Supplementary Online Content

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eTable 1. Known CA Genes

eTable 2. List of Possibly to Definitely Causative Variants

eTable 3. Variants of Unknown Significance

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Known CA genes

Gene Symbol	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
AARS2	*612035	COXPD8 (#614096) : combined oxidative phosphorylation deficiency-8 (infantile hypertrophic mitochondrial cardiomyopathy) (Gotz 2011)	LKENP (#615889) : Progressive leukoencephalopathy with ovarian failure (Dallabona 2014)	AR	
ABHD12	*613599	PHARC (#612674) : progressive polyneuropathy, hearing loss, ataxia, retinitis pigmentosa, and cataract (Fiskerstrand 2010)	Non-syndromic retinal degeneration (Nishiguchi 2014)	AR	
ACO2	*100805	ICRD (#614559) : infantile cerebellar - retinal degeneration (Spiegel 2012)	OPA9 (#616289) : Optic atrophy type 9 (Metodiev 2014)	AR	
ADCK3	*606980	COQ10D4 (#612016) : primary coenzyme Q deficiency-4 (Mollet 2008, Lagier-Tourenne 2008)		AR	
AFG3L2	*604581	SCA28 (#610246)(Di Bella 2010)	SPAX5 (#614487) (Pierson 2011); optic atrophy (Charif 2015)	AD / AR	Yes
AHI1	*608894	JBTS3 (#608629) : Joubert syndrome-3 (Ferland 2004, Dixon-Salazar 2004)		AR	
ALDH18A1	*138250	Autosomal recessive cutis laxa type IIIA (#219150) (Baumgartner 2005)	Autosomal dominant spastic paraplegia 9A (#601162) (Coutelier 2015) / autosomal recessive spastic paraplegia 9B (#601162) (Coutelier 2015) / autosomal dominant cutis laxa 3 (#616603) (Fischer-Zirnsak 2015)	AR / AD	
ALS2	*606352	Juvenile ALS 2 (#205100); juvenile primary lateral sclerosis (#606353) (Yang 2001, Hadano 2001)	Infantile ascending HSP (#607225) (Eymard-Pierre 2002)	AR	
AMPD2	*102771	PCH9: pontocerebellar hypoplasia type 9 (#615809) (Akizu 2013)	SPG63: spastic paraplegia type 63 (#615686) (Novarino 2014)	AR	
ANO10	*613726	SCAR10: autosomal recessive spinocerebellar ataxia type 10 (#613728) (Vermeer 2010)	Associated low CoQ10 levels (Balreira 2014)	AR	
AP4B1	*607245	SPG47: autosomal recessive spastic paraplegia type 47 = CPSQ5: Cerebral Palsy with Microcephaly & Intellectual Disability 5 (#614066) (Abou Jamra 2011, Bauer 2012, Tuysuz 2014, Abdollahpour 2015)		AR	
AP4E1	*607244	SPG51: autosomal recessive spastic paraplegia type 51 = CPSQ4 (#613744) (Moreno-De-Luca 2011, Abou Jamra 2011, Najmabadi 2011)		AR	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
AP4M1	*602296	SPG50: autosomal recessive spastic paraplegia type 50 / CPSQ3 (#612936) (Verkerk 2009)		AR	
AP4S1	*607243	SPG52: autosomal recessive spastic paraplegia type 52 = CPSQ6 (#614067) (Abou Jamra 2011)		AR	
AP5Z1	*613653	SPG48: autosomal recessive spastic paraplegia type 48 (#613647) (Slabicki 2010)		AR	
APTX	*606350	AOA1: Early-onset ataxia with oculomotor apraxia and hypoalbuminemia / adult-onset ataxia with oculomotor apraxia (#208920) (Date 2001, Moreira 2001)		AR	
ARL13B	*608922	JBTS8: Joubert syndrome type 8 (#612291) (Cantagrel 2008)		AR	
ARL6IP1	*607669	?SPG61: autosomal recessive spastic paraplegia type 61 (#615685) (Novarino 2014)		AR	
ARSI	*610009	?SPG66 (Novarino 2014)		AR	
ATCAY	*608179	Cayman type cerebellar ataxia (#601238) (Bomar 2003)		AR	
ATL1	*606439	SPG3A: autosomal dominant spastic paraplegia type 3A (#182600) (Zhao 2001)	Hereditary Sensory Neuropathy Type 1D (#613708) (Guelly 2011)	AD / AR (homozygous in 2 families)	
ATM	*607585	Ataxia-telangectasia (#208900) (Savitsky 1995)	Adult-onset ataxia / distal spinal muscular atrophy with little ataxia	AR	
ATP13A2	*610513	PARK9: Rufor-Kabed syndrome (#606693) (Ramirez 2006)	Ceroid lipofuscinosis type 12 (#606693) (Bras 2012)	AR	
ATP7B	*606882	Wilson disease (#277900) (Bull 1993, Tanzi 1993)		AR	
ATXN10	*611150	Spinocerebellar ataxia 10 (#603516) (Matsuura 2000)	Joubert syndrome (Sang 2011)	AD	
B4GALNT1	*601873	SPG26: autosomal recessive spastic paraplegia type 26 (#609195) (Boukhris 2013)		AR	
BICD2	*609797	Lower extremity-predominant spinal muscular atrophy-2 (#615290) (Neveling 2013)	HSP (Oates 2013)	AD	
BSCL2	*606158	Congenital generalized lipodystrophy type 2 (# 269700) (AR) (Magre 2001)	Distal hereditary motor neuropathy type VA (#600794) (AD) / SPG17: Silver spastic paraplegia syndrome (# 270685) (AD) (Windpassinger 2004) // Progressive encephalopathy with-without lipodystrophy (#615924) (AR) (Guillen-Navarro 2013)	AR (lipodystrophy) / AD (HSP)	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
C10orf2	*606075	PEOA3: Progressive external ophthalmoplegia with mitochondrial DNA deletions (#609286) (AD) (Spelbrink 2001)	Mitochondrial DNA depletion syndrome type 7 (hepatocerebral) = infantile onset spinocerebellar ataxia (IOSCA) (#271245) (AR) (Nikali 2005) / Perrault syndrome type 5 (#616138) (AR) (Morino 2014)	AD / AR	
C12orf65	*613541	COXPD7: Combined oxidative phosphorylation deficiency (#613559) (AR) (Antonicka 2010)	SPG55: spastic paraplegia type 55 (#615035) (Shimazaki 2012)	AR	
C19orf12	*614297	Neurodegeneration with brain iron accumulation type 4 (#614298) (Hartig 2011)	SPG43: spastic paraplegia type 43 (# 615043) (Landoure 2013)	AR	
C5orf42	*614571	Joubert syndrome-17 (#614615) (Srour 2012)	Orofaciodigital syndrome VI (#277170) (Lopez 2014)	AR	
CACNA1A	*601011	Episodic ataxia type 2 (#108500) / Familial hemiplegic migraine (#141500) (Ophoff 1996)	Spinocerebellar ataxia type 6 (#183086) (Zhuchenko 1997)	AD	Yes
CACNA1G	*604065	Spinocerebellar ataxia (Coutelier 2015)		AD	Yes
CACNB4	*601949	Episodic ataxia type 5 (#613855) / susceptibility to epilepsy (juvenile myoclonic / generalized)(#607682) (Escayg 2000)		AD	Yes
CC2D2A	*612013	Joubert syndrome type 9 (#612285) (Noor 2008)	Meckel syndrome type 6 (#612284) (Tallila 2008) / COACH syndrome: cerebellar vermis hypo/aplasia, oligophrenia, congenital ataxia, ocular coloboma, hepatic fibrosis (#216360) (Gorden 2008, Doherty 2010) - continuum	AR / digenic	
CCDC88C	*611204	Autosomal recessive nonsyndromic hydrocephalus (#236600) (Ekici 2010)	Spinocerebellar ataxia tyoe 40 (#616053) (Tsoi 2014)	AR / AD	
CCT5	*610150	Hereditary sensory neuropathy with spastic paraplegia (#256840) (Bouhouche 2006)		AR	
CEP290	*610142	Joubert syndrome type 5 (#610188) / Senior-Loken syndrome (610189) (Sayer 2006)	Wide continuum, no clear genotype-phenotype correlation: Leber congenital amaurosis 10 (#611755), Meckel syndrome 4 (#611134), ?Bardet-Biedl syndrome 14 (#615991)	AR / digenic	
CEP41	*610523	Joubert syndrome type 15 (#614464) (Lee 2012)		AR / digenic	
CISD2	*611507	Wolfram syndrome type 2 (#604928) (Amr 2007)		AR	
CLCN2	*600570	Leukoencephalopathy with ataxia (#615651) (Depienne 2013)		AR	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
CLN5	*608102	Neuronal ceroid lipofuscinosis-5 (#256731) (Savukoski 1998)	Late onset ataxia and progressive cognitive impairment (Mancini 2015)	AR	
CLN6	*606725	Neuronal ceroid lipofuscinosis-6 (#601780) (Gao 2002)	Kufs disease = neuronal ceroid lipofuscinosis-4A (#204300) (Arsov 2011)	AR	
CLPP	*601119	Perrault syndrome 3 (#614129) (Jenkinson 2013)		AR	
COASY	*609855	Neurodegeneration with brain iron accumulation type 6 (#615643) (Dusi 2014)		AR	
COL18A1	*120328	Knobloch syndrome 1 (#267750) (Sertie 2000)	Ataxia + epilepsy + eye disorder, still called Knobloch sundrome (Paisan-Ruiz 2009) (same frameshift mutation as one Knobloch family)	AR	
COQ2	*609825	Coenzyme Q10 deficiency-1 (#607426) (Quinzii 2006)	NB : high clinical heterogeneity in COQ10D	AR	
COQ9	*612837	Coenzyme Q10 deficiency-5 (#614654) (Duncan 2009)		AR	
COX20	*614698	Mitochondrial complex IV deficiency (#220110) (Szklarczyk 2013)		AR	
CP	*117700	Aceruloplasminemia, hemosiderosis, ataxia (#604290) (Yoshida 1995)	Hypoceruloplasminemia and ataxia (AD) (Miyajima 2001)	AR / AD	
CSPP1	*611654	Joubert syndrome type 21 (#615636) (Tuz 2014 / Akizu 2014)	Wide phenotypic variation, some with features reminiscent of Meckel syndrome and Jeune Asphyxiating Thoracic Dystrophy	AR	
CSTB	*601145	Progressive myoclonus epilepsy 1A (Unverricht Lundborg) (#254800) (Pennacchio 1996, Lafreniere 1997)		AR	
CTDP1	*604927	Congenital cataracts, facial dysmorphism, and neuropathy (#604168) (Varon 2003)	= variant of Marinesco Sjögren (neuromuscular)	AR	
CTSD	*116840	Ceroid lipofuscinosis 10 (#610127) (Steinfeld 2006)		AR	
CWF19L1	*616120	Autosomal recessive spinocerebellar ataxia 17 (SCAR17) (#616127) (Burns 2014)		AR	
CYP2U1	*610670	SPG56/49: autosomal recessive spastic paraplegia type 56/49 (#615030) (Tesson 2012)		AR	
CYP7B1	*603711	Congenital bile acid synthesis defect 3 (#613812) (Setchell 1998)	SPG5: spastic paraplegia type 5 (#270800) (Tsaousidou	AR	

