Solving patients with rare diseases through programmatic reanalysis of genome-phenome data

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gene	genotype	variant type	transcript	HGVS:cDNA	HGVS:protein	ERN	patient_hpos	omim_inheritance	Family_inheritance	Disease description year	ClinVar Variation ID	year_variant
ABCC9	0/1	missense_variant	NM_005691.3	c.1703C>T	p.Pro568Leu	ITHACA	Ureteral duplication//Macroglossia//Gingival fibromatosis//High palate//Coarse facial features//Epicanthus//Mandibular prognathia//Strabismus//Upslanted palpebral fissure//Delayed speech and language development//Edema//Hypertrichosis//Joint stiffness//Cardiomegaly//Patent ductus arteriosus//Hepatomegaly//Limb hypertonia//Spastic tetraplegia//Finger joint hypermobility//Infantile axial hypotonia	Hypertrichotic osteochondrodysplasia, 239850 (3), Autosomal dominant	dominant	Grange et al. (2006)	666318	Jan 1, 2014
ABCD1	1/1	missense_variant	NM_000033.4	c.565C>T	p.Arg189Trp	RND	Gaze-evoked nystagmus//Dysmetric saccades//Spasticity//Lower limb spasticity//Gait ataxia//Hyperactive deep tendon reflexes	Adrenoleukodystrophy, 300100 (3), X-linked recessive	X-linked	Mosser et al. (1993)	430349	Jul 06, 2018
ACTA1	0/1	missense_variant	NM_001100.4	c.1000C>T	p.Pro334Ser	NMD	High palate//Hypomimic face//Ptosis//Asymmetry of the thorax//Nasal speech//Scoliosis//Nocturnal hypoventilation//Myopathy//Increased muscle fatiguability//Abnormality of muscle fibers	Myopathy, congenital, with fiber-type disproportion 1, 255310 (3), Autosomal recessive, Autosomal dominant	dominant	Laing et al. (2004)	18291	Nov 01, 2004
AHDC1	0/1	frameshift_variant	NM_001029882.3	c.1402dupT	p.Cys468fs	ITHACA	Wide mouth//Thick lower lip vermilion//Macrocephaly//Long face//Coarse facial features//Epicanthus//Facial asymmetry//Abnormality of the pinna//Wide nose//Strabismus//Deeply set eye//Visual impairment//Ptosis//Proptosis//Widely spaced teeth//Delayed speech and language development//Abnormality of the thorax//Numerous nevi//Prominent fingertip pads//Intellectual disability//Muscular hypotonia//Motor delay//Abnormal facial shape//Hypoplasia of the corpus callosum//Drooling//Abnormality of calvarial	Xia-Gibbs syndrome, 615829 (3), Autosomal dominant	dominant	Xia et al. (2014)	224806	Sep 9, 2015
ANKRD11	0/1	frameshift_variant	NM_001256182.2	c.977delG	p.Gly326fs	ITHACA	Long face//Retrognathia//Hearing impairment//Myopia//Autistic behavior//Anxiety//Dysmetria//Abnormality of the voice//Abnormality of extrapyramidal motor function//Intellectual disability, moderate//High, narrow palate//Incisor macrodontia	KBG syndrome, 148050 (3), Autosomal dominant	dominant	Tekin et al. (2004)	545436	Mar 01, 2017
ANO10	1/1	frameshift_variant	NM_001346464.1	c.132dupA	p.Asp45fs	NMD	Ataxia	Spinocerebellar ataxia, autosomal recessive 10, 613728 (3), Autosomal recessive	recessive	Vermeer et al. (2010)	162016	Nov 01, 2014
ARID1B	0/1	stop_gained	NM_001371656.1	c.5653C>T	p.Arg1885*	ITHACA	Self-mutilation//Motor delay//Muscle weakness//Weight loss//Frequent falls//Short stature//Knee flexion contracture	Coffin-Siris syndrome 1, 135900 (3), Autosomal dominant	dominant	Hoyer et al. (2012)	210302	Jun 25, 2014
ASXL3	0/1	frameshift_variant	NM_030632.3	c.4219_4220delCT	p.Leu1407fs	ITHACA	Synophrys//Behavioral abnormality//Autism//Stereotypy//Intellectual disability//Seizures//Global developmental delay//Abnormal facial shape//Generalized seizures//Abnormal aggressive, impulsive or violent behavior//Repetitive compulsive behavior	Bainbridge-Ropers syndrome, 615485 (3), Autosomal dominant	dominant	Bainbridge et al. (2013)	524030	Mar 26, 2018
ATM	1/1	frameshift_variant	NM_000051.3	c.3894dupT	p.Ala1299fs	ITHACA	Cryptorchidism//Triangular face//Telangiectasia//Intellectual disability//Ataxia//Global developmental delay//Abnormality of the tricuspid valve//Asthma//Abnormality of the vertebrae//Oral-pharyngeal dysphagia	Ataxia-telangiectasia, 208900 (3), Autosomal recessive; {Breast cancer, susceptibility to}, 114480 (3), Autosomal dominant; Lymphoma, B-cell non-Hodgkin, somatic (3); Lymphoma, mantle cell, somatic (3); T-cell prolymphocytic leukemia, somatic (3)	recessive	Savitsky et al. (1995)	141534	Jun 27, 2017
ATP13A2	1/1	stop_gained	NM_022089.4	c.364C>T	p.Gln122*	RND	Cerebellar atrophy//Progressive cerebellar ataxia//Cerebral cortical atrophy//Progressive spastic paraparesis//Peripheral neuropathy	Kufor-Rakeb syndrome, 606693 (3), Autosomal recessive; Spastic paraplegia 78, autosomal recessive, 617225 (3), Autosomal recessive	recessive	Kara et al. (2016)	374889	Feb 01, 2017
AUTS2	0/1	stop_gained	NM_015570.4	c.901C>T	p.Gln301*	ITHACA	Open mouth//Short philtrum//Low-set ears//Autism//Abnormal facial shape//Prominent nasal tip//Intellectual disability, severe//Thick vermilion border//Self-injurious behavior	None	dominant	Beunders et al. (2013)	666574	Feb 15, 2019
B4GALNT1	1/1	missense_variant	NM_001478.5	c.1298A>C	p.Asp433Ala	RND	Psychosis//Intellectual disability//Spasticity//Dysarthria//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	Spastic paraplegia 26, autosomal recessive, 609195 (3), Autosomal recessive	recessive	Boukhris et al. (2013)	60527	Jul 11, 2013
CACNA1E	0/1	missense_variant&splice_region_variant	NM_001205293.3	c.1054G>A	p.Gly352Arg	ITHACA	Thin upper lip vermilion//Hypertelorism//Long philtrum//Bulbous nose//Anteverted nares//Strabismus//Global developmental delay//Dystonia//Large for gestational age//Morphological abnormality of the pyramidal tract//Depressed nasal bridge//Infantile axial hypotonia//Intellectual disability, severe	EPILEPTIC ENCEPHALOPATHY, EARLY INFANTILE, 69; Autosomal dominant	dominant	Helbig et al. (2018)	265066	Nov 28, 2016

CASQ1	0/1	missense_variant	NM_001231.5	c.731A>G	p.Asp244Gly	NMD	Muscle weakness//Elevated serum creatine phosphokinase//Muscular dystrophy//Limb muscle weakness//Abnormality of muscle morphology	Myopathy, vacuolar, with CASQ1 aggregates, 616231 (3), Autosomal dominant	dominant	Rossi et al. (2014)	183021	Oct 1, 2014
RS1	0/1	missense_variant	NM_000330.4	c.637C>T	p.Arg213Trp	ITHACA	High palate//Microcephaly//Aggressive behavior//Intellectual disability//Global developmental delay//Motor delay//Developmental regression	312700 RETINOSCHISIS 1, X-LINKED, JUVENILE; RS1	X-linked	Sauer et al. (1997)	99009	Dec 20, 2018
CHD3	0/1	missense_variant	NM_001005271.3	c.2922G>T	p.Leu974Phe	ITHACA	Abnormality of the outer ear//Low-set, posteriorly rotated ears//Conductive hearing impairment//Strabismus//Visual impairment//Blepharophimosis//Behavioral abnormality//Delayed speech and language development//Intellectual disability, mild//Global developmental delay//Generalized hypotonia//Abnormal facial shape//Delayed gross motor development//Delayed fine motor development//Prominent forehead//Broad thumb	SNIJDERS BLOK-CAMPEAU SYNDROME; SNIBCPS, autosomal dominant	dominant	Eising et al. (2019)	549730	May 03, 2018
