CoA carboxylase 2 deficiency #210210	Yes	Carriers Autosomal recessive

			Elevated plasma acylcarnitine Muscular hypotonia						
9	9 y	M	Hematuria Hypercalciuria Nephrolithiasis Hyperuricemia	*HPRT1*	c.424A>G	p=0.0018	HRPT-related hyperuricemia #300323	Yes	- X-linked recessive
10	1 m	M	Abnormality of fatty-acid metabolism Glutaric acidemia	*ETFDH*	c.1601C>T/ c.1601C>T	p=0.0481	Glutaric acidemia IIC #231680	Yes	Carriers Autosomal recessive
11	1 y	M	Hyperuricemia Episodic ataxia Xanthinuria	*MOCOS*	c.2356del/ c.512C>T	p=0.6593	Xanthinuria, type II #603592	Yes	Carriers Autosomal recessive
12	1 m	M	Hyperphenylalaninemia Abnormality tyrosine metabolism	*PAH*	c.782G>A/ c.1066-11G>A	p=0.0018	Hyperphenylalaninemia #261600	No	Carriers Autosomal recessive
13	23 d	M	Hyperphenylalaninemia Abnormality tyrosine metabolism	*PAH*	c.1162G>A/ c.728G>A	p=0.0018	Hyperphenylalaninemia #261600	No	Carriers Autosomal recessive
14	3 y	F	Hyperphenylalaninemia	*PAH*	c.898G>T/ c.1066-11G>A	p=0.3342	Hyperphenylalaninemia #261600	No	Carriers Autosomal recessive
15	13 d	F	Hyperphenylalaninemia Abnormality tyrosine metabolism	*PAH*	c.1169A>G/ c.116_118delTCT	p=0.0018	Hyperphenylalaninemia #261600	No	Carriers Autosomal recessive
16	6 y	M	Hyperphenylalaninemia Abnormality tyrosine metabolism	*PAH*	c.261C>A/ c.1315+1G>A	p=0.0018	Hyperphenylalaninemia #261600	No	Carriers Autosomal recessive
17	15 y	M	Myoclonus Action tremor	*ATP7A*	c.2068G>C	p=0.2510	Menkes disease #309400	Yes	NA X-linked recessive
18	2 m	M	Methylmalonic acidemia	*ACSF3*	c.1672C>T/ c.1075G>A	p=0.2151	Combined malonic and methylmalonic aciduria #614265	Yes	Carriers NA
19	14 y	M	Encephalopathy Hyperammonemia Hyperbilirubinemia	*OTC*	c.903A>C	p=0.5477	Hyperammonemia due to ornithine transcarbamylase deficiency #311250	Yes	Mother carrier, brother and maternal uncle affected Autosomal recessive
20	18 y	M	Hepatic steatosis	*AMACR*	c.43delG/ c.43delG	p=0.7096	Congenital bile acid synthesis defect type 4 #214950	Yes	Carriers Autosomal recessive

21	8 y	F	Hepatic steatosis Hepatomegaly Increased hepatic glycogen content	*PHKB*	c.2581A>G/ c.1459-9G>T	p=0.0036	Phosphorylase kinase deficiency of liver and muscle #261750	Yes	Carriers Autosomal recessive

** Changes in medication and/or diet after genetic diagnosis. d:days; F: female; m: month; M: male; NA: not available; y:years*

Supplementary Table S2 - Clinical data and genetic findings for each patient for which a positive diagnosis was established using the HYPO/HYPER panel.

Cases	Age	Sex	HPO	Gene	Variants	Phenomizer	Disorder MIM	Changes in Medication or Diet*	Parents/Inheritance
22	1 y	F	Hypoketotic hypoglycemia Abnormality of carnitine metabolism	*SLC22A5*	c.34G>A/ c.1463G>A	p=0.0534	Carnitine deficiency, systemic primary #212140	Yes	Carriers Autosomal recessive
23	-	M	Hepatomegaly Hypoglycemia Motor delay Growth delay	*PHKA2*	c.1245+1G>T	p=0.0160	Glycogen storage disease, type IXa #306000	Yes	Mother X-linked
24	-	M	Hypoglycemia Vertigo Polyphagia MODY Increased HbA1c levels	*CEL*	c.1810G>C/ c.1975G>C	p=0.0224	Maturity-onset diabetes of the young, type VIII #609812	Yes	Carriers Autosomal dominant
25	1 y	M	Ketotic hypoglycemia Hepatomegaly Increased hepatic transaminases Myopathy	*AGL*	c.100delC/ c.100delC	p=0.0718	Glycogen storage disease III #232400	Yes	Carriers Autosomal recessive
26	6 y	M	Hepatomegaly Hypoglycemia Hypercholesterolemia Elevated hepatic transaminases Short stature	*PHKA2*	c.3547_3548ins GGTGCCAT GGACACCC TGGAGA	p=0.0174	Glycogen storage disease, type IXa #306000	Yes	- X-linked
27	10 y	M	Hypergalactosemia Galactosuria Hypoglycemia	*GALT*	c.443G>A/ c.443G>A	p=0.0006	Galactosemia #230400	No	Carriers Autosomal recessive

28	1 m	M	Hypoketotic hypoglycemia Hyperammonemia Lethargy	*CPS1*	c.1201G>C/ c.2810T>A	p=0.0320	Carbamoyl phosphate synthetase I deficiency #237300	Yes	Carriers Autosomal recessive
29	-	M	Intrahepatic cholestasis Elevated alkaline phosphatase Hypercalcemia Hyperphosphatemia Vitamin D deficiency Elevated hepatic transaminases Hypoalphalipoproteinemia	*PHKA2*	c.3614C>T	p=0.0003	Glycogen storage disease, type IXa #306000	Yes	- X-linked
30	5 y	M	Hepatomegaly Hypoglycemia Fasting hypoglycemia	*PHKA2*	c.2746C>T	p=0.055	Glycogen storage disease, type IXa #306000	Yes	- X-linked
31	17 y	F	Abdominal pain Macrovesicular hepatic steatosis	*ALDOB*	c.448G>C/ c.448G>C	p=0.005	Fructose intolerance, hereditary #229600	Yes	Carriers Autosomal recessive
32	8 m	F	Hyperinsulinemia Abdominal distention Fasting hypoglycemia Intrauterine growth retardation	*INSR*	c.2621C>T/ c.3712C>T	p=0.0028	Hyperinsulinemic hypoglycemia, familial, 5 #609968	Yes	De novo/Mother Autosomal recessive

** Changes in medication and/or diet after genetic diagnosis .d:days; F: female; m: month; M: male; y:years*

Supplementary Table S3 - Clinical data and genetic findings for each patient for which a positive diagnosis was established using the MITO panel.

Cases	Age	Sex	HPO	Gene	Variants	Phenomizer	Disorder MIM	Changes in Medication or Diet*	Parents/Inheritance
33	3 y	F	Ventriculomegaly Epileptic spasms Hypoplasia of the corpus callosum Severe expressive language delay Slowly progressive spastic quadriparesis	*GFM1*	c.2011C>T/ c.1401delA	p=0.0302	Combined oxidative phosphorylation deficiency #609060	No	Carriers Autosomal recessive
34	9 y	M	Intrauterine growth retardation Delayed CNS myelination Athetosis Lactic acidosis	*FOXRED1*	c.920G>A/ c.733+1G>A	p=0.1400	Mitochondrial complex I deficiency #618241	No	Carriers Autosomal recessive
35	18 y	M	Decreased activity of mitochondrial complex I and IV Left ventricular hypertrophy Abnormality of coordination Dysdiadochokinesia Specific learning disability	*TSFM*	c.719G>C/ c.719G>C	p=0.0032	Combined oxidative phosphorylation deficiency #610505	No	Carriers Autosomal recessive
36	-	F	Epileptic encephalopathy Febrile seizures Status epilepticus Disinhibition Global developmental delay	*GFM2*	c.1925A>C/ c.1922T>A	p=0.2282	Combined oxidative phosphorylation deficiency #618397	No	Carriers Autosomal recessive
37	6 y	F	Abnormal mitochondria in muscle tissue Agenesis of corpus callosum Cerebral atrophy Increased CSF lactate Global developmental delay Seizures	*ADCK4*	c.418G>A	p=0.9010	Nephrotic syndrome, type 9 #615573	Yes	De novo Autosomal dominant
38	6 y	F	Hypomimic face Feeding difficulties Bilateral ptosis Optic atrophy Muscular hypotonia Areflexia	*DNM1L*	c.1337G>T	p=0.0288	Encephalopathy, lethal, due to defective mitochondrial peroxisomal fission 1 #614388	No	De novo Autosomal dominant

