ENDOCRINE DISORDERS

Genes	Name of disease	Orpha Code	Prevalence (Orphanet)	Variants Count
AAAS	Achalasia-addisonianism-alacrima syndrome, Triple A syndrome	ORPHA:869	<1 / 1 000 000	24
ABCC8	Autosomal dominant hyperinsulinism due to SUR1 deficiency	ORPHA:276575	Unknown	215
CASR	Hypocalciuric hypercalcemia I, neonatal hyperparathyroidism	ORPHA:428	Unknown	134
CYP11B1	Congenital adrenal hyperplasia due to 11-beta-hydroxylase deficiency	ORPHA:90795	1-9 / 1 000 000	55
CYP11B2	Familial hyperaldosteronism I	ORPHA:403	Unknown	21
CYP17A1	Congenital adrenal hyperplasia due to 17-alpha-hydroxylase deficiency	ORPHA:90793	1-9 / 1 000 000	37
CYP21A2*	Classical congenital adrenal hyperplasia due to 21-hydroxylase deficiency	ORPHA:418	1-9 / 100 000	0
CYP27B1	Vitamin D hydroxylation-deficient rickets I	ORPHA:289157	1-5 / 10 000	24
DUOX2	Thyroid hormonogenesis 6 defect	ORPHA:95716	1-9 / 100 000	37
DUOXA2	Thyroid hormonogenesis 5 defect	ORPHA:95716	1-9 / 100 000	7
HSD3B2	Congenital adrenal hyperplasia due to 3-beta-hydroxysteroid dehydrogenase 2 deficiency	ORPHA:90791	<1 / 1 000 000	22
IGF1	Growth delay due to insulin-like growth factor I deficiency	ORPHA:73272	<1 / 1 000 000	5
IGSF1	X-linked central congenital hypothyroidism with testicular enlargement	ORPHA:329235	<1 / 1 000 000	9
IRS4	Congenital hypothyroidism nongoitrous 9	ORPHA:442	1-5 / 10 000	3
IYD	Thyroid hormonogenesis 4 defect	ORPHA:95716	1-9 / 100 000	4
LHX3	Combined pituitary hormone deficiency	ORPHA:231720	<1 / 1 000 000	8
NKX2-5	Congenital hypothyroidism nongoitrous 5	ORPHA:95713	1-9 / 100 000	51
NR0B1	X-linked adrenal hypoplasia congenita	ORPHA:95702	1 / 12 500	69
PAX8	Congenital hypothyroidism due to thyroid dysgenesis or hypoplasia	ORPHA:95712, ORPHA:95720	1-5 / 10 000	10
POU1F1	Pituitary hormone deficiency 1, Combined pituitary hormone deficiencies	ORPHA:95494	1 / 4 000	18
PROP1	Combined pituitary hormone deficiency 2	ORPHA:95494	1 / 4 000	39
SCNN1A	Pseudohypoaldosteronism 1	ORPHA:756	1 / 47 000	17
SCNN1B	Pseudohypoaldosteronism 1	ORPHA:756	1 / 47 000	19
SECISBP2	Abnormal metabolism thyroid hormone	ORPHA:171706	Unknwon	4
SLC5A5	Thyroid hormonogenesis 1 defect	ORPHA:95716	1-9 / 100 000	10
TBL1X	Congenital hypothyroidism nongoitrous 8	ORPHA:442	1-5 / 10 000	1
TG	Thyroid hormonogenesis 3 defect	ORPHA:95716	1-9 / 100 000	26
THRA	Congenital hypothyroidism nongoitrous 6	ORPHA:566231	<1 / 1 000 000	8
TPO	Thyroid hormonogenesis 2A defect	ORPHA:95716	1-9 / 100 000	23
TRHR	Congenital hypothyroidism nongoitrous 7	ORPHA:99832	<1 / 1 000 000	4
TSHB	Congenital hypothyroidism nongoitrous 4	ORPHA:90674	1 / 4 000	4
TSHR	Congenital hypothyroidism nongoitrous 1	ORPHA:90673	Unknown	39