		Both enzymes affected?	2008)		
Gene Symbol (continued)	**OMIM #**	**Original phenotype**	**Phenotypic extension**	**Transmission mode**	**ADCA analysis**
DARS2	*610956	Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (#611105) (Scheper 2007)		AR	
DCAF17	*612515	Woodhouse-Sakati syndrome (#241080) (Alazami 2008)		AR	
DDB2	*600811	XPE: Xeroderma pigmentosum group E (#278740) (Nichols 1996)		AR	
DDHD1	*614603	SPG28: autosomal recessive spastic paraplegia type 28 (#609340) (Tesson 2012)		AR	
DDHD2	*615003	SPG54: autosomal recessive spastic paraplegia type 54 (#615033) (Schuurs-Hoeijmakers 2012)	Late-onset spastic ataxia (Doi 2014)	AR	
DNAJC19	*608977	3-methylglutaconic aciduria type V (#610198) (Davey 2006)		AR	
DNAJC3	*601184	Combined cerebellar and peripheral ataxia with hearing loss and diabetes mellitus (#616192) (Synofzik 2014)			
DNMT1	*126375	Hereditary sensory neuropathy type IE (#614116) (Klein 2011)	Cerebellar ataxia, deafness, narcolepsy (#604121) (Winkelmann 2012)	AD	Yes
EEF2	*130610	Spinocerebellar ataxia 26 (#609306) (Hekman 2012)		AD	Yes
EIF2B1	*606686	Leukoencephalopathy with vanishing white matter (#603896) (van der Knaap 2002)		AR	
EIF2B2	*606454	Leukoencephalopathy with vanishing white matter (#603896) (Leegwater 2001)	Ovarioleukodystrophy (#603896)	AR	
EIF2B3	*606273	Leukoencephalopathy with vanishing white matter (#603896) (van der Knaap 2002)		AR	
EIF2B4	*606687	Leukoencephalopathy with vanishing white matter (#603896) (van der Knaap 2002)	Ovarioleukodystrophy (#603896)	AR	
EIF2B5	*603945	Leukoencephalopathy with vanishing white matter (#603896) (Leegwater 2001) (most frequent gene, 2/3 of patients)	Ovarioleukodystrophy (#603896)	AR	
ELOVL4	*605512	Stargardt macular dystrophy (AD) (#600110) (Zhang 2001)	Ichthyosis, spastic quadriplegia, and mental retardation (AR) (#614457) (Aldahmesh 2011) / Spinocerebellar ataxia-34 (AD) (#133190) (Cadieux-Dion 2014)	AD / AR	Yes