39	24 h	M	Hypertrophic cardiomyopathy Muscle weakness Congenital cataract Increased serum lactate	*AGK*	c.518+1G>A/ c.518+1G>A	p=0.0160	Sengers syndrome #212350	No	Carriers Autosomal recessive
40	-	M	Decreased activities of mitochondrial complexes I and III Neonatal hypotonia Global development delay Seizures	*EARS2*	c.319C>T/ c.322C>T	p=0.0023	Combined oxidative phosphorylation deficiency 12 #614924	No	Carriers Autosomal recessive
41	-	F	Hypertrophic cardiomyopathy Hypotonia Lactic acidosis	*OPA1*	c.1710T>G	-	Optic atrophy #165500 Optic atrophy plus syndrome #125250	No	De novo Autosomal dominant
42	6 y	M	Muscular hypotonia Myalgia Ataxia Head tremor Limb tremor Ptosis Failure to thrive	*PDHA1*	c.787C>G	p=0.0366	Pyruvate dehydrogenase E1-alpha deficiency #312170	Yes	De novo X-linked dominant
43	8 m	F	Lactic acidosis Generalized hypotonia Global developmental delay Growth delay Increased serum lactate Thick eyebrow	*FBXL4*	c.858+5G>C/ c.1510T>C	p=0.0032	Mitochondrial DNA depletion syndrome 13 #615471	No	Carriers/Affected brother Autosomal recessive
44	5 y	M	Increased serum lactate Infantile axial hypotonia Ataxia Severe expressive language delay Short corpus callosum Hypotonia Seizures Lactic acidosis	*FARS2*	c.1256G>A/ g.(?_5404749)_(5404959_?)del	p=0.0012	Combined oxidative phosphorylation deficiency 14 #614946	No	Carriers Autosomal recessive
45	4 m	M	Increased serum lactate Sudden cardiac death, Encephalopathy	*ACAD9*	c.358delT/ c.809-2A>G	p=0.0018	Mitochondrial complex I deficiency, nuclear type 20	No	Carriers Autosomal recessive

			Hypoglycemia Acute liver failure				#611126		
46	12 y	M	Delayed psychomotor development Metabolic acidosis	*MTO1*	c.170G>T/	p=0.4211	Combined oxidative phosphorylation deficiency 10 #614702	No	Carriers Autosomal recessive
47	2 m	M	Lactic acidosis	*GFM1*	c.640A>T/ c.1199G>C	p=0.4194	Combined oxidative phosphorylation deficiency 1 #609060	No	Carriers Autosomal recessive
48	1 y	M	Lactic acidosis Nystagmus Ragged-red muscle fibers Global developmental delay Failure to thrive in infancy	*COX15*	c.649C>T/ c.649C>T	p=0.0548	Mitochondrial complex IV deficiency, nuclear type 6 #615119	No	Carriers Autosomal recessive
49	17 y	F	Leukodystrophy Agenesis of corpus callosum Decreased activity of mitochondrial complex I and III Lactic acidosis Increased CSF lactate	*EARS2*	c.670G>A/ c.376C>T	p=0.0013	Combined oxidative phosphorylation deficiency 12 #614924	No	Carriers Autosomal recessive
50	12 y	M	Muscle weakness Encephalopathy Lactic acidosis	*ACAD9*	c.737T>C/ c.860G>A	p=0.0005	Mitochondrial complex I deficiency, nuclear type 20 #611126	No	Carriers/Affected brother Autosomal recessive
51	-	M	Encephalopathy Generalized hypotonia Lactic academia Ptosis Generalized hypotonia Failure to thrive Global developmental delay	*C12orf65*	c.207_220del/ c.207_220del	p=0.0599	Combined oxidative phosphorylation deficiency 7 #613559	No	Carriers Autosomal recessive
52	17 y	F	Hypotonia Increased serum and CSF lactate	*PNPT1*	c.1177-2A>C/ c.1519G>T	p=0.0599	Combined oxidative phosphorylation deficiency 13 #614932	No	Carriers Autosomal recessive
53	1 y	F	Nystagmus Pigmentary retinopathy Ptosis Dystonia	*PET100*	c.1A>G	p=0.0055	Mitochondrial complex IV deficiency, nuclear type 12 #619055	No	Carriers Autosomal recessive

			Global developmental delay Respiratory insufficiency						
54	-	F	Hyperlacticaemia Metabolic acidosis Encephalopathy	*EARS2*	c.184A>T/ c.920T>C	p=0.0368	Combined oxidative phosphorylation deficiency 12 #614924	No	Carriers Autosomal recessive
55	1 m	M	Neonatal hypotonia Lethargy Focal seizures Diabetes insipidus Cerebellar and cerebral cortical atrophy	*COQ4*	c.202G>C/ c.718C>T	p=0.2884	Coenzyme Q10 deficiency, primary, 7 #616276	Yes	Carriers Autosomal recessive
56	1 m	F	Premature birth Hyperlacticaemia Intrauterine growth retardation Oligohydramnios Muscle weakness	*TMEM70*	c.317-2A>G/ c.317-2A>G	p=0.0417	Mitochondrial complex V (ATP synthase) deficiency, nuclear type 2 #614052	No	Carriers Autosomal recessive
57	12 y	F	Epileptic encephalopathy Status epilepticus Clonus Generalized hypotonia Progressive spasticity	*ATPAF2*	c.133+1G>T/ c.133+1G>T	p=0.053	Mitochondrial complex V (ATP synthase) deficiency, nuclear type 1 #604273	No	Carriers Autosomal recessive
58	2 m	M	Hyperlacticaemia Methylmalonic aciduria Mitochondrial DNA depletion Encephalopathy	*SUCLA2*	c.850C>T	p=0.0375	Mitochondrial DNA depletion syndrome 5 (encephalomyopathic form with or without methylmalonic aciduria) #612073	No	Carriers Autosomal recessive
59	8 y	M	Spastic tetraparesis Progressive encephalopathy Abnormality of the gastrointestinal tract	*MCCC1*	c.1441C>A/ c.1423G>A	p=0.3542	3-Methylcrotonyl-CoA carboxylase 1 deficiency #210200	Yes	Carriers Autosomal recessive
60	1 m	M	Metabolic acidosis Myocardial fibrosis Reduced consciousness/confusion Respiratory difficulties	*TK2*	c.230C>T/ c.31+470G>A	p=0.2884	Mitochondrial DNA depletion syndrome, myopathic form #609560	No	Carriers Autosomal recessive

** Changes in medication and/or diet after genetic diagnosis ;d:days; F: female; m: month; M: male; y:years*

Supplementary Table S4 - Clinical data and genetic findings for each patient for which a positive diagnosis was established using the COMP MOL panel.

Cases	Age	Sex	HPO	Gene	Variants	Phenomizer	Disorder MIM	Changes in Medication or Diet*	Parents/Inheritance
61	-	F	Thrombocytopenia Glaucoma Nystagmus Increased CSF interferon alpha	*TREX1*	c.218C>T/ c.404A>C	p=0.0525	Aicardi-Goutieres syndrome 1 #225750	No	Carriers, affected sister Autosomal recessive
62	10 y	M	Specific learning disability Ataxia Cerebellar atrophy EMG: axonal abnormality Attention deficit/hyperactivity Generalized myoclonic seizures Global developmental delay	*TPP1*	c.622C>T/ c.887-10T>C	p=0.0187	Ceroid lipofuscinosis, neuronal, 2 #204500	Yes	Carriers Autosomal recessive
63	5 y	F	Developmental regression Epileptic encephalopathy Apathy Generalized hypotonia	*HEXA*	c.533G>A/ c.380T>G	p=0.0628	Tay-Sachs disease #272800	No	Carriers Autosomal recessive
64	15 y	M	Bilateral ptosis Dysmetria Dysarthria Horizontal nystagmus Progressive cerebellar ataxia Learning disability	*POLR3B*	c.1244T>C/ c.2740G>A	p=0.0008	Leukodystrophy, hypomyelinating, 8, with or without oligodontia and/or hypogonadotropic hypogonadism #614381	No	Carriers/Affected brother Autosomal recessive
65	-	F	Increased neuronal autofluorescent lipopigment Ataxia Seizures	*PPT1*	c.541G>T/ c.541G>T	p=0.0411	Ceroid lipofuscinosis, neuronal, 1 #256730	No	Carriers Autosomal recessive
66	5 y	M	Arthralgia Joint stiffness	*GNPTAB*	c.1325G>A/ c.1325G>A	p=1.000	Mucolipidosis II alpha/beta #252500	No	Carriers Autosomal recessive