CIC	0/1	missense_variant	NM_001304815.1	c.3370C>T	p.Arg1124Trp	ITHACA	Thin vermilion border//Broad face//Short philtrum//Delayed speech and language development//Global developmental delay//Motor delay//Plagiocephaly//Hyperconvex nail//Clinodactyly of the 5th toe//Intellectual disability, borderline//Clinodactyly of the 3rd toe//Prominent ear helix//Prominent digit pad//Broad chin//Clinodactyly of the 4th toe//Anteverted ears	Mental retardation, autosomal dominant 45, 617600 (3), Autosomal dominant	dominant	Lu et al. (2017)	635170	May 21, 2019
CLN5	1/1	missense_variant	NM_006493.4	c.625T>G	p.Tyr209Asp	RND	Blindness//Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive extrapyramidal movement disorder//Progressive spastic paraparesis	Ceroid lipofuscinosis, neuronal, 5, 256731 (3), Autosomal recessive	recessive	Savukoski et al. (1998)	56545	May 19, 2013
COL6A1	0/1	splice_acceptor_variant&intron_variant	NM_001848.3	c.958-2A>G		NMD	Areflexia//Delayed gross motor development//Distal muscle weakness//Hip dislocation//Elbow flexion contracture//Skeletal muscle atrophy//Progressive muscle weakness//EMG abnormality//EMG: myopathic abnormalities//Proximal muscle weakness	Bethlem myopathy 1, 158810 (3), Autosomal recessive, Autosomal dominant; Ullrich congenital muscular dystrophy 1, 254090 (3), Autosomal recessive, Autosomal dominant	dominant	Jobsis et al. (1996)	542991	Jun 25, 2019
CSF1R	1/1	intron_variant	NM_001288705.2	c.1969+115_1969+116delAG		RND	Open mouth//High palate//Long face//Low-set ears//Spasticity//Spastic gait//Lower limb hyperreflexia//Spastic tetraplegia//Babinski sign//Hemiplegia/hemiparesis//Biconcave vertebral bodies//CNS demyelination//Periventricular white matter hyperdensities//Arachnoid cyst	Leukoencephalopathy, diffuse hereditary, with spheroids, 221820 (3), Autosomal dominant	recessive	Guo et al. (2019)	635123	Jun 21, 2019
CSNK2A1	0/1	start_lost	NM_001362770.2	c.1A>G	p.Met1?	ITHACA	Retrognathia//Epicanthus//Low-set ears//Abnormality of the nasal bridge//Delayed speech and language development//Motor delay//Plagiocephaly//Hip dysplasia	Okur-Chung neurodevelopmental syndrome, 617062 (3), Autosomal dominant	dominant	Okur et al. (2016)	619015	Feb 19, 2019
CTNNB1	0/1	frameshift_variant	NM_001098209.2	c.2273delA	p.His758fs	ITHACA	Strabismus//Hypotelorism//Jaundice//Spasticity//Spastic paraplegia//Generalized hypotonia//Specific learning disability//Scoliosis//Moderate global developmental delay	Colorectal cancer, somatic, 114500 (3); Exudative vitreoretinopathy 7, 617572 (3), Autosomal dominant; Hepatocellular carcinoma, somatic, 114550 (3); Medulloblastoma, somatic, 155255 (3); Mental retardation, autosomal dominant 19, 615075 (3), Autosomal dominant; Ovarian cancer, somatic, 167000 (3); Pilomatricoma, somatic, 132600 (3)	dominant	de Ligt et al. (2012)	666287	Jan 1, 2014
CUL4B	1/1	stop_gained	NM_003588.3	c.1450C>T	p.Arg484*	ITHACA	Inguinal hernia//Abnormality of the lip//Hydrocephalus//Epicanthus//Smooth philtrum//Plagiocephaly//Gait ataxia//Asthma//Language impairment//Calf muscle hypoplasia//Unilateral strabismus//Moderate global developmental delay//Delayed myelination//Short ear	Mental retardation, X-linked, syndromic 15 (Cabezas type), 300354 (3), X-linked recessive	X-linked	Tarpey et al. (2007)	426723	Apr 01, 2017
CUL4B	1/1	frameshift_variant	NM_003588.3	c.1007_1011delTTATA	p.Ile336fs	ITHACA	Micropenis//Hearing impairment//Agitation//Heterochromia iridis//Seizures//Global developmental delay//Neonatal hypotonia//Ventriculomegaly//Cutaneous syndactyly//Neurodevelopmental delay	Mental retardation, X-linked, syndromic 15 (Cabezas type), 300354 (3), X-linked recessive	X-linked	Tarpey et al. (2007)	666344	Jan 1, 2014
CUX1	0/1	stop_gained	NM_001202543.2	c.2617C>T	p.Gln873*	ITHACA	Recurrent urinary tract infections//Inguinal hernia//Brachycephaly//Delayed speech and language development//Intellectual disability//Muscular hypotonia//Motor delay//Muscle weakness//Joint hypermobility//Pes planus//Frontal bossing//Recurrent infections//Easy fatigability	None	dominant	Platzer et al. (2018)	618991	Aug 31, 2018

DDHD2	1/1	stop_gained	NM_001164232.1	c.859C>T	p.Arg287*	RND	Intellectual disability//Spasticity//Spastic tetraparesis//Lower limb spasticity//Spastic gait//Hypoplasia of the corpus callosum//Babinski sign//Progressive spastic paraparesis	Spastic paraplegia 54, autosomal recessive, 615033 (3), Autosomal recessive	recessive	Schuurs-Hoeijmakers et al. (2012)	39681	Jan 31, 2014
DDX3X	0/1	frameshift_variant	NM_001356.4	c.1563dupT	p.Ile522fs	ITHACA	Epicanthus//Microdontia//Diastema//Agitation//Aggressive behavior//Stereotypy//Inappropriate laughter//Delayed speech and language development//Pschomotor retardation	Mental retardation, X-linked 102, 300958 (3), X-linked recessive, X-linked dominant	dominant	Snijders Blok et al. (2015)	666561	Jun 5, 2018
DMD	0/1	splice_donor_variant&intron_variant	NM_004006.2	c.3603+2T>A		NMD	Multiple mitochondrial DNA deletions	Becker muscular dystrophy, 300376 (3), X-linked recessive; Cardiomyopathy, dilated, 3B, 302045 (3), X-linked; Duchenne muscular dystrophy, 310200 (3), X-linked recessive	X-linked	Tuffery-Giraud et al. (2009)	94598	Aug 22, 2016
DNM2	0/1	missense_variant	NM_001005360.2	c.1102G>A	p.Glu368Lys	NMD	Ptosis//Scoliosis//Myopathy	Centronuclear myopathy 1, 160150 (3), Autosomal dominant; Charcot-Marie-Tooth disease, axonal type 2M, 606482 (3), Autosomal dominant; Charcot-Marie-Tooth disease, dominant intermediate B, 606482 (3), Autosomal dominant; Lethal congenital contracture syndrome 5, 615368 (3), Autosomal recessive	dominant	Bitoun et al. (2005)	7282	Nov 01, 2006
DOK7	0/1	frameshift_variant	NM_001301071.2	c.1124_1127dupTGCC	p.Ala378fs	NMD	Myopathy	?Fetal akinesia deformation sequence, 208150 (3), Autosomal recessive; Myasthenic syndrome, congenital, 10, 254300 (3), Autosomal recessive	recessive	Beeson et al. (2006)	1273	Jul 01, 2008
DOK7	0/1	frameshift_variant	NM_001301071.2	c.1263dupC	p.Ser422fs	NMD	Myopathy	?Fetal akinesia deformation sequence, 208150 (3), Autosomal recessive; Myasthenic syndrome, congenital, 10, 254300 (3), Autosomal recessive	recessive	Beeson et al. (2006)	1274	Jul 01, 2008
DYRK1A	0/1	missense_variant	NM_001396.4	c.1763C>A	p.Thr588Asn	ITHACA	Movement abnormality of the tongue//Microcephaly//Abnormality of the face//Low anterior hairline//Short philtrum//Hypotelorism//Abnormality of dental enamel//Self-mutilation//Delayed speech and language development//Large hands//Intellectual disability//Seizures//Global developmental delay//Encephalopathy//Widely-spaced maxillary central incisors//Truncal obesity//Action tremor//Low hanging columella//Thickened ears//Stereotypical hand wringing//Stereotypical body rocking//Phonic tics//Long fingers	Mental retardation, autosomal dominant 7, 614104 (3), Autosomal dominant	dominant	van Bon et al. (2011)	162160	Jan 1, 2014
DYSF	1/1	missense_variant	NM_001130987.2	c.3167G>A	p.Arg1056Gln	NMD	Not available	Miyoshi muscular dystrophy 1, 254130 (3), Autosomal recessive; Muscular dystrophy, limb-girdle, type 2B, 253601 (3), Autosomal recessive; Myopathy, distal, with anterior tibial onset, 606768 (3), Autosomal recessive	recessive	Bashir et al. (1998)	242418	Apr 28, 2017