INMUNODEFICIENCIES

Genes	Name of disease	Orpha Code	Prevalence (Orphanet)	Omim Variants
ADA	Severe combined immunodeficiency due to adenosine deaminase deficiency	ORPHA:277	1-9 / 1 000 000	54
BTK	Agammaglobulinemia X-linked	ORPHA:47	1-9 / 1 000 000	148
CD3D	Severe Combined Immunodeficiency, Immunodeficiency 19	ORPHA:169160	1 / 58 000	3
CD3E	Severe Combined Immunodeficiency, Immunodeficiency 18	ORPHA:169160	1 / 58 000	7
CYBA	Chronic granulomatous disease	ORPHA:379	1-9 / 1 000 000	21
CYBB	Chronic granulomatous X-linked disease	ORPHA:379	1-9 / 1 000 000	91
CYBC1	Chronic granulomatous disease	ORPHA:379	1-9 / 1 000 000	2
DCLRE1C	Severe combined immunodeficiency Athabaskan	ORPHA:275	Unknown	31
DOCK8	Combined immunodeficiency due to DOCK8 deficiency	ORPHA:217390	<1 / 1 000 000	27
ELANE	Congenital cyclic neutropenia 1	ORPHA:2686	1-9 / 1 000 000	41
HAX1	Severe congenital neutropenia 3	ORPHA:99749	<1 / 1 000 000	15
IL2RG	Severe combined immunodeficiency X-linked	ORPHA:276	1-9 / 100 000	70
IL7R	Severe combined immunodeficiency due to IL-7Ralpha deficiency	ORPHA:169154	Unknown	25
JAK3	Severe Combined Immunodeficiency JAK3	ORPHA:35078	1 / 50 000	37
NCF1	Chronic granulomatous disease	ORPHA:379	1-9 / 1 000 000	10
NCF2	Chronic granulomatous disease	ORPHA:379	1-9 / 1 000 000	21
NCF4	Chronic granulomatous disease	ORPHA:379	1-9 / 1 000 000	7
RAG1	Severe combined immunodeficiency RAG-deficient	ORPHA:231154	<1 / 1 000 000	62
RAG2	Severe combined immunodeficiency B RAG-deficient	ORPHA:331206	1-9 / 100 000	43
RFX5	Bare lymphocyte syndrome II, complementation group C and E, Immunodeficiency by defective expression of MHC class I	ORPHA:572	Unknown	5
RFXANK	MHC class II deficiency, complementation group B	ORPHA:572	Unknown	8
RFXAP	Bare lymphocyte syndrome II, complementation group D	ORPHA:572	Unknown	3

INBORN ERRORS OF METABOLISM

Genes	Name of disease	Orpha Code	Prevalence (Orphanet)	Omim Variants
ABCD1	Adrenoleukodystrophy	ORPHA:139399	1 / 50 000	179
ABCD4	Methylmalonic aciduria and homocystinuria cb1J	ORPHA:26	1 / 37 000	5
ACADM	Medium chain Acyl-CoA dehydrogenase deficiency	ORPHA:42	1 - 9 / 100 000	135
ACADS	Short chain Acyl-CoA dehydrogenase deficiency	ORPHA:26792	1 / 50 000	55
ACADSB	2-methylbutyryl-CoA dehydrogenase deficiency, 2-methylbutyric aciduria	ORPHA:79157	<1 / 1 000 000	12
ACADVL	Very long chain Acyl-CoA dehydrogenase deficiency	ORPHA:26793	1-9 / 100 000	240
ACAD8	Isobutyryl-CoA dehydrogenase deficiency	ORPHA:79159	Unknown	17
ACAT1	Beta-ketothiolase deficiency	ORPHA:134	1 / 232 000	89
ACOX2	Congenital bile acid synthesis defect 6	ORPHA:485631	Unknown	1
ACSF3	Combined malonic and methylmalonic acidemia	ORPHA:289504	1 / 30 000	41
ADK	Hypermethioninemia due to adenosine kinase deficiency	ORPHA:289290	Unknown	6
AGA	Aspartylglucosaminuria	ORPHA:93	1 / 18 500	55
AGL	Glycogen storage disease III, Cori disease	ORPHA:366	1 / 100 000	194
AGXT	Primary hyperoxaluria 1	ORPHA:93598	1 / 58 000	180
AHCY	Hypermethioninemia with S-adenosylhomocysteine hydrolase deficiency	ORPHA:88618	<1 / 1 000 000	3
AKR1D1	Congenital bile acid synthesis defect 2	ORPHA:79303	Unknown	11
ALAD	Acute hepatic porphyria	ORPHA:100924	<1 / 1 000 000	4
ALDH4A1	Hyperprolinemia II	ORPHA:79101	1 / 700 000	5
ALDOB	Hereditary fructose intolerance	ORPHA:469	1-9 / 100 000	48