67	5 y	F	Progressive spasticity Abnormality of peripheral nerve conduction Developmental regression	*HSD17B4*	c.1273T>C/ c.1528G>A	p=0.1340	D-bifunctional protein deficiency #261515	No	Carriers Autosomal recessive
68	6 y	F	Encephalopathy CNS demyelination Generalized hypotonia Delayed speech and language development Seizures Global developmental delay	*SLC17A5*	c.918T>G/ c.1239C>G	p=0.0339	Salla disease #604369 Sialic acid storage disorder, infantile #269920	No	Carriers Autosomal recessive
69	8 m	M	Cerebral palsy Bilateral sensorineural hearing impairment Optic atrophy Abnormal basal ganglia MRI signal intensity Cerebellar atrophy Peripheral axonal neuropathy Seizures	*PLA2G6*	c.1460_1462del/ c.1460_1462del	p=0.0205	Neurodegeneration with brain iron accumulation 2B #610217	No	Carriers Autosomal recessive
70	3 y	M	Coarse facial features Global developmental delay Hyperactivity Sensorial ataxia	*NAGLU*	c.531+5G>A/ c.1045_1047del	p=0.3261	Mucopolysaccharidosis type IIIB (Sanfilippo B) #252920	No	Carriers Autosomal recessive
71	7 y	M	Abnormality of cerebral white matter Impaired smooth pursuit Abnormal emotion/affect behavior Vacuolated lymphocytes	*POLR3A*	c.2376_2377delAT/ c.2081G>A	p=0.489	Leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism #607694	No	Carriers Autosomal recessive
72	4 y	F	Hepatosplenomegaly Abnormality of blood and blood-forming tissues Hyposmia Pain Hypersplenism	*GBA*	c.1226A>G/ c.930T>A	p=0.0804	Gaucher disease, type I #230800	Yes	Carriers Autosomal recessive
73	5 m	F	Seizures Hypotonia	*PEX12*	c.888_889del/ c.888_889del	p=0.0055	Peroxisome biogenesis disorder 3	No	Carriers

			Increased very long chain fatty acids				#614859		Autosomal recessive
74	9 y	F	Motor deterioration Fingerprint intracellular accumulation of autofluorescent lipopigment storage material	*CLN6*	c.829_836delinsCCT	p=0.0028	Ceroid lipofuscinosis, neuronal, 6 #601780	No	Carriers Autosomal recessive
75	4 m	M	Hepatosplenomegaly Muscular dystrophy Generalized hypotonia	*CTSA*	c.1252G>T/ c.1252G>T	p=0.7652	Galactosialidosis #256540	No	Carriers Autosomal recessive
76	4 y	F	Macroglossia Relative macrocephaly Abnormality of mucopolysaccharide metabolism Hepatosplenomegaly Hearing impairment Corpus callosum atrophy	*SGSH*	c.355+1G>A/ c.1080delC	p=0.4196	Mucopolysaccharidosis type IIIA (Sanfilippo A) #252900	No	Carriers Autosomal recessive
77	7 m	F	Hepatomegaly Elevated hepatic transaminases Epicanthus Broad forehead Increased urinary O-linked Sialopeptides	*GNE*	c.797G>A	p=0.529	Sialuria #269921	No	Affected sisters Autosomal dominant
78	-	M	Delayed speech and language development Hepatomegaly Microcephaly Umbilical hernia Abnormality of joint mobility Broad eyebrow	*SGSH*	c.1127T>C/ c.197C>G	p=0.5943	Mucopolysaccharidosis type IIIA (Sanfilippo A) #252900	No	Carriers Autosomal recessive
79	1 y	M	Profound global developmental delay Strabismus Increased serum lactate Abnormal CNS myelination Increased CSF lactate	*SLC16A2*	c.46delC	p=0.4992	Allan-Herndon-Dudley syndrome #300523	No	Mother X-linked
80	5 y	M	Hepatosplenomegaly Thrombocytopenia	*GBA*	c.1193G>A/ c.155C>T	p=0.2962	Gaucher disease, type I #230800	Yes	Carriers Autosomal

									recessive
81	10 y	F	Coarse facial features Global developmental delay Urinary glycosaminoglycan excretion Hepatomegaly Splenomegaly Growth abnormality	*NAGLU*	c.1562C>T/ c.1693C>T	p=0.0425	Mucopolysaccharidosis type IIIB (Sanfilippo B) #252920	No	Carriers Autosomal recessive
82	6 y	M	Seizures Developmental regression Generalized hypotonia	*HEXA*	c.533G>A	p=0.3875	GM2-gangliosidosis #272800	No	Carriers Autosomal recessive
83	5 y	M	Muscular hypotonia Cardiomyopathy Elevated serum creatine phosphokinase	*GAA*	c.343C>T/ c.-32-13T>G	p=0.3778	Glycogen storage disease II #232300	Yes	Carriers Autosomal recessive

** Changes in medication and/or diet after genetic diagnosis ;d:days; F: female; m: month; M: male; y:years*

Supplementary Table S5 - Clinical data and genetic findings for each patient with a negative result on the MITO panel and subsequent positive diagnosis with the NeuroSeq panel. Highlighting indicates genes associated with metabolic disorders (orange) and neurological disorders (blue).

Cases	Age	Sex	HPO	Gene	Variants	Phenomizer	Disorder	MIM	Parents/Inheritance	Allocated Panel
84	2 y	M	Dilated cardiomyopathy Blindness Nystagmus	*ALMS1*	c.7586C>G/ c.11017C>T	p=0.2338	Alstrom syndrome	#203800	Carriers Autosomal recessive	**HYPO/HYPER**
85	10 y	M	Decreased activity of mitochondrial complex I	*SLC16A2*	c.99dupT	p=1.0000	Allan-Herndon-Dudley syndrome	#300523	De novo X-linked dominant	**COMP MOL**
86	5 m	M	Spastic tetraparesis Polyneuropathy Developmental regression Generalized hypotonia Global developmental delay	*POLR3A*	c.2248-1G>C/ c.1771-7C>G	p=0.0266	Wiedemann-Rautenstrauch syndrome	#264090	Carriers Autosomal recessive	**COM MOL**
87	2 m	M	Increased serum lactate Encephalopathy Seizures	*LIPT1*	c.212C>T/ c.292C>T	p=0.2631	Lipoyltransferase 1 deficiency	#616299	Carriers Autosomal recessive	**MITO updated**
88	2 y	F	Hypoglycemia Lactic acidosis Thin vermilion border Abnormal facial shape Widely spaced teeth	*LRPPRC*	c.1678A>T/ c.1736-7T>G	p=0.4006	Mitochondrial complex IV deficiency, nuclear type 5	#220111	Carriers Autosomal recessive	**MITO updated**
89	7 y	M	Epilepsia partialis continua Epileptic encephalopathy Mitochondrial depletion	*KCNT1*	c.785G>A/ c.3503-1G>A	p=0.0195	Epilepsy, nocturnal frontal lobe, 1	#615005	Father/*De novo* Autosomal dominant	**EPILEPSY**
90	3 y	F	Encephalopathy Dystonia Decreased activity of mitochondrial complex I Ragged-red muscle fibers	*GNAO1*	c.607G>A	p=0.064	Developmental and epileptic encephalopathy 17	#615473	*De novo* Autosomal dominant	**EPILEPSY**
91	4 y	M	Generalized hypotonia Muscular hypotonia Epileptic encephalopathy	*KCNQ2*	c.629G>A	p=0.0027	Developmental and epileptic encephalopathy 7	#613720	*De novo* Autosomal dominant	**EPILEPSY**

			Seizures Global developmental delay							
92	3 y	F	Encephalopathy Lactic acidosis Developmental regression Dystonia Psychomotor deterioration Abnormality of body weight	*GNAO1*	c.709G>A	p=0.0383	Developmental and epileptic encephalopathy 17	#615473	*De novo* Autosomal dominant	**EPILEPSY**
93	2 y	F	Epileptic encephalopathy Cortical atrophy Progressive leukoencephalopathy	*KCNQ2*	c.833T>C	p=0.0383	Developmental and epileptic encephalopathy 7	#613720	*De novo* Autosomal dominant	**EPILEPSY**
94	4 m	M	Hypotonia Diffuse hypomyelination	*SPTAN1*	c.6910_6918dup CAGCTGGGC	-	Developmental and epileptic encephalopathy 5	#613477	*De novo* Autosomal dominant	**EPILEPSY**
95	7 y	M	Ophthalmoplegia	SBF2	c.2380G>T/ c.2380G>T	p=0.3379	Charcot-Marie-Tooth disease, Type 4b2	#604563	Carriers Autosomal recessive	**NEUROMUSCULAR DISORDER**
96	18 y	M	Peripheral neuropathy Ataxia Pigmentary retinopathy	*FLVCR1*	c.721G>A/ c.721G>A	p=0.2157	Ataxia, posterior column, with retinitis pigmentosa	#609033	Carriers Autosomal recessive	***MOVEMENT DISORDERS***
97	5 y	F	Abnormality of coordination Delayed speech Language development	*STAG1*	c.2285T>A	-	Mental retardation, autosomal dominant 47	#617635	*De novo* Autosomal dominant	***INTELLECTUAL DISABILITY***

d:days; F: female; m: month; M: male; NA: not available; y:years

Supplementary Table S6 - Clinical data and genetic findings for each patient for which an inconclusive diagnosis was obtained. Highlighting indicates clinical cases in which pathogenic variants (dark grey) and variants of uncertain significance (light grey) were detected.