EEF1A2	0/1	missense_variant	NM_001958.4	c.271G>A	p.Asp91Asn	ITHACA	Macrocephaly//Retrognathia//High forehead//Macrotia//Anteverted nares//Abnormality of eye movement//Autism//Stereotypy//Short attention span//Delayed speech and language development//Poor eye contact//Abnormality of the thumb//Large hands//Seizures//Motor delay//Hypertonia//Gait disturbance//Hip dysplasia//Sleep disturbance//Intellectual disability, severe//Incisor macrodontia	Epileptic encephalopathy, early infantile, 33, 616409 (3), Autosomal dominant; Mental retardation, autosomal dominant 38, 616393 (3), Autosomal	dominant	Nakajima et al. (2015)	279803	Oct 13, 2016

EIF2B2	0/1	missense_variant	NM_014239.4	c.638A>G	p.Glu213Gly	RND	Dysarthria//Gait disturbance	Leukoencephalopathy with vanishing white matter, 603896 (3), Autosomal recessive; Ovarioleukodystrophy, 603896 (3), Autosomal recessive	recessive	Leegwater et al. (2001)	4336	Jun 01, 2003
EXOSC3	1/1	missense_variant	NM_016042.4	c.395A>C	p.Asp132Ala	NMD	Pontocerebellar atrophy	Pontocerebellar hypoplasia, type 1B, 614678 (3), Autosomal recessive	recessive	Wan et al. (2012)	31691	Dec 01, 2013
EXOSC3	1/1	missense_variant	NM_016042.4	c.92G>C	p.Gly31Ala	RND	Hypertelorism//Ophthalmoparesis//Nystagmus//Eczema//Muscular hypotonia//Dysarthria//Cerebellar atrophy//Lower limb spasticity//Limb ataxia//Progressive cerebellar ataxia//Truncal ataxia//Recurrent respiratory infections//Tetraparesis//Drooling//Psychomotor deterioration//Lower limb hyperreflexia//Thoracic scoliosis//Babinski sign//Progressive pulmonary function impairment//Cerebellar vermis atrophy//Lower limb hypertonia//Postnatal growth retardation//Seasonal allergy//Pschomotor retardation	Pontocerebellar hypoplasia, type 1B, 614678 (3), Autosomal recessive	recessive	Wan et al. (2012)	31688	Nov 01, 2013
FBXL4	1/1	frameshift_variant	NM_001278716.2	c.1648_1649delGA	p.Asp550fs	NMD	Not available	Mitochondrial DNA depletion syndrome 13 (encephalomyopathic type), 615471 (3), Autosomal recessive	recessive	Bonnen et al. (2013)	437499	Aug 10, 2017
FBXL4	1/1	stop_gained	NM_001278716.2	c.292C>T	p.Arg98*	NMD	Not available	Mitochondrial DNA depletion syndrome 13 (encephalomyopathic type), 615471 (3), Autosomal recessive	recessive	Bonnen et al. (2013)	437490	Aug 10, 2017
FGFR2	0/1	missense_variant	NM_022970.3	c.1945G>A	p.Ala649Thr	ITHACA	Hypertelorism//Sparse and thin eyebrow//Abnormality of the ear//Hypoplasia of teeth//Specific learning disability//Hyperconvex nail//Bronchiectasis//Sparse scalp hair//Scoliosis//2-3 toe syndactyly//Proximal placement of thumb//Symphalangism of the thumb//Low hanging columella//Cartilage destruction//Long fingers	Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis, 207410 (3), Autosomal dominant; Apert syndrome, 101200 (3), Autosomal dominant; Beare-Stevenson cutis gyrata syndrome, 123790 (3), Autosomal dominant; Bent bone dysplasia syndrome, 614592 (3), Autosomal dominant; Craniofacial-skeletal-dermatologic dysplasia, 101600 (3), Autosomal dominant; Craniosynostosis, nonspecific (3); Crouzon syndrome, 123500 (3), Autosomal dominant; Gastric cancer, somatic, 613659 (3); Jackson-Weiss syndrome, 123150 (3), Autosomal dominant; LADD syndrome, 149730 (3), Autosomal dominant; Pfeiffer syndrome, 101600 (3), Autosomal dominant; Saethre-Chotzen syndrome, 101400 (3), Autosomal dominant; Scaphocephaly and Axenfeld-Rieger anomaly (3); Scaphocephaly, maxillary retrusion, and mental retardation, 609579 (3)	dominant	Chun et al. (1998)	13296	Apr 01, 2006
FKBP14	1/1	frameshift_variant	NM_017946.4	c.362dupC	p.Glu122fs	ITHACA	Retrognathia//Arachnodactyly//Delayed gross motor development//Scoliosis//High, narrow palate//Abnormality of the fibula//Short stature//Pes valgus//Microtia//Infantile axial hypotonia//Short metatarsal//Unilateral strabismus//Severe Myopia	Ehlers-Danlos syndrome, kyphoscoliotic type, 2, 614557 (3), Autosomal recessive	recessive	Baumann et al. (2012)	279809	Feb 10, 2012

FLNA	1/1	missense_variant	NM_001110556.2	c.4660G>A	p.Gly1554Arg	ITHACA	Cryptorchidism//Triangular face//Telangiectasia//Intellectual disability//Ataxia//Global developmental delay//Abnormality of the tricuspid valve//Asthma//Abnormality of the vertebrae//Oral-pharyngeal dysphagia	Cardiac valvular dysplasia, X-linked, 314400 (3), X-linked recessive; Congenital short bowel syndrome, 300048 (3), X-linked recessive; ?FG syndrome 2, 300321 (3), X-linked; Frontometaphyseal dysplasia 1, 305620 (3), X-linked recessive; Heterotopia, periventricular, 300049 (3), X-linked dominant; Intestinal pseudoobstruction, neuronal, 300048 (3), X-linked recessive; Melnick-Needles syndrome, 309350 (3), X-linked dominant; Otopalatodigital syndrome, type I, 311300 (3), X-linked dominant; Otopalatodigital syndrome, type II, 304120 (3), X-linked dominant; Terminal osseous dysplasia, 300244 (3), X-linked	X-linked	Robertson et al. (2003)	635975	May 16, 2018
GBA2	1/1	stop_gained	NM_020944.3	c.700C>T	p.Arg234*	RND	Abnormality of eye movement//Intellectual disability//Dysphagia//Gait ataxia//Limb ataxia//Hypokinesia//Spastic dysarthria//Impaired vibratory sensation//Progressive spastic paraparesis//Cognitive impairment	Spastic paraplegia 46, autosomal recessive, 614409 (3), Autosomal recessive	recessive	Martin et al. (2013)	41486	Feb 07, 2013
GJB2	1/1	frameshift_variant	NM_004004.6	c.34delG	p.Gly12fs	ITHACA	Not available	Bart-Pumphrey syndrome, 149200 (3), Autosomal dominant; Deafness, autosomal dominant 3A, 601544 (3), Autosomal dominant; Deafness, autosomal recessive 1A, 220290 (3), Autosomal recessive; Hystrix-like ichthyosis with deafness, 602540 (3), Autosomal dominant; Keratitis-ichthyosis-deafness syndrome, 148210 (3), Autosomal dominant; Keratoderma, palmoplantar, with deafness, 148350 (3), Autosomal dominant; Vohwinkel syndrome, 124500 (3), Autosomal dominant	recessive	Kelsell et al. (1997)	17004	Jul 14, 2011
GNB1	0/1	missense_variant	NM_001282539.1	c.239T>C	p.Ile80Thr	ITHACA	Micropenis//Wide mouth//Mandibular prognathia//Round face//Proptosis//Recurrent respiratory infections//EEG abnormality//Febrile seizures//Developmental regression//Short stature//Decreased body weight//Abnormal pyramidal signs//Abnormality of skin adnexa morphology//Feeding difficulties//Chronic constipation//Epileptic encephalopathy	Leukemia, acute lymphoblastic, somatic, 613065 (3); Mental retardation, autosomal dominant 42, 616973 (3), Autosomal dominant	dominant	Petrovski et al. (2016)	208722	Dec 04, 2015
H1-4	0/1	frameshift_variant	NM_005321.2	c.430dupG	p.Ala144fs	ITHACA	Hypertelorism//Square face//Abnormality of the outer ear//Bulbous nose//Visual impairment//Global developmental delay//Generalized hypotonia//Obesity//Abnormal facial shape//Morphological abnormality of the central nervous system//Hypoplasia of the corpus callosum//Abnormality of the cerebral ventricles//Ventriculomegaly//Intellectual disability, moderate//Congenital myopia//Moderate global developmental delay//Abnormality of brain morphology//Moderate visual impairment//Short ear	Rahman syndrome, 617537 (3), Autosomal dominant	dominant	Tatton-Brown et al. (2017)	428605	Jun 27, 2017