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
ELOVL5	*611805	Spinocerebellar ataxia 38 (#615957) (Di Gregorio 2014)		AD	Yes
ENTPD1	*601752	SPG64: autosomal recessive spastic paraplegia type 64 (#615680) (Novarino 2014)	Regulation of immune cell levels	AR	
EPM2A	*607566	Progressive myoclonus epilepsy 2A (Lafora) (#254780) (Minassian 1998)		AR	
ERCC2	*126340	XPD: Xeroderma pigmentosum group D (#278730) (Frederick 1994)	TTD1: Trichothiodystrophy-1 (#601675) (Botta 1998) / COFS: Cerebrooculofacioskeletal syndrome-2 (#610756) (Graham 2001)	AR	
ERCC3	*133510	XPB: Xeroderma pigmentosum group B (# 610651) (Weeda 1990, Oh 2006) / Cockayne syndrome features	TTD2: Trichothiodystrophy (#616390) (Weeda 1997)	AR	
ERCC4	*133520	XPF: Xeroderma pigmentosum group F (#278760) (Sijbers 1996) / Cockayne syndrome features	Fanconi anemia group Q (#615272) (Kashiyama 2013) / XFE progeroid syndrome (#610965) (Niedernhofer 2006) (linked to ICL repair defect)	AR	
ERCC5	*133530	XPG: Xeroderma pigmentosum group G (#278780) (Nouspikel and Clarkson 1994) / Cockayne syndrome features	Cerebrooculofacioskeletal syndrome-3 (#616570) (Nouspikel 1997)	AR	
ERCC6	*609413	Cockayne syndrome type B (#133540) (Mallory 1998)	De Sanctis-Cacchione syndrome (#278800) (Colella 2000) // UV-sensitive syndrome-1 (#600630) (Horibata 2004) // Cerebrooculofacioskeletal Syndrome 1 (#214150) (Meira 2000)	AR	
ERCC8	*609412	Cockayne syndrome A (#216400) (Henning 1995)	UV-sensitive syndrome-2 (#614621) (Nardo 2009)	AR	
ERLIN1	*611604	SPG62: autosomal recessive spastic paraplegia type 62 (no OMIM #) (Novarino 2014)		AR	
ERLIN2	*611605	SPG18: autosomal recessive spastic paraplegia type 18 (#611225) (Alazami 2011)	Primary lateral sclerosis	AR	
ETFDH	*231675	Glutaric acidemia IIC = multiple acyl-CoA dehydrogenase deficiency (#231680) (Beard 1993)	Neonatal-onset form with congenital anomalies (type I), neonatal-onset form without congenital anomalies (type II), late-onset form (type III)	AR	
EXOC8	*615283	?Joubert syndrome (Dixon-Salazar 2012)		AR	
EXOSC3	*606489	Pontocerebellar hypoplasia, type 1B (#614678) (Wan 2012)	Milder spastic paraplegia with mild intellectual impairment phenotype (Zanni 2013)	AR	
FA2H	*611026	SPG35: autosomal recessive spastic paraplegia type 35 (#612319) (Edvradson 2008)		AR	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
FGF14	*601515	Spinocerebellar ataxia 27 (#609307) (van Swieten 2003)		AD	Yes
FLRT1	*604806	SPG68: autosomal recessive spastic paraplegia type 68 (Novarino 2014)		AR	
FLVCR1	*609144	Posterior column ataxia with retinitis pigmentosa (#609033) (Rajadhyaksha 2010)		AR	
FTL	*134790	Hyperferritinemia-Cataract syndrome (#600886) (Beaumont 1995)	Neurodegeneration with Brain Iron Accumulation type 3 (#606159) (Curtis 2001)/ L-ferritin deficiency (#615604) (Cremonesi 2004)	AD / AR	
FXN	*606829	Friedreich ataxia (#229300) (Delatycki 1999)		AR	
GAD1	*605363	Spastic quadriplegic cerebral palsy 1 (CPSQ1) (#603513) (Lynex 2004)		AR	
GBA2	*609471	SPG46: autosomal recessive spastic paraplegia type 46 (#614409) (Martin 2013, Hammer 2013)		AR	
GJA1	*121014	Hypoplastic left heart syndrome type 1 (#241550), atrioventricular canal defect (#600309) (Dasgupta 2001)	Oculodentodigital dysplasia (AD, #164200) (AR, #257850) (Paznekas 2003) / Syndactyly type III (#186100) (Richardson 2004) / Craniometaphyseal dysplasia (#218400) (Hu 2013) / Palmoplantar keratoderma and congenital alopecia type 1 (#104100) (Wang 2015) / erythrokeratodermia variabilis et progressiva (#133200) (Boyden 2015)	AD / AR	
GJC2	*608803	Hypomyelinating leukodystrophy type 2 (#608804) = Pelizaeus-Merzbacher-Like disease type 1 (Uhlenberg 2004)	Spastic paraplegia type 44 (#613206) (Orthmann-Murphy 2009) / Hereditary lymphedema IC (#613480) (AD) (Ferrell 2010)	AR / AD	
GOSR2	*604027	Progressive myoclonic epilepsy type 6 (#614018) (Corbett 2011)		AR	
GRID2	*602368	Autosomal recessive spinocerebellar ataxia 18 (#616204) (Utine 2013, Hills 2013)	AD congenital to late-onset ataxia (Coutelier 2015)	AR / AD	Yes
GRM1	*604473	Autosomal recessive spinocerebellar ataxia 13 (#614831) (Guergueltcheva 2012)		AR	
HEXA	*606869	Tay-Sachs disease (#272800) (Beutler 1975)		AR	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
HEXB	*606873	Sandhoff disease (#268800) (Bikker 1989)		AR	
HSD17B4	*601860	D-bifunctional protein deficiency (#261515) (Suzuki 1997)	Perrault syndrome type 1 (#233400) (Pierce 2010)	AR	
HSPD1	*118190	Autosomal dominant spastic paraplegia type 13 (#605280) (Hansen 2002)	AR hypomyelinating leukodystrophy type 4 (#612233) (Magen 2008)	AD / AR	
IFRD1	*603502	??Spinocerebellar ataxia 18 (#607458) (Brkanac 2009)		AD	Yes
INPP5E	*613037	Mental retardation, truncal obesity, retinal dystrophy, and micropenis syndrome (#610156) (Jacoby 2009) / Joubert syndrome type 1 (#213300) (Bielas 2009)		AR	
ITM2B	*603904	Familial British dementia (Vidal 1999)	Familial Danish dementia (Vidal 2000); retinal dystrophy with inner retinal dysfunction and ganglion cell abnormalities (#616079) (Audo 2014)	AD	Yes
ITPR1	*147265	Spinocerebellar ataxia 15 (#606658) (Van de Leemput 2007)	Spinocerebellar ataxia 29, congenital nonprogressive (#117360) (Huang 2012)	AD	Yes
KCNA1	*176260	Episodic ataxia / myokymia (#160120) (Browne 1994)		AD	Yes
KCNC3	*176264	Spinocerebellar ataxia 13 (#605259) (Waters 2006)		AD	Yes
KCND3	*605411	Brugada syndrome 9 (#616399) (Giudicessi 2011)	Spinocerebellar ataxia 19-22 (#607346) (Lee 2012, Duarri 2012)	AD	Yes
KCNJ10	*602208	SESAME syndrome (seizures, sensorineural deafness, ataxia, mental retardation, and electrolyte imbalance) (#612780) (Scholl 2009)		AR	
KCTD7	*611725	Progressive myoclonic epilepsy type 3 (#611726) (Van Bogaert 2007)	Pathologic findings of ceroid lipofuscinosis = CLN14	AR	
KIAA0196	*610657	Autosomal dominant spastic paraplegia type 8 (#603563) (Valdmanis 2007)	Ritscher-Schinzel syndrome-1 (#220210) (Elliott 2013)	AD / AR	
KIAA0226	*613516	Autosomal recessive spinocerebellar ataxia type 15 (#615705) (Assoum 2010)		AR	
KIF1A	*601255	SPG30: autosomal recessive spastic paraplegia type 30 (#610357) (Erlich 2011)	Hereditary sensory neuropathy type IIC (AR) (#614213) (Riviere 2011) / Nonsyndromic intellectual disability (AD) (#614255) (Hamdan 2011) / ID with variable symptoms (Lee 2015) / Progressive encephalopathy with edema, hypsarrhythmia and optic atrophy syndrome (AD) (#260565)	AR / AD	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
KIF1C	*603060	Spastic ataxia 2 (#611302) (Dor 2014)= spastic paraplegia 58 (Novarino 2014)		AR	
KIF5A	*602821	SPG10: autosomal dominant spastic paraplegia type 10 (#604187) (Reid 2002)	Charcot-Marie-Tooth type 2	AD	
KIF7	*611254	Acrocallosal syndrome (AR) (#200990) (Putoux 2011) / Hydrolethalus syndrome 2 (AR) (#614120) (Putoux 2011)	Joubert syndrome 12 (AR) (#200990) (Dafinger 2011)	AR	
L1CAM	*308840	X-linked hydrocephalus (#307000) (Rosenthal 1992)	X-linked spastic paraplegia type 1, MASA syndrome, CRASH syndrome (#303350) (Jouet 1994)	X-linked	
LAMA1	*150320	Poretti-Boltshauser syndrome (#615960), (Aldinger 2014)		AR	
LYST	*606897	Chediak-Higashi syndrome (#214500) (Nagle 1996)	Complicated spastic paraplegia (no OMIM, much milder) (2014)	AR	
MAG	*159460	Autosomal recessive spastic paraplegia type 75 (#616680) (Novarino 2014)		AR	
MARS	*156560	Interstitial lung and liver disease (#615486) (Van Meel 2013)	Charcot-Marie-Tooth type 2U (#616280) (Gonzalez 2013) (AD) / Spastic paraplegia (AR) (Novarino 2014)	AR / AD	
MARS2	*609728	Autosomal recessive spastic ataxia type 3 (#611390) (Bayat 2012)	Combined oxidative phosphorylation deficiency-25 (#616430) (Webb 2015)	AR	
MRE11A	*600814	Ataxia-telangectasia-like disorder (#604391) (Stewart 1999)		AR	
NDUFAF2	*609653	Mitochondrial complex I deficiency (#252010) (Ogilvie 2005)	Leigh syndrome (#256000) (Calvo 2010)	AR	
NIPA1	*608145	Autosomal dominant spastic paraplegia type 6 (#600363) (Rainier 2003)		AD	
NKX2-1	*600635				
NOL3	*605235	Familial cortical myoclonus (#614937) (Russell 2012)		AD	Yes
NPHP1	*607100	Juvenile nephronoptisis (#256100) (Konrad 1996)	Senior-Loken syndrome (#266900) (Caridi 1998) / Joubert syndrome (#213300) (Parisi 2004)	AR	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
NT5C2	*600417	Autosomal recessive spastic paraplegia type 45 (#613162) (Novarino 2014)		AR	
OFD1	*300170	Oral-facial-digital syndrome 1 (#311200) (Ferrante 2001)	Simpson-Golabi-Behmel Syndrome Type 2 (#300209) (Budny 2006) / Joubert syndrome 10 (#300804) (Coene 2009); Retinitis pigmentosa 23 (#300424) (Webb 2012)	XLD / XLR	
OPA1	*605290	Optic atrophy 1 (#165500)	Optic atrophy plus syndrome (#125250)	AD	Yes
PANK2	*606157	Neurodegeneration with brain iron accumulation 1 (#243200) (Zhou 2001)	HARP syndrome (#607236) (Ching 2002)	AR	
PCNA	*176740	Ataxia-telangiectasia-lie disorder 2(#615919)(Baple 2014)		AR	
PDE6D	*602676	Joubert syndrome type 22 (#615665) (Thomas 2014)		AR	
PDYN	*131340	Spinocerebellar ataxia type 23 (#610245) (Bakalkin 2010)		AD	Yes
PEX10	*602859	Peroxisome biogenesis disorder 6A (Zellweger) (#614870), peroxisome biogenesis disorder 6B (#614871) (Warren 1998)		AR	
PGAP1	*611655	Autosomal recessive mental retardation 42 (#615802)(Murakami 2014)	Spastic paraplegia type 67 (Novarino 2014)	AR	
PIK3R5	*611317	Ataxia-oculomotor apraxia type 3 (#615217) (Al Tassan 2012)		AR	
PLA2G6	*603604	Neurodegeneration with brain iron accumulation 2A = infantile neuroaxonal dystrophy (#256600); Neurodegeneration with brain iron accumulation 2B = Karak syndrome (#610217) (Morgan 2006)	Parkinson disease 14 (dystonia-parkinsonism) (#612953) (Paisan-Ruiz 2009)	AR	
PLP1	*300401	Pelizaeus-Merzbacher disease (#312080) (Cremers 1987)	Spastic paraplegia type 2 (#312920) (Saugier-Verber 1994)	XLR	
PMM2	*601785	Congenital disorder of glycosylation, type Ia (#212065) (Matthijs 1997)		AR	
PNPLA6	*603197	SPG39: autosomal recessive spastic paraplegia type 39 (#612020) (Rainier 2008)	Boucher-Neuhauser syndrome (#215470) / Gordon-Homes syndrome (#212840) (Synofzik 2014) / Oliver-McFarlane syndrome (#275400) / Laurence-Moon syndrome (#245800) (Hufnagel 2014)	AR	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
POLG	*174763	Progressive external ophtalmoplegia dominant (#157640) / recessive (#258450) (Van Goethem 2001)	Sensory Ataxic Neuropathy, Dysarthria and Ophtalmoparesis (SANDO) (#607459) (Van Goethem 2003) / mitochondrial DNA depletion syndrome type 4A (#203700) (Naviaux 2004) / mitochondrial DNA depletion syndrome type 4B (#613662) (Van Goethem 2003)	AD / AR	Yes
POLR3A	*614258	Hypomyelinating leukodystrophy 7, with or without oligodontia and / or hypogonadotropic hypogonadism (#607694) (Bernard 2011)		AR	
POLR3B	*614366	Hypomyelinating leukodystrophy 8, with or without oligodontia and / or hypogonadotropic hypogonadism (#614381) (Saitsu 2011)		AR	
PRICKLE1	*608500	Progressive myoclonic epilepsy 1B (#612437) (Bassuk 2008)		AR / ?AD	
PRKCG	*176980	Spinocerebellar ataxia type 14 (#605361) (Chen 2003)	Intellectual disability with ataxia (Najmabadi 2011)	AD / semidominant (Asai 2009) / AR	Yes
RAB3GAP2	*609275	Martsolf syndrome (#212720) (Aligianis 2006)	Warburg micro syndrome 2 (#614225) (Borck 2011) / spastic paraplegia (Novarino 2014)	AR	
REEP1	*609139	SPG31: autosomal dominant spastic paraplegia type 31 (#610250) (Zuchner 2006)	Autosomal dominant distal hereditary motor neuronopathy type VB (#614751) (Beetz 2012) / ?Spinal muscular atrophy with respiratory distress (AR) (#604320) (?Schottmann 2015)	AD / ?AR	Yes
REEP2	*609347	SPG72: spastic paraplegia type 72 (#615625) (Esteves 2014)		AD / AR	
RNF216	*609948	Gordon Holmes syndrome (#212840) (Margolin 2013)	Huntington-like disorder (Santens 2015)	AR	
RPGRIP1L	*610937	Joubert syndrome 7 (#611560) / Meckel syndrome 5 (#611561) (Delous 2007)	COACH syndrome (#216360) (Doherty 2010)	AR	
RTN2	*603183	SPH12: autosomal dominant spastic paraplegia type 12 (#604805) (Montenegro 2012)		AD	
SACS	*604490	Spastic ataxia of Charlevoix-Saguenay (#270550) (Engert 2000)		AR	
SCARB2	*602257	Progressive myoclonic epilepsy type 4, with or without renal failure (#254900) (Berkovic 2008)		AR	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
SETX	*608465	Autosomal recessive spinocerebellar 1 (SCAR1) = Ataxia with oculomotor apraxia 2 (AOA2) (AR) (#606002) (Moreira 2004)	Juvenile Amyotrophic Lateral Sclerosis 4 (AD) (#602433) (Chen 2004) / Distal motor neuropathy with upper motor neuron signs	AR / AD	
SIL1	*608005	Marinesco-Sjogren syndrome (#248800) (Anttonen 2005)		AR	
SLC16A2	*300095	Allan-Herndon-Dudley syndrome= spastic paraplegia 22 (#300523) (Dumitrescu 2004)		XLR	
SLC17A5	*604322	Sialic acid storage disease, infantile (#269920); Salla disease (adult form) (#604369) (Verheijen 1999)		AR	
SLC1A3	*600111	Episodic ataxia type 6 (#612656) (Jen 2005)		AD	Yes
SLC25A15	*603861	Hyperornithinemia-hyperammonemia-homocitrullinemia syndrome (#238970) (Camacho 1999)		AR	
SLC33A1	*603690	Autosomal dominant spastic paraplegia 42 (#612539) (Lin 2008)	Autosomal recessive congenital cataracts, hearing loss and neurodegeneration (#614482) (Huppke 2012)	AD / AR	
SLC9A1	*107310	Lichtenstein-Knorr syndrome (#616291) (Guissart 2015)	?[spastic diplegia, autism, seizures, intellectual disability, and behavioral problems] (Zhu 2015) (het de novo missense)	AR	
SNX14	*616105	Autosomal recessive spinocerebellar ataxia type 20 (#616354) (Thomas 2014)		AR	
SPAST	*604277	SPG4: autosomal dominant spastic paraplegia type 4 (#182601) (Hazan 1999)	AR-like to codominant transmission (Chinnery 2004, Lindsey 2000, Pantakani 2008)	AD / AR	
SPG11	*610844	SPG11: autosomal recessive spastic paraplegia type 11 (#604360) (Stevanin 2007)	Autosomal recessive juvenile-onset amyotrophic lateral sclerosis-5 (#602099) (Orlacchio 2010) / Autosomal recessive Charcot-Marie-Tooth disease type 2X (#616668) (Montecchiani 2016)	AR	
SPG20	*607111	SPG20: autosomal recessive spastic paraplegia type 20 = Troyer syndrome (#275900) (Patel 2002)		AR	
SPG21	*608181	Autosomal recessive spastic paraplegia type 21 = MAST syndrome (#248900) (Simpson 2003)		AR	
SPG7	*602783	SPG7: autosomal recessive spastic paraplegia type 7 (#607259) (Casari 1998)		AR / AD	Yes