Cases	Age	Sex	HPO	Panel	Gene	Variants	Disorder	Inheritance	Family Study
				DOMINANT GENES					
98	9 y	F	Hypoglycemia Focal seizures Hyperinsulinism	HYPO/HYPER	*GLUD1*	c.272C>T	Hyperinsulinism-hyperammonemia syndrome	AD	MOTHER (maternal family history)
99	5 y	M	Decreased activity of mitochondrial complex IV Seizures	MITO	*LETM1*	c.709C>T	Wolf-Hirschhorn Syndrome	AD	MOTHER (maternal family history)
100	3 y	M	Hyperinsulinemia Hypoglycemia	COM MOL	*KCNJ11*	c.1105C>A	Hyperinsulinemia Hypoglycemia, familial	AD	NA
101	18 y	F	Hyperglycemia Maturity-onset diabetes of the young	HYPO/HYPER	*HNF1A*	c.1295 C>T	MODY type II	AD	NA
102	4 y	M	Hyperalaninemia Hyperglutaminemia Increased serum lactate Asymmetric septal hypertrophy Hypertrophic cardiomyopathy Strabismus Encephalopathy Global developmental delay Increased CSF lactate Seizures	NeuroSeq	*WAC*	c.1583C>T	Desanto-Shinawi syndrome	AD	NA
103	-	F	Macrocephaly Hypoglycemia Metabolic acidosis Global developmental delay	INT MET	*IDH2*	c.419G>A	D-2-hydroxyglutaric aciduria 2	AD	NA

104	5 y	M	Mitochondrial depletion Global developmental delay Epilepsia partialis continua Generalized hypotonia	NeuroSeq	*ZEB2*	c.3202_3207delGG CTCG	Mowat-Wilson syndrome due to monosomy 2q22	AD	NA
105	2 y	M	Decreased mitochondrial complex I and II activity	NeuroSeq	*ARID1B*	c.2281+1G>C	Coffin-Siris syndrome	AD	NA
106	-	F	Dysmyelinating leukodystrophy Global developmental delay	COM MOL	*SOX10*	c.239T>C	Waardenburg syndrome type 2	AD	NA
107	10 y	M	Profound global developmental delay Gastroesophageal reflux Ventriculomegaly Agenesis of corpus callosum Microcephaly Upper airway obstruction Dysphagia Pontocerebellar atrophy	COM MOL	*LMNB1*	c.1025_1026delAA	Leukodystrophy, adult-onset, autosomal dominant	AD	NA
108	2 y	M	Recurrent bacterial infections Generalized hypotonia Mild receptive language delay	NeuroSeq	*ZNF41*	c.2057T>C	-	XL	NA
109	5 y	F	Ketotic hypoglycemia Episodic ketoacidosis	HYPO/HYPER	*PHKA2*	c.2911C>T	Glycogen storage disease, type IX	XLD	NA
110	6 y	F	Seizures Global developmental delay	NeuroSeq	*PDHA1*	c.577_578delTT	Pyruvate dehydrogenase E1-alpha deficiency	XL	NA
111	5 y	M	Decreased activity of mitochondrial complex IV Seizures	MITO	*NDUFB11*	c.152C>A	?Mitochondrial complex I deficiency, nuclear type 30	XL	MOTHER
RECESSIVE GENES									
112	3 y	M	Epileptic encephalopathy Abnormal CSF lactate level Cerebral cortical atrophy Leukoencephalopathy	MITO	*POLRMT*	c.3596T>C	? Autosomal dominant progressive external ophthalmoplegia and mitochondrial DNA depletion syndrome	-	TRANS

							4A		
113	6 y	M	NA	HYPO/HYPER	*ETFDH*	c.1274C>G	Glutaric acidemia IIC	AR	NA
114	2 y	F	Celiac disease Spastic diplegia Spastic paraparesis Leukoencephalopathy	COM MOL	*RNASEH2B*	c.655T>C	Aicardi-Goutieres Syndrome 2	AR	NA
115	9 y	M	Hyperornithinemia Hydroxyprolinemia Hydroxyprolinuria	INT MET	*PRODH*	c.1397C>T	Hyperprolinemia, type I	AR	MOTHER
116	9 y	M	Fatigue Recurrent infections Spinal rigidity	MITO	*DARS2*	c.396+2T>G	Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation	AR	NA
117	-	F	Global developmental delay Epileptic encephalopathy Postnatal microcephaly	COM MOL	*PPT1*	c.2T>C	Ceroid lipofuscinosis, neuronal, 2	AR	MOTHER
118	9 y	M	Dysphagia Optic neuritis Ptosis Strabismus Fatigable weakness Hypertonia Mitochondrial encephalopathy Increased CSF lactate	MITO	*BCS1L*	c.166C>T	Mitochondrial complex III deficiency, nuclear type 1	AR	FATHER
119	3 m	M	Orotic aciduria	INT MET	*UMPS*	c.1213C>T	Orotic aciduria	AR	NA
120	11 y	M	Lactic acidosis Decreased activity of cytochrome C oxidase in muscle tissue Cerebral palsy	MITO	*PNPT1*	c.493C>T	Combined oxidative phosphorylation deficiency 13	AR	MOTHER
121	12 y	M	Decreased activity of mitochondrial complex I	MITO	*ADCK4*	c.103G>A	Nephrotic syndrome, type 9 (coenzyme Q10 deficiency)	AR	MOTHER
122	8 y	F	Decreased activity of mitochondrial complex II Decreased activity of mitochondrial	MITO	*NDUFAF2*	c.490delG	Mitochondrial complex I deficiency, nuclear type 10	AR	MOTHER

			complex IV Cognitive impairment						
123	-	F	Seizures Global developmental delay	COM MOL	*CLN6*	c.314C>T	Ceroid lipofuscinosis, neuronal, 6	AR	NA
124	5 y	M	Focal autonomic seizures with altered responsiveness Mild microcephaly Central apnea Moderate postnatal growth retardation Generalized hypotonia Hypertelorism Wide nose Anemia Global developmental delay	NeuroSeq	*MTO1*	c.1390C>T	Combined oxidative phosphorylation deficiency 12	AR	NA
125	17 y	F	Ketotic hypoglycemia Episodic ketoacidosis Febrile seizures Global developmental delay	HYPO/HYPER	*PHKA2*	c.2870A>G	Glycogen storage disease, type IX	XLR	MOTHER
126	-	M	Decreased activity of mitochondrial complex I Decreased activity of mitochondrial complex II and III	MITO	*SLC6A8*	c.928G>A	Cerebral creatine deficiency syndrome 1	XLR	NA
			DOMINANT AND RECESSIVE INHERITANCE						
127	8 y	F	Decreased activity of mitochondrial complex II Decreased activity of mitochondrial complex IV Pyramidal syndrome	MITO	*DNM1L*	c.1921G>A	Encephalopathy, lethal, due to defective mitochondrial peroxisomal fission 1	AD, AR	NA
128	2 y	M	Noninsulin-dependent diabetes mellitus	HYPO/HYPER	*PDX1*	c.779G>A	MODY, type IV	AD, AR	FATHER (paternal family history)
129	-	M	Hyperinsulinemia Hypoglucemia+ macrosomia	HYPO/HYPER	*ABCC8*	g.(?_17464699)_(17464884_?)del g.(?_17464241)_(17464454_?)del	Familial hyperinsulinemic hypoglycemia	AD, AR	NA

130	1 y	M	Abnormality of coordination Gait disturbance	MITO	*SPG7*	c.1529C>T	Spastic Paraplegia Type 7	AD, AR	NA
POSSIBLE CASE OF DIGENIC INHERITANCE									
131	1 y	F	Ketotic hypoglycemia Compensated hypothyroidism	HYPO/HYPER	*ABCC8* *SLC37A4*	c.3004G>A c.1225A>G/ c.1022C>T	Hypoglycemia of infancy, leucine-sensitive Glycogen storage disease	AD, AR AR	*DE NOVO* TRANS

d:days; F: female; m: month; M: male; NA: not available; y:years

Supplementary Table S7 – Design of five different multi-gene panels consisting of a group of genes previously associated with: inborn errors of intermediary metabolism (INT MET), hypoglycemic/hyperglycemic events (HYPO/HYPER) associated with metabolic disorders or other processes, mitochondrial diseases (MITO), complex molecular defects including leukodystrophies (COMP MOL), and NeuroSeq panel which includes all the genes from the individual panels, along with genes associated with neurological disorders.

