

SUPPLEMENTARY MATERIAL

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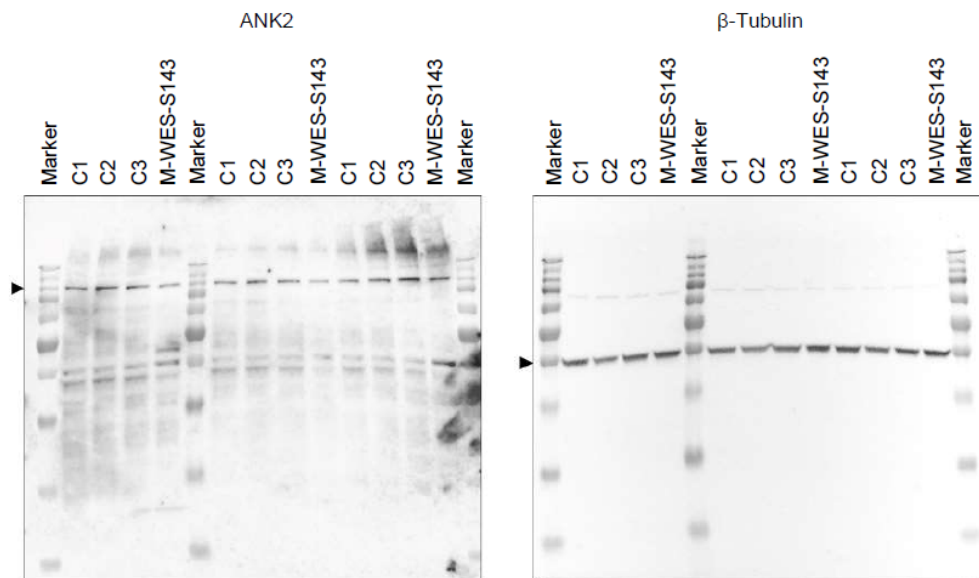
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Supplementary References

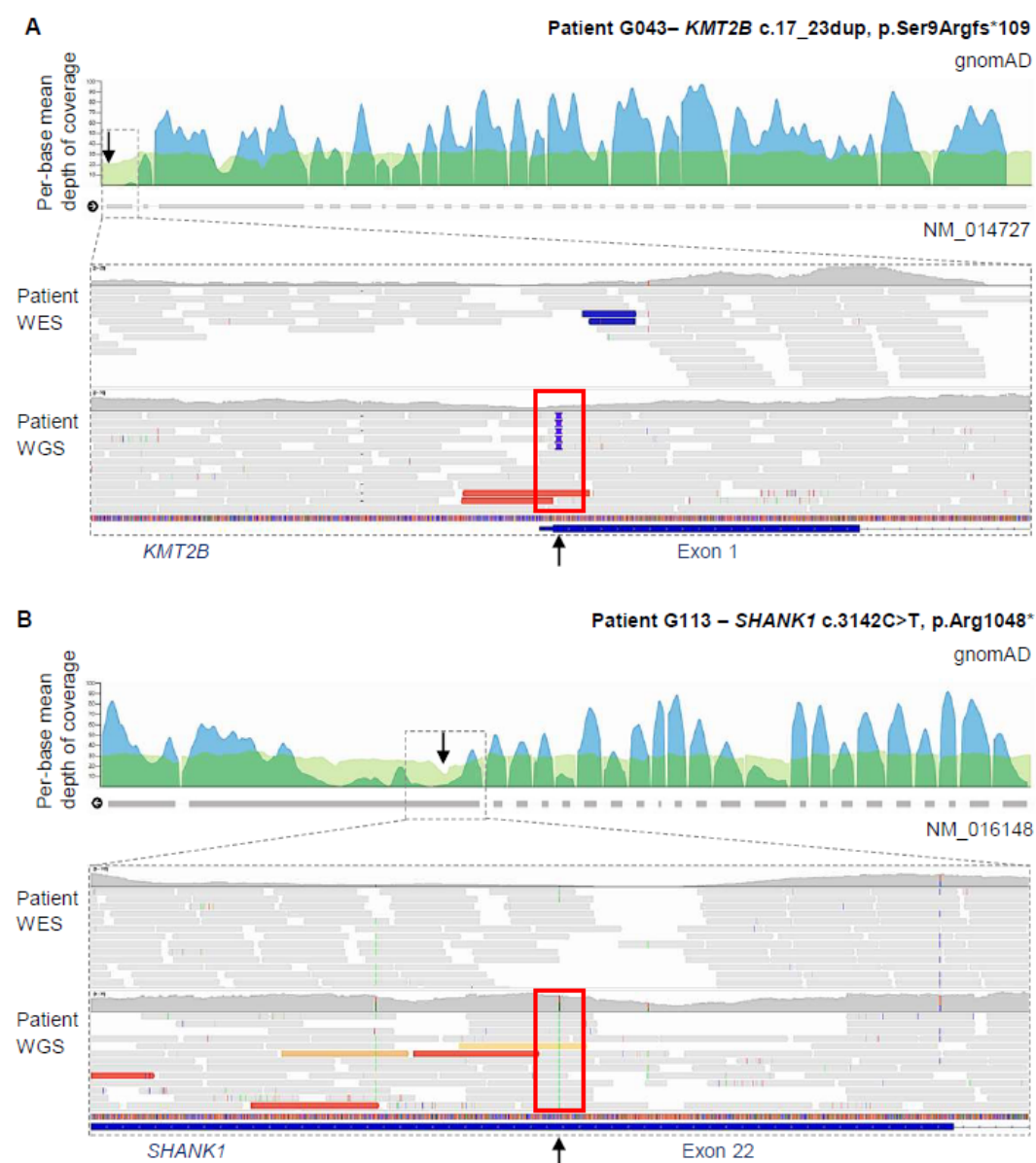
Supplementary Figures

Suppl. Figure 1 *ANK2* variant effect on protein expression in patient fibroblasts



Immunoblot analysis of the lysates of patient-derived fibroblast cells carrying the *ANK2* variant c.3804dup, p.Thr1269Hisfs*19 and three control cell lines (C1-C3). An *ANK2*-specific antibody was used (Santa Cruz, sc-12718); β -tubulin (abcam, 11-13002) was analyzed as a loading control. Three biological replicates were produced.

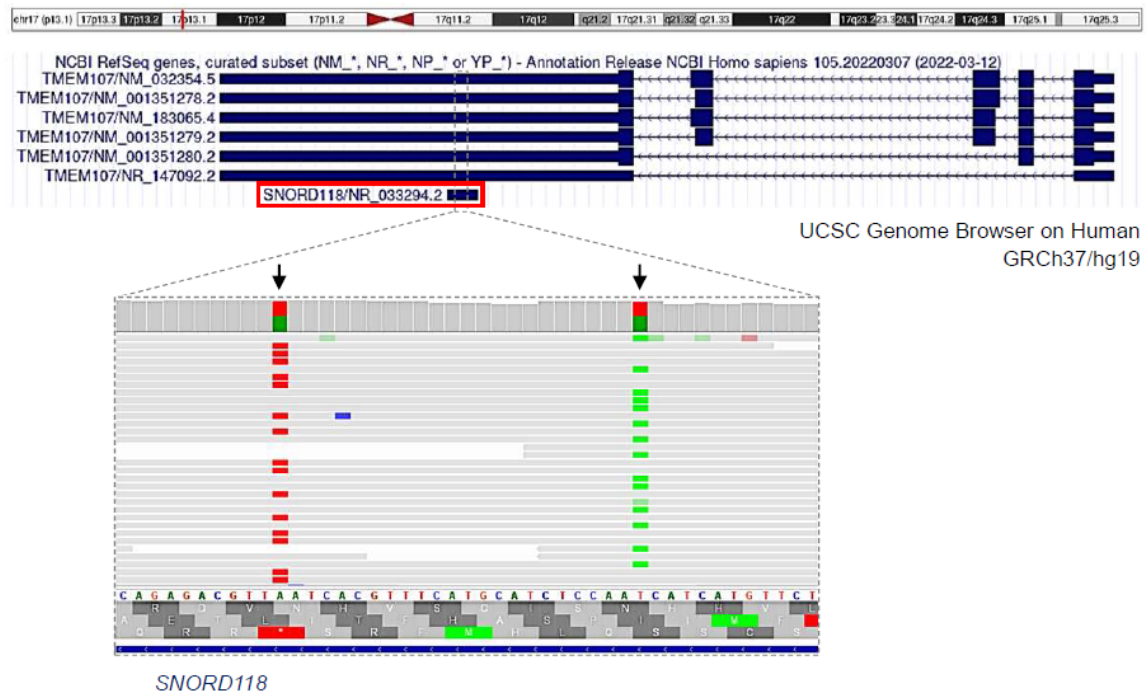
Suppl. Figure 2 Coding variants uniquely identified by WGS



Comparison of IGV views of WES and WGS data and depth-of-coverage plots from gnomAD gene pages for coding variants covered by an insufficient number of reads in targeted exomic experiments. **(A)** IGV screenshots of WES and WGS reads mapped onto exon 1 of *KMT2B* (NM_014727.2) in index patient G043 with dystonia, developmental delay, and microcephaly. The frameshift indel (red box) falls into an exome coverage drop-out region, as indicated by black arrows. Note poor read depth at the variant position in our WES data and in gnomAD exome data. *KMT2B* exon 1 with the frameshift indel was completely captured by WGS. **(B)** IGV screenshots of WES and WGS reads mapped onto exon 22 of *SHANK1* (NM_016148.5) in index patient G113 with dystonia, ataxia, and developmental delay. The nonsense SNV (red box) falls into an exome coverage drop-out region, as indicated by black arrows. Note poor read depth at the variant position in our WES data and in gnomAD exome data. *SHANK1* exon 22 with the nonsense SNV was completely captured by WGS. gnomAD, Genome Aggregation Database; IGV, Integrative Genomics Viewer¹; indel, short insertion/deletion; SNV, single-nucleotide variant; WES, whole-exome sequencing; WGS, whole-genome sequencing.

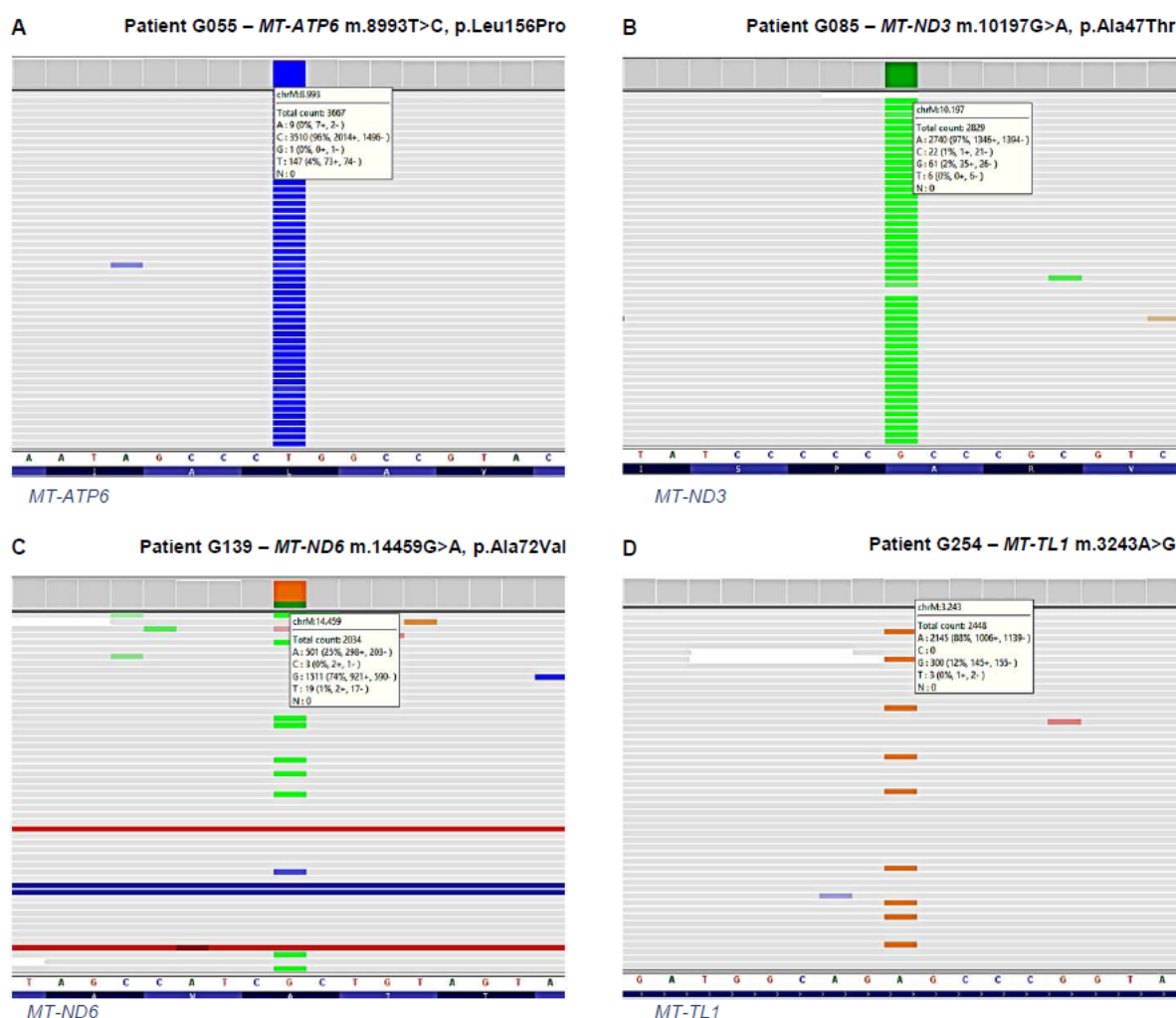
Suppl. Figure 3 Identification of non-coding RNA variants by WGS