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
SPTBN2	*604985	Spinocerebellar ataxia type 5 (#600224) (Ikeda 2006)	Autosomal recessive spinocerebellar ataxia type 14 (#615386) (Lise 2012)	AD / AR	Yes
SRD5A3	*611715	Congenital disorder of glycosylation type Iq (#612379) (Al Gazali 2008)		AR	
STUB1	*607207	Autosomal recessive spinocerebellar ataxia type 16 (#615768) (Shi 2013)		AR	Yes
SYNE1	*608441	Spinocerebellar ataxia type 8 (ARCA1, SCAR8) (#610743) (Gros-Louis 2007) (AR)	Emery-Dreifuss muscular dystrophy (#612998) (Zhang 2007) (AD)	AR / AD	
SYT14	*610949	Autosomal recessive spinocerebellar ataxia type 11 (#614229) (Doi 2011)		AR	
TCTN1	*609863	Joubert syndrome type 13 (#614173) (Garcia-Gonzalo 2011)		AR	
TCTN2	*613846	Joubert syndrome type 24 (#616654) (Sang 2011), Meckel syndrome type 8 (#613885) (Shaheen 2011)		AR	
TCTN3	*613847	Joubert syndrome type 18 (#614815); orofaciodigotal syndrome IV (#258860) (Thomas 2012)		AR	
TDP1	*607198	Spinocerebellar ataxia with axonal neuropathy (#607250) (Takashima 2002)		AR	
TDP2	*605764	Ataxia with epilepsy and mental retardation (Gomez-Herreros 2014)		AR	
TECPR2	*615000	Autosomal recessive spastic paraplegia type 49 (#615031) (Oz-Levi 2012)		AR	
TFG	*602498	Hereditary motor and sensory neuropathy type Okinawa (#604484) (Ishiura 2012)	?Autosomal recessive spastic paraplegia type 57 (#615658) (Beetz 2013)	AD / ?AR	
TGM6	*613900	Spinocerebellar ataxia type 35 (#613908) (Wang 2010)		AD	Yes
TMEM138	*614459	Joubert syndrome type 16 (#614465) (Lee 2012)		AR	
TMEM216	*613277	Joubert syndrome type 2 (#608091) (Edvardson 2010) / Meckel syndrome type 2 (#603194) (Valente 2010)		AR	
TMEM231	*614949	Joubert syndrome type 20 (#614970) (Srour 2012) / Meckel syndrome type 11 (#615397) (Shaheen 2013)		AR	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
TMEM237	*614423	Joubert syndrome type 14 (#614424) (Huang 2011)		AR	
TMEM240	*616101	Spinocerebellar ataxia type 21 (#607454) (Delplanque 2014)		AD	
TMEM67	*609884	Meckel syndrome 3 (#607361) (Smith 2006)	Joubert syndrome 6 (#610688) (Baala 2007) / Bardet-Biedl syndrome (#209900) (Leitch 2008) / COACH syndrome (#216360) (Brancati 2008) / Nephronoptisis 11 (#613550) (Otto 2009)	AR	
TPPA	*600415	Ataxia with isolated vitamin E deficiency (#277460) (Ouahchi 1995)		AR	
TRAPPC11	*614138	Limb-girdle muscular dystrophy type 2S (#615346) (Bogershausen 2013)		AR	
TTBK2	*611695	Spinocerebellar ataxia type 11 (#604432) (Houlden 2007)		AD	Yes
TTC19	*613814	Mitochondrial complex III deficiency nuclear type 2 (#615157) (Ghezzi 2011)		AR	
UCHL1	*191342	Neurodegeneration with optic atrophy (#615491) (Bilguvar 2013)	Possible role in Parkinson disease (Leroy 1998)	AR	
USP8	*603158	?Autosomal recessive spsatic paraplaegia type 59 (Novarino 2014)		AR	
VAMP1	*185880	Spastic ataxia 1 (#108600) (Bourassa 2012)		AD	Yes
VCP	*601023	Inclusion body myopathy with Paget disease of bone and frontotemporal dementia (#167320) (Watts 2004)	Amyotrophic lateral sclerosis 14 with or without frontotemporal dementia (#613954) (Johnson 2010) / Charcot-Marie-Tooth disease type 2Y (#616687) (Gonzalez 2014)	AD	
VPS37A	*609927	Autosomal recessive spastic paraplegia type 53 (#614898) (Zivony-Elboum 2012)		AR	
WDR45	*300526	Neurodegeneration with brain iron accumulation 5 (#300894) (Haack 2012)		XLD	
WDR48	*612167	?Spastic paraplegia 60 (Novarino 2014)		AR	
WFS1	*606201	Wofram syndrome 1 (#222300) (Strom 1998) (AR)	Nonsyndromic sensorineural deafness (#600965) (Bespalova 2001) (AD) / Wolfram-like syndrome (#614296) (AD) (Domenech 2002)	AR / AD	