INBORN ERRORS OF METABOLISM

Genes	Name of disease	Orpha Code	Prevalence (Orphanet)	Omim Variants
ALPL	Hypophosphatasia	ORPHA:247623, ORPHA:247651, ORPHA:247676	1 / 300 000	115
AMACR	Congenital bile acid synthesis defect 4	ORPHA:79302	<1 / 1 000 000	2
AMT	Glycine encephalopathy	ORPHA:407	1-9 / 1 000 000	57
ARG1	Argininemia	ORPHA:90	<1 / 1 000 000	38
ARSA	Metachromatic leukodystrophy	ORPHA:512	1-9 / 1 000 000	157
ARSB	Mucopolysaccharidosis VI, Maroteaux-Lamy disease	ORPHA:583	1-9 / 1 000 000	130
ASL	Argininosuccinic aciduria	ORPHA:23	1-9 / 100 000	77
ASS1	Citrullinemia 1	ORPHA:247525	1-9 / 100 000	92
ATP7A	Menkes disease	ORPHA:565	1 / 35 000	122
ATP7B	Wilson disease	ORPHA:905	1-9 / 100 000	306
AUH	3-methylglutaconic aciduria 1	ORPHA:67046	<1 / 1 000 000	19
BCAT2	Hypervalinemia and hyperleucine-isoleucinemia	ORPHA:511	1-9 / 1 000 000	1
BCKDHA	Maple syrup urine Ia disease	ORPHA:268145, ORPHA:268162, ORPHA:268173, ORPHA:511, ORPHA:268184	1-9 / 1 000 000	70
BCKDHB	Maple syrup urine Ib disease	ORPHA:268145, ORPHA:268162, ORPHA:268173, ORPHA:511, ORPHA:268184	1-9 / 1 000 000	107
BTD	Biotinidase deficiency	ORPHA:79241	1-9 / 100 000	209
CBS	Classic homocystinuria	ORPHA:394	1-9 / 100 000	112
CD320	Methylmalonic aciduria due to transcobalamin receptor defect	ORPHA:280183	<1 / 1 000 000	1
CLPB	3-methylglutaconic aciduria 7	ORPHA:445038	<1 / 1 000 000	25
CPS1	Carbamoyl-phosphate synthetase 1 deficiency	ORPHA:147	1/1.300.000	92
CPT1A	Carnitine palmitoyl transferase 1a deficiency	ORPHA:156	<1 / 1 000 000	67
CPT2	Carnitine palmitoyl transferase 2 deficiency	ORPHA:228302, ORPHA:228308, ORPHA:228305	<1 / 1 000 000	94
CTH	Cystathioninuria	ORPHA:212	1-9 / 100 000	2
CTNS	Cystinosis	ORPHA:411629, ORPHA:411634	1 / 200 000	81
CYP27A1	Cerebrotendinous xanthomatosis	ORPHA:909	<5 / 100 000	88
DBT	Maple syrup urine disease	ORPHA:268145, ORPHA:268162, ORPHA:268173, ORPHA:511, ORPHA:268184	1-9 / 1 000 000	47
DNAJC12	Mild non-BH4-deficient hyperphenylalaninemia	ORPHA:508523	<1 / 1 000 000	11
ETFA	Glutaric Acidemia II, multiple acyl-CoA dehydrogenase deficiency	ORPHA:26791	1-9 / 1 000 000	15
ETFB	Glutaric Acidemia II, multiple acyl-CoA dehydrogenase deficiency	ORPHA:26791	1-9 / 1 000 000	6
ETFDH	Glutaric Acidemia II, multiple acyl-CoA dehydrogenase deficiency	ORPHA:26791	1-9 / 1 000 000	67
FAH	Tyrosinemia 1	ORPHA:882	1 / 120 000	77
FBP1	Fructose-1,6-bisphosphatase deficiency	ORPHA:348	1 / 147 575	28
FECH	Erytrhopoietic protoporphyria	ORPHA:79278	1-9 / 1 000 000	15
