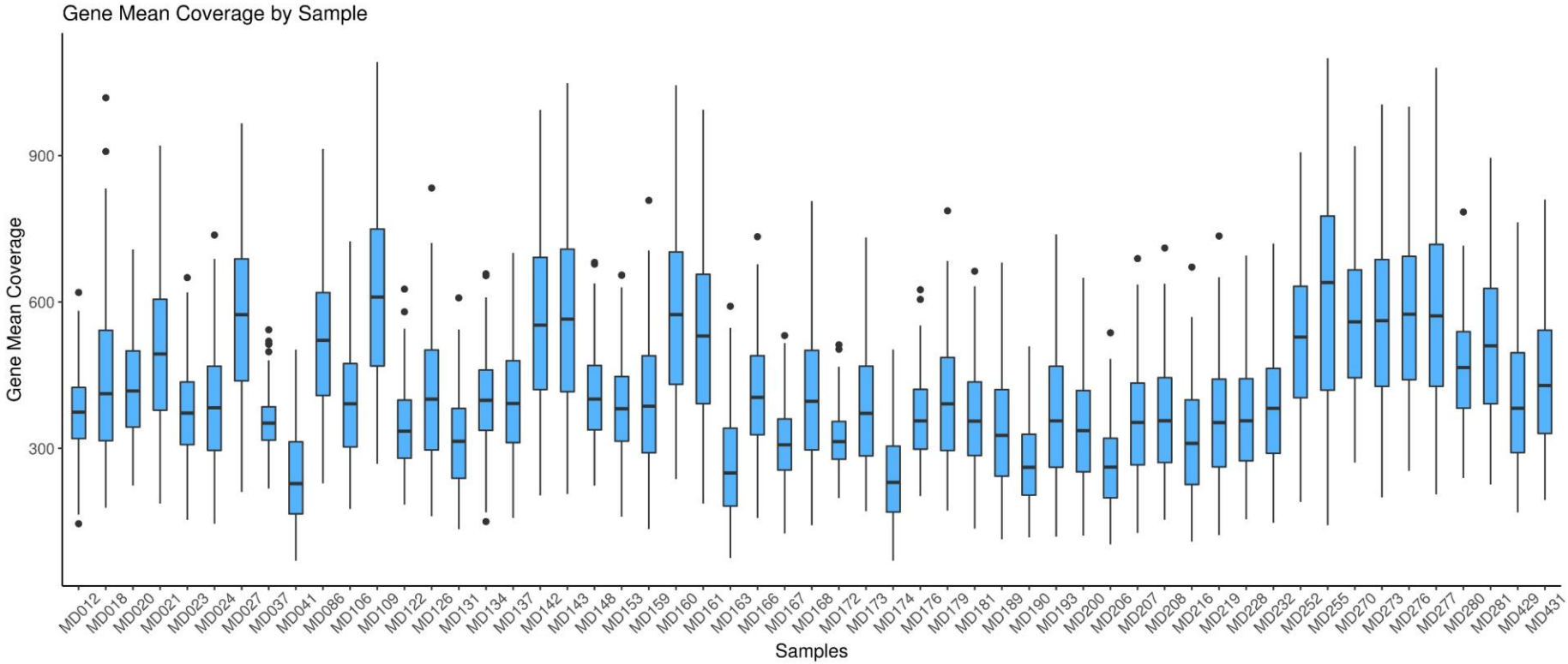
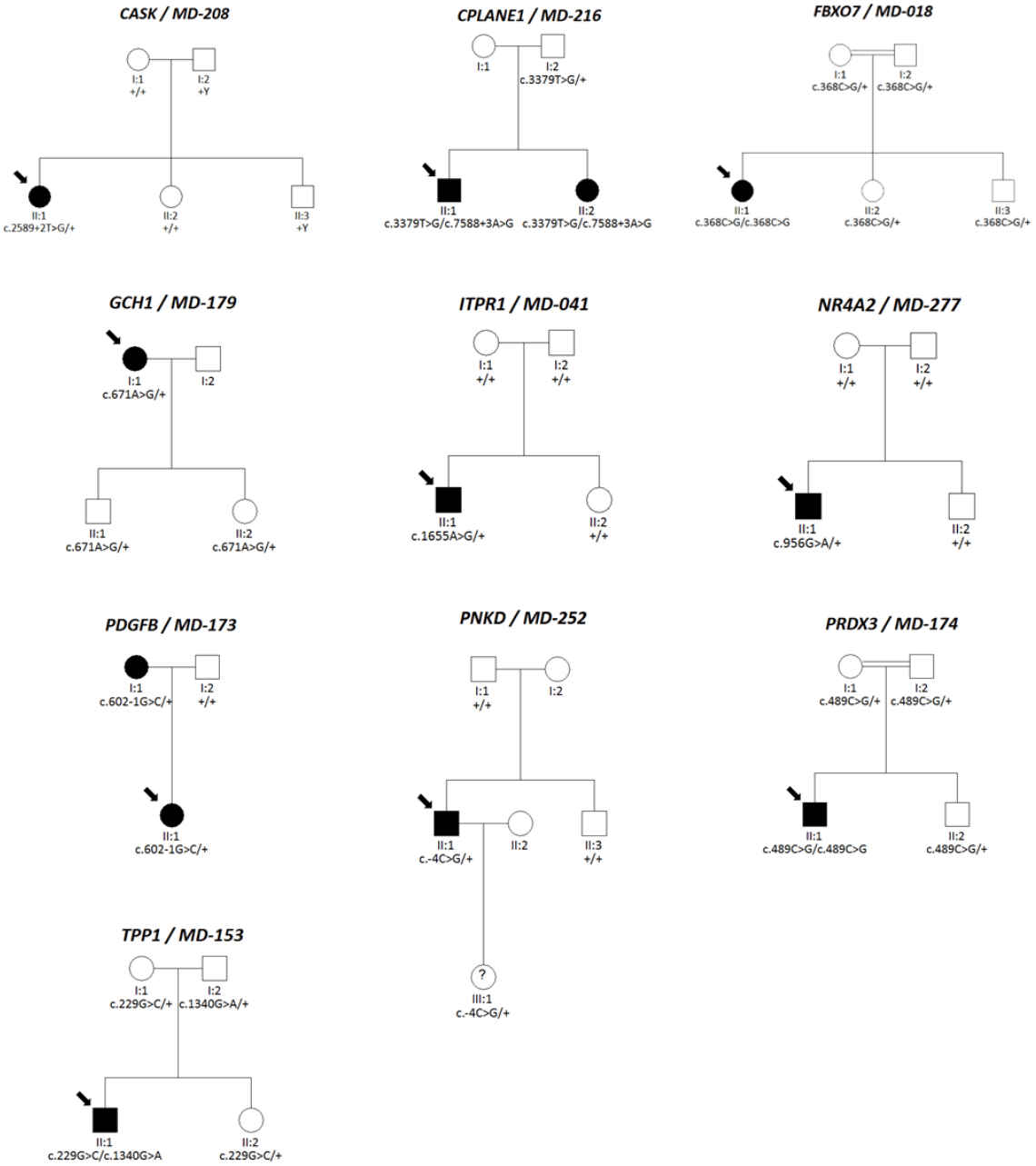
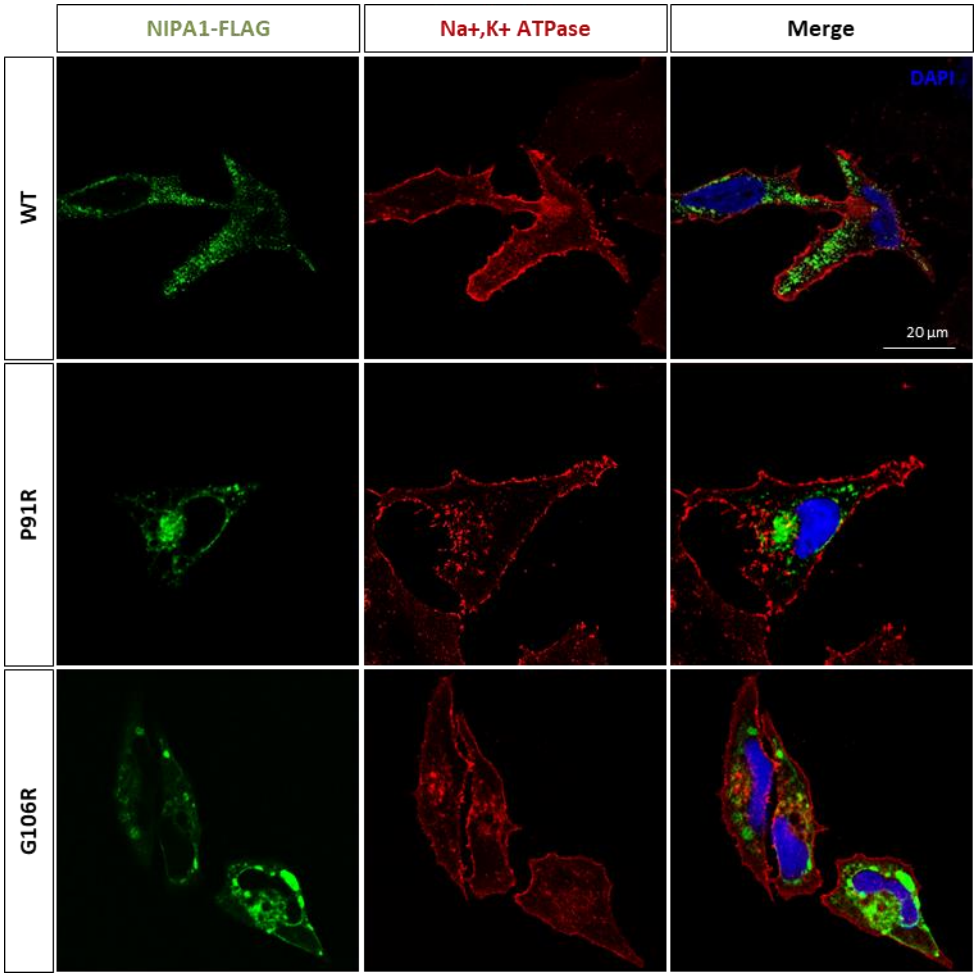


Supplementary Figure S1. Depth of coverage of each of the 55 samples analysed using the custom gene panel MovDisord.



Supplementary Figure S2. Segregation analysis of disease-causing mutations. Only families for which DNA was available from parents and other relatives are included. At the top of each pedigree, the responsible gene and the proband's code are indicated. The arrow points out the proband. Genotypes for each deleterious variant are shown below each symbol/subject; those individuals without genotype were not investigated because DNA was not available. Plus (+) symbol refers to the absence of the causative changes. A question mark (?) on the MD-252's daughter (*PNKD*) means that this girl (25 years old) is currently asymptomatic. All the implicated genes are located in autosomes, except *CASK* that is located on chromosome X. MD-018 (*FBXO7*) and MD-174 (*PRDX3*) were born to consanguineous parents.