Gene Symbol (continued)	OMIM #	Original phenotype	Phenotypic extension	Transmission mode	ADCA analysis
WWOX	*605131	Autosomal recessive spinocerebellar ataxia-12 (SCAR12) (#614322) (Mallaret 2014)	Early infantile epileptic encephalopathy-28 (#616211) (Abdel-Salam 2014) / NB: mutated in ovarian carcinoma and esophageal squamous cell carcinoma (somatic)	AR	
XPA	*611153	XPA: Xeroderma pigmentosum group A (#278700) (Tanaka 1990)		AR	
XPC	*613208	XPC: Xeroderma pigmentosum group C (#278720) (Li 1993)		AR	
ZFR	*615635	?Spastic paraplegia 71 (Novarino 2014)		AR	
ZFYVE26	*612012	SPG15: autosomal recessive spastic paraplegia type 15 (#270700) (Hanein 2008)		AR	
ZNF423	*604557	Nephronoptisis 14 (#614844) (Alcaraz 2006) (AR)	Joubert syndrome 19 (#614844) (Chaki 2012) (AD)	AR / AD	

eTable 2. List of Possibly to Definitely Causative Variants

Patient ID	Clinical Group	Conclusion[a]	AR or AD	Gene	Variant	Pathogenic Predictions	GERP++	Comments	Coverage of Both Alleles	Sanger Sequencing	Segregation
AAR-130-1	AOA-like	1a	AR	*ADCK3*	NM_020247.4:c.125delC:p.A42fs;c.148C>T:p.Q50X	Frameshift/nonsense	NA	*Trans* on bam files	29,26;18,12	NA	NA
AAR-646-1	Spastic	1a	AR	*ADCK3*	NM_020247.4:c.811C>T:p.R271C;c.1460C>G:p.T487R	4/4	4.09/5.51	Matching clinics	31,23;41,22	NA	TRUE (*trans*) (1)
AAR-311-13	Metabolic	2	AR	*ADCK3*	hom NM_020247.4:c.238C>T:p.H80Y	1/4	4.52	Divergent clinics	0,36	NA	TRUE (2)
AAR-615-1	Pure	2	AR	*ADCK3*	hom NM_020247.4:c.911C>T:p.A304V	4/4	5.57	Matching clinics but unusually late age of onset	0,79	NA	NA
SAL-399-32	Late complex	1a	AD	*AFG3L2*	NM_006796.2:c.1961C>T:p.T654I	Known	NA	Matching clinics	9,11	NA	NA
SAL-399-307	Metabolic	1a	AD	*AFG3L2*	NM_006796.2:c.121C>T:p.R41X	Nonsense	NA	Matching clinics	26,16	NA	NA
SAL-399-489	Spastic	2	AD	*AFG3L2*	NM_006796.2:c.232C>T:p.P78S	2/4	5.36	Not in hotspot domains, matching clinics	22,20	NA	NA
AAR-182-9	Spastic	1a	AR	*ALS2*	hom NM_020919.3:c.3619delA:p.M1207X	Nonsense	NA	Matching clinics (SLA-like)	0,44	TRUE	NA
AAR-180-11	Spastic	1a	AR	*ANO10*	hom NM_018075.4:c.132dupA:p.D45fs	Frameshift	NA	Recurrent	0,23	NA	NA
SAL-399-177	Spastic	1a	AR	*ANO10*	hom NM_018075.4:c.289delA:p.M97X	Nonsense	NA	Matching clinics	2,26	NA	NA
AAR-645-1	Spastic	1a	AR	*ANO10*	hom NM_018075.4:c.132dupA:p.D45fs	Frameshift	NA	Recurrent, segregates	0,2	TRUE	TRUE (1)
AAR-211-3	AOA-like	2	AR	*ANO10*	NM_018075.4:c.132dupA:p.D45fs;c.1537T>C:p.C513R	Frameshift/4/4	5.24	Unusual clinics (sensory polyneuropathy, AOA-like)	33,18;19,24	NA	TRUE (*trans*) (1)
AAR-355-3	AOA-like	1a	AR	*APTX*	hom NM_001195249.1:c.837G>A:p.W279X	Nonsense	NA	Matching clinics	0,30	TRUE	TRUE (1)