G6PC1	Glycogen storage Ia disease	ORPHA:79258	1 / 100 000	69
G6PD	Favism	ORPHA:466026	<1 / 1 000 000	44
GAA	Glycogen storage disease II, Pompe disease	ORPHA:308552	1 / 40 000	301
GALC	Krabbe disease	ORPHA:206448, ORPHA:206436, ORPHA:206443	1 / 100 000	144
GALE	Galactosemia due to galactose epimerase deficiency	ORPHA:352	1 / 60 000	14
GALK1	Galactosemia due to galactokinase deficiency	ORPHA:79237	<1 / 100 000	22
GALM	Galactosemia due to mutarotase deficiency, galactosemia IV	ORPHA:570422	Unknown	31
GALNS	Mucopolysaccharidosis IVA, Morquio A syndrome	ORPHA:309297	1-5 / 10 000	82
GALT	Classic galactosemia, galactosemia I	ORPHA:79239	1 / 60 000	269
GAMT	Cerebral creatine deficiency 2 syndrome	ORPHA:382	<1 / 1 000 000	38
GATM	Cerebral creatine deficiency 3 syndrome	ORPHA:35704	<1 / 1 000 000	12
GBA	Gaucher disease	ORPHA:85212, ORPHA:77259, ORPHA:77260, ORPHA:77261, ORPHA:2072	1-9 / 100 000	125
GCDH	Glutaric acidemia I	ORPHA:25	1 / 100 000	142
GLA	Fabry disease	ORPHA:324	1 / 60 000	312
GLB1	GM1-gangliosidosis 1, Morquio B syndrome	ORPHA:79255	1 / 1 000 000	119
GLUD1	Hyperinsulinemic hypoglycemia 6, hyperinsulinism-hyperammonemia syndrome	ORPHA:35878	Unknown	11
GNMT	Hypermethioninemia due to glycine N-methyltransferase deficiency	ORPHA:289891	Unknown	3
GNS	Mucopolysaccharidosis IIID, Sanfilippo D	ORPHA:79272	1 / 250 000	12
GRHPR	Primary hyperoxaluria 2	ORPHA:93599	<1 / 1 000 000	65
GSS	Glutathione synthetase deficiency	ORPHA:32	<1 / 1 000 000	12
GUSB	Mucopolysaccharidosis 7, Sly syndrome	ORPHA:584	<1 / 1 000 000	36
GYS2	Glycogen storage disease 0	ORPHA:2089	<1 / 1 000 000	14
HADH	Hyperinsulinemic hypoglycemia 4	ORPHA:71212	<1 / 1 000 000	9
HADHA	Long-chain 3-hydroxyacyl-Coa dehydrogenase (subunit A) deficiency	ORPHA:5	1-9 / 100 000	79
HADHB	Long-chain 3-hydroxyacyl-Coa dehydrogenase (subunit B) deficiency	ORPHA:746	1-9 / 100 000	27
HEXA	Tay-Sachs disease	ORPHA:845	1 / 320 000	145
HCFC1	Methylmalonic acidemia and homocysteinemia cblX	ORPHA:369962	<1 / 1 000 000	4
HGD	Alkaptonuria	ORPHA:56	1-9 / 1 000 000	57
HGSNAT	Mucopolysaccharidosis IIIC, Sanfilippo C	ORPHA:581	1-9 / 1 000 000	62
HLCS	Holocarboxylase synthetase deficiency	ORPHA:79242	1 / 200 000	38
HMGCL	3-hydroxy-3-methylglutaric aciduria	ORPHA:20	1 / 125 000	31
HOGA1	Primary hyperoxaluria 3	ORPHA:93600	<1 / 1 000 000	42
HPD	Tyrosinemia 3	ORPHA:69723	<1 / 1 000 000	9
HSD3B7	Congenital bile acid synthesis defect 1	ORPHA:79301	1-9 / 1 000 000	11