HIVEP2	0/1	stop_gained	NM_006734.4	c.2827C>T	p.Arg943*	ITHACA	Unilateral renal agenesis//Global developmental delay//Myelomeningocele//Abnormality of the anus//Irregular chondrocostal junctions	Mental retardation, autosomal dominant 43, 616977 (3), Autosomal dominant	dominant	Rauch et al. (2012)	224791	Apr 06, 2016

HRAS	0/1	missense_variant	NM_001130442.2	c.38G>T	p.Gly13Val	ITHACA	Cleft palate//Retrognathia//Low-set ears//Short neck//Cystic hygroma//Growth delay//Abnormal facial shape//Hepatomegaly	{Bladder cancer, somatic}, 109800 (3); Congenital myopathy with excess of muscle spindles, 218040 (3), Autosomal dominant, Isolated cases; Costello syndrome, 218040 (3), Autosomal dominant, Isolated cases; {Nevus sebaceous or woolly hair nevus, somatic}, 162900 (3); Schimmelpenning-Feuerstein-Mims syndrome, somatic mosaic, 163200 (3); {Spitz nevus or nevus spilus, somatic}, 137550 (3); {Thyroid carcinoma, follicular, somatic}, 188470 (3)	dominant	Tartaglia et al. (2003)	180848	Jul 14, 2015
HRAS	0/1	missense_variant	NM_001130442.2	c.37G>T	p.Gly13Cys	ITHACA	Retrognathia//Coarse facial features//Epicanthus//Low-set, posteriorly rotated ears//Prominent antihelix//Bulbous nose//Anteverted nares//Abnormality of vision//Ptosis//Long eyelashes//Thick eyebrow//Nystagmus//Delayed speech and language development//Dry skin//Intellectual disability//Motor delay//Growth abnormality//Fragile nails//Overlapping toe//Deep philtrum//Frontal bossing//Sparse scalp hair//Short stature//Deep palmar crease//Feeding difficulties in infancy//Abnormality of the distal phalanx of finger//Cleft helix//Short 5th metacarpal//Tented upper lip vermilion	{Bladder cancer, somatic}, 109800 (3); Congenital myopathy with excess of muscle spindles, 218040 (3), Autosomal dominant, Isolated cases; Costello syndrome, 218040 (3), Autosomal dominant, Isolated cases; {Nevus sebaceous or woolly hair nevus, somatic}, 162900 (3); Schimmelpenning-Feuerstein-Mims syndrome, somatic mosaic, 163200 (3); {Spitz nevus or nevus spilus, somatic}, 137550 (3); {Thyroid carcinoma, follicular, somatic}, 188470 (3)	dominant	Tartaglia et al. (2003)	12606	Jun 29, 2010
KCNA2	0/1	missense_variant	NM_004974.4	c.890G>A	p.Arg297Gln	RND	Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	Epileptic encephalopathy, early infantile, 32, 616366 (3), Autosomal dominant	dominant	Pena and Coimbra (2015)	190328	Apr 01, 2015
KCNH1	0/1	missense_variant&splice_region_variant	NM_172362.3	c.1465C>T	p.Leu489Phe	ITHACA	Ptosis//Seizures//Muscular hypotonia//Joint laxity//Patent ductus arteriosus//Abnormal facial shape//Short stature//Decreased body weight//Feeding difficulties in infancy//Intellectual disability, severe	Temple-Baraitser syndrome, 611816 (3), Autosomal dominant; Zimmermann-Laband syndrome 1, 135500 (3), Autosomal dominant	dominant	Kortum et al. (2015)	449572	Aug 22, 2017
KIF1A	0/1	missense_variant	NM_001244008.1	c.761G>A	p.Arg254Gln	RND	Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	Mental retardation, autosomal dominant 9, 614255 (3), Autosomal dominant; Neuropathy, hereditary sensory, type IIC, 614213 (3), Autosomal recessive; Spastic paraplegia 30, autosomal recessive, 610357 (3), Autosomal recessive	dominant	Hamdan et al. (2011)	280500	Aug 05, 2016
KIF1A	0/1	missense_variant	NM_001244008.1	c.761G>A	p.Arg254Gln	RND	Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	Mental retardation, autosomal dominant 9, 614255 (3), Autosomal dominant; Neuropathy, hereditary sensory, type IIC, 614213 (3), Autosomal recessive; Spastic paraplegia 30, autosomal recessive, 610357 (3), Autosomal recessive	dominant	Hamdan et al. (2011)	280500	Aug 05, 2016

KIF1A	0/1	missense_variant	NM_001244008.1	c.38G>A	p.Arg13His	ITHACA	Recurrent urinary tract infections//Delayed speech and language development//Eczema//Ataxia//Intellectual disability, mild//Motor delay//Cerebellar hypoplasia//Constipation//Broad-based gait//Gait imbalance//Unsteady gait//Myopathy//Hyperlordosis//Increased muscle fatiguability	Mental retardation, autosomal dominant 9, 614255 (3), Autosomal dominant; Neuropathy, hereditary sensory, type IIC, 614213 (3), Autosomal recessive; Spastic paraplegia 30, autosomal recessive, 610357 (3), Autosomal recessive	dominant	Hamdan et al. (2011)	209165	Jul 19, 2013
KIF5A	0/1	missense_variant	NM_004984.4	c.611G>A	p.Arg204Gln	RND	Urinary urgency//Urinary incontinence//Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	{Amyotrophic lateral sclerosis, susceptibility to, 25}, 617921 (3), Autosomal dominant; Myoclonus, intractable, neonatal, 617235 (3), Autosomal dominant; Spastic paraplegia 10, autosomal dominant, 604187 (3), Autosomal dominant	dominant	Hamdan et al. (2011)	37127	Feb 01, 2009
KIF5A	0/1	missense_variant	NM_004984.4	c.611G>A	p.Arg204Gln	RND	Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	{Amyotrophic lateral sclerosis, susceptibility to, 25}, 617921 (3), Autosomal dominant; Myoclonus, intractable, neonatal, 617235 (3), Autosomal dominant; Spastic paraplegia 10, autosomal dominant, 604187 (3), Autosomal dominant	dominant	Hamdan et al. (2011)	37127	Feb 01, 2009
KIF5A	0/1	missense_variant	NM_004984.4	c.751G>A	p.Glu251Lys	RND	Cataract//Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis//Peripheral neuropathy	{Amyotrophic lateral sclerosis, susceptibility to, 25}, 617921 (3), Autosomal dominant; Myoclonus, intractable, neonatal, 617235 (3), Autosomal dominant; Spastic paraplegia 10, autosomal dominant, 604187 (3), Autosomal dominant	dominant	Hamdan et al. (2011)	37129	Aug 12, 2014
KLHL7	1/1	splice_donor_variant&intron_variant	NM_001031710.3	c.618+1G>A		ITHACA	Pierre-Robin sequence//Abnormal facial shape//Limb hypertonia//Distal arthrogryposis//Infantile axial hypotonia	Cold-induced sweating syndrome 3, 617055 (3), Autosomal recessive; Retinitis pigmentosa 42, 612943 (3), Autosomal dominant	recessive	Friedman et al. (2009)	487514	Jan 01, 2014

LMNA	0/1	frameshift_variant	NM_170707.4	c.1961dupG	p.Thr655fs	ITHACA	Coarse facial features//Prominent supraorbital ridges//Wide nasal bridge//Broad nasal tip//Anteverted nares//Delayed speech and language development//Sprengel anomaly//Expressive language delay//Cervical C2/C3 vertebral fusion//Abnormal vertebral segmentation and fusion//Congenital muscular torticollis//Moderately short stature//High anterior hairline//Mild expressive language delay//Left superior vena cava draining directly to the left atrium	Cardiomyopathy, dilated, 1A, 115200 (3), Autosomal dominant; Charcot-Marie-Tooth disease, type 2B1, 605588 (3), Autosomal recessive; Emery-Dreifuss muscular dystrophy 2, AD, 181350 (3), Autosomal dominant; Emery-Dreifuss muscular dystrophy 3, AR, 616516 (3), Autosomal recessive; Heart-hand syndrome, Slovenian type, 610140 (3), Autosomal dominant; Hutchinson-Gilford progeria, 176670 (3), Autosomal recessive, Autosomal dominant; Lipodystrophy, familial partial, type 2, 151660 (3), Autosomal dominant; Malouf syndrome, 212112 (3), Autosomal dominant; Mandibuloacral dysplasia, 248370 (3), Autosomal recessive; Muscular dystrophy, congenital, 613205 (3), Autosomal dominant; Muscular dystrophy, limb-girdle, type 1B, 159001 (3), Autosomal dominant; Restrictive dermopathy, lethal, 275210 (3), Autosomal recessive	dominant	Mercuri et al. (2004)	66878	Jul 19, 2013
