Table S1. Genetic diagnosis identified after reanalysis of genome sequencing data and the reason for positive results in 29 individuals.

ID	Sex	Phenotype	Sample	Gene	Variant(s)	Pathogenicity	Mutation type	IP	Zygosity	Origin	Novelty	Diagnosis (OMIM number)	Reasons not detected at the first analysis
Reclassification, n = 9													
069	M	DD Epilepsy	DNA	*TBC1D24*	c.1499C>T (p.Ala500Val)/ c.1499C>T (p.Ala500Val)	P/ P	Missense/ Missense	AR	homo	Paternal/ Maternal	N/ N	Developmental and epileptic encephalopathy 16 (OMIM 615338)	Re-classification from VUS (PM5, PM2, PM1) to Pathogenic variant after literature/ClinVar database (PP5) and genetic analysis (PM3)
122	M	DD Epilepsy	DNA	*SLC12A1*	c.2291_2293del(p.Leu764del)/ c.2722A>G(p.Lys908Glu)	LP/ LP	Deletion/ Missense	AR	Compound het	Maternal/ Paternal	Y/ Y	Bartter syndrome, type 1 (OMIM 601678)	Re-classification from VUS (PP3, PP2, PM2) to Likely Pathogenic variant after incorporating clinical update (PP4) and genetic analysis (PM3)
155	F	DD Epilepsy	DNA	*TBC1D24*	c.1499C>T (p.Ala500Val)/ c.1499C>T (p.Ala500Val)	P/ P	Missense/ Missense	AR	homo	Paternal/ Maternal	N/ N	Developmental and epileptic encephalopathy 16 (OMIM 615338)	Heterozygote identified on initial SNV calling Re-classification from VUS (PM5, PM2, PM1) to Pathogenic variant after literature/ClinVar database (PP5) and genetic analysis (PM3)
174	M	DD Epilepsy	DNA	*SATB2*	c.1204G>A (p.Glu402Lys)	LP	Missense	AD	het	*de novo*	N	Glass syndrome (OMIM 612313)	Re-classification from VUS (PS2, PM2) to Likely Pathogenic variant after literature/ClinVar database (PP5)
175	M	DD Epilepsy	DNA	*SATB2*	c.1204G>A (p.Glu402Lys)	LP	Missense	AD	het	*de novo*	N	Glass syndrome (OMIM 612313)	Re-classification from VUS (PS2, PM2) to Likely Pathogenic variant after literature/ClinVar database (PP5)
207	M	DD	DNA	*GRIN2B*	c.2284T>C (p.Tyr762His)	LP	Missense	AD	het	*de novo*	Y	Intellectual developmental disorder, autosomal dominant 6, with or without seizures (OMIM 613970)	Re-classification from VUS (PP3, PM2) to Likely Pathogenic variant after genetic analysis (PS2)
214	F	DD Epilepsy	DNA	*TBCD*	c.1561C>T (p.Gln521Ter)/ c.3365C>T (p.Pro1122Leu)	P/ LP	Nonsense/ Missense	AR	Compound het	Paternal/ Maternal	N/ N	Encephalopathy, progressive, early-onset, with brain atrophy and thin corpus callosum (OMIM 617193)	Re-classification from VUS (PP3, PM2) to Likely Pathogenic variant after literature/ClinVar database (PP5) and genetic analysis (PM3)
272	F	DD	DNA	*STXBP1*	c.770_772del (p.Leu257del)	LP	deletion	AD	het	*de novo*	Y	Developmental and epileptic encephalopathy 4 (OMIM 612164)	Re-classification from VUS (PP3, PM2) to Likely Pathogenic variant after genetic analysis (PS2)
323	M	ID Epilepsy	DNA	*HCN1*	c.459G>A (p.Met153Ile)	LP	Missense	AD	het	*de novo*	Y	Developmental and epileptic encephalopathy 24 (OMIM 615871)	Re-classification from VUS (PM2) to Likely Pathogenic variant after pathogenicity re-evaluation (PP3) and genetic analysis (PS2)
Analytical issues, n = 9													
051	F	DD Epilepsy	DNA	*CREBBP*	Chr 16p13.3(35880_4552153) x3 [0.24] encompassing *CREBBP*	P	Duplication	AD	het	*de novo*	N	Chromosome 16p13.3 duplication syndrome (mosaicism 24%) (OMIM 613458) encompassing CREBBP	Not identified on initial SV calling

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Table S1. Genetic diagnosis identified after reanalysis of genome sequencing data and the reason for positive results in 29 individuals (Cont)