INBORN ERRORS OF METABOLISM

Genes	Name of disease	Orpha Code	Prevalence (Orphanet)	Omim Variants
HSD17B10	2-methyl-3-hydroxybutyric aciduria	ORPHA:391457, ORPHA:391428, ORPHA:85295	<1 / 1 000 000	13
IDS	Mucopolysaccharidosis II, Hunter disease	ORPHA:217093, ORPHA:217085	1 / 166 000	108
IDUA	Mucopolysaccharidosis I, Hurler syndrome, Hurler-Scheie syndrome, Scheie syndrome	ORPHA:93476, ORPHA:93473, ORPHA:93474	1-9 / 1 000 000	133
IVD	Isovaleric acidemia	ORPHA:33	1-9 / 100 000	74
LIPA	Lysosomal acid lipase deficiency, Wolman disease	ORPHA:75233	Unknown	74
LMBRD1	Methylmalonic aciduria and homocystinuria cblF	ORPHA:79284	<1 / 1 000 000	4
MAN2B1	Alpha-mannosidosis	ORPHA:61	1-9 / 1 000 000	106
MAT1A	Methionine adenosyltransferase deficiency	ORPHA:168598	<1 / 1 000 000	23
MCCC1	3-methylcrotonyl-CoA carboxylase 1 deficiency	ORPHA:6	1-9 / 100 000	63
MCCC2	3-methylcrotonyl-CoA carboxylase 2 deficiency	ORPHA:6	1-9 / 100 000	49
MCEE	Methylmalonic acidemia due to methylmalonyl-CoA epimerase deficiency	ORPHA:308425	<1 / 1 000 000	2
MLYCD	Malonyl-CoA decarboxylase deficiency, malonic aciduria	ORPHA:943	<1 / 1 000 000	10
MMAA	Methylmalonic acidemia cblA	ORPHA:28	Unknown	64
MMAB	Methylmalonic acidemia cblB	ORPHA:79311	Unknown	36
MMACHC	Methylmalonic aciduria and homocystinuria cblC	ORPHA:79282	Unknown	76
MMADHC	Methylmalonic aciduria and homocystinuria cblD	ORPHA:79283	<1 / 1 000 000	22
MMUT	Methylmalonic acidemia due to methylmalonyl-CoA mutase deficiency	ORPHA:79312, ORPHA:289916	Unknown	206
MTHFR	Homocystinuria due to methylenete trahydrofolatereductase deficiency	ORPHA:395	Unknown	73
MTR	Homocystinuria-megaloblastic anemia due to defect in cobalamin metabolism cbIG	ORPHA:2170	<1 / 1 000 000	20
MTRR	Homocystinuria-megaloblastic anemia due to defect in cobalamin metabolism cblE	ORPHA:2169	<1 / 1 000 000	23
MVK	Mevalonic aciduria	ORPHA:29	<1 / 1 000 000	42
NAGLU	Mucopolysaccharidosis IIIA, Sanfilippo B syndrome	ORPHA:79270	1-9 / 1 000 000	89
NAGS	Hyperammonemia due to N-acetylglutamate synthase deficiency	ORPHA:927	<1 / 1 000 000	24
NPC1	Niemann-Pick C disease	ORPHA:646	1-9 / 100 000	218
NPC2	Niemann-Pick C disease	ORPHA:646	1-9 / 100 000	23
OAT	Ornithine aminotransferase deficiency	ORPHA:414	1 / 50 000	73
OPA3	3-methylglutaconic aciduria 3	ORPHA:67047	1 / 10 000	14
OTC	Ornithine transcarbamylase deficiency	ORPHA:664	1-9 / 100 000	356
PAH	Phenylketonuria	ORPHA:2209	1 / 10 000	477
PCBD1	Pterin-4-alpha-carbinolamine dehydratase deficiency	ORPHA:1578	Unknown	6
PCCA	Propionic acidemia	ORPHA:35	1-9 / 1 000 000	108
PCCB	Propionic acidemia	ORPHA:35	1-9 / 1 000 000	98
PPM1K	Maple syrup urine disease	ORPHA:268162	1-9 / 1 000 000	1
PRDX1	Methylmalonic aciduria and homocystinuria cblC	ORPHA:26	1 / 67 000	2
PRODH	Hyperprolinemia 1	ORPHA:419	1 / 700 000	2
PYGL	Glycogen storage disease VI	ORPHA:369	1 / 85 000	23
SGSH	Mucopolysaccharidosis IIIA, Sanfilippo A syndrome	ORPHA:79269	1-9 / 1 000 000	75
SLC22A5	Systemic primary carnitine deficiency	ORPHA:158	1 / 100 000	132
SLC25A13	Citrullinemia 2	ORPHA:247585	1 / 57 000	44
SLC25A15	Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome	ORPHA:415	<1 / 1 000 000	31
SLC25A20	Carnitine-acylcarnitine translocase deficiency	ORPHA:159	<1 / 1 000 000	18
SLC37A4	Glycogen storage disease IB and IC	ORPHA:79259	1 / 100 000	70
SLC3A1	Cystinuria	ORPHA:163690	<1 / 1 000 000	34
SLC6A8	Cerebral creatine deficiency syndrome 1	ORPHA:52503	Unknown	47
SLC7A7	Lysinuric protein intolerance	ORPHA:470	1 / 60 000	52
SLC7A9	Cystinuria	ORPHA:214	1-5 / 10 000	29
SMPD1	Niemann-Pick A and B disease	ORPHA:77292, ORPHA:77293	1-9 / 1 000 000	146
SPR	Dystonia dopa-responsive due to sepiapterin reductase deficiency	ORPHA:70594	<1 / 1 000 000	16
TAT	Tyrosinemia 2	ORPHA:28378	<1 / 1 000 000	22
TCN2	Transcobalamin II deficiency	ORPHA:859	<1 / 1 000 000	18
THAP11	Methylmalonic Acidemia and Homocysteinemia cblX	ORPHA:369962	<1 / 1 000 000	1
TIMM50	3-methylglutaconic aciduria 9	ORPHA:505216	<1 / 1 000 000	7
TPP1	Neuronal ceroid lipofuscinosis 2	ORPHA:79264	1-2 / 9 000 000	94
UGT1A1	Crigler-Najjar syndrome 1 and 2	ORPHA:79234, ORPHA:79235	1 / 1 000 000	30