Patient G132 – *SNORD118* compound heterozygous variants n.61A>T and n.84T>A



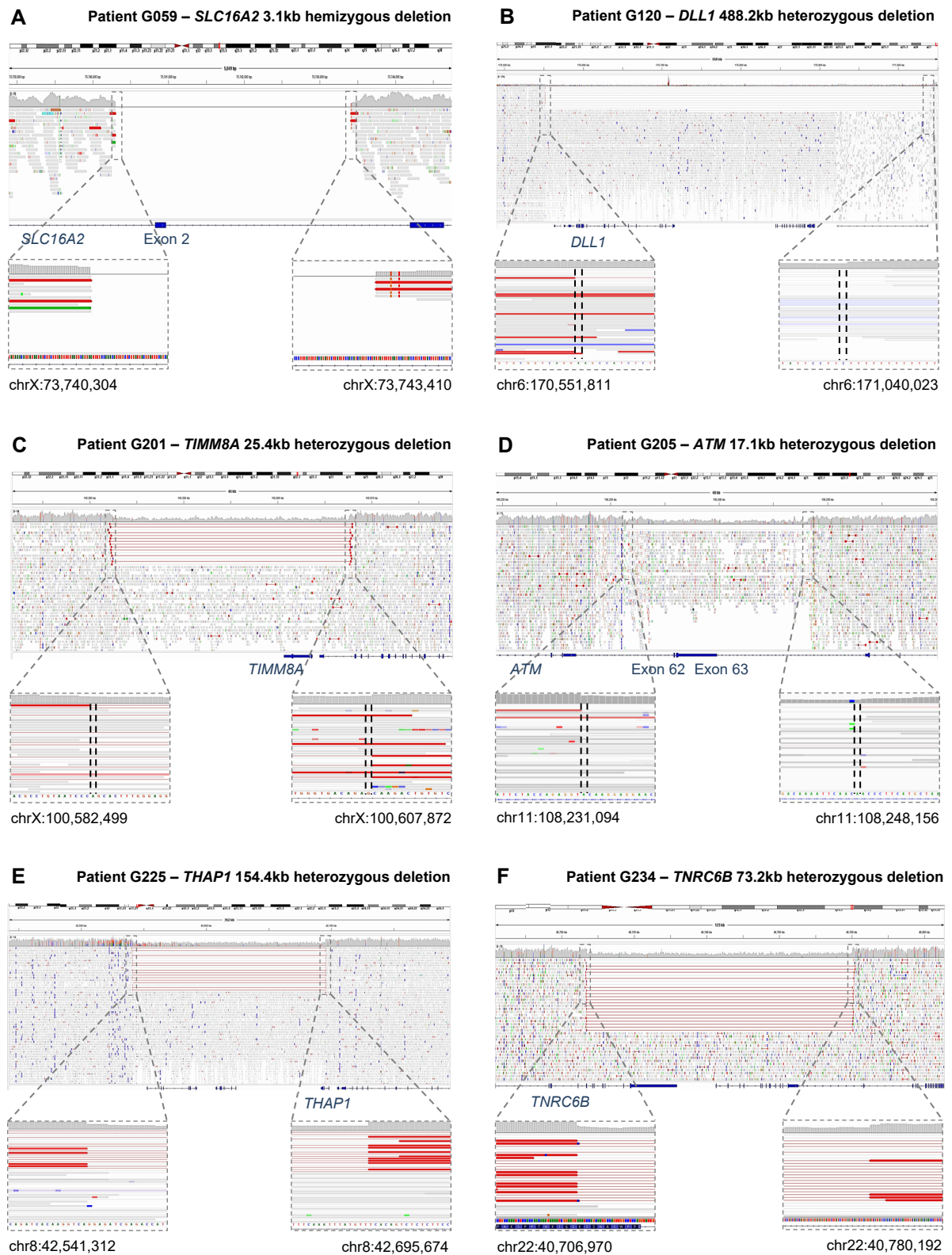
Compound heterozygous variants in a non-protein coding gene, *SNORD118*, in index patient G132 with dystonia, epilepsy, and leukoencephalopathy. *SNORD118* encodes a small nucleolar RNA (small nucleolar RNA, C/D box 118) required for ribosome biogenesis, which is no specific target in most standard WES capture kits^{2,3}. The location of the identified variants is highlighted on the ideogram of chromosome 17, where *SNORD118* is embedded in the 3'-UTR of the protein-coding gene *TMEM107*. UCSC genome browser session (hg19) with different *TMEM107* isoforms and the *SNORD118* transcript NR_033294.2 (red box) is depicted. The variants are highlighted in the IGV screenshot with black arrows. IGV, Integrative Genomics Viewer¹; UCSC, University of California, Santa Cruz; UTR, untranslated region; WES, whole-exome sequencing; WGS, whole-genome sequencing.

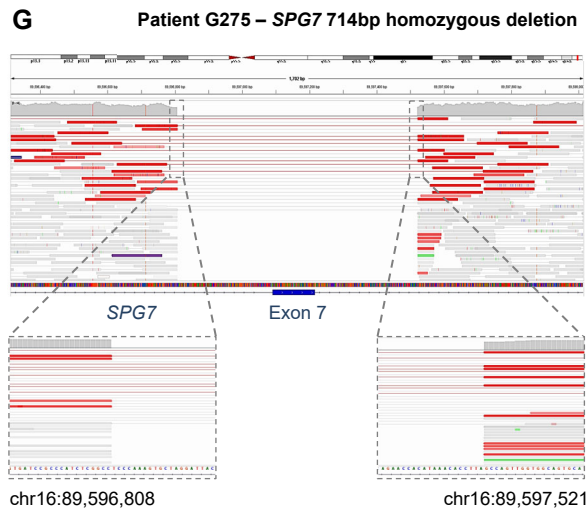
Suppl. Figure 4 Identification of MT variants with different degrees of heteroplasmy by WGS



Our WGS approach enabled analysis of the mitochondrial genome with sequencing depth of >2000x. IGV screenshots of identified MT variants with confirmed pathogenicity status according to MITOMAP⁴ are illustrated. **(A)** *MT-ATP6* variant detected with mutational load of 96% (3510/3667 reads supporting the alternate allele) in index patient G055 with dystonia, ataxia, and developmental delay. **(B)** *MT-ND3* variant detected with mutational load of 97% (2740/2829 reads supporting the alternate allele) in index patient G085 with dystonia and symmetrical signal abnormalities in the basal ganglia. **(C)** *MT-ND6* variant detected with mutational load of 25% (501/2034 reads supporting the alternate allele) in index patient G139 with isolated dystonia. **(D)** *MT-TL1* variant detected with mutational load of 12% (300/2448 reads supporting the alternate allele) in index patient G254 with dystonia and cognitive decline. IGV, Integrative Genomics Viewer¹; MT variant, mitochondrial variant; WGS, whole-genome sequencing.

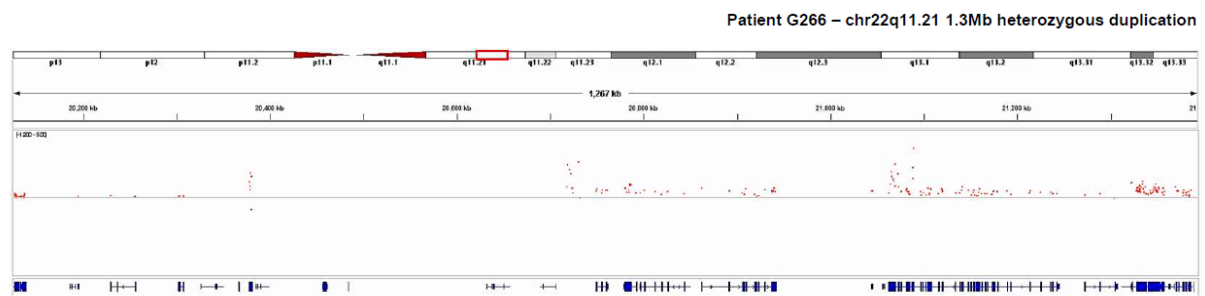
Suppl. Figure 5 Genomic alignment of WGS data supporting additional CNVs reported in this study





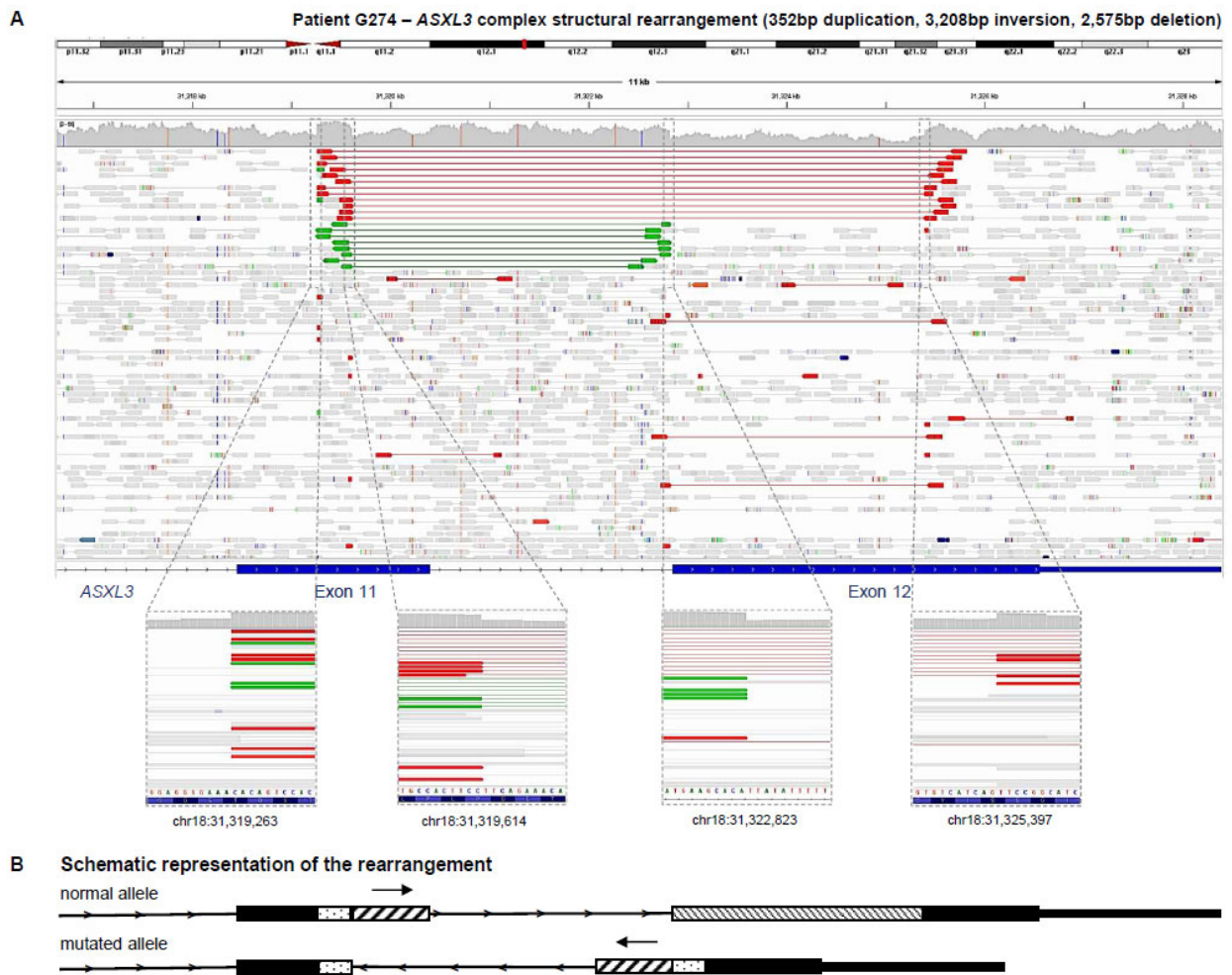
IGV screenshots are shown along with zoom-in panels depicting genomic breakpoints of CNVs. Uniform coverage allowed for resolution at the nucleotide level; genomic coordinates (hg19) of the breakpoint positions are provided. (A) A hemizygous single-exon deletion in *SLC16A2* (NM_006517.5: exon 2) in index patient G059 with dystonia and developmental delay. (B) A heterozygous deletion of the whole coding region of *DLL1* (NM_005618.4) in index patient G120 with dystonia, intellectual disability, and dysmorphism. (C) A heterozygous deletion of the whole coding region of *TIMM8* (NM_004085.4) in index patient G201 with isolated dystonia. (D) A heterozygous deletion of the last two exons of *ATM* (NM_000051.3: exons 62-63) and its 3'-UTR, found in combination with a pathogenic SNV, in index patient G205 with dystonia and chorea. (E) A heterozygous deletion of the last two exons of *THAP1* (NM_018105.3: exons 2-3) and its 3'-UTR in index patient G225 with isolated dystonia. (F) A heterozygous deletion of exons 17-23 of *TNRC6B* (NM_001162501.2) and its 3'-UTR in index patient G234 with dystonia and cognitive impairment. (G) A homozygous single-exon deletion in *SPG7* (NM_003119.4: exon 7) in index patient G275 with dystonia and spasticity. CNV, copy-number variant; IGV, Integrative Genomics Viewer¹; SNV, single-nucleotide variant; UTR, untranslated region; WGS, whole-genome sequencing.