ID	Sex	Phenotype	Sample	Gene	Variant(s)	Pathogenicity	Mutation type	IP	Zygosity	Origin	Novelty	Diagnosis (OMIM number)	Reasons not detected at the first analysis
171	F	ID SP	DNA	*TUBB4*	c.1228G>A (p.Glu410Lys)	P	Missense	AD	het	*de novo*	N	Leukodystrophy, hypomyelinating, 6 (OMIM 612438)	Not identified on initial SNV calling Classification as Pathogenic variant after pathogenicity reanalysis (PP3, PM2), literature database (PP5, PS3), and genetic analysis (PS2)
283	F	DD Neuropathy	DNA	*MORC2*	c.260C>T (p.Ser87Leu)	P	Missense	AD	het	*de novo*	N	Charcot-Marie-Tooth disease, axonal, type 2Z (OMIM 616688)	Not identified on initial SNV calling Classification as Pathogenic variant after pathogenicity reanalysis (PP3, PM2), literature database (PM1, PP5, PS3), and genetic analysis (PS2)
291	M	DD SS, RTA	DNA	*TRIP12*	Chr 2q36.3q37.1(229486750_ 230345306) x1 encompassing *TRIP12*	P	Deletion	AD	het	*de novo*	N	Chromosomal microdeletion disorder encompassing TRIP12 (OMIM 617752)	Not identified on initial SV calling
335	M	DD, FTT, SS	DNA	*BPTF*	c.2521C>T (p.Arg841Ter)	P	Nonsense	AD	het	*de novo*	Y	Neurodevelopmental disorder with dysmorphic facies and distal limb anomalies (OMIM 617755)	Not identified on initial SNV calling Classification as Pathogenic variant after pathogenicity reanalysis (PVS1, PM2) and genetic analysis (PS2)
342	M	DD Epilepsy	RNA	*GLS*	c.785G>A (p.Gly262Asp)/ c.736-406A>G	LP/ P	Missense/ Splicing	AR	Compound het	Paternal/ Maternal	Y/ Y	Developmental and epileptic encephalopathy 71 (OMIM 618328)	Heterozygote identified on initial SNV calling Deep intronic splicing variation, not included on initial analysis
374	F	DD Epilepsy	DNA	*FGF12*	Chr 3q28q29 (192156981_ 192751325) x3 encompassing *FGF12*	P	Duplication	AD	het	*de novo*	N	Developmental and epileptic encephalopathy 47 (OMIM 617166)	Not identified on initial SV calling
384	F	High myopia lens subluxation	RNA	*SLC25A13*	c.1638_1660dup(p.Ala554GlyfsTer17)/ c.934-1926A>G	P/ P	Duplication/ Splicing	AR	Compound het	Maternal/ Paternal	Y/ Y	Citrullinemia, type II, neonatal-onset (OMIM 605814)	Heterozygote identified on initial SNV calling Deep intronic splicing variation, not included on initial analysis
498	F	DD Myopathy	DNA	*TTN*	c.31147G>T(p.Glu10383Ter)/ c.83231A>G(p.Tyr27744Cys)	P/ LP	Nonsense/ Missense	AR	Compound het	Maternal/ Paternal	Y/ Y	Congenital myopathy 5 with cardiomyopathy (OMIM 611705)	Heterozygote identified on initial SNV calling (PS1) New symptom emerging Classification as Pathogenic variant after pathogenicity reanalysis (PP3), population evidence (PM2), and parental genetic analysis (PP4, PM3)

Table S1. Genetic diagnosis identified after reanalysis of genome sequencing data and the reason for positive results in 29 individuals (Cont)

ID	Sex	Phenotype	Sample	Gene	Variant(s)	Pathogenicity	Mutation type	IP	Zygosity	Origin	Novelty	Diagnosis (OMIM number)	Reasons not detected at the first analysis
New emerging disease-gene association, n = 8													
007	M	DD Dystonia	DNA	*SHQ1*	c.195T>A (p.Tyr65Ter)/ c.997C>G (p.Leu333Val)	P/ LP	Nonsense/ Missense	AR	Compound het	Maternal/ Paternal	Y/ Y	Neurodevelopmental disorder with dystonia and seizures (OMIM 619922)	Emerging disease Newly discovered disease-gene association Classification as Pathogenic/Likely pathogenic variants after computational/predictive evidence (PP3), absence in population databases (PM2), parental genetic analysis (PM3), and functional study (PS3)
108	M	ID Dystonia	DNA	*SHQ1*	c.812T>A (p.Val271Glu)/ c.997C>G (p.Leu333Val)	LP/ LP	Missense/ Missense	AR	Compound het	Paternal/ Maternal	Y/ Y	Neurodevelopmental disorder with dystonia and seizures (OMIM 619922)	Emerging disease Newly discovered disease-gene association Classification as Likely pathogenic variants after computational/predictive evidence (PP3), absence in population databases (PM2), parental genetic analysis (PM3), and functional study (PS3)
109	M	ID Dystonia	DNA	*SHQ1*	c.812T>A (p.Val271Glu)/ c.997C>G (p.Leu333Val)	LP/ LP	Missense/ Missense	AR	Compound het	Paternal/ Maternal	Y/ Y	Neurodevelopmental disorder with dystonia and seizures (OMIM 619922)	Emerging disease Newly discovered disease-gene association Classification as Likely pathogenic variants after computational/predictive evidence (PP3), absence in population databases (PM2), parental genetic analysis (PM3), and functional study (PS3)
228	M	DD Dystonia	DNA	*SHQ1*	c.195T>A (p.Tyr65Ter)/ c.997C>G (p.Leu333Val)	P/ LP	Nonsense/ Missense	AR	Compound het	Maternal/ Paternal	Y/ Y	Neurodevelopmental disorder with dystonia and seizures (OMIM 619922)	Emerging disease Newly discovered disease-gene association Classification as Pathogenic/Likely pathogenic variants after computational/predictive evidence (PP3), absence in population databases (PM2), parental genetic analysis (PM3), and functional study (PS3)
355	F	DD Dystonia	DNA	*SHQ1*	c.997C>G (p.Leu333Val)/ c.997C>G (p.Leu333Val)	LP/ LP	Missense/ Missense	AR	homo	Paternal/ Maternal	Y/ Y	Neurodevelopmental disorder with dystonia and seizures (OMIM 619922)	Emerging disease Newly discovered disease-gene association Classification as Likely pathogenic variants after computational/predictive evidence (PP3), absence in population databases (PM2), parental genetic analysis (PM3), and functional study (PS3)