GENETIC HEARING LOSS

Genes	Name of disease	Orpha Code	Prevalence (Orphanet)	Omim Variants
CDH23	Usher 1D syndrome	ORPHA:231169	1-9 / 100 000	180
GJB2	Autosomal recessive 1A deafness	ORPHA:90635	1 / 1000	155
GJB6	Autosomal recessive 1B deafness	ORPHA:90636	1 / 1000	10
MYO7A	Usher syndrome 1b	ORPHA:231169	1-9 / 100 000	343
TMIE	Deafness 6	ORPHA:90636	Unknown	8
TMPRSS3	Deafness 8 and 10	ORPHA:90636	Unknown	27
TPRN	Autosomal recessive deafness 79	ORPHA:90636	Unknown	6
TRIOBP	Autosomal recessive deafness 28	ORPHA:90636	Unknown	31
USH1C	Autosomal recessive deafness 18a, Usher syndrome 1c	ORPHA:231169	1-9 / 100 000	64
USH1G	Usher syndrome 1g	ORPHA:231169	1-9 / 100 000	16
USH2A	Retinitis pigmentosa 39, Usher syndrome 2a	ORPHA:231178, ORPHA:791	1-5 / 10 000	697
WHRN	Autosomal recessive deafness 31, Usher syndrome 2d	ORPHA:231178	1-9 / 100 000	17