Suppl. Figure 6 Identification of a chromosome 22q11.2 duplication event by WGS



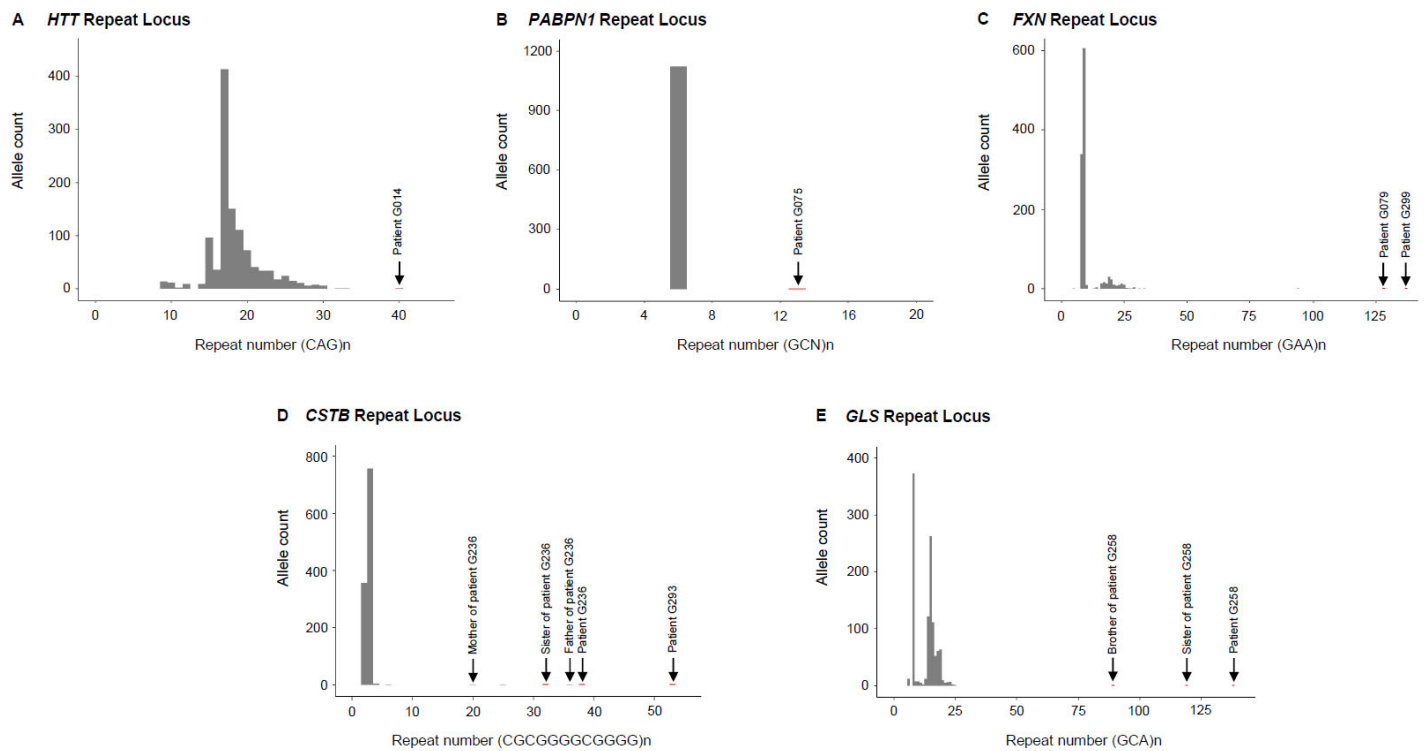
A heterozygous ~1.3Mb duplication at 22q11.21 in index patient G266 with infantile-onset dystonia. The location of the duplicated segment is highlighted on the ideogram of chromosome 22 (red box). IGV visualization of the WGS result is illustrated for the recurrent microduplication event, which has only recently been shown to be associated with pediatric dystonia⁵. IGV, Integrative Genomics Viewer¹; WGS, whole-genome sequencing.

Suppl. Figure 7 Identification of a complex genomic rearrangement by WGS



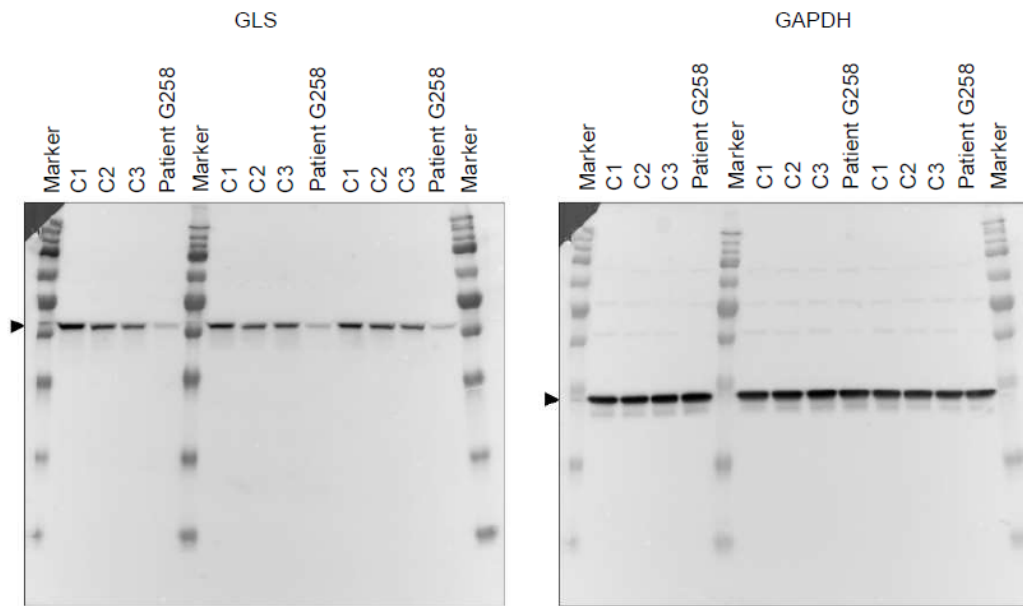
A heterozygous structural rearrangement affecting coding and non-coding sequence of *ASXL3* (NM_030632.3: exons 11-12) in index patient G274 with dystonia, spasticity, and developmental delay. **(A)** An IGV screenshot is shown along with zoom-in panels depicting breakpoints of the rearranged chromosomal region. Genomic coordinates (hg19) of the breakpoint positions for the SV are provided. The rearrangement is supported by the presence of split and discordant read pairs and called segments that were duplicated (coverage increase) or deleted (coverage decrease) in the region of interest. **(B)** Diagram of part of *ASXL3* illustrating the nature of the SV with observed pattern of inverted, duplicated, and deleted genomic intervals involving the last two exons of the gene. The boxes represent blocks of sequence and the black arrows indicate mapping orientation on the normal reference genome or the identified mutant allele. In the patient, an inversion and a smaller duplicated segment of parts of exon 11 with inverted orientation were observed, followed by a partial deletion of exon 12. IGV, Integrative Genomics Viewer¹; SV, structural variant; WGS, whole-genome sequencing.

Suppl. Figure 8 Identification of STR alleles by WGS across 564 samples



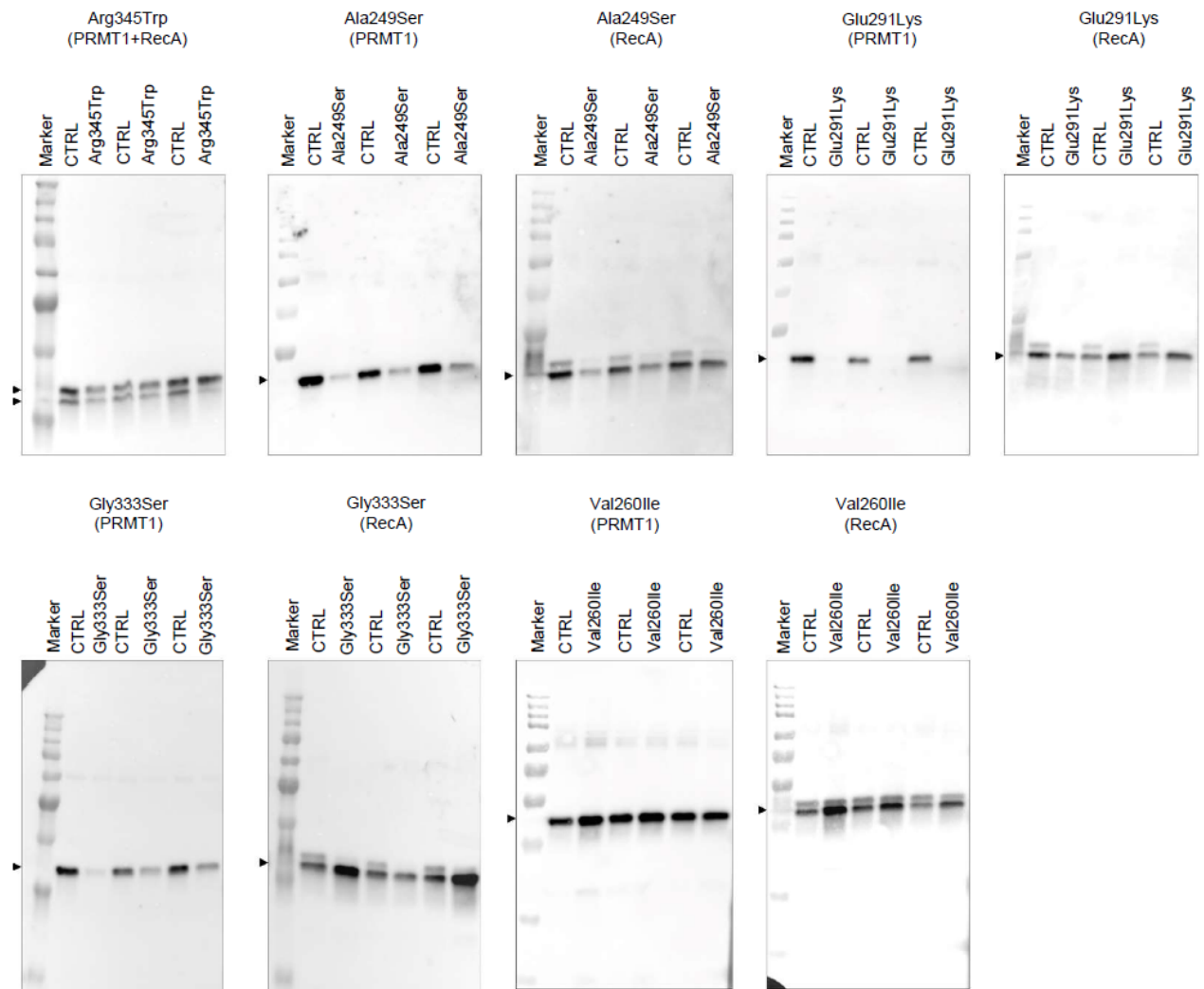
EH⁶ was used to predict sizes of STRs at each allele for each corresponding locus in WGS data of 305 dystonia index patients and 259 relatives. STR size distribution is plotted for calls in (A) *HTT*, (B) *PABPN1*, (C) *FXN*, (D) *CSTB*, and (E) *GLS*. STR sizes are shown on the x axes and the numbers of alleles on y axes. Note abnormal STR lengths in the families diagnosed with repeat-expansion disorders (family members indicated by black arrows). EH, ExpansionHunter⁶; STR, short tandem repeat; WGS, whole-genome sequencing.

Suppl. Figure 9 Effect of *GLS* variants on protein expression in patient fibroblasts



Immunoblot analysis of the lysates of patient-derived fibroblast cells carrying the *GLS* variant c.1197+2T>C in combination with a 5'-UTR GCA repeat expansion and three control cell lines (C1-C3). A *GLS*-specific antibody was used (GeneTex, GTX131263); GAPDH (Sigma, G8795-25UL) was analyzed as a loading control. Three biological replicates were produced.

Suppl. Figure 10 Effect of missense variants on PRMT1 expression



Immunoblot analysis of the lysates of bacterial cells expressing normal control (CTRL) PRMT1 or the PRMT1 mutants: p.Arg345Trp, p.Ala249Ser, p.Glu291Lys, p.Gly333Ser (published variant⁷), and the gnomAD-listed p.Val260Ile substitution⁸. PRMT1 was detected by ab73246 (Abcam); the internal reference RecA was probed with ab63797 (Abcam). Three biological replicates were produced for each missense variant.

Supplementary Tables

Suppl. Table 1 Overview of demographics, clinical characteristics and WES design for the entire dystonia cohort (N=1,825 index patients)

Characteristics	No (%)
Gender	
Female	955 (52.3)
Male	870 (47.7)
Inclusive recruitment	
Underrepresented populations ^a	154 (8.4)
Age at testing	
Infancy (0-2 years)	104 (5.7)
Childhood (3-12 years)	336 (18.4)
Adolescence (13-20 years)	246 (13.5)
Adulthood (≥21 years)	1,139 (62.4)
Age at dystonia onset	
Infancy (0-2 years)	463 (25.4)
Childhood (3-12 years)	387 (21.2)
Adolescence (13-20 years)	265 (14.5)
Adulthood (≥21 years)	710 (38.9)
Body distribution	
Generalized dystonia	647 (35.5)
Segmental dystonia	652 (35.7)
Focal dystonia	526 (28.8)
Associated features	
Isolated dystonia	814 (44.6)
Dystonia combined with additional movement disorder(s)	306 (16.8)
Dystonia combined with other neurologic and/or systemic features (with or without additional movement disorder/s)	705 (38.6)
Brain MRI abnormality ^b	
Yes	375 (30.4) ^b
No	858 (69.6) ^b
Family history ^c	
Positive	394 (21.6)
Negative	1,431 (78.4)
Sequencing mode ^d	
Solo	1,287 (70.5)
Duo	55 (3.0)
Trio	450 (24.7)
Quartet	28 (1.5)
Multiplex	5 (0.3)

^aFamilies from Ukraine and Slovakian minority groups.

^bBrain magnetic resonance imaging (MRI) data available for 1,233 index patients (67.6%) of the cohort.

^cReported to have first/second degree relatives with dystonia and/or tremor and/or a multisymptomatic neurologic condition related to the phenotype of the index patient in the cohort.