MAPK8IP3	0/1	missense_variant	NM_001318852.1	c.1735C>T	p.Arg579Cys	ITHACA	Thin upper lip vermilion//Microcephaly//Short philtrum//Abnormality of the outer ear//Delayed speech and language development//Seizures//Global developmental delay//Generalized hypotonia//Delayed gross motor development//Intellectual disability, moderate//Short stature//Bronchodysplasia//Delayed fine motor development//Intellectual disability, severe//Stereotypical hand wringing	NEURODEVELOPMENTAL DISORDER WITH OR WITHOUT VARIABLE BRAIN ABNORMALITIES; NEDBA, autosomal dominant	dominant	Platzer et al. (2019)	632564	Feb 07, 2019
MAP3K20	1/1	frameshift_variant &stop_gained	NM_016653.3	c.282dupT	p.Asn95fs	NMD	Scoliosis//Progressive muscle weakness//Myalgia//EMG: myopathic abnormalities//Scapular winging//Proximal muscle weakness in lower limbs//Proximal muscle weakness in upper limbs//Hypertrophy of the lower limb//Ring fibers	Centronuclear myopathy 6 with fiber-type disproportion, 617760 (3), Autosomal recessive; Split-foot malformation with mesoaxial polydactyly, 616890 (3), Autosomal recessive	recessive	Vasli et al. (2017)	446160	Nov 7, 2017
MAP3K20	1/1	frameshift_variant &stop_gained	NM_016653.3	c.282dupT	p.Asn95fs	NMD	Motor delay//Hyperlordosis//Progressive muscle weakness//Scapular winging//Proximal muscle weakness in lower limbs//Proximal muscle weakness in upper limbs	Centronuclear myopathy 6 with fiber-type disproportion, 617760 (3), Autosomal recessive; Split-foot malformation with mesoaxial polydactyly, 616890 (3), Autosomal recessive	recessive	Vasli et al. (2017)	446160	Nov 7, 2017
MT-TM	1/1	mitochondrial	NC_012920.1	m.8993T>G		NMD	Decreased activity of mitochondrial complex III	None	mitochondrial	Vissing et al. (1998)	9641	Aug 01, 2009
MUTYH	1/1	frameshift_variant	NM_001128425.1	c.1147delC	p.Ala385fs	GENTURIS	Adenomatous colonic polyposis//Large intestinal polyposis//Intestinal polyposis//Colorectal polyposis	Adenomas, multiple colorectal, 608456 (3), Autosomal recessive; Colorectal adenomatous polyposis, autosomal recessive, with pilomatricomas, 132600 (3), Somatic mutation; Gastric cancer, somatic, 613659 (3)	recessive	Al-Tassan et al. (2002)	134860	Sep 19, 2013

MYH7	0/1	missense_variant	NM_000257.4	c.4258C>T	p.Arg1420Trp	NMD	Myopathy	Cardiomyopathy, dilated, 1S, 613426 (3), Autosomal dominant; Cardiomyopathy, hypertrophic, 1, 192600 (3), Autosomal dominant; Laing distal myopathy, 160500 (3), Autosomal dominant; Left ventricular noncompaction 5, 613426 (3), Autosomal dominant; Myopathy, myosin storage, autosomal dominant, 608358 (3), Autosomal dominant; Myopathy, myosin storage, autosomal recessive, 255160 (3), Autosomal recessive; Scapuloperoneal syndrome, myopathic type, 181430 (3), Autosomal dominant	dominant	Tajsharghi et al. (2003)	43003	Jun 01, 2014
NAA10	0/1	missense_variant	NM_003491.4	c.382T>A	p.Phe128Ile	ITHACA	Progressive microcephaly//Dolichocephaly//Small forehead//Astigmatism//Abnormality of eye movement//Hypermetropia//Exotropia//Abnormality of ocular smooth pursuit//Agitation//Delayed speech and language development//Hypoplasia of the corpus callosum//Limb hypertonia//Thoracic kyphosis//Decreased body weight//Hyperactive deep tendon reflexes//Congenital blindness//Infantile axial hypotonia//EEG with generalized slow activity//Dyskinesia	?Microphthalmia, syndromic 1, 309800 (3), X-linked; Ogden syndrome, 300855 (3), X-linked recessive, X-linked dominant	X-linked	Rope et al. (2011)	236259	Jan 01, 2014
NAA15	0/1	frameshift_variant	NM_057175.5	c.228_232delCTTGA	p.Asp76fs	ITHACA	High forehead//Delayed speech and language development//Hyperhidrosis//Hyporeflexia//Motor delay//Gait disturbance//Ventricular septal defect//Abnormality of the tricuspid valve//Toe clinodactyly//Intellectual disability, moderate//Abnormality of movement	Mental retardation, autosomal dominant 50, 617787 (3), Autosomal dominant	dominant	Stessman et al. (2017)	446520	Dec 05, 2017
NACC1	0/1	missense_variant	NM_052876.4	c.892C>T	p.Arg298Trp	ITHACA	Microcephaly//Congenital cataract//Abnormality of the skeletal system//Global developmental delay//Generalized hypotonia//Extrapyramidal dyskinesia	Neurodevelopmental disorder with epilepsy, cataracts, feeding difficulties, and delayed brain myelination, 617393 (3), Autosomal dominant	dominant	Schoch et al. (2017)	417784	Feb 02, 2017
NFIB	0/1	missense_variant	NM_001369458.1	c.442A>G	p.Lys148Glu	ITHACA	Astigmatism//Strabismus//Nystagmus//Delayed speech and language development//Arachnodactyly//Intellectual disability//Global developmental delay//Motor delay//Neonatal hypotonia//Febrile seizures//Meningocele//Scoliosis	MACROCEPHALY, ACQUIRED, WITH IMPAIRED INTELLECTUAL DEVELOPMENT; MACID, autosomal dominant	dominant	Schanze et al. (2018)	560026	Jan 23, 2019
NIPA1	0/1	missense_variant&splice_region_variant	NM_144599.5	c.316G>A	p.Gly106Arg	RND	Seizures//Spastic paraplegia//Lower limb spasticity//Spastic gait//Spastic paraparesis//Lower limb hyperreflexia//Babinski sign//Lower limb muscle weakness//Ankle clonus	Spastic paraplegia 6, autosomal dominant, 600363 (3), Autosomal dominant	dominant	Chai et al. (2003)	2523	Feb 01, 2005
NPHS1	1/1	missense_variant	NM_004646.3	c.2417C>A	p.Ala806Asp	ITHACA	Gingival overgrowth//Dolichocephaly//Delayed speech and language development//Global developmental delay//Overlapping toe//Delayed gross motor development//Intellectual disability, moderate//Short stature//Decreased body weight//Delayed fine motor development//Torsion of the penis	Nephrotic syndrome, type 1, 256300 (3), Autosomal recessive	recessive	Kestila et al. (1998)	56473	Jun 12, 2014
OSGEP	1/1	missense_variant	NM_017807.4	c.332T>C	p.Ile111Thr	ITHACA	Nephrotic syndrome//Microcephaly//Delayed speech and language development//Muscular hypotonia//Intellectual disability, mild//Abnormal facial shape//Short stature	Galloway-Mowat syndrome 3, 617729 (3), Autosomal recessive	recessive	Edvardson et al. (2017)	444891	Oct 26, 2017
PAX9	0/1	missense_variant	NM_001372076.1	c.51C>G	p.Asn17Lys	ITHACA	Anodontia//Dry skin//Ectodermal dysplasia//Generalized keratosis follicularis	Tooth agenesis, selective, 3, 604625 (3), Autosomal dominant	dominant	Stockton et al. (2000)	666317	Jan 1, 2014
PBX1	0/1	stop_gained	NM_002585.4	c.145C>T	p.Gln49*	ITHACA	Cryptorchidism//Hearing impairment//Specific learning disability//Dyscalculia//Expressive language delay//Abnormality of the 4th finger//External ear malformation//Bilateral renal hypoplasia	Congenital anomalies of kidney and urinary tract syndrome with or without hearing loss, abnormal ears, or developmental delay, 617641 (3), Autosomal dominant	dominant	Heidet et al. (2017)	666556	Jul 25, 2018