AAR-550-1	Metabolic	1b	AR	*ATM*	hom NM_000051.3:c.9022C>T:p.R3008C; hom c.5185G>C:p.V1729L	4/4	5.22	Recurrent, matching clinics	1,19;0,18	NA	NA
AAR-431-5	Metabolic	1a	AR	*C10orf2*	NM_021830.4:c.716C>A:p.P239H;c.1502T>C:p.M501T	3/4/4/4	5.54/5.73	Matching clinics	51,39;24,14	NA	TRUE (*trans*) (1)
AFT-76-10	Metabolic	1a	AD	*CACNA1A*	NM_001127222.1:c.2493dupC:p.N832fs	Frameshift	NA	Divergent clinics (epilepsy)	53,37	NA	NA
AAR-173-1	Pure	1a	AD	*CACNA1A*	NM_001127222.1:c.4633C>T:p.R1545X	Nonsense	NA	Matching clinics (episodic ataxia)	22,17	NA	NA
SAL-399-9	Pure	1a	AD	*CACNA1A*	NM_001127222.1:c.4979G>A:p.R1660H	4/4	3.26	Near to known variants, matching clinics	33,23	NA	NA
SAL-399-186	Spastic	1a	AD	*CACNA1A*	NM_001127222.1:c.4997G>A:p.R1666Q	4/4	4.96	Aminoacid known to be mutated, matching clinics	28,32	NA	NA
SAL-399-498	Pure	2	AD	*CACNA1A*	NM_001127222.1:c.889G>A:p.G297R	4/4	5.42	Near to known variants, matching clinics	39,44	NA	NA
AAR-492-3	Pure	2	AD	*CACNA1A*	NM_001127222.1:c.4034G>A:p.R1345Q	4/4	5.4	Near to known variants, matching clinics	26,24	NA	NA
SAL-399-194	Metabolic	1a	AR	*CEP290*	NM_025114.3:c.1079G>A:p.R360Q;c.4962_4963del:p.Q1654fs	Frameshift/3/4	5.43	Matching clinics	15,15;19,13	NA	NA
AAR-120-4	Metabolic	1a	AR	*CLN5*	hom NM_006493.2:c.755A>G:p.N252S	4/4	5.84	Matching clinics (cardiomyopathy, optic atrophy)	1,14	NA	NA
AAR-320-1	Spastic	1a	AR	*CYP7B1*	NM_004820.4:c.440G>A:p.G147D;c.825T>A:p.Y275X	Nonsense/3/4	5.17	Matching clinics	14,16;10,8	NA	NA
AAR-463-3	Spastic	1a	AR	*CYP7B1*	hom NM_004820.4:c.907T>G:p.W303G	4/4	5.67	Matching clinics	0,13	NA	TRUE (2)
SAL-399-229	Spastic	1b	AR	*CYP7B1*	hom NM_004820.4:c.524G>A:p.W175X	NA	NA	Matching clinics, very high levels of oxysterols	0,32	NA	NA
AAR-73-4	Spastic	1a	AR	*ERCC5*	hom NM_000123.3:c.3004C>T:p.Q1002X	Nonsense	NA	Matching clinics	0,31	TRUE	TRUE (2)
AAR	Spasti	1a	AR	*GB*	M_020944.2:c.517T>C:p.W17	Frameshi	4.2	Matching clinics	44,32;3	NA	NA

-69-4	c			*A2*	3R;c.712_715del:p.V238fs	ft/4/4	7		1,15		
AAR-498-1	AOA-like	1a	AR	*HEXA*	hom NM_000520.5:c.1511G>A:p.R504H	2/4	5.71	Matching clinics, very low hexaminidase	0,20	NA	NA
AAR-354-1	Spastic	2	AR	*HEXA*	NM_000520.5:c.739C>T:p.R247W;c.1033G>A:p.G345S	3/4/3/4	3.72/3.33	Matching clinics	21,20;21,35	NA	NA
AAR-224-1	Metabolic	1b	AR	*HSD17B4*	NM_001199291.2:c.817C>T:p.R273C;c.1207G>A:p.G403R	4/4/4/4	5.51/5.49	Matching clinics (white matter changes)	18,30;39,38	NA	TRUE (*trans*) (2, monozygous twins)
SAL-399-257	Pure	2	AD	*ITPR1*	NM_001168272.1:c.3785T>A:p.I1262N	4/4	5.24	Matching clinics	6,4	NA	NA
AAR-266-1	Late complex	2	AD	*ITPR1*	NM_001168272.1:c.2012A>G:p.N671S	1/4	1.3	Matching clinics (late complex, dystonia, parkinsonism)	58,54	NA	NA
AAR-636-3	Pure	2	AD	*KCND3*	NM_004980.4:c.641A>G:p.K214R	2/4	5.51	Matching clinics (episodic ataxia)	0,5	TRUE (het)	NA; unaffected mother carries the variant
SAL-208-1	Spastic	1a	AR	*KIF1C*	hom NM_006612.5:c.2836C>T:p.Q946X	Nonsense	NA	Matching clinics	0,27	TRUE	TRUE (1)
AAR-388-6	Spastic	1a	AR	*KIF1C*	hom NM_006612.5:c.1019dupG:p.R340fs	Frameshift	NA	Matching clinics	0,106	TRUE	TRUE (2)
SAL-399-457	AOA-like	2	AR	*PLA2G6*	NM_003560.3:c.1116C>G:p.F372L;c.2233_2244del:p.745_748del	Indel/3/4	2.08	Divergent clinics (AOA-like)	32,42;61,23	NA	NA
FSP-819-3	Spastic	1a	AR	*PLA2G6*	NM_003560.3:c.1903C>T:p.R635X;c.T2411C:p.L804P	Nonsense/2/4	4.29	Matching clinics, mathcing RMI signs (T2 hyposignals of the pallidum)	8,9;25,16	NA	TRUE (trans) (1)
SAL-244-3	Metabolic	1b	AR	*PMM2*	NM_000303.2:c.T470C:p.F157S;c.G722C:p.C241S	4/4/3/4	5.22/5.22	Matching clinics	17,29;54,59	NA	NA
AAR-45-13	Spastic	1a	AR	*PNPLA6*	hom NM_001166111.1:c.2633G>A:p.G878D	4/4	4.98	In hotspot domain, matching clinics	0,14	NA	NA
AAR-611-14	Pure	2	AR	*PNPLA6*	NM_001166111.1:c.1483C>A:p.P495T;c.1857G>T:p.Q619H	2/4/2/4	4.99/1.72	Matching clinics (hypogonadism)	49,51;20,33	NA	NA
SAL-399-222	Spastic	1a	AR	*POLG*	hom NM_001126131.1:c.2243G>C:p.W748S	3/4	5.57	Recurrent, matching clinics (spastic, sensory polyneuropathy)	0,90	NA	NA
AAR	Meta	1a	AR	*PO*	hom	3/4	5.5	Recurrent, matching clinics	0,64	NA	TRUE (2)

-407-13	bolic			*LG*	NM_001126131.1:c.2243G>C:p.W748S		7	(ophthalmoplegia, polyneuropathy)			
AAR-127-1	Pure	1a	AR	*PRKCG*	hom NM_002739.4:c.767T>C:p.M256T	3/3 (LRT NA)	4.11	Near to known homozygous variants	0,48	NA	NA
AAR-132-7	Pure	1a	AD	*PRKCG*	NM_002739.4:c.303C>G:p.H101Q	Known	NA	Matching clinics	51,46	NA	NA
SAL-399-897	Late complex	1a	AD	*PRKCG*	NM_002739.4:c.368G>T:p.G123V	3/3 (LRT NA)	4.75	Aminoacid known to be mutated, matching clinics	20,17	NA	NA
SAL-399-443	Spastic	2	AD	*PRKCG*	NM_002739.4:c.221A>G:p.H74R	3/3 (LRT NA)	4.68	Near to known variants, divergent clinics (deafness, late onset)	39,26	NA	NA
AAR-350-3	Metabolic	1a	AR	*RNF216*	hom NM_207111.3:c.1754C>T:p.T585M	3/4	5.6	Matching clinics (white matter changes, psychiatric)	0,54	NA	NA
AAR-408-7	Pure	1a	AR	*RNF216*	hom NM_207111.3:c.1489T>A:p.F497I	3/4	5.48	Matching clinics	2,25	NA	NA
AAR-111-5	Spastic	1a	AR	*SACS*	hom NM_014363.5:c.12220G>C:p.A4074P	3/4	5.31	Recurrent, matching clinics (spastic, deafness)	0,22	NA	NA
AAR-196-10	Spastic	1a	AR	*SACS*	hom NM_014363.5:c.2018dupA:p.N673fs	Frameshift	NA	Matching clinics (demyelinating polyneuropathy)	0,12	TRUE	TRUE (1)
AAR-334-9	Spastic	1b	AR	*SACS*	NM_014363.5:c.2881C>T:p.R961X;c.8108G>A:p.R2703H	Nonsense/4/4	5.56	Matching clinics	52,56;40,47	NA	NA
AAR-340-3	Spastic	1a	AR	*SACS*	hom NM_014363.5:c.11779dupG:p.A3927fs	Frameshift	NA	Matching clinics though late onset (43)	1,24	TRUE	TRUE (2)
AAR-618-1	Metabolic	1a	AR	*SACS*	hom NM_014363.5:c.12220G>C:p.A4074P	3/4	5.31	Recurrent, matching clinics (demyelinating polyneuropathy)	0,28	NA	NA
SAL-249-3	Metabolic	2	AR	*SACS*	NM_014363.5:c.8339T>G:p.F2780C;c.12677A>T:p.Q4226L	4/4/3/4	5.44/5.32	Non excluding clinics (epilepsy, myoclony)	54,48;47,35	NA	NA
SAL-399-77	Spastic	2	AR	*SACS*	NM_014363.5:c.4718T>G:p.M1573R;c.8227delC:p.H2743fs	Frameshift/2/4	4.98	Matching clinics	16,20;55,41	NA	NA
AAR-532-3	Spastic	2	AR	*SACS*	NM_014363.5:c.2983G>T:p.V995F;c.7586C>T:p.T2529I	0/4/4/4	-6.84/5.	Matching clinics	26,19;22,20	NA	NA