^dSolo, exome analysis of the index patient only; duo, exome analysis of the index patient and 1 affected family member (affected parent or affected sibling); trio, exome analysis of the index patient and the parents; quartet, exome analysis of the index patient and the parents plus 1 affected sibling; multiplex, exome analysis of the index patient and 2 affected family members (first/second degree relatives).

Suppl. Table 2 Diagnostic likely pathogenic/pathogenic^{9,10} variants identified by WES in 396 index patients of the dystonia cohort

Solved index patient ID ^a	Sequencing mode ^b	Dystonia category ^c	Gene/locus	RefSeq transcript for gene	Variant cDNA	Predicted protein change(s)	Zygosity	Disorder - mode of inheritance (AD, autosomal dominant; AR, autosomal recessive; XL, X-linked)	Associated disorder (OMIM; N/A, not available)	Variant inheritance (AR, autosomal recessive, i.e. homozygous or compound heterozygous) ^d	NDD-linked gene according to SysNDD database ¹¹	Variant finding published previously - PMID
M-WES-S1	solo	isolated	<i>ANO3</i>	NM_031418.2	c.1199G>T	p.Gly400Val	heterozygous	AD	<i>ANO3</i> -related dystonia (615034)	dominantly inherited		33098801
M-WES-S2	solo	isolated	<i>ANO3</i>	NM_031418.4	c.1693G>A	p.Val565Met	heterozygous	AD	<i>ANO3</i> -related dystonia (615034)	undetermined		
M-WES-S3 ^e	trio	isolated	<i>AOPEP</i>	NM_001193329.1	c.1477C>T	p.Arg493*	homozygous	AR	<i>AOPEP</i> -related dystonia (619565)	AR		34596301
M-WES-S4	solo	isolated	<i>AOPEP</i>	NM_001193329.1	c.1201C>T	p.Arg401Trp	homozygous	AR	<i>AOPEP</i> -related dystonia (619565)	AR		35306330
M-WES-S5	solo	isolated	<i>ATM</i>	NM_000051.3	c.2838+6T>C	p.Gly880Valfs*22	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S5	solo	isolated	<i>ATM</i>	NM_000051.3	c.7469dupT	p.Trp2491Leufs*3	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S6	trio	isolated	<i>ATM</i>	NM_000051.3	c.5573G>A	p.Trp1858*	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S6	trio	isolated	<i>ATM</i>	NM_000051.3	c.6154G>A	p.Glu2052Lys	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S7	solo	isolated	<i>ATM</i>	NM_000051.3	c.5177+5G>A	p.Glu1669Valfs*12	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S7	solo	isolated	<i>ATM</i>	NM_000051.3	c.8147T>C	p.Val2716Ala	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S8 ^e	solo	isolated	<i>ATP5F1B</i>	NM_001686.4	c.1445T>C	p.Val482Ala	heterozygous	AD	N/A	dominantly inherited		36860166
M-WES-S9	solo	isolated	<i>CHD3</i>	NM_001005273.3	c.5092C>T	p.Arg1698*	heterozygous	AD	Snijders Blok-Campeau syndrome (618205)	undetermined	yes	
M-WES-S10	solo	isolated	<i>CHD3</i>	NM_001005273.3	c.3822dup	p.Asp1275*	heterozygous	AD	Snijders Blok-Campeau syndrome (618205)	undetermined	yes	
M-WES-S11	solo	isolated	<i>CHD3</i>	NM_001005273.3	c.1652_1653del	p.Phe551Cysfs*35	heterozygous	AD	Snijders Blok-Campeau syndrome (618205)	undetermined	yes	
M-WES-S12 ^e	solo	isolated	<i>CHD3</i>	NM_001005273.3	c.793+1G>A	p.?	heterozygous	AD	Snijders Blok-Campeau syndrome (618205)	undetermined	yes	
M-WES-S13	solo	isolated	<i>CHD8</i>	NM_020920.3	c.2995dup	p.Asp999Glyfs*2	heterozygous	AD	Intellectual developmental disorder with autism and macrocephaly (615032)	undetermined	yes	38441608
M-WES-S14 ^f	solo	isolated	<i>COQ8A</i>	NM_020247.4	c.1332_1336dup	p.Glu446Alafs*33	compound heterozygous	AR	Coenzyme Q10 deficiency, primary, 4 (612016)	AR	yes	
M-WES-S14 ^f	solo	isolated	<i>COQ8A</i>	NM_020247.4	c.1750_1752del	p.Thr584del	compound heterozygous	AR	Coenzyme Q10 deficiency, primary, 4 (612016)	AR	yes	

M-WES-S15	multiplex	isolated	<i>EIF2AK2</i>	NM_002759.3	c.388G>A	p.Gly130Arg	heterozygous	AD	<i>EIF2AK2</i> -related dystonia (619687)	dominantly inherited	yes	33866603
M-WES-S16 ^e	multiplex	isolated	<i>EIF4A2</i>	NM_001967.4	c.896_897del	p.Thr299Serfs*7	heterozygous	AD	Neurodevelopmental disorder with hypotonia and speech delay, with or without seizures (620455)	undetermined	yes	37485550
M-WES-S17 ^e	duo	isolated	<i>EIF4A2</i>	NM_001967.4	c.896_897del	p.Thr299Serfs*7	heterozygous	AD	Neurodevelopmental disorder with hypotonia and speech delay, with or without seizures (620455)	dominantly inherited	yes	37485550
M-WES-S18 ^e	solo	isolated	<i>GCH1</i>	NM_000161.2	c.626+2_626+3insT	p.?	heterozygous	AD	Dystonia, DOPA-responsive (128230)	dominantly inherited	yes	
M-WES-S19 ^f	solo	isolated	<i>GCH1</i>	NM_000161.3	c.287G>A	p.Trp96*	heterozygous	AD	Dystonia, DOPA-responsive (128230)	undetermined	yes	
M-WES-S20 ^f	solo	isolated	<i>GCH1</i>	NM_000161.3	c.631_632del	p.Met211Valfs*38	heterozygous	AD	Dystonia, DOPA-responsive (128230)	undetermined	yes	
M-WES-S21	solo	isolated	<i>GCH1</i>	NM_000161.2	c.317C>G	p.Thr106Ser	heterozygous	AD	Dystonia, DOPA-responsive (128230)	undetermined	yes	
M-WES-S22	solo	isolated	<i>GNAL</i>	NM_001142339.2	c.529T>A	p.Tyr177Asn	heterozygous	AD	<i>GNAL</i> -related dystonia (615073)	undetermined		33098801
M-WES-S23	solo	isolated	<i>GNAL</i>	NM_001142339.2	c.478G>A	p.Asp160Asn	heterozygous	AD	<i>GNAL</i> -related dystonia (615073)	undetermined		33949708
M-WES-S24	solo	isolated	<i>KMT2B</i>	NM_014727.1	c.3632G>A	p.Gly1211Glu	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33098801
M-WES-S25	solo	isolated	<i>KMT2B</i>	NM_014727.1	c.6866delC	p.Pro2289Argfs*36	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	undetermined	yes	33098801
M-WES-S26	trio	isolated	<i>KMT2B</i>	NM_014727.1	c.6406delC	p.Leu2136Serfs*17	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33098801
M-WES-S27	trio	isolated	<i>KMT2B</i>	NM_014727.1	c.3700G>A	p.Glu1234Lys	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33098801
M-WES-S28	trio	isolated	<i>KMT2B</i>	NM_014727.2	c.7693C>G	p.Arg2565Gly	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	dominantly inherited	yes	34590685
M-WES-S29	solo	isolated	<i>MECP2</i>	NM_004992.3	c.1162_1169del	p.Pro388Thrfs*2	heterozygous	XL	Rett syndrome, atypical (312750)	undetermined	yes	
M-WES-S30	solo	isolated	<i>MECP2</i>	NM_004992.3	c.1152_1203del	p.Pro387Serfs*5	heterozygous	XL	Rett syndrome, atypical (312750)	undetermined	yes	
M-WES-S31 ^f	solo	isolated	<i>PNKD</i>	NM_015488.5	c.26C>T	p.Ala9Val	heterozygous	AD	Paroxysmal nonkinesigenic dyskinesia 1 (118800)	undetermined		
M-WES-S32	solo	isolated	<i>SCP2</i>	NM_002979.4	c.825+1G>T	p.?	homozygous	AR	Leukoencephalopathy with dystonia and motor neuropathy (613724)	AR		33098801
M-WES-S33	solo	isolated	<i>SLC20A2</i>	NM_006749.4	c.82G>A	p.Asp28Asn	heterozygous	AD	Basal ganglia calcification, idiopathic, 1 (213600)	undetermined		33098801
M-WES-S34	quartet	isolated	<i>THAP1</i>	NM_018105.2	c.14G>A	p.Cys5Tyr	heterozygous	AD	<i>THAP1</i> -related dystonia (602629)	dominantly inherited		33098801
M-WES-S35	solo	isolated	<i>THAP1</i>	NM_018105.2	c.112delG	p.Ala38Glnfs*35	heterozygous	AD	<i>THAP1</i> -related dystonia (602629)	undetermined		33098801
M-WES-S36	solo	isolated	<i>THAP1</i>	NM_018105.2	c.11C>T	p.Ser4Phe	heterozygous	AD	<i>THAP1</i> -related dystonia (602629)	undetermined		33949708
M-WES-S37 ^e	trio	isolated	<i>THAP1</i>	NM_018105.2	c.403C>T	p.His135Tyr	heterozygous	AD	<i>THAP1</i> -related dystonia (602629)	dominantly inherited		
M-WES-S38	solo	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	dominantly inherited	yes	33098801

M-WES-S39	solo	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	dominantly inherited	yes	33098801
M-WES-S40	solo	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	undetermined	yes	33098801
M-WES-S41	trio	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	dominantly inherited	yes	33949708
M-WES-S42	trio	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	dominantly inherited	yes	33949708
M-WES-S43	solo	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	undetermined	yes	
M-WES-S44 ^f	solo	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	undetermined	yes	
M-WES-S45 ^f	solo	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	undetermined	yes	
M-WES-S46	solo	isolated	<i>TOR1A</i>	NM_000113.2	c.907_909delGAG	p.Glu303del	heterozygous	AD	<i>TOR1A</i> -related dystonia (128100)	undetermined	yes	
M-WES-S47 ^e	solo	isolated	<i>VPS16</i>	NM_022575.2	c.1903C>T	p.Arg635*	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	undetermined	yes	32808683
M-WES-S48 ^e	solo	isolated	<i>VPS16</i>	NM_022575.2	c.1903C>T	p.Arg635*	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	undetermined	yes	32808683
M-WES-S49 ^e	solo	isolated	<i>VPS16</i>	NM_022575.2	c.1988_1989insG	p.Asn663Lysfs*2	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	undetermined	yes	32808683
M-WES-S50 ^e	trio	isolated	<i>VPS16</i> /20p13	NM_022575.2	CNV (chr20:2816108-3955033, deletion)	CNV (chr20:2816108-3955033, deletion)	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	de novo	yes	32808683
M-WES-S51	solo	isolated	<i>VPS16</i>	NM_022575.2	c.1204-2A>G	p.?	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	undetermined	yes	
M-WES-S52	solo	isolated	<i>VPS16</i>	NM_022575.2	c.2140C>T	p.Gln714*	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	undetermined	yes	38291845
M-WES-S53	trio	isolated	<i>VPS16</i>	NM_022575.4	c.2066dup	p.Gln690Profs*9	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	dominantly inherited	yes	
M-WES-S54	trio	isolated	<i>VPS16</i>	NM_022575.2	c.1903C>T	p.Arg635*	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	dominantly inherited	yes	
M-WES-S55	solo	combined-MD	<i>ADCY5</i>	NM_183357.2	c.1378A>T	p.Ile460Phe	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		33098801
M-WES-S56 ^f	trio	combined-MD	<i>ADCY5</i>	NM_183357.2	c.2088+1G>A	p.?	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		
M-WES-S57	solo	combined-MD	<i>ANO3</i>	NM_031418.2	c.1528G>A	p.Glu510Lys	heterozygous	AD	<i>ANO3</i> -related dystonia (615034)	de novo		33098801
M-WES-S58	solo	combined-MD	<i>ANO3</i>	NM_031418.2	c.1969G>A	p.Ala657Thr	heterozygous	AD	<i>ANO3</i> -related dystonia (615034)	undetermined		33098801
M-WES-S59	solo	combined-MD	<i>AOPEP</i>	NM_001193329.1	c.1909G>T	p.Glu637*	homozygous	AR	<i>AOPEP</i> -related dystonia (619565)	AR		35306330
M-WES-S60	duo	combined-MD	<i>ATL1</i>	NM_015915.4	c.1243C>T	p.Arg415Trp	heterozygous	AD	Spastic paraplegia 3A, autosomal dominant (182600)	dominantly inherited		
M-WES-S61	solo	combined-MD	<i>ATM</i>	NM_000051.3	c.449T>C	p.Leu150Pro	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S61	solo	combined-MD	<i>ATM</i>	NM_000051.3	c.9137G>A	p.Ser3046Asn	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S62 ^f	solo	combined-MD	<i>ATM</i>	NM_000051.3	c.8147T>C	p.Val2716Ala	homozygous	AR	Ataxia-telangiectasia (208900)	AR		