PHIP	0/1	stop_gained	NM_017934.7	c.3571C>T	p.Gln1191*	ITHACA	Cryptorchidism//Thick eyebrow//Synophrys//Behavioral abnormality//Stereotypy//Short attention span//Delayed speech and language development//Dry skin//Eczema//Muscular hypotonia//Motor delay//Abnormality of the hair//Premature birth//Recurrent respiratory infections//Increased body weight//Depigmentation/hyperpigmentation of skin//Abnormality of the palmar creases//Intellectual disability, severe//Toxemia of pregnancy	Developmental delay, intellectual disability, obesity, and dysmorphic features, 617991 (3), Autosomal dominant	dominant	de Ligt et al. (2012)	545398	Dec 2, 2019
PIK3CA	0/1	missense_variant	NM_006218.4	c.3140A>G	p.His1047Arg	GENTURIS	Stomach cancer	Breast cancer, somatic, 114480 (3); CLOVE syndrome, somatic, 612918 (3); Colorectal cancer, somatic, 114500 (3); Cowden syndrome 5, 615108 (3); Gastric cancer, somatic, 613659 (3); Hepatocellular carcinoma, somatic, 114550 (3); Keratosis, seborrheic, somatic, 182000 (3); Megalencephaly-capillary malformation-polymicrogyria syndrome, somatic, 602501 (3); Nevus, epidermal, somatic, 162900 (3); Nonsmall cell lung cancer, somatic, 211980 (3); Ovarian cancer, somatic, 167000 (3)	mosaic	Orloff et al. (2013)	13652	Aug 05, 2010
PNPLA6	0/1	missense_variant	NM_001166111.2	c.787G>A	p.Val263Ile	RND	Gait ataxia//Impaired vibratory sensation//Peripheral axonal neuropathy//Motor polyneuropathy//Progressive spastic paraparesis	Boucher-Neuhauser syndrome, 215470 (3), Autosomal recessive; ?Laurence-Moon syndrome, 245800 (3), Autosomal recessive; Oliver-McFarlane syndrome, 275400 (3), Autosomal recessive; Spastic paraplegia 39, autosomal recessive, 612020 (3), Autosomal recessive	recessive	Rainier et al. (2008)	101043	Jan 01, 2014
PNPLA6	0/1	missense_variant	NM_001166111.2	c.2519G>A	p.Gly840Glu	RND	Gait ataxia//Impaired vibratory sensation//Peripheral axonal neuropathy//Motor polyneuropathy//Progressive spastic paraparesis	Boucher-Neuhauser syndrome, 215470 (3), Autosomal recessive; ?Laurence-Moon syndrome, 245800 (3), Autosomal recessive; Oliver-McFarlane syndrome, 275400 (3), Autosomal recessive; Spastic paraplegia 39, autosomal recessive, 612020 (3), Autosomal recessive	recessive	Rainier et al. (2008)	101044	Jan 1, 2014
PNPLA6	0/1	frameshift_variant	NM_001166111.2	c.3088_3091dupAGCC	p.Arg1031fs	RND	Urinary urgency//Urinary incontinence//Abnormality of eye movement//Gaze-evoked nystagmus//Gait ataxia//Limb ataxia//Progressive cerebellar ataxia//Progressive spastic paraparesis//Impaired tactile sensation	Boucher-Neuhauser syndrome, 215470 (3), Autosomal recessive; ?Laurence-Moon syndrome, 245800 (3), Autosomal recessive; Oliver-McFarlane syndrome, 275400 (3), Autosomal recessive; Spastic paraplegia 39, autosomal recessive, 612020 (3), Autosomal recessive	recessive	Rainier et al. (2008)	6607	Mar 01, 2008
POLR3A	0/1	splice_acceptor_variant&intron_variant	NM_007055.4	c.2617-1G>A		RND	Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	Leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism, 607694 (3), Autosomal recessive	recessive	Bernard et al. (2011)	31146	Sep 09, 2011

POLR3A	0/1	splice_region_variant&intron_variant	NM_007055.4	c.1048+5G>T		RND	Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	Leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism, 607694 (3), Autosomal recessive	recessive	Bernard et al. (2011)	549560	Apr 01, 2018
PTRH2	1/1	frameshift_variant	NM_001015509.2	c.272_273delCT	p.Ala91fs	RND	Hearing impairment//Intellectual disability//Peripheral neuropathy	Infantile-onset multisystem neurologic, endocrine, and pancreatic disease, 616263 (3), Autosomal recessive	recessive	Hu et al. (2014)	183428	Dec 1, 2014
PUF60	0/1	disruptive_inframe_deletion	NM_001362895.2	c.560_568delCCCCTTTG	p.Ala187_Phe189del	ITHACA	Smooth philtrum//High forehead//Hearing impairment//Visual impairment//Telecanthus//Ptosis//Carious teeth//Delayed speech and language development//Pectus excavatum//Intellectual disability, mild//Obesity//Deep philtrum//Recurrent infections//Short nose//Attention deficit hyperactivity disorder//Broad uvula	Verheij syndrome, 615583 (3), Autosomal dominant	dominant	Dauber et al. (2013)	430808	Oct 08, 2015
REEP1	0/1	stop_gained&splice_region_variant	NM_001371279.1	c.182G>A	p.Trp61*	RND	Spasticity//Lower limb spasticity//Babinski sign//Hyperactive deep tendon reflexes	?Neuronopathy, distal hereditary motor, type VB, 614751 (3), Autosomal dominant; Spastic paraplegia 31, autosomal dominant, 610250 (3), Autosomal dominant	dominant	Zuchner et al. (2006)	620230	Jun 14, 2018
SCN8A	0/1	intron_variant	NM_001330260.2	c.615-221G>A		ITHACA	Abnormality of the pinna//Downslanted palpebral fissures//Autism//Delayed speech and language development//Seizures//Obesity//Sleep disturbance//Intellectual disability, severe	?Cognitive impairment with or without cerebellar ataxia, 614306 (3), Autosomal dominant; Epileptic encephalopathy, early infantile, 13, 614558 (3), Autosomal dominant; Seizures, benign familial infantile, 5, 617080 (3), Autosomal dominant	dominant	Trudeau et al. (2006)	253276	Feb 19, 2016
SELENON	1/1	stop_gained&splice_region_variant	NM_020451.3	c.1090C>T	p.Gln364Ter	NMD	High palate//Facial asymmetry//Myopia//Growth hormone deficiency//Muscular hypotonia//Hyporeflexia//Muscle weakness//Joint hypermobility//Weak cry//Pes planus//Respiratory insufficiency//Tetraparesis//Frequent falls//Hyporeflexia of lower limbs//Scoliosis//Respiratory insufficiency due to muscle weakness//Myopathy//Skeletal muscle atrophy//Generalized muscle weakness//Generalized amyotrophy//Proximal muscle weakness//Short stature//Craniofacial asymmetry//Arnold-Chiari type I malformation//Congenital facial diplegia//Infantile muscular hypotonia//Proximal muscle weakness in lower limbs//Decreased Achilles reflex//Abnormal elasticity of skin//Complete breech presentation//Hyporeflexia of upper limbs//Fatty replacement of skeletal muscle//Abnormality of the brachial nerve plexus	Muscular dystrophy, rigid spine, 1, 602771 (3), Autosomal recessive; Myopathy, congenital, with fiber-type disproportion, 255310 (3), Autosomal recessive, Autosomal dominant	recessive	Moghadaszadeh et al. (2001)	280366	Mar 30, 2016
SET	0/1	missense_variant	NM_001122821.2	c.283T>G	p.Trp95Gly	ITHACA	Delayed speech and language development//Motor delay//Incoordination//Abnormality of movement	MENTAL RETARDATION, AUTOSOMAL DOMINANT	dominant	Stevens et al. (2018)	560206	Aug 31, 2018
SIN3A	0/1	frameshift_variant	NM_001145357.2	c.2955_2956delGA	p.Glu985fs	ITHACA	Hypospadias//Malar flattening//Delayed speech and language development//Intellectual disability//Clinodactyly of the 5th finger	Witteveen-Kolk syndrome, 613406 (3), Autosomal dominant	dominant	Witteveen et al. (2016)	253073	Aug 12, 2016