Supplementary Figure S3. Intracellular distribution of transiently expressed wild-type (WT) NIPA1 protein and two NIPA1 mutated forms: p.P91R identified in patient MD-232 and the recurrent clinical mutation p.G106R. HeLa cells were transfected with NIPA1 constructs, tagged with FLAG in C-ter, for 24 hours and subsequently fixed and immunostained using anti-FLAG antibody (green), anti-sodium potassium ATPase (Na^+,K^+ ATPase) antibody (red) as a marker of plasma membrane, and DAPI (blue). Representative confocal microscopy images are shown. WT-NIPA1 displays a diffuse cytoplasmatic pattern extended to the cell surface; minimal or no co-localization with Na^+, K^+ATPase is detected. In contrast, NIPA1-P91R predominantly shows perinuclear distribution and sporadically localizes in larger vesicle-like structures, while NIPA1-G106R is accumulated in large aggregates, as previously described.

Supplementary Table S1. Haplotype constructed for the *PANK2* locus in twelve unrelated carriers of the c.1583C>T (rs137852967) mutation.

			***PANK2* gene**								
Patients ID	**Origin**	***PANK2* c.1583C>T**	**rs1078152**	***D20S867***	**rs6084513**	**rs137852967**	**rs6037695**	**rs7270329**	***D20S889***	***D20S116***	**rs1628323**
MD-002	Spain	HOMOZYGOSIS Roma	A	268	C	**T**	C	G	285	115	T
			A	268	C	**T**	C	G	285	119	T
MD-004			A	268	C	**T**	C	G	285	115	T
			A	268	C	**T**	C	G	285	119	T
MD-007			A	268	C	**T**	C	G	285	115	T
			A	268	C	**T**	C	G	285	119	T
MD-008			A	268	C	**T**	C	G	285	115	T
			A	268	C	**T**	C	G	285	119	T
MD-040			A	268	C	**T**	C	G	285	115	T
			A	268	C	**T**	C	G	285	119	T
MD-101			A	268	C	**T**	C	G	285	115	T
			A	268	C	**T**	C	G	285	119	T
MD-132			A	268	C	**T**	C	G	285	115	T
			A	268	C	**T**	C	G	285	119	T
MD-046	Hungary		C	268	C	**T**	C	G	285	115	T
			C	271	C	**T**	C	G	289	119	T
MD-114	Greece	HETEROZYGOUS Non-Roma	A	268	C	**T**	C	G	285	115	T
			A	270	C	C	C	G	287	109	C
MD-115			A	268	C	**T**	C	G	285	115	T
			A	270	C	C	C	G	287	109	C
MD-112			A	268	C	**T**	C	G	278	103	C
			A	270	C	C	C	G	281	103	C
MD-102	Spain		A	268	A	**T**	T	C	270	109	C
			A	272	A	C	T	C	268	103	C

Supplementary Table S2. Sequencing coverage summary for the 55 samples investigated with the custom gene panel MovDisord.