M-WES-S63	solo	combined-MD	<i>ATP1A3</i>	NM_152296.4	c.2767G>A	p.Asp923Asn	heterozygous	AD	<i>ATP1A3</i> -related dystonia /Alternating hemiplegia of childhood 2/CAPOS syndrome/Developmental and epileptic encephalopathy 99 (128235/614820/601338/619606)	undetermined	yes	33098801
M-WES-S64	trio	combined-MD	<i>ATP1A3</i>	NM_152296.4	c.1838C>T	p.Thr613Met	heterozygous	AD	<i>ATP1A3</i> -related dystonia /Alternating hemiplegia of childhood 2/CAPOS syndrome/Developmental and epileptic encephalopathy 99 (128235/614820/601338/619606)	dominantly inherited	yes	35872528
M-WES-S65	solo	combined-MD	<i>ATP1A3</i>	NM_152296.5	c.2501T>C	p.Leu834Ser	heterozygous	AD	<i>ATP1A3</i> -related dystonia /Alternating hemiplegia of childhood 2/CAPOS syndrome/Developmental and epileptic encephalopathy 99 (128235/614820/601338/619606)	undetermined	yes	
M-WES-S66 ^e	trio	combined-MD	<i>ATP2B2</i>	NM_001001331.4	c.3028G>A	p.Glu1010Lys	heterozygous	AD	N/A	de novo	yes	37675773
M-WES-S67 ^e	trio	combined-MD	<i>ATP5MC3</i>	NM_001689.4	c.318C>G	p.Asn106Lys	heterozygous	AD	Dystonia, early-onset, and/or spastic paraplegia (619681)	de novo		33949708
M-WES-S68	solo	combined-MD	<i>ATP7B</i>	NM_000053.3	c.2332C>G	p.Arg778Gly	compound heterozygous	AR	Wilson disease (277900)	AR		33098801
M-WES-S68	solo	combined-MD	<i>ATP7B</i>	NM_000053.3	c.3207C>A	p.His1069Gln	compound heterozygous	AR	Wilson disease (277900)	AR		33098801
M-WES-S69	trio	combined-MD	<i>C19orf12</i>	NM_031448.5	c.105_106del	p.Ala37Hisfs*34	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 4 (614298)	AR		
M-WES-S69	trio	combined-MD	<i>C19orf12</i>	NM_031448.5	c.164_166del	p.Gly55del	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 4 (614298)	AR		
M-WES-S70	trio	combined-MD	<i>CACNA1A</i>	NM_000068.3	c.1997C>T	p.Thr666Met	heterozygous	AD	Spinocerebellar ataxia 6/Migraine, familial hemiplegic, 1/Developmental and epileptic encephalopathy 42 (183086/141500/617106)	dominantly inherited	yes	33098801
M-WES-S71	solo	combined-MD	<i>CACNA1A</i>	NM_000068.3	c.5005C>T	p.Arg1669*	heterozygous	AD	Spinocerebellar ataxia 6/Migraine, familial hemiplegic, 1/Developmental and epileptic encephalopathy 42 (183086/141500/617106)	undetermined	yes	
M-WES-S59	solo	combined-MD	<i>CHD8</i>	NM_020920.3	c.2888G>A	p.Arg963Gln	heterozygous	AD	Intellectual developmental disorder with autism and macrocephaly (615032)	de novo	yes	35306330
M-WES-S72	solo	combined-MD	<i>CHD8</i>	NM_020920.3	c.2687_2688insC	p.Leu896Phefs*3	heterozygous	AD	Intellectual developmental disorder with autism and macrocephaly (615032)	undetermined	yes	38441608
M-WES-S73	duo	combined-MD	<i>COQ8A</i>	NM_020247.4	c.656-1G>T	p.Gly219_Ala230del + p.Gly219_Ser243del	homozygous	AR	Coenzyme Q10 deficiency, primary, 4 (612016)	AR	yes	33098801
M-WES-S74	solo	combined-MD	<i>COQ8A</i>	NM_020247.4	c.638G>A	p.Arg213Gln	compound heterozygous	AR	Coenzyme Q10 deficiency, primary, 4 (612016)	AR	yes	33949708
M-WES-S74	solo	combined-MD	<i>COQ8A</i>	NM_020247.4	c.911C>T	p.Ala304Val	compound heterozygous	AR	Coenzyme Q10 deficiency, primary, 4 (612016)	AR	yes	33949708
M-WES-S75	trio	combined-MD	<i>FGF14</i>	NM_004115.3	CNV (chr13:102521075-	CNV (chr13:102521075-	heterozygous	AD	Spinocerebellar ataxia 27A (193003)	de novo		33949708

			102568994, deletion)			102568994, deletion)						
M-WES-S76	trio	combined-MD	<i>GCH1</i>	NM_000161.2	c.287G>A	p.Trp96*	heterozygous	AD	Dystonia, DOPA-responsive (128230)	dominantly inherited	yes	33949708
M-WES-S77	trio	combined-MD	<i>GCH1</i>	NM_000161.2	c.281C>T	p.Thr94Met	heterozygous	AD	Dystonia, DOPA-responsive (128230)	dominantly inherited	yes	33949708
M-WES-S78	duo	combined-MD	<i>GCH1</i>	NM_000161.2	CNV (chr14:55309757-55424352, deletion)	CNV (chr14:55309757-55424352, deletion)	heterozygous	AD	Dystonia, DOPA-responsive (128230)	dominantly inherited	yes	33611074
M-WES-S79 ^e	solo	combined-MD	<i>KCNJ10</i>	NM_002241.5	c.511C>T	p.Arg171Trp	heterozygous	AD	N/A	undetermined	yes	
M-WES-S80 ^e	solo	combined-MD	<i>KCTD17</i>	NM_024681.3	c.411+1G>A	p.?	heterozygous	AD	<i>KCTD17</i> -related dystonia (616398)	undetermined		
M-WES-S81	solo	combined-MD	<i>KIF5A</i>	NM_004984.4	c.1A>G	p.?	heterozygous	AD	Spastic paraplegia 10, autosomal dominant (604187)	undetermined		
M-WES-S82	solo	combined-MD	<i>LRRK2</i>	NM_198578.3	c.6055G>A	p.Gly2019Ser	heterozygous	AD	Parkinson disease 8 (607060)	undetermined		33949708
M-WES-S83	solo	combined-MD	<i>MECP2</i>	NM_004992.3	c.1129_1143del	p.Lys377_Pro381del	heterozygous	XL	Rett syndrome, atypical (312750)	undetermined	yes	
M-WES-S84	solo	combined-MD	<i>MRE11</i>	NM_005591.3	c.77T>C	p.Met26Thr	compound heterozygous	AR	Ataxia-telangiectasia-like disorder 1 (604391)	AR	yes	33098801
M-WES-S84	solo	combined-MD	<i>MRE11</i>	NM_005591.3	c.820_821delCT	p.Leu274Phefs*16	compound heterozygous	AR	Ataxia-telangiectasia-like disorder 1 (604391)	AR	yes	33098801
M-WES-S85	solo	combined-MD	<i>NKX2-1</i>	NM_003317.4	c.556del	p.Leu186Cysfs*12	heterozygous	AD	Chorea, hereditary benign/Choreoathetosis, hypothyroidism, and neonatal respiratory distress (118700/610978)	undetermined		
M-WES-S86	solo	combined-MD	<i>PARK7</i>	NM_007262.5	CNV (chr1:8029405-8031022, deletion)	CNV (chr1:8029405-8031022, deletion)	homozygous	AR	Parkinson disease 7, autosomal recessive early-onset (606324)	AR		33611074
M-WES-S87	duo	combined-MD	<i>PDE10A</i>	NM_001130690.2	c.1001T>G	p.Phe334Cys	heterozygous	AD	Striatal degeneration, autosomal dominant (616922)	dominantly inherited		33098801
M-WES-S88	solo	combined-MD	<i>PINK1</i>	NM_032409.2	c.745T>G	p.Leu249Val	compound heterozygous	AR	Parkinson disease 6, early onset (605909)	AR		33098801
M-WES-S88	solo	combined-MD	<i>PINK1</i>	NM_032409.2	c.1015G>A	p.Ala339Thr	compound heterozygous	AR	Parkinson disease 6, early onset (605909)	AR		33098801
M-WES-S89	solo	combined-MD	<i>PLA2G6</i>	NM_003560.2	c.757G>A	p.Gly253Ser	compound heterozygous	AR	Infantile neuroaxonal dystrophy 1/Neurodegeneration with brain iron accumulation 2B/Parkinson disease 14, autosomal recessive (256600/610217/612953)	AR	yes	33098801
M-WES-S89	solo	combined-MD	<i>PLA2G6</i>	NM_003560.2	c.986G>A	p.Arg329His	compound heterozygous	AR	Infantile neuroaxonal dystrophy 1/Neurodegeneration with brain iron accumulation 2B/Parkinson disease 14, autosomal recessive (256600/610217/612953)	AR	yes	33098801
M-WES-S90	trio	combined-MD	<i>PNPLA6</i>	NM_006702.4	c.721C>T	p.Arg241Trp	compound heterozygous	AR	Boucher-Neuhauser syndrome (215470)	AR	yes	
M-WES-S90	trio	combined-MD	<i>PNPLA6</i>	NM_006702.4	c.2944_2947dup	p.Arg983Glnfs*38	compound heterozygous	AR	Boucher-Neuhauser syndrome (215470)	AR	yes	
M-WES-S91	solo	combined-MD	<i>POLG</i>	NM_002693.2	c.651dup	p.Ser218Leufs*26	compound heterozygous	AR	Mitochondrial DNA depletion syndrome 4A (Alpers type)/Mitochondrial DNA depletion syndrome 4B (MNGIE	AR	yes	

M-WES-S91	solo	combined-MD	<i>POLG</i>	NM_002693.2	c.3212G>A	p.Arg1071His	compound heterozygous	AR	type)/Mitochondrial recessive ataxia syndrome (includes SANDO and SCAE)/Progressive external ophthalmoplegia, autosomal recessive 1 (203700/613662/607459/258450) Mitochondrial DNA depletion syndrome 4A (Alpers type)/Mitochondrial DNA depletion syndrome 4B (MNGIE type)/Mitochondrial recessive ataxia syndrome (includes SANDO and SCAE)/Progressive external ophthalmoplegia, autosomal recessive 1 (203700/613662/607459/258450)	AR	yes	
M-WES-S92 ^e	trio	combined-MD	<i>POLR1A</i>	NM_015425.6	c.3721G>A	p.Val1241Ile	heterozygous	AD	N/A	de novo	yes	37075751
M-WES-S93	trio	combined-MD	<i>PRKN</i>	NM_004562.3	c.1244C>A	p.Thr415Asn	compound heterozygous	AR	Parkinson disease, juvenile, type 2 (600116)	AR		35872528
M-WES-S93	trio	combined-MD	<i>PRKN</i>	NM_004562.3	c.1358G>A	p.Trp453*	compound heterozygous	AR	Parkinson disease, juvenile, type 2 (600116)	AR		35872528
M-WES-S94	trio	combined-MD	<i>PRRT2</i>	NM_145239.3	c.324_325delAG	p.Ser110Glnfs*23	heterozygous	AD	Convulsions, familial infantile, with paroxysmal choreoathetosis/Episodic kinesigenic dyskinesia 1 (602066/128200)	dominantly inherited	yes	35872528
M-WES-S95 ^e	trio	combined-MD	<i>PRRT2</i>	NM_145239.3	c.649dup	p.Arg217Profs*8	heterozygous	AD	Convulsions, familial infantile, with paroxysmal choreoathetosis/Episodic kinesigenic dyskinesia 1 (602066/128200)	dominantly inherited	yes	37476319
M-WES-S96	solo	combined-MD	<i>PRRT2</i>	NM_145239.3	c.457_458del	p.Lys153Alafs*16	heterozygous	AD	Convulsions, familial infantile, with paroxysmal choreoathetosis/Episodic kinesigenic dyskinesia 1 (602066/128200)	undetermined	yes	
M-WES-S97	solo	combined-MD	<i>SGCE</i>	NM_003919.2	c.812G>A	p.Cys271Tyr	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	undetermined		33098801
M-WES-S98	trio	combined-MD	<i>SGCE</i>	NM_003919.2	c.619delA	p.Arg207Glyfs*12	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	dominantly inherited		33098801
M-WES-S99	solo	combined-MD	<i>SGCE</i>	NM_003919.2	c.549_552delTCTT	p.Phe183Leufs*4	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	dominantly inherited		33098801
M-WES-S100	quartet	combined-MD	<i>SGCE</i>	NM_003919.2	c.742T>A	p.Cys248Ser	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	dominantly inherited		33098801
M-WES-S101	trio	combined-MD	<i>SGCE</i>	NM_003919.2	c.289C>T	p.Arg97*	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	dominantly inherited		33098801
M-WES-S102	solo	combined-MD	<i>SGCE</i>	NM_003919.2	c.314A>G	p.Gln105Arg	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	undetermined		33098801
M-WES-S103	solo	combined-MD	<i>SGCE</i>	NM_003919.2	c.786delT	p.Arg263Valfs*26	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	undetermined		33949708
M-WES-S104	trio	combined-MD	<i>SGCE</i>	NM_003919.2	c.170T>G	p.Leu57Arg	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	dominantly inherited		33949708