SLC16A2	1/1	missense_variant	NM_006517.5	c.439G>A	p.Gly147Arg	ITHACA	Epicanthus//Generalized hypotonia//Encephalopathy//Cerebral cortical atrophy//Corpus callosum atrophy//EEG with periodic abnormalities//Delayed myelination//Abnormal T3/T4 ratio	Allan-Herndon-Dudley syndrome, 300523 (3), X-linked	X-linked	Dumitrescu et al. (2004)	666343	Jan 1, 2014
SLC25A24	0/1	missense_variant	NM_013386.5	c.649C>T	p.Arg217Cys	ITHACA	Microcephaly//Atresia of the external auditory canal//Atrial septal defect//Pulmonary hypoplasia//Delayed skeletal maturation//Clinodactyly of the 5th finger//Short stature//Decreased body weight//2-3 toe syndactyly	Fontaine progeroid syndrome, 612289 (3), Autosomal dominant	dominant	Ehmke et al. (2017)	369980	Jan 26, 2018
SLC52A2	0/1	missense_variant	NM_001253815.2	c.368T>C	p.Leu123Pro	NMD	Decreased activity of mitochondrial complex I	Brown-Vialetto-Van Laere syndrome 2, 614707 (3), Autosomal recessive	recessive	Johnson et al. (2012)	39576	Nov 01, 2012
SLC52A2	0/1	missense_variant	NM_001253815.2	c.916G>A	p.Gly306Arg	NMD	Decreased activity of mitochondrial complex I	Brown-Vialetto-Van Laere syndrome 2, 614707 (3), Autosomal recessive	recessive	Johnson et al. (2012)	35470	Jan 01, 2014

SLC6A1	0/1	missense_variant	NM_001348250.1	c.1377C>A	p.Ser459Arg	ITHACA	Brachycephaly//Long face//Retrognathia//Prominent nasal bridge//Misalignment of teeth//Anxiety//Delayed speech and language development//Hyperactivity//Pectus excavatum//Enuresis//Arachnodactyly//Intellectual disability, mild//Limited elbow extension//Disproportionate tall stature//Pes planus//Scoliosis//High, narrow palate//Cubitus valgus//Muscular hypotonia of the trunk//Aplasia/Hypoplasia of the mandible//Long toe//Mild global developmental delay//Feeding difficulties//Delayed social development//Down-sloping shoulders	Myoclonic-atonic epilepsy, 616421 (3), Autosomal dominant	dominant	Hirunsatit et al. (2007)	421382	Jun 03, 2016
SMAD4	0/1	frameshift_variant	NM_005359.6	c.1231_1232delAG	p.Ser411fs	GENTURIS	Adenomatous colonic polyposis//Large intestinal polyposis//Intestinal polyposis//Colorectal polyposis	Juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome, 175050 (3), Autosomal dominant; Myhre syndrome, 139210 (3), Autosomal dominant; Pancreatic cancer, somatic, 260350 (3); Polyposis, juvenile intestinal, 174900 (3), Autosomal dominant	dominant	Howe et al. (1998)	182867	May 11, 2016
TMEM107	1/1	missense_variant	NM_183065.4	c.134A>G	p.Glu45Gly	ITHACA	Macrocephaly//Cerebellar hypoplasia//Absent speech//Ventricular septal defect//Abnormal facial shape//Delayed gross motor development//Severe global developmental delay//Hamartoma of tongue//Delayed ability to sit//Postaxial polydactyly	Leukoencephalopathy, brain calcifications, and cysts, 614561 (3), Autosomal recessive	recessive	Jenkinson et al. (2016)	430703	Jul 14, 2017
SPAST	0/1	disruptive_inframe_deletion	NM_014946.3	c.1209_1211delCTT	p.Phe404del	RND	Not available	Spastic paraplegia 4, autosomal dominant, 182601 (3), Autosomal dominant	dominant	Hazan et al. (1999)	448449	Dec 07, 2015
SPAST	0/1	disruptive_inframe_deletion	NM_014946.3	c.1209_1211delCTT	p.Phe404del	RND	Not available	Spastic paraplegia 4, autosomal dominant, 182601 (3), Autosomal dominant	dominant	Hazan et al. (1999)	448449	Dec 07, 2015
SPAST	0/1	stop_gained	NM_014946.3	c.1291C>T	p.Arg431*	RND	Urinary urgency//Urinary incontinence//Dysphagia//Limb ataxia//Progressive spastic paraparesis//Distal lower limb amyotrophy	Spastic paraplegia 4, autosomal dominant, 182601 (3), Autosomal dominant	dominant	Hazan et al. (1999)	188179	Apr 28, 2016
SPAST	0/1	splice_donor_variant&intron_variant	NM_014946.3	c.1245+1G>A		RND	Sensory neuropathy//Intellectual disability//Dysarthria//Limb ataxia//Progressive spastic paraparesis//Impaired tactile sensation//Abnormality of movement//Cognitive impairment	Spastic paraplegia 4, autosomal dominant, 182601 (3), Autosomal dominant	dominant	Hazan et al. (1999)	226113	Feb 19, 2016
SPAST	0/1	splice_donor_variant&intron_variant	NM_014946.3	c.1245+1G>A		RND	Impaired vibratory sensation//Chronic mucocutaneous candidiasis//Progressive spastic paraparesis//Distal lower limb amyotrophy//Cognitive impairment	Spastic paraplegia 4, autosomal dominant, 182601 (3), Autosomal dominant	dominant	Hazan et al. (1999)	226113	Feb 19, 2016
SPAST	0/1	stop_gained	NM_014946.3	c.1684C>T	p.Arg562*	RND	Urinary urgency//Spasticity//Lower limb spasticity//Sensory impairment//Hyperactive deep tendon reflexes	Spastic paraplegia 4, autosomal dominant, 182601 (3), Autosomal dominant	dominant	Hazan et al. (1999)	448449	Dec 07, 2015
SPAST	0/1	disruptive_inframe_deletion	NM_014946.3	c.1206CTT[1]	p.Phe404del	RND	Urinary urgency//Spasticity//Lower limb spasticity//Sensory impairment//Hyperactive deep tendon reflexes	Spastic paraplegia 4, autosomal dominant, 182601 (3), Autosomal dominant	dominant	Hazan et al. (1999)	521727	Jun 12, 2017
SPG11	0/1	stop_gained	NM_025137.4	c.6856C>T	p.Arg2286*	NMD	Spastic paraplegia	Amyotrophic lateral sclerosis 5, juvenile, 602099 (3), Autosomal recessive; Charcot-Marie-Tooth disease, axonal, type 2X, 616668 (3), Autosomal recessive; Spastic paraplegia 11, autosomal recessive, 604360 (3), Autosomal recessive	recessive	Stevanin et al. (2007)	41353	Jan 31, 2013
SPG11	0/1	frameshift_variant	NM_025137.4	c.4307_4308delAA	p.Gln1436fs	NMD	Spastic paraplegia	Amyotrophic lateral sclerosis 5, juvenile, 602099 (3), Autosomal recessive; Charcot-Marie-Tooth disease, axonal, type 2X, 616668 (3), Autosomal recessive; Spastic paraplegia 11, autosomal recessive, 604360 (3), Autosomal recessive	recessive	Stevanin et al. (2007)	241590	Nov 01, 2017

SPG11	0/1	stop_gained	NM_025137.4	c.1951C>T	p.Arg651*	RND	Urinary urgency//Urinary incontinence//Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	Amyotrophic lateral sclerosis 5, juvenile, 602099 (3), Autosomal recessive; Charcot-Marie-Tooth disease, axonal, type 2X, 616668 (3), Autosomal recessive; Spastic paraplegia 11, autosomal recessive, 604360 (3), Autosomal recessive	recessive	Stevanin et al. (2007)	41284	Jan 31, 2013
SPG11	0/1	frameshift_variant	NM_025137.4	c.1818_1819delTT	p.Ser607fs	RND	Urinary urgency//Spasticity//Lower limb spasticity//Hyperactive deep tendon reflexes//Upper limb spasticity	Amyotrophic lateral sclerosis 5, juvenile, 602099 (3), Autosomal recessive; Charcot-Marie-Tooth disease, axonal, type 2X, 616668 (3), Autosomal recessive; Spastic paraplegia 11, autosomal recessive, 604360 (3), Autosomal recessive	recessive	Stevanin et al. (2007)	648623	Dec 3, 2018
SPG11	0/1	frameshift_variant	NM_025137.4	c.1348dupA	p.Ile450fs	RND	Urinary urgency//Spasticity//Lower limb spasticity//Gait ataxia//Hyperactive deep tendon reflexes	Amyotrophic lateral sclerosis 5, juvenile, 602099 (3), Autosomal recessive; Charcot-Marie-Tooth disease, axonal, type 2X, 616668 (3), Autosomal recessive; Spastic paraplegia 11, autosomal recessive, 604360 (3), Autosomal recessive	recessive	Stevanin et al. (2007)	41315	Jan 31, 2013