Patient	Mean Coverage	% Bases							
		>1	>10	>15	>20	>50	>100	>150	>200
MD-012	369.93	100	100	100	99.9	99.7	98.7	95.9	90
MD-018	424.68	100	100	100	100	99.7	98.6	95.7	89.5
MD-020	417.2	100	100	100	100	99.7	98.8	96.5	91.6
MD-021	493.46	100	100	100	100	99.8	98.9	97.1	93.4
MD-023	368.66	100	100	100	99.9	99.7	98.5	95.2	88.6
MD-024	379.66	100	100	100	100	99.6	97.6	93	85.4
MD-027	568.79	100	100	100	100	99.8	99.3	98.1	95.9
MD-037	353.92	100	100	100	99.9	99.7	98.8	96.7	91.5
MD-041	233.64	100	99.9	99.8	99.7	97.2	86	70.7	55.2
MD-086	516.01	100	100	100	100	99.8	99	97.2	94.2
MD-106	386.23	100	100	100	100	99.7	98	93.9	86.9
MD-109	605.06	100	100	100	100	99.8	99.3	98	95.8
MD-122	335.85	100	100	100	99.9	99.6	98.3	94	84.9
MD-126	397.78	100	100	100	99.9	99.6	97.5	92.8	85.6
MD-131	310.47	100	100	100	99.9	99.3	95.8	88.1	76.9
MD-134	395.8	100	100	100	99.9	99.7	98.8	96.4	91.3
MD-137	390.44	100	100	100	100	99.8	98.5	95.2	88.6
MD-142	554.74	100	100	100	100	99.8	99.1	97.6	94.9
MD-143	560.46	100	100	100	100	99.8	99.1	97.5	94.6
MD-148	400.55	100	100	100	100	99.8	99	96.9	92.2
MD-153	376.61	100	100	100	100	99.8	98.7	95.7	89.6
MD-159	386.92	100	100	100	100	99.5	97.2	92.1	84.1
MD-160	564.34	100	100	100	100	99.8	99.1	97.4	94.5
MD-161	527.56	100	100	100	100	99.8	98.8	96.7	93.1
MD-163	257.78	100	99.9	99.8	99.7	97.9	88.9	75.5	60.9
MD-166	403.67	100	100	100	100	99.8	98.7	96	90.5
MD-167	306.19	100	100	100	100	99.6	97.7	91.9	80.8
MD-168	393.89	100	100	100	100	99.6	97.4	92.7	85.2
MD-172	316.42	100	100	100	100	99.7	98.7	95.2	86.6
MD-173	370.92	100	100	100	100	99.7	98.1	93.6	85.2
MD-174	233.33	100	99.9	99.9	99.7	97.8	88	72.6	56.5
MD-176	356.49	100	100	100	100	99.7	98.6	95.2	88
MD-179	388.04	100	100	100	99.9	99.6	97.6	93	85.5
MD-181	354.44	100	100	100	100	99.7	98.1	93.6	85.2
MD-189	329.95	100	100	100	99.9	99.3	95.7	87.8	77.3
MD-190	261.91	100	100	99.9	99.9	99	93.4	81.6	66.8
MD-193	359.08	100	100	100	99.9	99.2	95.7	88.5	79.1
MD-200	331.37	100	100	100	99.9	99.3	96	88.6	78.3
MD-206	259	100	100	99.9	99.8	98.6	91.9	79.9	65.1
MD-207	348.49	100	100	100	99.9	99.4	96.6	90.2	81
MD-208	354.47	100	100	100	100	99.5	97.1	91.3	82.4
MD-216	310.6	100	100	99.9	99.9	98.9	94.1	84.8	73.4
MD-219	350.26	100	100	99.9	99.9	99.3	96.2	89.3	80
MD-228	355.98	100	100	100	100	99.5	97.1	91.3	82.7
MD-232	375.09	100	100	100	100	99.6	97.4	92.6	84.6
MD-252	517.62	100	100	100	100	99.7	98.8	96.9	93.8
MD-255	592.28	100	100	99.9	99.9	98.9	95.6	91.4	86.7
MD-270	557.4	100	100	100	100	99.8	99.3	98	95.7
MD-273	559.72	100	100	100	100	99.8	99.2	97.7	95.1
MD-276	567.85	100	100	100	100	99.8	99.1	97.7	95
MD-277	572.34	100	100	100	100	99.8	99.1	97.5	94.7
MD-280	465.06	100	100	100	100	99.8	99.2	97.6	94.4
MD-281	509.95	100	100	100	100	99.8	99	97.1	93.7
MD-429	391.91	100	100	100	100	99.6	97.6	92.9	85.4
MD-431	435.52	100	100	100	100	99.8	98.5	95.4	89.9

Supplementary Table S3. Genes included in the last version of the custom panel MovDisord.