M-WES-S105	trio	combined-MD	SGCE	NM_003919.2	c.314A>G	p.Gln105Arg	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	dominantly inherited		33949708
M-WES-S106	solo	combined-MD	SGCE	NM_003919.3	c.289C>T	p.Arg97*	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	undetermined		35872528
M-WES-S107 ⁱ	duo	combined-MD	SGCE	NM_003919.2	c.491T>C	p.Phe164Ser	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	dominantly inherited		
M-WES-S108	trio	combined-MD	SGCE	NM_003919.3	c.898_899del	p.Glu300Ilefs*6	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	dominantly inherited		
M-WES-S109	solo	combined-MD	SGCE	NM_003919.3	c.778A>T	p.Lys260*	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	undetermined		
M-WES-S110 ⁱ	solo	combined-MD	SGCE	NM_003919.3	c.272T>G	p.Leu91*	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	undetermined		
M-WES-S111	trio	combined-MD	SGCE	NM_003919.3	c.783dup	p.Phe262Ilefs*8	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	dominantly inherited		
M-WES-S112 ⁱ	solo	combined-MD	SGCE	NM_003919.3	c.289C>T	p.Arg97*	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	undetermined		
M-WES-S113	trio	combined-MD	SGCE	NM_003919.3	c.391-1G>A	p.?	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	dominantly inherited		
M-WES-S114 ⁱ	solo	combined-MD	SGCE	NM_003919.2	c.289C>T	p.Arg97*	heterozygous	AD	SGCE-related myoclonus-dystonia (159900)	undetermined		
M-WES-S115	solo	combined-MD	SLC2A1	NM_006516.3	c.997C>T	p.Arg333Trp	heterozygous	AD	SLC2A1-related dystonia/GLUT1 deficiency syndrome 2, childhood onset (601042/612126)	undetermined	yes	
M-WES-S116	solo	combined-MD	SPG7	NM_003119.4	c.1529C>T	p.Ala510Val	compound heterozygous	AR	Spastic paraplegia 7, autosomal recessive (607259)	AR		35872528
M-WES-S116	solo	combined-MD	SPG7	NM_003119.4	c.2228T>C	p.Ile743Thr	compound heterozygous	AR	Spastic paraplegia 7, autosomal recessive (607259)	AR		35872528
M-WES-S117	solo	combined-MD	SPG7	NM_003119.4	c.2225A>G	p.Asp742Gly	compound heterozygous	AR	Spastic paraplegia 7, autosomal recessive (607259)	AR		
M-WES-S117	solo	combined-MD	SPG7	NM_003119.4	c.1529C>T	p.Ala510Val	compound heterozygous	AR	Spastic paraplegia 7, autosomal recessive (607259)	AR		
M-WES-S118	solo	combined-MD	SPG7	NM_003119.4	c.233T>A	p.Leu78*	compound heterozygous	AR	Spastic paraplegia 7, autosomal recessive (607259)	AR		
M-WES-S118	solo	combined-MD	SPG7	NM_003119.4	c.1045G>A	p.Gly349Ser	compound heterozygous	AR	Spastic paraplegia 7, autosomal recessive (607259)	AR		
M-WES-S119	solo	combined-MD	SYNE1	NM_182961.3	c.4908C>A	p.Tyr1636*	compound heterozygous	AR	Spinocerebellar ataxia, autosomal recessive 8 (610743)	AR		33098801
M-WES-S119	solo	combined-MD	SYNE1	NM_182961.3	c.12247C>T	p.Gln4083*	compound heterozygous	AR	Spinocerebellar ataxia, autosomal recessive 8 (610743)	AR		33098801
M-WES-S120 ⁱ	solo	combined-MD	TH	NM_000360.4	c.605G>A	p.Arg202His	compound heterozygous	AR	Segawa syndrome, recessive (605407)	AR	yes	
M-WES-S120 ⁱ	solo	combined-MD	TH	NM_000360.4	c.1171G>A	p.Gly391Arg	compound heterozygous	AR	Segawa syndrome, recessive (605407)	AR	yes	
M-WES-S121	solo	combined-MD	TMEM240	NM_001114748.2	c.509C>T	p.Pro170Leu	heterozygous	AD	Spinocerebellar ataxia 21 (607454)	undetermined	yes	35872528
M-WES-S122	solo	combined-MD	TMEM240	NM_001114748.2	c.509C>T	p.Pro170Leu	heterozygous	AD	Spinocerebellar ataxia 21 (607454)	dominantly inherited	yes	38617829
M-WES-S123 ⁱ	solo	combined-MD	TTPA	NM_000370.3	c.513_514insTT	p.Thr172Leufs*5	homozygous	AR	Ataxia with isolated vitamin E deficiency (277460)	AR		
M-WES-S124	solo	combined-MD	VPS16	NM_022575.2	c.2170_2171del	p.Lys724Glufs*44	heterozygous	AD	VPS16-related dystonia (619291)	undetermined	yes	38291845

M-WES-S125	duo	combined-MD	<i>VPS16</i>	NM_022575.2	c.1939C>T	p.Arg647*	heterozygous	AD	<i>VPS16</i> -related dystonia (619291)	dominantly inherited	yes	38291845
M-WES-S126	trio	combined-other	<i>AARS1</i>	NM_001605.2	c.2873T>C	p.Phe958Ser	homozygous	AR	Developmental and epileptic encephalopathy 29 (616339)	AR	yes	
M-WES-S127	solo	combined-other	<i>ACTB</i>	NM_001101.3	c.547C>T	p.Arg183Trp	heterozygous	AD	Dystonia-deafness syndrome 1 (607371)	de novo	yes	33098801
M-WES-S128	solo	combined-other	<i>ACTB</i>	NM_001101.3	c.547C>T	p.Arg183Trp	heterozygous	AD	Dystonia-deafness syndrome 1 (607371)	de novo	yes	36183459
M-WES-S129	trio	combined-other	<i>ADAR</i>	NM_001111.5	c.3019G>A	p.Gly1007Arg	heterozygous	AD	Dyschromatosis symmetrica hereditaria/Aicardi-Goutieres syndrome 6 (127400/615010)	dominantly inherited	yes	
M-WES-S130	solo	combined-other	<i>ADCY5</i>	NM_183357.2	c.1252C>T	p.Arg418Trp	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		33098801
M-WES-S131	trio	combined-other	<i>ADCY5</i>	NM_183357.2	c.1322C>T	p.Ala441Val	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		33098801
M-WES-S132	trio	combined-other	<i>ADCY5</i>	NM_183357.2	c.2071A>G	p.Lys691Glu	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		33098801
M-WES-S133	solo	combined-other	<i>ADCY5</i>	NM_183357.2	c.1252C>T	p.Arg418Trp	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	undetermined		33098801
M-WES-S134	trio	combined-other	<i>ADCY5</i>	NM_183357.2	c.1253G>A	p.Arg418Gln	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		35872528
M-WES-S135	trio	combined-other	<i>ADCY5</i>	NM_183357.2	c.1252C>T	p.Arg418Trp	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		35872528
M-WES-S136 ^f	solo	combined-other	<i>ADCY5</i>	NM_183357.2	c.1252C>T	p.Arg418Trp	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	undetermined		
M-WES-S137 ^f	trio	combined-other	<i>ADCY5</i>	NM_183357.2	c.1252C>T	p.Arg418Trp	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		
M-WES-S138	trio	combined-other	<i>ADCY5</i>	NM_183357.2	c.1252C>T	p.Arg418Trp	heterozygous	AD	Dyskinesia with orofacial involvement, autosomal dominant (606703)	de novo		
M-WES-S139	trio	combined-other	<i>AFG3L2</i>	NM_006796.2	c.1119T>A	p.Ser373Arg	heterozygous	AD	Spinocerebellar ataxia 28 (610246)	de novo		33098801
M-WES-S140	trio	combined-other	<i>ALS2</i>	NM_020919.3	c.601C>T	p.Arg201*	homozygous	AR	Spastic paralysis, infantile onset ascending (607225)	AR		33098801
M-WES-S141	trio	combined-other	<i>ALS2</i>	NM_020919.3	c.913delC	p.Leu305*	compound heterozygous	AR	Spastic paralysis, infantile onset ascending (607225)	AR		33098801
M-WES-S141	trio	combined-other	<i>ALS2</i>	NM_020919.3	c.1867_1868delCT	p.Leu623Valfs*24	compound heterozygous	AR	Spastic paralysis, infantile onset ascending (607225)	AR		33098801
M-WES-S142	solo	combined-other	<i>ALS2</i>	NM_020919.3	c.3583G>T	p.Gly1195*	homozygous	AR	Spastic paralysis, infantile onset ascending (607225)	AR		33098801
M-WES-S143	trio	combined-other	<i>ANK2</i>	NM_001148.6	c.3804dup	p.Thr1269Hisfs*19	heterozygous	AD	N/A	dominantly inherited	yes	
M-WES-S144 ^e	trio	combined-other	<i>ANK2</i>	NM_001148.6	c.4279C>T	p.Arg1427*	heterozygous	AD	N/A	mosaic mother (10%)	yes	
M-WES-S145	trio	combined-other	<i>ANO3</i>	NM_031418.4	c.1943A>G	p.Asn648Ser	heterozygous	AD	<i>ANO3</i> -related dystonia (615034)	de novo		

M-WES-S146	trio	combined-other	<i>ARHGEF9</i>	NM_015185.3	c.792_793del	p.His264Glnfs*2	hemizygous	XL	Developmental and epileptic encephalopathy 8 (300607)	de novo	yes	
M-WES-S147 ⁱ	solo	combined-other	<i>ARSA</i>	NM_000487.5	c.1276G>A	p.Glu426Lys	homozygous	AR	Metachromatic leukodystrophy (250100)	AR	yes	33949708
M-WES-S148	trio	combined-other	<i>ASXL3</i>	NM_030632.1	c.1210C>T	p.Gln404*	heterozygous	AD	Bainbridge-Ropers syndrome (615485)	de novo	yes	35872528
M-WES-S149	trio	combined-other	<i>ASXL3</i>	NM_030632.1	c.1419dup	p.Pro474Thrfs*2	heterozygous	AD	Bainbridge-Ropers syndrome (615485)	de novo	yes	
M-WES-S150	trio	combined-other	<i>ATL1</i>	NM_015915.4	c.1220_1222delAGA	p.Lys407del	heterozygous	AD	Spastic paraplegia 3A, autosomal dominant (182600)	de novo		33098801
M-WES-S151	solo	combined-other	<i>ATM</i>	NM_000051.3	c.1564_1565delGA	p.Glu522Ilefs*43	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S151	solo	combined-other	<i>ATM</i>	NM_000051.3	c.6898T>G	p.Trp2300Gly	compound heterozygous	AR	Ataxia-telangiectasia (208900)	AR		33098801
M-WES-S152	solo	combined-other	<i>ATP1A3</i>	NM_152296.4	c.2401G>A	p.Asp801Asn	heterozygous	AD	<i>ATP1A3</i> -related dystonia /Alternating hemiplegia of childhood 2/CAPOS syndrome/Developmental and epileptic encephalopathy 99 (128235/614820/601338/619606)	undetermined	yes	33098801
M-WES-S153	trio	combined-other	<i>ATP1A3</i>	NM_152296.4	c.2425G>C	p.Ala809Pro	heterozygous	AD	<i>ATP1A3</i> -related dystonia /Alternating hemiplegia of childhood 2/CAPOS syndrome/Developmental and epileptic encephalopathy 99 (128235/614820/601338/619606)	de novo	yes	33098801
M-WES-S154	trio	combined-other	<i>ATP1A3</i>	NM_152296.4	c.266G>C	p.Gly89Ala	heterozygous	AD	<i>ATP1A3</i> -related dystonia /Alternating hemiplegia of childhood 2/CAPOS syndrome/Developmental and epileptic encephalopathy 99 (128235/614820/601338/619606)	de novo	yes	33098801
M-WES-S155	trio	combined-other	<i>ATP1A3</i>	NM_152296.4	c.2443G>A	p.Glu815Lys	heterozygous	AD	<i>ATP1A3</i> -related dystonia /Alternating hemiplegia of childhood 2/CAPOS syndrome/Developmental and epileptic encephalopathy 99 (128235/614820/601338/619606)	de novo	yes	33098801
M-WES-S156	solo	combined-other	<i>ATP1A3</i>	NM_152296.4	c.2332A>C	p.Thr778Pro	heterozygous	AD	<i>ATP1A3</i> -related dystonia /Alternating hemiplegia of childhood 2/CAPOS syndrome/Developmental and epileptic encephalopathy 99 (128235/614820/601338/619606)	undetermined	yes	33949708
M-WES-S157	trio	combined-other	<i>ATP5F1A</i>	NM_004046.6	c.545G>A	p.Arg182Gln	heterozygous	AD	Mitochondrial complex V (ATP synthase) deficiency, nuclear type 4A (620358)	de novo		34954817
M-WES-S158	trio	combined-other	<i>ATP8A2</i>	NM_016529.4	c.1874G>A	p.Arg625Gln	compound heterozygous	AR	Cerebellar ataxia, impaired intellectual development, and dysequilibrium syndrome 4 (615268)	AR	yes	33098801
M-WES-S158	trio	combined-other	<i>ATP8A2</i>	NM_016529.4	c.1936_1939delTATC	p.Tyr646Argfs*7	compound heterozygous	AR	Cerebellar ataxia, impaired intellectual development, and dysequilibrium syndrome 4 (615268)	AR	yes	33098801