SPG7	0/1	frameshift_variant	NM_001363850.1	c.1049_1077delCCCCCGGCTGTGGGAAGACGCTGCTGGCC	p.Pro350fs	RND	Urinary urgency//Urinary incontinence//Gait ataxia//Impaired vibratory sensation//Progressive spastic paraparesis//Abnormality of movement	Spastic paraplegia 7, autosomal recessive, 607259 (3), Autosomal recessive, Autosomal dominant	dominant	Casari et al. (1998)	495055	Aug 07, 2017
SPG7	0/1	stop_gained	NM_001363850.1	c.1192C>T	p.Arg398*	RND	Spasticity//Lower limb spasticity//Spastic gait//Progressive cerebellar ataxia//Babinski sign//Progressive spastic paraparesis	Spastic paraplegia 7, autosomal recessive, 607259 (3), Autosomal recessive, Autosomal dominant	dominant	Casari et al. (1998)	545964	May 17, 2018
STUB1	0/1	missense_variant	NM_005861.4	c.194A>G	p.Asn65Ser	RND	Gait disturbance	Spinocerebellar ataxia, autosomal recessive 16, 615768 (3), Autosomal recessive	recessive	Shi et al. (2013)	162097	Sep 26, 2014
STUB1	0/1	missense_variant	NM_005861.4	c.194A>G	p.Asn65Ser	RND	Saccadic smooth pursuit//Gait disturbance	Spinocerebellar ataxia, autosomal recessive 16, 615768 (3), Autosomal recessive	recessive	Shi et al. (2013)	162097	Sep 26, 2014
SYNGAP1	0/1	splice_donor_variant&intron_variant	NM_006772.3	c.2294+1G>A		ITHACA	Behavioral abnormality//Autism//Delayed speech and language development//Hypopigmentation of the skin//Intellectual disability//Muscular hypotonia//Hip dysplasia//Absence seizures//Recurrent infections//Neonatal hyperbilirubinemia//Equinovarus deformity//Feeding difficulties in infancy	Mental retardation, autosomal dominant 5, 612621 (3), Autosomal dominant	dominant	Hamdan et al. (2009)	41460	May 01, 2011
TAF1	1/1	missense_variant	NM_001286074.1	c.3736C>T	p.Arg1246Trp	ITHACA	Triangular mouth//Hearing impairment//Narrow nose//Astigmatism//Visual impairment//Synophrys//Abnormality of dental enamel//Abnormality of the skin//Intellectual disability//Coarctation of aorta//Morphological abnormality of the central nervous system//High, narrow palate//Recurrent lower respiratory tract infections//Atrioventricular canal defect//Feeding difficulties in infancy//Prominent ear helix//Interrupted aortic arch//Abnormal shape of the palpebral fissure	Dystonia-Parkinsonism, X-linked, 314250 (3), X-linked recessive; Mental retardation, X-linked, syndromic 33, 300966 (3), X-linked recessive	X-linked	O'Rawe et al. (2015)	219116	Dec 03, 2015
TAF2	1/1	missense_variant	NM_003184.4	c.2531C>T	p.Pro844Leu	ITHACA	Wide mouth//Progressive microcephaly//Synophrys//Seizures//Profound global developmental delay	Mental retardation, autosomal recessive 40, 615599 (3), Autosomal recessive	recessive	Najmabadi et al. (2011)	666328	Jan 01, 2014

TBL1XR1	0/1	missense_variant	NM_001321193.2	c.1336T>G	p.Tyr446Asp	ITHACA	Glossoptosis//Cleft palate//Micrognathia//Intellectual disability//Seizures//Short stature	Mental retardation, autosomal dominant 41, 616944 (3), Autosomal dominant; Pierpont syndrome, 602342 (3), Autosomal dominant	dominant	Saitsu et al. (2014)	559571	Apr 09, 2018
TRIO	0/1	missense_variant	NM_007118.4	c.4283G>A	p.Arg1428Gln	ITHACA	Delayed speech and language development//Abnormal heart morphology//Abnormality of the mitral valve//Birth length less than 3rd percentile	Mental retardation, autosomal dominant 44, 617061 (3), Autosomal dominant	dominant	Riazuddin et al. (2006)	253084	Mar 27, 2017
TRIP4	1/1	stop_gained	NM_016213.5	c.760C>T	p.Arg254*	NMD	Pontocerebellar atrophy	?Muscular dystrophy, congenital, Davignon-Chauveau type, 617066 (3), Autosomal recessive; Spinal muscular atrophy with congenital bone fractures 1, 616866 (3), Autosomal recessive	recessive	Knierim et al. (2016)	224631	Aug 10, 2016
TTN	0/1	missense_variant	NM_001267550.2	c.107840T>A	p.Ile35947Asn	NMD	obsolete Respiratory difficulties//Contractures of the joints of the lower limbs//Proximal muscle weakness in lower limbs//Proximal muscle weakness in upper limbs	Cardiomyopathy, dilated, 1G, 604145 (3); Cardiomyopathy, familial hypertrophic, 9, 613765 (3), Autosomal dominant; Muscular dystrophy, limb-girdle, type 2J, 608807 (3), Autosomal recessive; Myopathy, proximal, with early respiratory muscle involvement, 603689 (3); Salih myopathy, 611705 (3), Autosomal recessive; Tibial muscular dystrophy, tardive, 600334 (3), Autosomal dominant	dominant	Lange et al. (2005)	12654	Aug 01, 2003
TUBB	0/1	missense_variant	NM_178014.4	c.895A>G	p.Met299Val	ITHACA	Wide mouth//Thick lower lip vermilion//Wide nose//Megalocornea//Ptosis//Photophobia//Horizontal nystagmus//Delayed speech and language development//Severe visual impairment//Prominent fingertip pads//Muscular hypotonia//Motor delay//Agenesis of corpus callosum//Pes planus//Short foot//Hallux valgus//Constipation//Gray matter heterotopias//Abnormality of the caudate nucleus//Aplasia/Hypoplasia of the optic nerve//Low insertion of columella//Unilateral strabismus//Severe Myopia//Cortical visual impairment//Long fingers	Cortical dysplasia, complex, with other brain malformations 6, 615771 (3), Autosomal dominant; Symmetric circumferential skin creases, congenital, 1, 156610 (3), Autosomal dominant	dominant	Breuss et al. (2012)	127189	Dec 27, 2012
TUBB3	0/1	missense_variant	NM_006086.4	c.763G>A	p.Val255Ile	ITHACA	Recurrent urinary tract infections//Microcephaly//Round face//Short philtrum//Deeply set eye//Hypermetropia//Aggressive behavior//Self-mutilation//Delayed speech and language development//Pectus carinatum//Hemangioma//Global developmental delay//Short foot//Toe clinodactyly//Constipation//Hypoplasia of the corpus callosum//Ventriculomegaly//Phonophobia//Sleep disturbance//Recurrent upper respiratory tract infections//Inverted nipples//Short stature//Impaired pain sensation//Intellectual disability, severe	Cortical dysplasia, complex, with other brain malformations 1, 614039 (3), Autosomal dominant; Fibrosis of extraocular muscles, congenital, 3A, 600638 (3), Autosomal dominant	dominant	Poirier et al. (2010)	372654	Oct 12, 2016
UBAP1	0/1	frameshift_variant	NM_016525.5	c.286_290dup	p.Glu97fs	RND	Spastic paraplegia	UBIQUITIN-ASSOCIATED PROTEIN 1; UBAP1, autosomal dominant	dominant	Farazi Fard et al. (2019)	627554	May 10, 2019
UBAP1	0/1	frameshift_variant	NM_001171201.1	c.478_482dup CCAGA	p.Glu161fs	RND	Spasticity//Lower limb spasticity//Spastic gait//Babinski sign//Progressive spastic paraparesis	UBIQUITIN-ASSOCIATED PROTEIN 1; UBAP1, autosomal dominant	dominant	Farazi Fard et al. (2019)	627554	May 10, 2019
WDR45	1/1	disruptive_inframe_deletion	NM_007075.3	c.752_754delCCT	p.Ser251del	ITHACA	Myopia//Delayed speech and language development//Slender finger//Intellectual disability//Seizures//Motor delay//Abnormal mitochondria in muscle tissue	Neurodegeneration with brain iron accumulation 5, 300894 (3), X-linked	X-linked	Haack et al. (2012)	418542	Jan 16, 2019
ZFYVE26	0/1	stop_gained	NM_015346.4	c.2182C>T	p.Arg728*	RND	Urinary urgency//Urinary incontinence//Spastic dysarthria//Progressive spastic paraparesis//Distal lower limb amyotrophy	Spastic paraplegia 15, autosomal recessive, 270700 (3), Autosomal recessive	recessive	Hanein et al. (2008)	553395	Aug 18, 2017