INT MET panel

ABCD4	ACADM	ACADS	ACADSB	ACADVL	ACAT1	ACAT2	ACSF3	ADA	ADK	ADSL	AGL	AGXT	AGXT2	AHCY	ALDH4A1	ALDH5A1
ALDH6A1		ALDOB	AMT	APRT	ARG1	ASL	ASS1	AUH	BCKDHA		BCKDHB	BTD	C2ORF25	C7ORF10	CBS	CD320	CLPB
CLPX	CPS1	CPT1A	CPT2	CTH	D2HGDH		DBT	DHTKD1	DLD	DNAJC12	DNAJC19	DPYD	DPYS	ETFA	ETFB	ETFDH	ETHE1
FAH	FBP1	FH	FMO3	FTCD	G6PC	GALE	GALK1	GALT	GBE1	GCDH	GCH1	GCSH	GGT1	GLDC	GLUL	GLYCTK	GNMT
GPHN	GRHPR	GSTZ1	GYS2	HADHA	HADHB	HAL	HCFC1	HGD	HLCS	HMGCL	HMGCS2	HOGA1	HPD	HPRT1	HSD17B10		HTRA2
IDH2	IVD	L2HGDH	LMBRD1	MAT1A	MCCC1	MCCC2	MCEE	MDH1	MLYCD	MMAA	MMAB	MMACHC		MMADHC		MOCOS	MOCS1
MOCS2	MTHFR	MTR	MTRR	MUT	NAGS	NT5C3A	OAT	OGDH	OPA3	OTC	OXCT1	PAH	PC	PCBD1	PCCA	PCCB	PCK1
PCK2	PEPD	PGM1	PHKA2	PHKB	PHKG2	PKLR	PMM2	PNP	PRODH	PRPS1	PTS	PYGL	QDPR	SERAC1	SLC1A1	SLC22A5	SLC25A1
SLC25A13		SLC25A15		SLC25A20		SLC2A2	SLC37A4	SLC46A1	SLC52A1	SLC6A19	SLC6A9	SUCLA2	SUCLG1	SUOX	TAT	TAZ	TCN2
TIMM50	UMPS	UPB1	XDH														

HYPO/HYPER panel

ABCC8	AKT2	ALMS1	APPL1	ASXL2	BLK	BSCL2	CAPN10	CDKAL1	CEL	DIS3L2	ENPP1	GCGR	GCK	GLIS3	GLUD1	GPD2	HADH
HMGA1	HNF1A	HNF1B	HNF4A	IGF2BP2	IL6	INS	INSR	IRS1	IRS2	KCNJ11	KLF11	LEP	LEPR	LIPC	LMNA	MAFA	MAPK8IP1
MC4R	MEN1	MPI	MTNR1B	NEUROD1		NSD1	PAX4	PCSK1	PDX1	PGM1	PLAGL1	PLIN1	PLUT	POMC	PPARA	PPARG	PPP1R3A
PTPN1	PYGL	RETN	SH2B1	SIM1	SLC16A1	SLC2A1	SLC2A2	SLC30A8	SLC5A1	TCF2	TCF7L2	UBE3B	UCP2	UMOD	WFS1	ZFP57	

MITO panel

AARS2	ABCB11	ACAD8	ACAD9	ACO2	ADCK1	ADCK2	ADCK3	ADCK4	ADCK5	ADSL	AFG3L2	AGK	AIFM1	AKR1B15	APOPT1	APTX	ATAD1
ATAD3A	ATP5A1	ATP5B	ATP5C1	ATP5D	ATP5E	ATP5F1	ATP5F1D	ATP5G1	ATP5G2	ATP5G3	ATP5O	ATPAF1	ATPAF2	BCS1L	BOLA3	C10ORF2	C12ORF65
C19ORF12		C1QBP	CA5A	CARS2	CCDC88A		CEP89	CHCHD10		CLPB	CLPP	COA5	COA6	COA7	COQ10A	COQ10B	COQ2
COQ3	COQ4	COQ5	COQ6	COQ7	COQ9	COX10	COX11	COX14	COX15	COX16	COX17	COX18	COX19	COX4I1	COX4I2	COX6A1	COX6A2
COX6B1	COX6B2	COX7B	COX8A	CPS1	CYC1	CYCS	DARS2	DEAF1	DGUOK	DLAT	DLD	DNA2	DNAJC19	DNM1L	E4F1	EARS2	ECHS1
ELAC2	ETHE1	FAM36A	FARS2	FARSB	FASTKD2		FBXL4	FDX1L	FH	FLAD1	FOXRED1		GARS	GFER	GFM1	GFM2	GLRX5
GOT2	GPT2	GTPBP3	GYG2	HARS2	HCCS	HIBCH	HSD17B10		HSD17B4	HSPD1	HSPE1	HTRA2	IARS	IARS2	IBA57	ISCA1	ISCA2
ISCU	ITPA	KARS	LARS2	LETM1	LGI1	LIAS	LIPT1	LIPT2	LONP1	LRP4	LRPPRC	LYRM4	LYRM7	MARS2	MDH2	MECP2	MFF
MFN1	MFN2	MGME1	MICU1	MIPEP	MNF1	MPV17	MRPL12	MRPL3	MRPL44	MRPS16	MRPS22	MRPS23	MRPS34	MRPS7	MTCH1	MTERF1	MTFMT
MTHFD1L		MTO1	MTPAP	NADK2	NARS2	NAT8L	NAXE	NDUFA1	NDUFA10		NDUFA11		NDUFA12		NDUFA13		NDUFA2

NDUFA3	NDUFA4	NDUFA4L2	NDUFA5	NDUFA9	NDUFAF1	NDUFAF2	NDUFAF3	NDUFAF4	NDUFAF5	NDUFAF6							
NDUFB1	NDUFB10	NDUFB11	NDUFB2	NDUFB3	NDUFB4	NDUFB5	NDUFB6	NDUFB7	NDUFB8	NDUFB9	NDUFS1	NDUFS2	NDUFS3	NDUFS4	NDUFS5		
NDUFS6	NDUFS7	NDUFS8	NDUFV1	NDUFV2	NDUFV3	NFS1	NFU1	NUBPL	OPA1	OPA3	PARS2	PC	PCK2	PDHA1	PDHA2	PDHB	PDHX
PDK3	PDP1	PDP2	PDSS1	PDSS2	PET100	PET117	PGAP2	PIGN	PMPCB	PNPLA4	PNPLA8	PNPT1	POLG	POLG2	POLRMT	PTCD1	PUS1
QRSL1	RANBP2	RARS2	RERE	RMND1	RNASEH1	RPIA	RRM2B	RTN4IP1	SARS	SARS2	SCO1	SCO2	SDHA	SDHAF1	SDHAF2	SDHB	
SDHC	SDHD	SERAC1	SFXN4	SLC19A3	SLC25A12	SLC25A19	SLC25A26	SLC25A3	SLC25A4	SLC25A42	SLC25A46	SLC52A2					
SLC6A8	SLC6A9	SPG20	SPG7	SUCLA2	SUCLG1	SURF1	TACO1	TANGO2	TARS2	TAZ	TAZ	TBCD	TBCE	TFAM	TIMM8A	TK2	TKT
TMEM126A	TMEM126B	TMEM70	TOP3A	TPK1	TRAK1	TRIT1	TRMT10C	TRMT5	TRMU	TRNT1	TSFM	TTC19	TUBB	TUBB6			
TUFM	TXN2	TYMP	UPB1	UQCC3	UQCR10	UQCR11	UQCRB	UQCRC1	UQCRC2	UQCRFS1	UQCRH	UQCRHL	UQCRQ	VAC14	VARS2	VDAC1	
VDAC2	WARS2	YARS2	YME1L1														

COMP MOL panel

AARS	AARS2	ABCD1	ABCD3	ABHD12	ABHD5	ACAA1	ACER3	ACOX1	ADAR	AGA	AGPS	AIFM1	AIMP1	AIMP2	AKR1D1	ALDH3A2	
AMACR	APOPT1	ARSA	ARSB	ASAH1	ASPA	ATP13A2	ATRN	BCAP31	C11ORF73		C19ORF12		CLCN2	CLN3	CLN5	CLN6	CLN8
CNTNAP1		COL4A1	CP	CRAT	CSF1R	CTBP1	CTC1	CTSA	CTSD	CTSF	CYP27A1	CYP7B1	DARS	DHCR24	DHCR7	DNAJC5	DYM
EBP	EIF2B1	EIF2B2	EIF2B3	EIF2B4	EIF2B5	EPRS	ERAL1	FA2H	FAM126A		FDFT1	FUCA1	GAA	GALC	GALNS	GBA	GBE=GBE1
GFAP	GJC2	GLA	GLB1	GM2A	GM1	GNE	GNPAT	GNPTAB	GNPTG	GNS	GPHN	GRN	GUSB	HEPACAM		HEXA	HEXB
HGSNAT	HSD17B4	HSD3B7	HSPD1	HTRA1	HYAL1	IBA57	IDS	IDUA	IFIH1	ITPA	KCNT1	KCTD7	LAMP2	LIPA	LMNB1	MAG	MAN2B1
MANBA	MCOLN1	MFSD8	MLC1	MSMO1	MVK	NAGA	NAGLU	NALCN	NANS	NDUFA2	NEU1	NKX6-2	NOTCH3	NPC1	NPC2	NPL	NSDHL
NUBPL	PEX1	PEX10	PEX11B	PEX12	PEX13	PEX14	PEX16	PEX19	PEX2	PEX26	PEX3	PEX5	PEX6	PEX7	PHYH	PLEKHG2	
PLP1	PMM2	POLR1A	POLR1C	POLR3A	POLR3B	PPT1	PSAP	PYCR2	RAB33B	RARS	REPS1	RNASEH2A		RNASEH2B		RNASEH2C	
RNASET2		SAMHD1	SC5D	SCARB2	SCP2	SGSH	SIGMAR1		SLC16A2	SLC17A5	SLC1A4	SLC25A12		SMPD1	SNORD118		SOX10
SPTAN1	SUMF1	TBCD	TMEM106B		TPP1	TREX1	TUBB4A	UBTF	UFM1	VPS11	VPS33A						