M-WES-S159	trio	combined-other	<i>ATP8A2</i>	NM_016529.4	c.691_701del	p.Leu231Ilefs*7	homozygous	AR	Cerebellar ataxia, impaired intellectual development, and dysequilibrium syndrome 4 (615268)	AR	yes	33949708
M-WES-S160	trio	combined-other	<i>AUTS2</i>	NM_015570.2	c.946C>T	p.Arg316*	heterozygous	AD	Intellectual developmental disorder, autosomal dominant 26 (615834)	de novo	yes	33098801
M-WES-S161	trio	combined-other	<i>AUTS2</i>	NM_015570.2	c.1604A>C	p.His535Pro	heterozygous	AD	Intellectual developmental disorder, autosomal dominant 26 (615834)	de novo	yes	33098801
M-WES-S162	trio	combined-other	<i>BCL11B</i>	NM_138576.4	c.2513A>G	p.Lys838Arg	heterozygous	AD	Intellectual developmental disorder with dysmorphic facies, speech delay, and T-cell abnormalities (618092)	de novo	yes	35872528
M-WES-S163	solo	combined-other	<i>BRAF</i>	NM_004333.4	c.1574T>A	p.Leu525Gln	heterozygous	AD	Cardiofaciocutaneous syndrome (115150)	de novo	yes	33949708
M-WES-S164	solo	combined-other	<i>BRPF1</i>	NM_004634.2	CNV (chr3:9593958-9788137, deletion)	CNV (chr3:9593958-9788137, deletion)	heterozygous	AD	Intellectual developmental disorder with dysmorphic facies and ptosis (617333)	undetermined	yes	33949708
M-WES-S165 ⁱ	trio	combined-other	<i>C19orf12</i>	NM_031448.5	c.105_106del	p.Ala37Hisfs*34	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 4 (614298)	AR		
M-WES-S165 ⁱ	trio	combined-other	<i>C19orf12</i>	NM_031448.5	c.171_181del	p.Gly58Argfs*10	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 4 (614298)	AR		
M-WES-S166	solo	combined-other	<i>CACNA1A</i>	NM_000068.3	c.3536delC	p.Pro1179Hisfs*11	heterozygous	AD	Spinocerebellar ataxia 6/Migraine, familial hemiplegic, 1/Developmental and epileptic encephalopathy 42 (183086/141500/617106)	undetermined	yes	33949708
M-WES-S167	duo	combined-other	<i>CACNA1E</i>	NM_000721.4	c.901_904del	p.Thr301Serfs*21	heterozygous	AD	Developmental and epileptic encephalopathy 69 (618285)	undetermined	yes	
M-WES-S168	solo	combined-other	<i>CACNA1E</i>	NM_000721.4	c.1054G>A	p.Gly352Arg	heterozygous	AD	Developmental and epileptic encephalopathy 69 (618285)	undetermined	yes	
M-WES-S169	trio	combined-other	<i>CAMK4</i>	NM_001744.4	c.981+1G>A	p.Lys303Serfs*28	heterozygous	AD	N/A	de novo	yes	33098801
M-WES-S170	trio	combined-other	<i>CAMK4</i>	NM_001744.4	c.981+1G>T	p.?	heterozygous	AD	N/A	de novo	yes	33098801
M-WES-S171	solo	combined-other	<i>CAMTA1</i>	NM_015215.2	c.3585_3592del	p.Trp1197Argfs*28	heterozygous	AD	Cerebellar dysfunction with variable cognitive and behavioral abnormalities (614756)	dominantly inherited	yes	33949708
M-WES-S172	solo	combined-other	<i>CASK</i>	NM_001367721.1	c.1233+2T>C	p.?	heterozygous	XL	Intellectual developmental disorder and microcephaly with pontine and cerebellar hypoplasia (300749)	undetermined	yes	
M-WES-S173	solo	combined-other	<i>CD40LG</i>	NM_000074.3	c.761C>T	p.Thr254Met	hemizygous	XL	Immunodeficiency, X-linked, with hyper-IgM (308230)	undetermined		35267244
M-WES-S174	trio	combined-other	<i>CHD4</i>	NM_001273.2	c.637A>G	p.Ser213Gly	heterozygous	AD	Sifrim-Hitz-Weiss syndrome (617159)	de novo	yes	33949708
M-WES-S175	solo	combined-other	<i>CHD8</i> /14q11.2	NM_020920.3	CNV (chr14:21788176-22676026, deletion)	CNV (chr14:21788176-22676026, deletion)	heterozygous	AD	Intellectual developmental disorder with autism and macrocephaly (615032)	undetermined	yes	33098801
M-WES-S176	solo	combined-other	<i>CHD8</i>	NM_020920.3	c.5812C>T	p.Arg1938*	heterozygous	AD	Intellectual developmental disorder with autism and macrocephaly (615032)	undetermined	yes	33098801

M-WES-S177	quartet	combined-other	<i>CNTNAP1</i>	NM_003632.3	c.530del	p.Phe177Serfs*47	compound heterozygous	AR	Hypomyelinating neuropathy, congenital, 3 (618186)	AR	yes	
M-WES-S177	quartet	combined-other	<i>CNTNAP1</i>	NM_003632.3	c.1507T>C	p.Phe503Leu	compound heterozygous	AR	Hypomyelinating neuropathy, congenital, 3 (618186)	AR	yes	
M-WES-S178 ^f	duo	combined-other	<i>CP</i>	NM_000096.4	c.2670C>G	p.Tyr890*	homozygous	AR	Aceruloplasminemia (604290)	AR		
M-WES-S179 ^e	solo	combined-other	<i>CSDE1</i>	NM_001242891.1	c.2291dup	p.Phe765Valfs*6	heterozygous	AD	N/A	undetermined	yes	
M-WES-S180	solo	combined-other	<i>CTNNB1</i>	NM_001904.3	c.214C>T	p.Gln72*	heterozygous	AD	Neurodevelopmental disorder with spastic diplegia and visual defects (615075)	undetermined	yes	33098801
M-WES-S181 ⁱ	trio	combined-other	<i>CTNNB1</i>	NM_001904.3	c.999C>G	p.Tyr333*	heterozygous	AD	Neurodevelopmental disorder with spastic diplegia and visual defects (615075)	de novo	yes	
M-WES-S182	solo	combined-other	<i>CTNNB1</i>	NM_001904.3	c.1543C>T	p.Arg515*	heterozygous	AD	Neurodevelopmental disorder with spastic diplegia and visual defects (615075)	undetermined	yes	
M-WES-S183	multiplex	combined-other	<i>CUL3</i>	NM_003590.4	c.664C>T	p.Gln222*	heterozygous	AD	Neurodevelopmental disorder with or without autism or seizures (619239)	dominantly inherited		33949708
M-WES-S184	trio	combined-other	<i>CUX1</i>	NM_181552.4	c.1942C>T	p.Arg648*	heterozygous	AD	Global developmental delay with or without impaired intellectual development (618330)	de novo	yes	
M-WES-S185	solo	combined-other	<i>CWF19L1</i>	NM_018294.4	c.665G>A	p.Arg222Gln	compound heterozygous	AR	Spinocerebellar ataxia, autosomal recessive 17 (616127)	AR	yes	33098801
M-WES-S185	solo	combined-other	<i>CWF19L1</i>	NM_018294.4	c.1114C>T	p.Gln372*	compound heterozygous	AR	Spinocerebellar ataxia, autosomal recessive 17 (616127)	AR	yes	33098801
M-WES-S186	solo	combined-other	<i>DCAF17</i>	NM_025000.3	c.436delC	p.Ala147Hisfs*9	homozygous	AR	Woodhouse-Sakati syndrome (241080)	AR	yes	33098801
M-WES-S187	solo	combined-other	<i>DDC</i>	NM_000790.3	c.304G>A	p.Gly102Ser	homozygous	AR	Aromatic L-amino acid decarboxylase deficiency (608643)	AR	yes	33098801
M-WES-S188	trio	combined-other	<i>DDC</i>	NM_000790.4	c.849G>C	p.Glu283Asp	compound heterozygous	AR	Aromatic L-amino acid decarboxylase deficiency (608643)	AR	yes	
M-WES-S188	trio	combined-other	<i>DDC</i>	NM_000790.4	c.1066_1068del	p.Arg356del	compound heterozygous	AR	Aromatic L-amino acid decarboxylase deficiency (608643)	AR	yes	
M-WES-S189	trio	combined-other	<i>DHCR24</i>	NM_014762.3	c.1504G>A	p.Ala502Thr	compound heterozygous	AR	Desmosterolosis (602398)	AR	yes	33098801
M-WES-S189	trio	combined-other	<i>DHCR24</i>	NM_014762.3	c.1532G>A	p.Cys511Tyr	compound heterozygous	AR	Desmosterolosis (602398)	AR	yes	33098801
M-WES-S190	trio	combined-other	<i>DHDDS</i>	NM_024887.3	c.632G>A	p.Arg211Gln	heterozygous	AD	Developmental delay and seizures with or without movement abnormalities (617836)	de novo	yes	
M-WES-S191	trio	combined-other	<i>DLG4</i>	NM_001365.4	c.659G>T	p.Gly220Val	heterozygous	AD	Intellectual developmental disorder, autosomal dominant 62 (618793)	de novo	yes	
M-WES-S192	solo	combined-other	<i>DLL1</i>	NM_005618.4	c.1903del	p.Arg635Alafs*85	heterozygous	AD	Neurodevelopmental disorder with nonspecific brain abnormalities and with or without seizures (618709)	undetermined	yes	

M-WES-S193	trio	combined-other	<i>DNAJC6</i>	NM_014787.3	c.817C>T	p.Arg273*	homozygous	AR	Parkinson disease 19b, early-onset (615528)	AR		33949708
M-WES-S194	trio	combined-other	<i>DNM1L</i>	NM_005690.4	c.428C>G	p.Thr143Arg	heterozygous	AD	Encephalopathy, lethal, due to defective mitochondrial peroxisomal fission 1 (614388)	de novo	yes	33949708
M-WES-S195	solo	combined-other	<i>DNMT1</i>	NM_001379.2	c.4250T>C	p.Met1417Thr	heterozygous	AD	Cerebellar ataxia, deafness, and narcolepsy, autosomal dominant (604121)	de novo		33098801
M-WES-S196	trio	combined-other	<i>DNMT1</i>	NM_001379.2	c.1775T>G	p.Leu592Arg	heterozygous	AD	Cerebellar ataxia, deafness, and narcolepsy, autosomal dominant (604121)	de novo		33949708
M-WES-S197 ^f	trio	combined-other	<i>EBF3</i> /10q26.2-q26.3	NM_001005463.3	CNV (chr10:129676413-133109897, deletion)	CNV (chr10:129676413-133109897, deletion)	heterozygous	AD	Hypotonia, ataxia, and delayed development syndrome (617330)	de novo	yes	
M-WES-S198	trio	combined-other	<i>EBF3</i> /10q26.3	NM_001005463.3	CNV (chr10:131506159-135379032, deletion)	CNV (chr10:131506159-135379032, deletion)	heterozygous	AD	Hypotonia, ataxia, and delayed development syndrome (617330)	de novo	yes	
M-WES-S199 ^g	trio	combined-other	<i>EBF3</i>	NM_001005463.3	c.454C>T	p.Arg152Cys	heterozygous	AD	Hypotonia, ataxia, and delayed development syndrome (617330)	de novo	yes	
M-WES-S200	trio	combined-other	<i>ECHS1</i>	NM_004092.4	c.518C>T	p.Ala173Val	compound heterozygous	AR	Mitochondrial short-chain enoyl-CoA hydratase 1 deficiency (616277)	AR	yes	
M-WES-S200	trio	combined-other	<i>ECHS1</i>	NM_004092.4	c.583G>A	p.Gly195Ser	compound heterozygous	AR	Mitochondrial short-chain enoyl-CoA hydratase 1 deficiency (616277)	AR	yes	
M-WES-S201	trio	combined-other	<i>EEF1A2</i>	NM_001958.5	c.364G>A	p.Glu122Lys	heterozygous	AD	Developmental and epileptic encephalopathy 33 (616409)	de novo	yes	
M-WES-S202	trio	combined-other	<i>EFTUD2</i>	NM_004247.4	CNV (chr17:42949814-42949937, deletion)	CNV (chr17:42949814-42949937, deletion)	heterozygous	AD	Mandibulofacial dysostosis, Guion-Almeida type (610536)	de novo	yes	33611074
M-WES-S203	solo	combined-other	<i>ERCC4</i>	NM_005236.2	c.2026G>T	p.Glu676*	compound heterozygous	AR	Xeroderma pigmentosum, type F/Cockayne syndrome (278760)	AR		33949708
M-WES-S203	solo	combined-other	<i>ERCC4</i>	NM_005236.2	c.2395C>T	p.Arg799Trp	compound heterozygous	AR	Xeroderma pigmentosum, type F/Cockayne syndrome (278760)	AR		33949708
M-WES-S204 ^e	trio	combined-other	<i>ERCC8</i>	NM_000082.3	c.551-1G>A	p.?	homozygous	AR	Cockayne syndrome, type A (216400)	AR	yes	
M-WES-S205	trio	combined-other	<i>FA2H</i>	NM_024306.4	c.102C>G	p.Tyr34*	compound heterozygous	AR	Spastic paraplegia 35, autosomal recessive (612319)	AR	yes	35872528
M-WES-S205	trio	combined-other	<i>FA2H</i>	NM_024306.4	c.968C>T	p.Pro323Leu	compound heterozygous	AR	Spastic paraplegia 35, autosomal recessive (612319)	AR	yes	35872528
M-WES-S206	trio	combined-other	<i>FA2H</i>	NM_024306.5	c.133G>T	p.Gly45Trp	compound heterozygous	AR	Spastic paraplegia 35, autosomal recessive (612319)	AR	yes	
M-WES-S206	trio	combined-other	<i>FA2H</i>	NM_024306.5	c.786G>A (synonymous variant with effect on splicing, determined by conventional cDNA analysis)	p.Glu205Glyfs*31	compound heterozygous	AR	Spastic paraplegia 35, autosomal recessive (612319)	AR	yes	
M-WES-S207	trio	combined-other	<i>FBXO31</i>	NM_024735.3	c.1000G>A	p.Asp334Asn	heterozygous	AD	N/A	de novo		33949708
M-WES-S208	trio	combined-other	<i>FITM2</i>	NM_001080472.1	c.694G>A	p.Gly232Arg	homozygous	AR	Siddiqi syndrome (618635)	AR	yes	33098801
M-WES-S209	solo	combined-other	<i>FOXG1</i>	NM_005249.4	c.406G>T	p.Glu136*	heterozygous	AD	Rett syndrome, congenital variant (613454)	undetermined	yes	33949708