OTHER GROUPS				
Genes	Name of disease	Orpha Code	Prevalence (Orphanet)	Omim Variants
ALDH7A1	Pyridoxine-dependent epilepsy	ORPHA:3006	1 / 783 000	68
AQP2	Nephrogenic diabetes insipidus 2	ORPHA:223	1-9 / 1 000 000	31
AVPR2	Nephrogenic diabetes insipidus 1	ORPHA:223	1-9 / 1 000 000	47
CFTR	Cystic fibrosis	ORPHA:586	1-9 / 100 000	831
DMD**	Duchenne muscular dystrophy	ORPHA:98896	1-9 / 100 000	964
F8	Hemophilia A	ORPHA:169802, ORPHA:169805	1-9 / 100 000	754
F9	Hemophilia B	ORPHA:98879	1-9 / 100 000	137
FGFR3	Achondroplasia	ORPHA:15	1-9 / 100 000	53
GCH1	Autosomal dominant and recessive GTP cyclohydrolase I	ORPHA:98808	1-9 / 1 000 000	55
HBB	Sickle cell anemia	ORPHA:232	1-5 / 10 000	296
JAG1	Alagille syndrome	ORPHA:52	1 / 70 000	202
KCNQ2	Benign familial neonatal epilepsy	ORPHA:1949	Unknown	420
NLRP3	Cryopyrin-associated periodic syndrome	ORPHA:1451	1 / 360 000	30
PHEX	X-linked hypophosphatemic rickets	ORPHA:89936	1-9 / 1 000 000	385
PIGA	Paroxysmal nocturnal hemoglobinuria	ORPHA:447	1-9 / 100 000	29
PNPO	Pyridoxamine 5-prime-phosphate oxidase deficiency	ORPHA:79096	1-9 / 1 000 000	19
PROSC	Epilepsy vitamin B6-dependent	ORPHA:3006	1/783.000	7
PTS	6-pyruvoyl-tetrahydropterin synthase deficiency	ORPHA:13	Unknown	40
QDPR	Q-dihydropteridine reductase deficiency	ORPHA:226	Unknown	15
RPE65	RPE65-associated retinal dystrophy	ORPHA:364055	Unknown	98
SERPING1	Hereditary angioedema 1 and 2	ORPHA:100050	1-9 / 100 000	68
SCN1A	Developmental and epileptic encephalopathy 6, Dravet syndrome	ORPHA:33069	<1 / 40 000	1031
SLC2A1	GLUT1 deficiency syndrome 1, Paroxysmal exertion-induced dyskinesia	ORPHA:98811	<1 / 1 000 000	151
SLC34A3	Hypophosphatemic rickets with hypercalciuria	ORPHA:157215	<1 / 1 000 000	22
SLC39A4	Acrodermatitis enteropathica	ORPHA:37	1 / 500 000	14
SMN1***	Spinal muscular atrophy I, II, III and IV	ORPHA:83330, ORPHA:83418, ORPHA:83419, ORPHA:83420	1 / 100 000	0
TSC1	Tuberous sclerosis complex 1	ORPHA:805	1 / 25 000	280
TSC2	Tuberous sclerosis complex 2	ORPHA:805	1 / 25 000	564
TTPA	Ataxia with isolated vitamin E deficiency	ORPHA:96	1-9 / 1 000 000	33
TTR	Hereditary amyloidosis transthyretin-related	ORPHA:85447	1 / 1 000 000	76
VDR	Vitamin D-dependent rickets 2	ORPHA:93160	Unknown	19
TH	Autosomal recessive Segawa syndrome, autosomal recessive DOPA-responsive dystonia	ORPHA:101150	1-9 / 1 000 000	51

* **CYP21A2** - Frequent disease-causing variants of the CYP21A2 gene by mini-sequencing. Additionally, 20-30% of clinical cases present with large deletions/duplications of this gene. For this reason, a comprehensive study of these variants by qPCR is included in the analysis.

** **DMD** - Only 20-35% of reported cases can be detected by NGS. Large deletions/duplications are responsible of the 65-80% remaining clinical cases. For this reason, an MLPA analysis is included within this test.

*** **SMN1** - The main disease-causing mutation of SMA (around 96% of clinical cases) is the presence of large biallelic deletions in the SMN1 gene. In order to detect these variants, qPCR testing is included in this test.