NeuroSeq panel

AARS	AARS2	AASS	ABAT	ABCB11	ABCB7	ABCC8	ABCD1	ABCD3	ABCD4	ABHD12	ABHD5	ACAA1	ACAD8	ACAD9	ACADM	ACADS	ACADSB
ACADVL	ACAT1	ACAT2	ACBD5	ACER3	ACHE	ACMSD	ACO2	ACOX1	ACSF3	ACSL4	ACTA1	ACTB	ACTG1	ADA	ADAM22	ADAMTS2	
ADAR	ADAT3	ADCK1	ADCK2	ADCK3	ADCK4	ADCK5	ADCY5	ADCY6	ADD3	ADGRG1	ADGRG6	ADGRV1	ADK	ADNP	ADPRHL2		ADSL
ADSSL1	AEBP1	AFF2	AFG3L2	AGA	AGK	AGL	AGMO	AGO1	AGPS	AGRN	AGXT	AGXT2	AHCY	AHDC1	AHI1	AIFM1	AIMP1
AIMP2	AKR1B15		AKR1D1	AKT1	AKT2	AKT3	ALAD	ALAS2	ALDH18A1		ALDH3A2		ALDH4A1		ALDH5A1		ALDH6A1
ALDH7A1		ALDOA	ALDOB	ALG1	ALG11	ALG12	ALG13	ALG14	ALG2	ALG3	ALG6	ALG8	ALG9	ALMS1	ALPK3	ALS2	ALX4
AMACR	AMPD1	AMPD2	AMT	ANK3	ANKLE2	ANKRD11		ANO10	ANO3	ANO5	AP1S2	AP3B2	AP4B1	AP4E1	AP4M1	AP4S1	AP5Z1
APBB1	APOA1BP	APOL2	APOL4	APOPT1	APPL1	APRT	APTX	ARCN1	ARF1	ARFGEF2		ARG1	ARHGEF10		ARHGEF15		ARHGEF2
ARHGEF6		ARHGEF9		ARID1A	ARID1B	ARL13B	ARL3	ARL6	ARL6IP1	ARMC4	ARMC9	ARSA	ARSB	ARSI	ARV1	ARX	ASAH1
ASCC1	ASH1L	ASL	ASNS	ASPA	ASPM	ASS1	ATAD1	ATAD3A	ATAD3B	ATAD3C	ATCAY	ATG5	ATL1	ATL3	ATM	ATP13A2	ATP1A2
ATP1A3	ATP1B1	ATP2A1	ATP2B3	ATP5A1	ATP5B	ATP5C1	ATP5D	ATP5E	ATP5F1	ATP5F1D	ATP5G1	ATP5G2	ATP5G3	ATP5O	ATP6AP2	ATP6V0A2	
ATP6V1A		ATP7A	ATP7B	ATP8A2	ATPAF1	ATPAF2	ATR	ATRN	ATRX	AUH	AUTS2	B3GALNT2		B3GNT1	B4GALNT1		B4GALT1

B4GALT7	B9D1	B9D2	BAG3	BBIP1	BBS1	BBS10	BBS12	BBS2	BBS4	BBS5	BBS7	BBS9	BCAP31	BCKDHA		BCKDHB	BCKDK	
BCL11A	BCL11B	BCS1L	BEAN1	BICD2	BIN1	BLK	BMP1	BOLA3	BPTF	BRAF	BRAT1	BRF1	BRPF1	BRWD3	BSCL2	BTD	BVES	
C6ORF66		C10ORF2		C11ORF73		C12ORF65		C19ORF12		C2ORF86	C5ORF42	C7ORF10	C8ORF37	CA5A	CA8	CACNA1A		
CACNA1B		CACNA1C		CACNA1D		CACNA1G		CACNA1H		CACNA1S		CACNA2D1		CACNA2D2		CACNB4	CACNG2	
CAD	CAMK2A		CAMK2B		CAMTA1		CAPN1	CAPN3	CARS2	CASC5	CASK	CASQ1	CASR	CAV3	CBL	CBS	CC2D1A	
CC2D2A	CCDC115	CCDC174	CCDC28B		CCDC78	CCDC88A		CCDC88C		CCM1	CCND2	CCT5	CD320	CDH15	CDK13	CDK5	CDK5RAP2	
CDK6	CDKL5	CDON	CEL	CENPE	CENPF	CENPJ	CEP104	CEP120	CEP135	CEP152	CEP164	CEP290	CEP41	CEP63	CEP89	CERS1	CFL2	
CHAMP1	CHAT	CHCHD10		CHD1	CHD2	CHD7	CHD8	CHI3L1	CHKB	CHMP1A	CHMP1B	CHRNA1	CHRNA2	CHRNA4	CHRNB1	CHRNB2	CHRND	
CHRNE	CHRNG	CHST14	CIC		CIT	CIZ1	CLCN1	CLCN2	CLCN4	CLCN6	CLIC2	CLN3	CLN5	CLN6	CLN8	CLP1	CLPB	
CLPP	CLPX	CLTC	CNKSR2	CNNM2	CNOT3	CNPY3	CNTN1	CNTN2	CNTNAP1		CNTNAP2		COA5	COA6	COA7	COASY	COG1	
COG2	COG4	COG5	COG6	COG7	COG8	COL12A1	COL13A1	COL18A1	COL1A1	COL1A2	COL3A1	COL4A1	COL4A2	COL4A3BP		COL5A1	COL5A2	
COL5A3	COL6A1	COL6A2	COL6A3	COL6A6	COLEC11		COLQ	COMT	COQ10A	COQ10B	COQ2	COQ3	COQ4	COQ5	COQ6	COQ7	COQ9	
COX10	COX11	COX14	COX15	COX16	COX17	COX18	COX19	COX4I1	COX4I2	COX6A1	COX6A2	COX6B1	COX6B2	COX7B	COX8A	CP	CPA6	
CPLX1	CPOX	CPS1	CPT1A	CPT1C	CPT2	CRADD	CRAT	CRBN	CRTAP	CRYAB	CSDE1	CSF1R	CSNK1G1		CSNK2B	CSPP1	CSTB	
CTBP1	CTC1	CTCF	CTH	CTNNA2	CTNNB1	CTSA	CTSD	CTSF	CTTNBP2		CTU2	CUL4B	CUX2	CWF19L1	CXORF56	CYC1	CYCS	
CYFIP2	CYP26B1	CYP27A1	CYP2U1	CYP7B1		D2HGDH		DAB1	DAG1	DAO	DAOA	DARS	DARS2	DBT	DCAF17	DCAF8	DCC	
DCHS1	DCX	DDC	DDHD1	DDHD2	DDOST	DDX3X	DEAF1	DENND5A		DEPDC5	DES	DGAT2	DGUOK	DHCR24	DHCR7	DHDDS	DHFR	
DHTKD1	DHX30	DIAPH1	DISC1	DISP1	DLAT	DLD	DLG3	DLGAP4	DLL1	DMD	DNA2	DNAJB2	DNAJB6	DNAJC12	DNAJC19	DNAJC3	DNAJC5	
DNM1	DNM1L	DNM2	DNMT1	DNMT3A		DOCK3	DOCK7	DOCK8	DOK7	DOLK	DPAGT1	DPM1	DPM2	DPM3	DPP6	DPYD	DPYS	
DRD3	DRD4	DRD5	DRP2	DSCAM	DST	DSTYK	DYM	DYNC1H1		DYRK1A	DYSF	E4F1	EARS2	EBF3	EBP	ECEL1	ECHS1	
EDC3	EEF1A2	EEF2	EFHC1	EFNB1	EFTUD2	EGR2	EIF2AK2	EIF2B1	EIF2B2	EIF2B3	EIF2B4	EIF2B5	EIF2S3	EIF4E	ELAC2	ELOVL4	ELOVL5	
ELP2	EMD	EMILIN1	EML1	EMX2	ENTPD1	EOMES	EPB41L1	EPM2A	EPRS	EPT1	ERAL1	ERBB3	ERBB4	ERF	ERGIC1	ERLIN1	ERLIN2	
ERMARD		ETFA	ETFB	ETFDH	ETHE1		EVL	EXOSC3	EXOSC9	EXT2	EZH2	FA2H	FAH	FAM111B	FAM126A		FAM36A	
FARS2	FARSB	FAS	FASTKD2		FAT2	FAT4	FBN1	FBN2	FBP1	FBXL4	FBXO11	FBXO31	FDFT1	FDX1L	FECH	FGD1	FGD4	
FGF12	FGF14	FGF8	FGFR1	FGFR2	FGFR3	FH	FHL1	FIG4	FKBP10	FKBP14	FKRP	FKTN	FLAD1	FLNA	FLNC	FLVCR1	FMN2	
FMO3	FMR1	FOLR1	FOXA2	FOXG1	FOXH1	FOXP1	FOXP2	FOXRED1		FREM1	FRMD4A	FRMPD4	FRRS1L	FTCD	FTL	FTSJ1	FUCA1	FUS
FUT8	G6PC	GAA	GABBR2	GABRA1	GABRA5	GABRB1	GABRB2	GABRB3	GABRD	GABRG2	GAD1	GALC	GALE	GALK1	GALNS	GALT	GAN	
GARS	GAS1	GATAD2B		GBA	GBA2	GBE1	GCDH	GCH1	GCK	GCSH	GDAP1	GDI1	GEMIN4	GFAP	GFER	GFM1	GFM2	
GFPT1	GGT1	GJB1	GJC2	GLA	GLB1	GLDC	GLDN	GLE1	GLI2	GLI3	GLIS2	GLIS3	GLRA1	GLRB	GLRX5	GLUD1	GLUL	
GLYCTK	GM2A	GMPPA	GMPPB	GNAL	GNAO1	GNAQ	GNB1	GNB4	GNB5	GNE	GNMT	GNPAT	GNPTAB	GNPTG	GNS	GOLGA2	GOSR2	
GOT2	GPAA1	GPC3	GPHN	GPR88	GPRASP1		GPSM2	GPT2	GRB14	GRHPR	GRIA3	GRIA4	GRID2	GRIK2	GRIN1	GRIN2A	GRIN2B	
GRIN2D	GRM1	GRM5	GRN	GSTZ1	GTPBP3	GUF1	GUSB	GYG1	GYG2	GYS1	GYS2	GZF1	HACD1	HACE1	HADH	HADHA	HADHB	
HAL	HARS	HARS2	HBA1	HCCS	HCFC1	HCN1	HCN2	HCN4	HDAC8	HECW2	HEPACAM		HERC2	HESX1	HEXA	HEXB	HFE	
HGD	HGSNAT	HIBCH	HINT1	HINT3	HIVEP2	HK1	HLCS	HMBS	HMGCL	HMGCS2	HNF1A	HNF4A	HNF6	HNMT	HNRNPA1		HNRNPA2B1	
HNRNPDL		HNRNPH1		HNRNPH2		HNRNPU		HOGA1	HOXA1	HPCA	HPD	HPRT1	HRAS	HSD17B10		HSD17B4	HSD3B7	
HSPB1	HSPB3	HSPB8	HSPD1	HSPE1	HSPG2	HTR2A	HTRA1	HTRA2	HUWE1	HYAL1	HYOU1	IARS	IARS2	IBA57	ICK	IDH2	IDS	
IDUA	IER3IP1	IFIH1	IFITM5	IFT122	IFT27	IFT64	IGBP1	IGHMBP2		IKBKAP	IL11RA	IL1RAPL1		IMPA1	INAVA	INF2	INPP5E	
INPP5K	INS	INSR	INVS	IQCB1	IQSEC1	IQSEC2	IRF2BPL	ISCA1	ISCA2	ISCU	ISPD	ITGA5	ITGA7	ITPA	ITPR1	IVD	JPH1	
KANK1	KARS	KAT6A	KATNB1	KBTBD13	KCNA1	KCNA2	KCNB1	KCNC1	KCNC3	KCND3	KCNH1	KCNH5	KCNJ10	KCNJ11	KCNMA1		KCNQ2	
KCNQ3	KCNQ5	KCNT1	KCNT2	KCTD17	KCTD7	KDM5B	KDM5C	KDM6A	KIAA0196		KIAA0226		KIAA0556		KIAA0586		KIAA1109	