CLINICAL SIGN (no. genes)	517 GENES
Ataxia (210)	*ABCB7, ACO2, ADCK3, AHI1, ALG6, AMACR, ANO10, APTX, ARL13B, ARSA, ATCAY, ATG5, ATM, ATP1A3, ATP2B3, ATP7A, ATP8A2, ATR, ATXN2, BCKDHA, BCKDHB, BTD, C10ORF2, C5ORF42, CACNA1G, CACNB4, CAMTA1, CASK, CC2D2A, CCDC88C, CEP290, CEP41, CHMP1A, CHP1, CLCN2, CLN5, CLN6, CLP1, COG5, COL18A1, COQ2, COQ4, COQ5, COQ7, COQ9, COX20, CSTB, CTDP1, CTSD, CUL4B, CWF19L1, DAB1, DBT, DCLRE1B, DHTKD1, DKC1, DNAJC19, DNMT1, DYRK1A, EEF2, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, ELOVL4, ELOVL5, EMC1, EP300, EPM2A, ERCC2, ERCC3, ERCC5, ERCC6, ERCC8, EXOSC3, EXOSC8, FAAH2, FAT1, FAT2, FGF14, FLVCR1, FOLR1, FOXC1, GAN, GOSR2, GPR56, GRM1, HEXA, HSD17B4, IFRD1, INPP5E, ITPR1, KCNA1, KCNA2, KCNC3, KCND3, KCNJ10, KCTD7, KDM6A, KIAA0226, KIF26B, KIF7, KMT2D, L2HGDH, LAMA1, LMNB2, MAN2B1, MCEE, MLC1, MMACHC, MMADHC, MORC2, MRE11A, MRPL10, MTFMT, MTTP, NALCN, NHLRC1, NKX2-1, NKX6-2, NOL3, NPC1, OFD1, OPHN1, PARN, PAX6, PC, PCNA, PDHB, PDSS1, PDSS2, PEX10, PEX6, PEX7, PHYH, PIK3R5, PITRM1, PITX2, PLD3, PLP1, PMPCA, PNKP, POLG2, POLR3B, PRICKLE1, PRKCG, PRPS1, PTEN, PUM1, RAD1, RARS2, RIPPLY1, RPGRIP1L, RTEL1, SAMD9L, SCARB2, SCN1A, SCN2A, SCN8A, SCYL1, SEPSECS, SETX, SLC17A5, SLC1A3, SLC25A46, SLC2A1, SLC46A1, SLC52A2, SLC52A3, SLC6A19, SLC9A1, SLC9A6, SNAP25, SNX14, SPTAN1, SPTBN2, SURF1, SYNE1, SYT14, TCTN1, TCTN2, TCTN3, TDP2, TERT, TGFB1, TGM6, THG1L, TINF2, TMEM138, TMEM216, TMEM231, TMEM237, TMEM240, TMEM67, TRAPPC11, TRPC3, TSEN2, TSEN54, TTBK2, TTPA, TTR, UBA5, VHL, VLDLR, VPS53, VRK1, WFS1, XPA, XRCC1*
SPAX (41)	*AARS2, ABHD12, AFG3L2, AIMP1, ARX, CA8, CYP27A1, DARS2, ERLIN1, FAM126A, FXN, GALC, GBA2, GFAP, GJC2, GRID2, KIF1C, L1CAM, LMNB1, LYST, MAG, MARS2, MECP2, MTPAP, OPA1, OPA3, PDYN, PNPLA6, POLR3A, RARS, RPIA, SACS, SIL1, SPG7, STUB1, TPP1, TTC19, VAMP1, VWA3B, WDR73, WWOX*