Table S1. Genetic diagnosis identified after reanalysis of genome sequencing data and the reason for positive results in 29 individuals (Cont)

ID	Sex	Phenotype	Sample	Gene	Variant(s)	Pathogenicity	Mutation type	IP	Zygosity	Origin	Novelty	Diagnosis (OMIM number)	Reasons not detected at the first analysis
415	F	DD Dystonia	DNA	*SHQ1*	c.146T>C(p.Leu49Ser)/ c.997C>G(p.Leu333Val)	LP/ LP	Missense/ Missense	AR	Compound het	Maternal/ *de novo*	Y/ Y	Neurodevelopmental disorder with dystonia and seizures (OMIM 619922)	Emerging disease Newly discovered disease-gene association Classification as Likely pathogenic variants after computational/predictive evidence (PP3), absence in population databases (PM2), parental genetic analysis (PM3), and functional study (PS3)
419	F	DD Dystonia	DNA	*SHQ1*	c.195T>A(p.Tyr65Ter)/ c.997C>G(p.Leu333Val)	P/ LP	Nonsense/ Missense	AR	Compound het	Maternal/ NA	Y/ Y	Neurodevelopmental disorder with dystonia and seizures (OMIM 619922)	Emerging disease Newly discovered disease-gene association Classification as Pathogenic/Likely pathogenic variants after computational/predictive evidence (PP3), absence in population databases (PM2), parental genetic analysis (PM3), and functional study (PS3)
434	F	DD Dystonia	DNA	*SHQ1*	c.195T>A(p.Tyr65Ter)/ c.997C>G(p.Leu333Val)	P/ LP	Nonsense/ Missense	AR	Compound het	Maternal/ Paternal	Y/ Y	Neurodevelopmental disorder with dystonia and seizures (OMIM 619922)	Emerging disease Newly discovered disease-gene association Classification as Pathogenic/Likely pathogenic variants after computational/predictive evidence (PP3), absence in population databases (PM2), parental genetic analysis (PM3), and functional study (PS3)
Clinical update, n = 3													
169	F	Stroke Epilepsy	DNA	*RNF213*	c.12043_12045dup (p.Val4015dup)	P	Duplication	AD	het	*de novo*	Y	Moyamoya disease 2, susceptibility to (OMIM 607151)	New symptom emerging Classification as Pathogenic variants after clinical update (PP4), protein/predictive evidence (PM1, PM4), population data (PM2), and parental genetic analysis (PS2)
234	M	Neuropathy	DNA	*MFN2*	c.2222T>G (p.Leu741Trp)	P	Missense	AD	het	Maternal	N	Charcot-Marie-Tooth disease, axonal, type 2A2A (OMIM 609260)	Excluded on initial familiar genetic analysis; the mother had cryptic phenotype Classification from VUS (PP3, PM5, PM2) to Pathogenic variant due to maternal data (PP4) and literature database (PP5)

Table S1. Genetic diagnosis identified after reanalysis of genome sequencing data and the reason for positive results in 29 individuals (Cont)

ID	Sex	Phenotype	Sample	Gene	Variant(s)	Pathogenicity	Mutation type	IP	Zygosity	Origin	Novelty	Diagnosis (OMIM number)	Reasons not detected at the first analysis
299	M	Neuropathy	DNA	*MFN2*	c.281G>A (p.Arg94Gln)	P	Missense	AD	het	Paternal	N	Charcot-Marie-Tooth disease, axonal, type 2A2A (OMIM 609260)	Excluded on initial familiar genetic analysis of mosaic mutation; the father had cryptic phenotype Classification from VUS (PP3, PM5, PM2) to Pathogenic variant due to paternal data (PP4) and literature database (PP5)

aCGH: array comparative genomic hybridization; AD: autosomal dominant; AR: autosomal recessive; DD: developmental delay; DNA: deoxyribonucleic acid; EIEE: early infantile epileptic encephalopathy; F: female; FTT: failure to thrive; HD SNP-array: high-density single-nucleotide polymorphism-array; ID: intellectual disability; IP: Inheritance pattern; LP: likely pathogenic; het: heterozygous; homo: homozygous; P: pathogenic; RNA: ribonucleic acid; RTA: renal tubular acidosis; SP: spastic paraplegia; SS: short stature.