KIAA1279		KIAA2022		KIDINS220		KIF11	KIF14	KIF1A	KIF1B	KIF1C	KIF22	KIF2A	KIF4A	KIF5A	KIF5C	KIF7	KIRREL3
KLC2	KLF11	KLHL15	KLHL40	KLHL41	KMT2B	KMT5B	KPTN	KRAS	KY	L1CAM	L2HGDH	LAMA2	LAMB1	LAMB2	LAMC3	LAMP2	LARGE
LARS2	LAS1L	LDB3	LDHA	LEPRE1	LETM1	LGI1	LGI4	LIAS	LIMS2	LINGO1	LINS	LIPA	LIPT1	LIPT2	LITAF	LMAN2L	LMBRD1
LMNA	LMNB1	LMNB2	LMOD3	LNPK	LONP1	LRP2	LRP4	LRPPRC	LRRC56	LRSAM1	LTC4S	LYRM4	LYRM7	LZTFL1	LZTR1	MAFA	MAG
MAGEL2	MAGI2	MAN1B1	MAN2B1	MANBA	MAOA		MAP2	MAPK10	MAPT	MARS	MARS2	MASP1	MAT1A	MAT2A	MATR3	MBD5	MBOAT7
MCCC1	MCCC2	MCEE	MCM3AP		MCOLN1	MCPH1	MDH1	MDH2	MECP2	MECR	MED12	MED13L	MED17	MED20	MED23	MED25	MEF2C
MEGF10	MEIS2	METTL23	MFF	MFN1	MFN2	MFSD2A	MFSD8	MGAT2	MGME1	MICU1	MID2	MIPEP	MIR17HG		MKKS	MKS1	MLC1
MLYCD	MMAA	MMAB	MMACHC		MMADHC		MME	MNF1	MOCOS	MOCS1	MOCS2	MOGS	MORC2	MPDU1	MPDZ	MPI	MPV17
MPZ	MR1	MRE11A	MRPL12	MRPL3	MRPL44	MRPS16	MRPS22	MRPS23	MRPS34	MRPS7	MRTO4	MSMO1	MSTO1	MSX2	MTCH1	MTERF	MTFMT
MTHFD1L		MTHFR	MTM1	MTMR14	MTMR2	MTO1	MTOR	MTPAP	MTR	MTRR	MUSK	MUT	MVK	MYBPC1	MYCN	MYF6	MYH14
MYH2	MYH3	MYH7	MYH8	MYO18B	MYO9A	MYOT	MYPN	MYT1L	NAA15	NACC1	NADK2	NAGA	NAGLU	NAGS	NALCN	NANS	NAPB
NARS2	NAT8L	NCAPD2	NCAPD3	NCAPH	NCKAP1	NDE1	NDP	NDRG1	NDST1	NDUFA1	NDUFA10		NDUFA11		NDUFA12		NDUFA13
NDUFA2	NDUFA3	NDUFA4	NDUFA4L2		NDUFA5	NDUFA6	NDUFA9	NDUFAF1		NDUFAF2		NDUFAF3		NDUFAF4		NDUFAF5	
NDUFAF6		NDUFB1	NDUFB10		NDUFB11		NDUFB2	NDUFB3	NDUFB4	NDUFB5	NDUFB6	NDUFB7	NDUFB8	NDUFB9	NDUFS1	NDUFS2	NDUFS3
NDUFS4	NDUFS5	NDUFS6	NDUFS7	NDUFS8	NDUFV1	NDUFV2	NDUFV3	NEB	NECAP1	NEDD4L	NEFH	NEFL	NEK1	NEK8	NEK9	NEU1	NEUROD1
NFIA	NFS1	NFU1	NGLY1	NGN3	NHEJ1	NHLRC1	NIN	NIPA1	NIPA2	NKX6-2	NLGN4X	NONO	NOTCH3	NPC1	NPC2	NPHP1	NPHP3
NPHP4	NPL	NPRL2	NPRL3	NRAS	NRXN1	NSDHL	NSUN2	NT5C2	NT5C3A	NTNG1	NTRK2	NUAK1	NUBPL	NUP37	NUS1	OAT	OCLN
OFD1	OGDH	OGT	OPA1	OPA3	OPHN1	ORAI1	OTC	OTUD6B	OTX2	OXCT1	P4HB	PABPN1	PACS1	PACS2	PAFAH1B1		PAH
PAK1	PAK3	PANK2	PARK2	PARK7	PARS2	PAX3	PAX4	PAX5	PBX1	PC	PCBD1	PCCA	PCCB	PCDH12	PCDH19	PCDH7	PCK1
PCK2	PCNA	PDE10A	PDE6D	PDGFB	PDHA1	PDHA2	PDHB	PDHX	PDK3	PDP1	PDP2	PDSS1	PDSS2	PDX1	PDYN	PEPD	PET100
PET117	PEX1	PEX10	PEX11B	PEX12	PEX13	PEX14	PEX16	PEX19	PEX2	PEX26	PEX3	PEX5	PEX6	PEX7	PFKFB2	PFKM	PGAM2
PGAP1	PGAP2	PGK1	PGM1	PHC1	PHF6	PHF8	PHIP	PHKA1	PHKA2	PHKB	PHKG2	PHYH	PIBF1	PIEZO2	PIGA	PIGC	PIGG
PIGH	PIGN	PIGO	PIGQ	PIGS	PIK3CA	PIK3R2	PIK3R5	PINK1	PIP5K1C	PKLR	PLA2G6	PLAA	PLCB1	PLD3	PLEC	PLEKHG2	
PLEKHG5		PLOD1	PLOD2	PLOD3	PLP1	PMM2	PMP22	PMPCA	PMPCB	PNKP	PNP	PNPLA2	PNPLA4	PNPLA6	PNPLA8	PNPO	PNPT1
POGLUT1		POGZ	POLG	POLG2	POLR1A	POLR1C	POLR2M	POLR3A	POLR3B	POLRMT	POMGNT1		POMGNT2		POMK	POMT1	POMT2
PPIB	PPM1D	PPOX	PPP1CB	PPP1R15B		PPP2R1A	PPP2R5D	PPP3CA	PPT1	PQBP1	PRDM8	PRICKLE1		PRICKLE2		PRKAG2	PRKCG
PRKRA	PRNP	PRODH	PROSC	PRPF39	PRPS1	PRRT2	PRSS12	PRUNE1	PRX	PSAP	PSMD12	PTCD1	PTCH1	PTCHD1	PTEN	PTPN11	PTS
PUM1	PURA	PUS1	PUS3	PYCR2	PYGL	PYGM	PYROXD1		QARS	QDPR	QRSL1	RAB11A	RAB11B	RAB18	RAB23	RAB33B	RAB39B
RAB3GAP1		RAB3GAP2		RAB40AL		RAB7A	RAC1	RAF1	RALGAPA1		RANBP2	RAPSN	RARS	RARS2	RBBP8	RBCK1	RBFOX1
RBFOX3	RBM12	RBMX	RECQL4	REEP1	REEP2	RELN	REPS1	RERE	RFT1	RHOBTB2		RIT1	RLIM	RMND1	RNASEH1		RNASEH2A
RNASEH2B		RNASEH2C		RNASET2		RNF170	RNF216	ROBO1	ROGDI	RORA	RORB	RP2	RPGRIP1L		RPIA	RPL10	RPS23
RPS6KA3	RRM2B	RTN2	RTN4IP1	RTN4R	RTTN	RYR1	RYR3	SACS	SAMD9L	SAMHD1	SARS	SARS2	SASS6	SBF1	SBF2	SC5D	SCA2
SCAPER	SCARB2	SCN10A	SCN1A	SCN1B	SCN2A	SCN3A	SCN4A	SCN7A	SCN8A	SCN9A	SCO1	SCO2	SCP2	SCYL1	SDCCAG8		SDHA
SDHAF1	SDHAF2	SDHB	SDHC	SDHD	SELENON		SEMA3E	SEPSECS	SERAC1	SERPINF1		SERPINH1		SERPINI1	SET	SETBP1	SETD2
SETD5	SETDB2	SETX	SFXN4	SGCA	SGCB	SGCD	SGCE	SGCG	SGSH	SH3TC2	SHANK2	SHANK3	SHH	SHOC2	SHROOM4		SIGMAR1
SIK1	SIL1	SIN3A	SIX3	SKI	SLC12A5	SLC12A6	SLC13A5	SLC16A1	SLC16A2	SLC17A5	SLC18A2	SLC18A3	SLC19A3	SLC1A1	SLC1A2	SLC1A3	SLC1A4
SLC22A5	SLC25A1	SLC25A12		SLC25A13		SLC25A15		SLC25A19		SLC25A20		SLC25A22		SLC25A26		SLC25A3	SLC25A32
SLC25A4	SLC25A42		SLC25A46		SLC2A1	SLC2A10	SLC2A2	SLC30A10		SLC30A9	SLC33A1	SLC35A1	SLC35A2	SLC35A3	SLC35C1	SLC37A4	SLC39A13
SLC39A14		SLC39A8	SLC3A1	SLC45A1	SLC46A1	SLC52A1	SLC52A2	SLC52A3	SLC5A1	SLC5A7	SLC6A1	SLC6A17	SLC6A19	SLC6A3	SLC6A5	SLC6A8	SLC6A9
SLC9A1	SLC9A6	SLC9A9	SMARCA1		SMARCA4		SMARCB1		SMARCC2		SMC1A	SMCHD1	SMPD1	SMS	SNAP25	SNAP29	SNORD118