							72				
AAR-152-3	Metabolic	1a	AR	SETX	hom NM_015046.6:c.7138C>G:p.R2380G	4/4	5.17	Matching clinics	1,43	NA	TRUE (trans) (1)
AAR-268-3	AOA-like	1a	AR	SETX	NM_015046.6:c.6017G>A:p.C2006Y;c.7319A>G:p.D2440G	4/4/4/4	4.58/4.84	Matching clinics, elevated alpha-fetoprotein	59,74;3,3	TRUE	TRUE (trans) (1)
AAR-308-14	AOA-like	1a	R	SETX	hom NM_015046.6:c.2659C>T:p.Q887X	Nonsense		Matching clinics, elevated alpha-fetoprotein	0,12	NA	NA
AAR-328-15	Pure	1a	AR	SETX	hom NM_015046.6:c.7267G>A:p.G2423R	4/4	5.31	Matching clinics (demyelinating polyneuropathy)	0,10	NA	TRUE (2)
SAL-399-144	Sensory	1a	AAR	SETX	hom NM_015046.6:c.5224G>A:p.D1742N;c.5227T>C:p.Y1743H	4/4/3/4	5.71/5.71	Matching clinics	0,25	NA	NA
AAR-586-6	AOA-like	1a	AR	SETX	NM_015046.6:c.4075C>T:p.Q1359X;c.6694C>T:p.R2232C	Nonsense/4/4	5.69	Matching clinics, elevated alpha-fetoprotein	10,12;16,10	NA	TRUE (*trans*) (1)
AAR-171-1	Sensory	2	AR	SETX	hom NM_015046.6:c.7249T>G:p.Y2417D	2/4	5.31	Matching clinics (sensory ataxia, demyelinating polyneuropathy)	0,9	TRUE	NA
AAR-3-5	Metabolic	1a	AR	*SNX14*	NM_153816.5:c.709C>T:p.R237X;c.1108G>A:p.E370K	Nonsense/3/3 (SIFT NA)	5.39	Matching clinics (deafness)	16,15;15,10	NA	TRUE (*trans*) (2)
AAR-12-26	Spastic	1a	AR	*SPG11*	hom NM_025137.3:c.2315T>A:p.L772X	Nonsense	NA	Matching clinics	0,63	NA	TRUE (1); unaffected sibling heterozygous
SAL-607-4	Spastic	1b	AR	*SPG11*	NM_025137.3:c.4252delA:p.M1418fs;ex7 del	Frameshift/Del	NA	Matching clinics	3,13;coverage drop	TRUE/confirmed on MLPA	NA
AAR-40-9	Spastic	1a	AR	*SPG7*	hom NM_003119.3:c.1529C>T:p.A510V	Known	NA	Matching clinics	1,32	NA	NA
AAD-81-8	Spastic	1a	AR	*SPG7*	NM_003119.3:c.1529C>T:p.A510V;c.1747T>C:p.W583R	Known/4/4	4.73	Matching clinics	19,19;30,12	NA	TRUE (3)
AAR-331-6	NA	1a	AR	*SPG7*	hom NM_003119.3:c.1529C>T:p.A510V	Known	NA	NA	0,42	NA	NA
AAR-339-1	Spastic	1a	AR	*SPG7*	hom NM_003119.3:c.1529C>T:p.A510V	Known	NA	Matching clinics	0,37	NA	TRUE (2)

SAL-399-45	Spastic	1a	AR	*SPG7*	NM_003119.3:c.233T>A:p.L78X;c.1529C>T:p.A510V	Nonsense/Known	NA	Matching clinics	18,24;5,2	TRUE (A510V)	NA
SAL-399-216	Spastic	1a	AR	*SPG7*	NM_003119.3:c.1529C>T:p.A510V;c.2084T>C:p.L695P	Known/4/4	5.21	Matching clinics	5,2;34,24	New DNA sample requested	NA
SAL-399-225	Spastic	1a	AR	*SPG7*	NM_003119.3:c.1894G>A:p.G632R;c.1529C>T:p.A510V	Known/4/4	5.93	Matching clinics	35,24;17,15	NA	NA
SAL-399-327	Spastic	1a	AR	*SPG7*	NM_003119.3:c.233T>A:p.L78X;c.1529C>T:p.A510V	Nonsense/Known	NA	Matching clinics + cognitive decline	32,32;21,28	NA	NA
SAL-399-473	Spastic	1a	AR	*SPG7*	NM_003119.3:c.86G>A:p.W29X;c.1529C>T:p.A510V	Nonsense/Known	NA	Matching clinics	2,8;23,23	NA	NA
SAL-399-566	Metabolic	1a	AR	*SPG7*	NM_003119.3:c.1529C>T:p.A510V;c.2228T>C:p.I743T	Known/4/4	4.49	Matching clinics	25,43;38,21	NA	NA
SAL-399-961	Metabolic	1a	AR	*SPG7*	NM_003119.3:c.1529C>T:p.A510V;c.1972G>A:p.A658T	Known/3/4	5.06	Matching clinics (ophtalmoplegia, brisk reflexes)	4,7;47,18	TRUE (A510V)	NA
AAR-541-9	Spastic	1a	AR	*SPG7*	NM_003119.3:c.1519C>T:p.Q507X;c.1529C>T:p.A510V	Nonsense/Known	NA	Matching clinics	4,13;14,4	NA	TRUE (3)
AAD-847-18	Metabolic	1a	AR	*SPG7*	hom NM_003119.3:c.1529C>T:p.A510V	Known	NA	Matching clinics	3,40	NA	TRUE (3)
AAR-628-1	Spastic	1b	AR	*SPG7*	NM_003119.3:c.1408C>T:p.R470X;c.1715C>T:p.A572V	Known	NA	Matching clinics	40,45;49,42	NA	NA
AAR-449-3	Spastic	1a	AD	*SPTBN2*	NM_006946.2:c.1472T>C:p.L491P	4/4	4.47	Second spectrin repeat, matching clinics	32,22	NA	NA
AAR-61-11	Pure	1a	AR	*SYNE1*	hom NM_182961.3:c.11946_11947insTT:p.L3983fs	Frameshift	NA	Matching clinics	0,67	NA	NA
AAR-163-6	Late complex	1a	AR	*SYNE1*	hom NM_182961.3:c.16228C>T:p.R5410X	Nonsense	NA	Matching clinics	0,21	NA	NA
SAL-399-573	Spastic	1a	AR	*SYNE1*	NM_182961.3:c.14273T>G:p.L4758X;c.23346G>A:p.W7782X	Nonsense/nonsense	NA	Matching clinics	31,38;59,37	NA	NA
AAR-536-	Pure	1a	AR	*SYNE*	hom NM_182961.3:c.4561C>T:p.R	Nonsense	NA	Matching clinics	0,35	TRUE	TRUE (1); unaffected

4				*1*	1521X						sibling heterozygous
AAR-241-13	Pure	1b	AR	*SYNE1*	NM_182961.3:c.638T>C:p.F213S;c.2755A>T:p.K919X;c.24931C>G:p.Q8311E	NA	NA	Matching clinics	5,4;14,22;5,5	NA	NA
SAL-399-1023	Sensory	2	AR	*SYNE1*	NM_182961.3:c.11187G>T:p.K3729N;c.23179G>A:p.D7727N	2/4/3/4	3.05/5.99	Nonexcluding clinics (ganglionopathy)	20,16;6,8	NA	NA
SAL-399-171	Spastic	1a	AD	*TTBK2*	NM_173500.3:c.1302dupC:p.R435fs	Frameshift	NA	Matching clinics	18,14	NA	NA
AAR-218-3	Sensory	1b	AR	*TTPA*	hom NM_000370.3:c.744delA:p.E248fs	NA	NA	Matching clinics	0,12	NA	NA
SAL-399-1035	Spastic	2	AR	*TTPA*	NM_000370.3:c.265C>T:p.P89S;c.515C>G:p.T172S	4/4/0/4	3.74/1.30	Divergent clinics, normal vitamin E levels	30,17;23,25	NA	NA

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; NA, not applicable.