SPG (69)	*ALDH18A1, ALS2, AMPD2, AP4B1, AP4E1, AP4S1, AP5Z1, ARG1, ARL6IP1, ARSI, ATAD3A, ATL1, B4GALNT1, BICD2, BSCL2, C12ORF65, CAV1, CCT5, CHCHD10, CPT1C, CYP2U1, CYP7B1, DDHD1, DDHD2, DNM2, DSTYK, ENTPD1, EPT1, ERLIN2, FAM134B, FIG4, FLRT1, GAD1, GBE1, GRN, HACE1, HSPD1, IBA57, IFIH1, KIAA0196, KIF1A, KIF5A, KLC2, MARS, NIPA1, NT5C2, PEX16, PGAP1, RAB3GAP2, REEP1, REEP2, RTN2, SARS2, SLC16A2, SPAST, SPG11, SPG20, SPG21, TARDBP, TECPR2, TFG, TRMT5, UBQLN2, USP8, VPS37A, WDR48, ZFR, ZFYVE26, ZFYVE27*
Dystonia (93)	*ACAT1, ANO3, ATP1A2, ATP7B, BCS1L, CACNA1B, CIZ1, COL6A3, COX10, COX15, COX8A, DDC, DLAT, DLD, DNAJC12, EARS2, ECHS1, ETHE1, FARS2, FBXL4, FOXG1, FOXRED1, GCDH, GCH1, GFM1, GFM2, GLB1, GNAL, GNAO1, GTPBP3, HIBCH, HPCA, HPRT1, IARS2, KCTD17, KMT2B, LIAS, LIPT1, LRPPRC, MCOLN1, MICU1, MUT, NARS2, NDUFA1, NDUFA10, NDUFA11, NDUFA12, NDUFA2, NDUFA4, NDUFA9, NDUFAF2, NDUFAF5, NDUFAF6, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS7, NDUFS8, NDUFV1, NDUFV2, PCCA, PCCB, PDHX, PET100, PNPT1, PRKRA, PTS, QDPR, SCO2, SDHA, SDHAF1, SERAC1, SGCE, SLC19A3, SLC25A19, SLC30A10, SLC39A14, SLC6A3, SPR, SUCLA2, SUCLG1, TACO1, TH, THAP1, TIMM8A, TOR1A, TPK1, TRMU, TSFM, TUBB2B, TUBB4A, UQCRQ*
Choreas (6)	*ADCY5, HTT, PRNP, RNF216, VPS13A, XK*
NBIA (14)	*AP4M1, ATP13A2, C19ORF12, COASY, CP, CRAT, DCAF17, FA2H, FTL, PANK2, PLA2G6, REPS1, SCP2, WDR45*
BGC (5)	*ISG15, PDGFB, PDGFRB, XPR1, SLC20A2*
Parkinson (14)	*CHCHD2, DNAJC13, DNAJC6, FBXO7, GBA, HTRA2, LRRK2, PARK2, PARK7, PINK1, POLG, SNCA, SYNJ1, VPS35*
Others (65)	*ACTB, ADAR, AIFM1, ALDH3A2, AMT, ASPA, ASS1, ATP6AP2, BCAP31, CACNA1A, CAPN1, DCTN1, ETFA, ETFB, ETFDH, FTH1, FUCA1, FUS, GAMT, GATM, GLDC, GLRX5, GTPBP2, HEXB, HTRA1, KIDINS220, KLC4, MECR, MTHFR, NPC2, NUP62, PCSK2, PDE10A, PDE8B, PDHA1, PMM2, PNKD, PPCDC, PPCS, PRRT2, PSEN1, RAB39B, RELN, RNASEH2A, RNASEH2B, RNASEH2C, RNF170, SAMHD1, SCN4A, SLC11A2, SLC25A15, SLC25A42, SLC40A1, SLC6A8, SMPD1, SQSTM1, SUOX, TENM4, TBCD, TBCE, TREX1, TXN2, UCHL1, VCP, WDR81*

SPAX: Spastic Ataxia; SPG: Spastic Paraplegia; NBIA: Neurodegeneration with Brain Iron Accumulation; BGC: Basal Ganglia Calcification