SNX14 SOD1 SON SOS1 SOS2 SOX10 SOX11 SOX2 SOX3 SP7 SPAST SPATA5 SPEG SPG11 SPG20 SPG21 SPG7 SPR
SPTAN1 SPTBN2 SPTBN4 SQSTM1 SRD5A3 SRGAP2 SRGAP2C SRPX2 SSR4 ST3GAL3 ST3GAL5 STAC3 STAG1 STIL STIM1 STRADA STT3A
STT3B STUB1 STX1B STXBP1 STYXL1 SUCLA2 SUCLG1 SUCO SUFU SUMF1 SUOX SURF1 SYN1 SYN2 SYNE1 SYNE2 SYNGAP1
SYNJ1 SYP SYT14 SYT1 SYT2 SZT2 TACO1 TAF1 TAF13 TAF2 TANGO2 TARDBP TARS2 TAT TAZ TBC1D23 TBC1D24 TBC1D7
TBCD TBCE TBCK TBL1XR1 TBR1 TCAP TCF12 TCF2 TCF3 TCF4 TCF7L2 TCN2 TCTN1 TCTN2 TCTN3 TDGF1 TDP1 TDP2
TECPR2 TECR TELO2 TENM4 TERF2 TFAM TFG TGFB1 TGFB2 TGFB3 TGFBR1 TGIF1 TGM6 TH THAP1 THOC2 TIA1 TIMM50
TIMM8A TIMMDC1 TK2 TKT TLK2 TM4SF20 TMEM106B TMEM107 TMEM126A TMEM126B TMEM138 TMEM165
TMEM199 TMEM216 TMEM231 TMEM237 TMEM240 TMEM38B TMEM43 TMEM5 TMEM67 TMEM70 TMLHE TMTC3
TNIK TNNI2 TNNT1 TNNT3 TNPO3 TNXB TOP3A TOR1A TOR1AIP1 TOR1AIP2 TPK1 TPM2 TPM3 TPP1 TRAF3IP1
TRAIP TRAK1 TRAPPC11 TRAPPC12 TRAPPC6B TRAPPC9 TREX1 TRIM2 TRIM32 TRIM36 TRIM54 TRIM63 TRIM8 TRIO
TRIP12 TRIP4 TRIT1 TRMT10A TRMT10C TRMT5 TRMU TRNT1 TROVE2 TRPC3 TRPV4 TSC1 TSC2 TSEN15 TSEN2 TSEN34
TSEN54 TSFM TSPAN7 TTBK2 TTC19 TTC21B TTC8 TTI2 TTN TTPA TTR TUBA1A TUBA8 TUBB TUBB2A TUBB2B TUBB3 TUBB4A
TUBB6 TUBG1 TUBGCP4 TUBGCP6 TUFM TUSC3 TWIST1 TXN2 TYMP UBA1 UBA5 UBE2A UBE3A UBR3 UBR4 UBTF
UCHL1 UCP2 UFC1 UFM1 UMOD UMPS UNC13A UNC80 UPB1 UPF3B UQCC3 UQCR10 UQCR11 UQCRB UQCRC1 UQCRC2 UQCRFS1
UQCRH UQCRHL UQCRQ UROC1 UROD UROS USP18 USP27X USP8 USP9X VAC14 VAMP1 VARS VARS2 VCP VDAC1 VDAC2 VLDLR
VMA21 VPS11 VPS13A VPS13D VPS33A VPS37A VPS53 VRK1 VWA3B WAC WARS WARS2 WASHC4 WDFY3 WDR19 WDR26 WDR33 WDR45
WDR45B WDR48 WDR62 WDR73 WDR81 WWOX XDH XRCC1 XRCC4 YARS YARS2 YME1L1 YWHAG YY1 ZAK ZBTB18 ZBTB42 ZC3H14
ZDHHC15 ZDHHC9 ZEB2 ZFR ZFYVE26 ZFYVE27 ZIC2 ZMYM2 ZMYM3 ZMYND11 ZNF148 ZNF335 ZNF41 ZNF423 ZNF469 ZNF592
ZNF674 ZNF711 ZNF81 ZSWIM6