[a]Variants are classified according to their pathogenicity classification as 1a (very probable/definite diagnosis), 1b (diagnosis made elsewhere during the study process, confirmed by our study, hence considered definite), or 2 (possible diagnosis). Reasons for classifying variants in categories 1a and 2 are listed for each variant. In silico pathogenicity software used were sorting intolerant from tolerant (SIFT), polymorphism phenotyping 2 (Polyphen2) HumDiv, LRT, and MutationTaster. Higher Genomic Evolutionary Rate Profiling (GERP++) conservation scores[35] (http://mendel.stanford.edu/SidowLab/downloads/gerp/) indicates better conservation. Variants were annotated with Annovar (http://annovar.openbioinformatics.org/en/latest).

eTable 3. Variants of Unknown Significance

Patient ID	Clinical group	AR/AD	Gene	Variant
SAL-399-861	Pure	AR	*ARL6IP1*	NM_015161.2:c.310A>T:p.R104X;c.349C>T:p.R117C
SAL-399-264	Late complex	AR/AD	*ATM / RNF216 / SPTBN2*	NM_000051.3:c.320G>A:p.C107Y;c.334G>A:p.A112T;c.7313C>T:p.T2438I / NM_207111.3:c.436A>C:p.T146P;c.2686G>A:p.V896I / NM_006946.2:c.643G>A:p.V215M
AAR-155-4	Metabolic	AR	*ATP7B*	NM_000053.3:c.1934T>G:p.M645R;c.4301C>T:p.T1434M
SAL-399-545	Spastic ataxia	AR	*BSCL2*	NM_001122955.3:c.940G>A:p.V314M;c.1280T>C:p.L427P
AAR-27-12	Sensory ataxia	AD	*CACNA1A*	NM_001127222.1:c.6001C>T:p.P2001S
AAR-641-1	Sensory ataxia	AD	*CACNA1A*	NM_001127222.1:c.5700C>G:p.I1900M
AAR-400-10	Spastic ataxia	AR	*CACNA1A*	hom NM_001127222.1:c.1357G>A:p.A453T
AAR-95-16	Spastic ataxia	AR	*CLN5*	hom NM_006493.2:c.65G>T:p.R22L
AAR-592-1	Pure	AR	*CLN6*	NM_017882.2:c.34G>A:p.A12T;c.44G>A:p.G15D
AAR-613-1	Metabolic	AR/AD	*COL18A1 / KCNA1*	NM_030582.3:c.2597G>A:p.R866Q;c.3842C>G:p.P1281R; NM_000217.2:c.922C>A:p.H308N
AAR-262-5	No group	AR/AD	*CWF19L1 / CACNA1A*	hom NM_018294.5:c.1363G>A:p.D455N; NM_001127222.1:c.6325G>A:p.G2109R;c.6335T>C:p.L2112P
SAL-399-836	Spastic ataxia	AD	*EEF2*	NM_001961.3:c.487G>A:p.A163T
SAL-399-1034	Late complex	AD	*ELOVL5*	NM_001242828.1:c.952G>T:p.V318L
AAR-661-1	Late complex	AD	*ELOVL5*	NM_001242828.1:c.212G>T:p.G71V
AAR-289-3	Pure	AD	*GRID2*	NM_001510.3:c.2147A>G:p.N716S
AAR-383-7	Pure	AD	*IFRD1 / POLG*	NM_001550.3:c.440C>A:p.A147E / NM_001126131.1:c.1493A>C:p.K498T
AAR-493-9	Metabolic	AD	*ITPR1*	NM_001168272.1:c.2107C>G:p.Q703E

Patient ID (continued)	Clinical group	AR/AD	Gene	Variant
AAR-59-13	Spastic ataxia	AD	*ITPR1*	NM_001168272.1:c.8194C>T:p.P2732S
SAL-209-1	Late complex	AD	*KCNC3*	NM_004977.2:c.1696C>T:p.P566S
AAR-29-9	Spastic ataxia	AD	*KCNC3*	NM_004977.2:c.2096G>A:p.G699D
SAL-399-588	Pure	AR	*KIF1C*	NM_006612.5:c.1111G>A:p.A371T;c.2989G>A:p.G997R
SAL-399-871	Pure	AR	*KIF1C*	NM_006612.5:c.1346A>G:p.K449R;c.2920G>A:p.D974N
SAL-399-1040	Late complex	AR	*LYST*	NM_000081.3:c.8913T>G:p.N2971K;c.9017A>G:p.K3006R
AAR-329-1	No clinic	AD	*NOL3*	NM_001276319.1:c.356G>C:p.R119T
MET-35-4	Metabolic	AR	*OFD1*	hom NM_003611.2:c.1294A>G:p.K432E
AAR-159-16	Spastic ataxia	AD	*OPA1*	NM_130836.2:c.2341G>A:p.A781T
AAR-287-4	Metabolic	AD	*PDYN*	NM_001190898.2:c.616C>T:p.R206C
AAR-356-1	Metabolic	AR	*PEX10*	NM_153818.1:c.80G>A:p.S27N;c.88G>T:p.G30C
AAR-606-1	Metabolic	AD	*POLG*	NM_001126131.1:c.729C>A:p.D243E
SAL-231-23	Sensory ataxia	AD	*POLG*	NM_001126131.1:c.3151G>C:p.G1051R
AAR-256-3	Metabolic	AD	*POLG*	NM_001126131.1:c.655G>T:p.A219S
AAR-272-9	Metabolic	AR/AD	*POLG / ITPR1*	NM_001126131.1:c.1550G>T:p.G517V;c.3076C>T:p.R1026C / NM_001168272.1:c.4288G>A:p.V1430M
AAR-539-1	Metabolic	AR	*POLG/ (SYNE1)*	hom NM_001126131.1:c.127_128insGGC:p.Q43delinsRQ / hom NM_182961.3:c.7976C>A:p.T2659N
AAR-141-7	Metabolic	AR	*PRICKLE1*	NM_153026.2:c.370G>A:p.A124T;c.2236C>T:p.P746S
AAR-264-6	Late complex	AD	*SLC1A3*	NM_004172.4:c.1544A>G:p.E515G
SAL-399-1013	Pure	AD	*SLC1A3*	NM_004172.4:c.67C>T:p.R23C

Patient ID (continued)	Clinical group	AR/AD	Gene	Variant
SAL-399-934	No group	AR	*SLC33A1*	NM_001190992.1:c.1136C>A:p.A379D;c.1141C>A:p.P381T
AAD-254-7	No group	AR	*SPAST*	NM_014946.3:c.775G>A:p.G259S;c.844T>C:p.S282P;c.922A>G:p.T308A
SAL-399-1042	Metabolic	AD	*SPTBN2*	NM_006946.2:c.5168G>T:p.G1723V
AAR-432-5	Metabolic	AD	*SPTBN2*	NM_006946.2:c.2546_2548del:p.849_850del
AAR-18-10	Spastic ataxia	AD	*SPTBN2*	NM_006946.2:c.5137C>T:p.R1713C
AAR-240-15	Spastic ataxia	AD	*SPTBN2*	NM_006946.2:c.805A>G:p.I269V
AAR-281-3	Late complex	AR	*SYNE1*	NM_182961.3:c.1964A>G:p.Q655R;c.13253A>G:p.N4418S
AAR-129-1	Spastic ataxia	AR	*SYNE1*	NM_182961.3:c.8779C>T:p.R2927C;c.20182C>T:p.R6728C
AAR-546-3	Metabolic	AR	*SYNE1*	NM_182961.3:c.5693A>G:p.N1898S,c.6908C>T:p.T2303M,c.22891C>T:p.L7631F
AAR-413-9	Pure	AR	*SYNE1*	NM_182961.3:c.2995G>A:p.E999K;c.12565G>A:p.V4189M;c.21758C>T:p.S7253L
AAR-291-4	Pure	AD	*TGM6*	NM_198994.2:c.730G>A:p.G244S
SAL-399-966	Pure	AD	*TTBK2*	NM_173500.3:c.3406A>G:p.N1136D
AAR-590-1	Late complex	AD	*VAMP1*	NM_016830.3:c.344G >A:p.R115Q