M-WES-S210	solo	combined-other	<i>FOXP1</i>	NM_005249.4	c.703C>T	p.Leu235Phe	heterozygous	AD	Rett syndrome, congenital variant (613454)	de novo	yes	33949708
M-WES-S211	solo	combined-other	<i>FOXP1</i>	NM_005249.5	c.630C>A	p.Phe210Leu	heterozygous	AD	Rett syndrome, congenital variant (613454)	undetermined	yes	
M-WES-S212 ⁱ	solo	combined-other	<i>FOXP1</i>	NM_005249.5	c.653A>C	p.Tyr218Ser	heterozygous	AD	Rett syndrome, congenital variant (613454)	undetermined	yes	
M-WES-S213 ⁱ	solo	combined-other	<i>FOXP2/7q31</i>	NM_014491.4	CNV (chr7:114174672-117880014, deletion)	CNV (chr7:114174672-117880014, deletion)	heterozygous	AD	Speech-language disorder-1/7q31 deletion syndrome (602081)	undetermined	yes	
M-WES-S214	solo	combined-other	<i>FRMD5</i>	NM_032892.5	c.1052G>A	p.Ser351Asn	heterozygous	AD	Neurodevelopmental disorder with eye movement abnormalities and ataxia (620094)	undetermined	yes	
M-WES-S215 ^e	solo	combined-other	<i>FRYL</i>	NM_015030.2	c.1855_1858del	p.Val619Ilefs*7	heterozygous	AD	N/A	undetermined	yes	
M-WES-S216 ^f	solo	combined-other	<i>FTL</i>	NM_000146.4	c.485_489dup	p.Glu164Trpfs*30	heterozygous	AD	Neurodegeneration with brain iron accumulation 3 (606159)	undetermined		
M-WES-S217	trio	combined-other	<i>GABBR2</i>	NM_005458.7	c.1699G>A	p.Ala567Thr	heterozygous	AD	Neurodevelopmental disorder with poor language and loss of hand skills (617903)	de novo	yes	33949708
M-WES-S218	trio	combined-other	<i>GABRA1</i>	NM_000806.5	c.647A>T	p.Asn216Ile	heterozygous	AD	Developmental and epileptic encephalopathy 19 (615744)	de novo	yes	34399161
M-WES-S219 ^{e,f}	trio	combined-other	<i>GAD1</i>	NM_000817.3	c.1370G>A	p.Arg457His	homozygous	AR	Developmental and epileptic encephalopathy 89 (619124)	AR	yes	
M-WES-S220	solo	combined-other	<i>GCH1</i>	NM_000161.3	c.745A>G	p.Arg249Gly	homozygous	AR	Dystonia, DOPA-responsive (128230)	AR	yes	
M-WES-S221 ^f	solo	combined-other	<i>GJA1</i>	NM_000165.5	c.413G>A	p.Gly138Asp	heterozygous	AD	Oculodentodigital dysplasia (164200)	undetermined		
M-WES-S222	solo	combined-other	<i>GJC2</i>	NM_020435.4	c.108C>G	p.Ile36Met	homozygous	AR	Spastic paraplegia 44, autosomal recessive/Leukodystrophy, hypomyelinating, 2 (613206/608804)	AR	yes	
M-WES-S223	solo	combined-other	<i>GNAL/18p</i>	NM_001142339.2	CNV (chr18:158699-14852478, deletion)	CNV (chr18:158699-14852478, deletion)	heterozygous	AD	Chromosome 18p deletion syndrome (146390)	undetermined		
M-WES-S224 ^f	solo	combined-other	<i>GNAL/18p</i>	NM_001142339.2	CNV (chr18:158699-14852478, deletion)	CNV (chr18:158699-14852478, deletion)	heterozygous	AD	Chromosome 18p deletion syndrome (146390)	undetermined		
M-WES-S225	trio	combined-other	<i>GNAO1</i>	NM_138736.2	c.709G>A	p.Glu237Lys	heterozygous	AD	Neurodevelopmental disorder with involuntary movements (617493)	de novo	yes	33098801
M-WES-S226	trio	combined-other	<i>GNAO1</i>	NM_138736.2	c.626G>A	p.Arg209His	heterozygous	AD	Neurodevelopmental disorder with involuntary movements (617493)	de novo	yes	33098801
M-WES-S227	trio	combined-other	<i>GNAO1</i>	NM_138736.2	c.625C>T	p.Arg209Cys	heterozygous	AD	Neurodevelopmental disorder with involuntary movements (617493)	de novo	yes	33098801
M-WES-S228	trio	combined-other	<i>GNAO1</i>	NM_138736.2	c.625C>T	p.Arg209Cys	heterozygous	AD	Neurodevelopmental disorder with involuntary movements (617493)	de novo	yes	33949708
M-WES-S229 ^e	duo	combined-other	<i>GNAO1</i>	NM_138736.2	CNV (chr16:56362543-56423286, deletion)	CNV (chr16:56362543-56423286, deletion)	heterozygous	AD	Neurodevelopmental disorder with involuntary movements (617493)	dominantly inherited	yes	36273395
M-WES-S230	trio	combined-other	<i>GNAO1</i>	NM_138736.2	c.4G>C	p.Gly2Arg	heterozygous	AD	Neurodevelopmental disorder with involuntary movements (617493)	de novo	yes	

M-WES-S231 ^f	solo	combined-other	<i>GNAO1</i>	NM_138736.2	c.626G>A	p.Arg209His	heterozygous	AD	Neurodevelopmental disorder with involuntary movements (617493)	undetermined	yes	
M-WES-S232	solo	combined-other	<i>GNB1</i>	NM_002074.3	c.226G>A	p.Asp76Asn	heterozygous	AD	Intellectual developmental disorder, autosomal dominant 42 (616973)	undetermined	yes	33949708
M-WES-S233 ^e	trio	combined-other	<i>GRIA2</i>	NM_000826.4	c.2188A>T	p.Asn730Tyr	heterozygous	AD	Neurodevelopmental disorder with language impairment and behavioral abnormalities (618917)	de novo	yes	
M-WES-S234	trio	combined-other	<i>GRIA3</i>	NM_000828.4	c.1949C>T	p.Ala650Val	heterozygous	XL	Intellectual developmental disorder, X-linked syndromic, Wu type (300699)	de novo	yes	37163803
M-WES-S235	quartet	combined-other	<i>GRID2</i>	NM_001510.2	c.671G>A	p.Arg224Gln	homozygous	AR	Spinocerebellar ataxia, autosomal recessive 18 (616204)	AR	yes	33098801
M-WES-S236	trio	combined-other	<i>GRIN1</i>	NM_000832.6	c.352G>A	p.Val118Met	heterozygous	AD	Neurodevelopmental disorder with or without hyperkinetic movements and seizures, autosomal dominant (614254)	de novo	yes	33098801
M-WES-S237	solo	combined-other	<i>GRIN2A</i>	NM_000833.3	c.1681_1683delATG	p.Met561del	heterozygous	AD	Epilepsy, focal, with speech disorder and with or without impaired intellectual development (245570)	de novo	yes	33098801
M-WES-S238	trio	combined-other	<i>HECW2</i>	NM_020760.1	c.3829T>C	p.Tyr1277His	heterozygous	AD	Neurodevelopmental disorder with hypotonia, seizures, and absent language (617268)	de novo	yes	33098801
M-WES-S239 ^f	trio	combined-other	<i>HEXA</i>	NM_000520.6	c.805G>A	p.Gly269Ser	compound heterozygous	AR	Tay-Sachs disease (272800)	AR		
M-WES-S239 ^f	trio	combined-other	<i>HEXA</i>	NM_000520.6	c.1510C>T	p.Arg504Cys	compound heterozygous	AR	Tay-Sachs disease (272800)	AR		
M-WES-S240 ^f	solo	combined-other	<i>HIBCH</i>	NM_014362.4	c.452C>T	p.Ser151Leu	homozygous	AR	3-hydroxyisobutryl-CoA hydrolase deficiency (250620)	AR	yes	
M-WES-S241	trio	combined-other	<i>IFIH1</i>	NM_022168.3	c.2159G>A	p.Arg720Gln	heterozygous	AD	Aicardi-Goutieres syndrome 7 (615846)	de novo	yes	33098801
M-WES-S242	trio	combined-other	<i>IMPDH2</i>	NM_000884.3	c.338G>A	p.Gly113Glu	heterozygous	AD	N/A	de novo	yes	33098801
M-WES-S243 ^e	solo	combined-other	<i>INTS11</i>	NM_017871.6	c.881_882del	p.Phe294Cysfs*7	compound heterozygous	AR	Neurodevelopmental disorder with motor and language delay, ocular defects, and brain abnormalities (620428)	AR	yes	
M-WES-S243 ^e	solo	combined-other	<i>INTS11</i>	NM_017871.6	c.629T>C	p.Ile210Thr	compound heterozygous	AR	Neurodevelopmental disorder with motor and language delay, ocular defects, and brain abnormalities (620428)	AR	yes	
M-WES-S166	solo	combined-other	<i>IRF2BPL</i>	NM_024496.3	c.2135delCinsGGT	p.Pro712Argfs*56	heterozygous	AD	Neurodevelopmental disorder with regression, abnormal movements, loss of speech, and seizures (618088)	undetermined	yes	33949708
M-WES-S244	solo	combined-other	<i>KCNA2</i>	NM_004974.4	c.881G>A	p.Arg294His	heterozygous	AD	Developmental and epileptic encephalopathy 32 (616366)	undetermined	yes	
M-WES-S245	solo	combined-other	<i>KCNB1</i>	NM_004975.4	c.916C>T	p.Arg306Cys	heterozygous	AD	Developmental and epileptic encephalopathy 26 (616056)	undetermined	yes	
M-WES-S246	trio	combined-other	<i>KCNMA1</i>	NM_002247.4	c.2725C>T	p.Gln909*	heterozygous	AD	Liang-Wang syndrome (618729)	de novo	yes	

M-WES-S247	trio	combined-other	<i>KIF1A</i>	NM_004321.7	c.914C>T	p.Pro305Leu	heterozygous	AD	Spastic paraplegia 30, autosomal dominant (610357)	de novo	yes	35872528
M-WES-S248	trio	combined-other	<i>KIF1A</i>	NM_004321.7	c.760C>T	p.Arg254Trp	heterozygous	AD	Spastic paraplegia 30, autosomal dominant (610357)	de novo	yes	
M-WES-S167	duo	combined-other	<i>KIF5A</i>	NM_004984.4	c.751G>A	p.Glu251Lys	heterozygous	AD	Spastic paraplegia 10, autosomal dominant (604187)	undetermined		
M-WES-S249	solo	combined-other	<i>KMT2B</i>	NM_014727.1	c.424C>T	p.Arg142*	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	undetermined	yes	33098801
M-WES-S250	trio	combined-other	<i>KMT2B</i>	NM_014727.1	c.7050-2A>G	p.Phe2321Serfs*93	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33098801
M-WES-S251	trio	combined-other	<i>KMT2B</i>	NM_014727.1	c.4549C>T	p.Arg1517*	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33098801
M-WES-S252	trio	combined-other	<i>KMT2B</i>	NM_014727.1	c.521dupC	p.Thr176Aspfs*8	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33098801
M-WES-S253	solo	combined-other	<i>KMT2B</i>	NM_014727.1	c.2428C>T	p.Gln810*	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	dominantly inherited	yes	33098801
M-WES-S254	solo	combined-other	<i>KMT2B</i>	NM_014727.1	c.4759_4760delTA	p.Tyr1587Argfs*90	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	undetermined	yes	33098801
M-WES-S255	trio	combined-other	<i>KMT2B</i>	NM_014727.1	c.4847C>T	p.Ala1616Val	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33098801
M-WES-S256	trio	combined-other	<i>KMT2B</i>	NM_014727.1	c.1633C>T	p.Arg545*	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33098801
M-WES-S257	trio	combined-other	<i>KMT2B</i>	NM_014727.1	c.17_23dup	p.Ser9Argfs*109	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	33949708
M-WES-S258	solo	combined-other	<i>KMT2B</i>	NM_014727.1	c.3335-9_3363del	p.?	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	undetermined	yes	33949708
M-WES-S259	solo	combined-other	<i>KMT2B</i>	NM_014727.1	CNV (chr19:36220867-36223036, deletion)	CNV (chr19:36220867-36223036, deletion)	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	undetermined	yes	37365401
M-WES-S260 ^f	trio	combined-other	<i>KMT2B</i>	NM_014727.1	c.3043C>T	p.Arg1015*	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	de novo	yes	37365401
M-WES-S261	solo	combined-other	<i>KMT2B</i>	NM_014727.1	c.5003G>C	p.Arg1668Pro	heterozygous	AD	<i>KMT2B</i> -related dystonia (617284)	undetermined	yes	37365401
M-WES-S222	solo	combined-other	<i>LIG4</i>	NM_001098268.2	c.833G>A	p.Arg278His	homozygous	AR	LIG4 syndrome (606593)	AR	yes	
M-WES-S262	solo	combined-other	<i>MAG</i>	NM_002361.3	c.1126C>T	p.Gln376*	homozygous	AR	Spastic paraplegia 75, autosomal recessive (616680)	AR	yes	33949708
M-WES-S263 ^e	trio	combined-other	<i>MATR3</i>	NM_018834.6	c.1306G>A	p.Glu436Lys	heterozygous	AD	N/A	de novo		34173818
M-WES-S264	solo	combined-other	<i>MECP2</i>	NM_004992.3	c.397C>T	p.Arg133Cys	heterozygous	XL	Rett syndrome (312750)	de novo	yes	33098801
M-WES-S265	solo	combined-other	<i>MECP2</i>	NM_001110792.1	c.1A>G	p.?	hemizygous	XL	Rett syndrome (312750)	de novo	yes	33098801
M-WES-S266	solo	combined-other	<i>MECP2</i>	NM_004992.3	c.1163dupC	p.Pro389Thrfs*4	heterozygous	XL	Rett syndrome, atypical (312750)	undetermined	yes	34399161
M-WES-S267	trio	combined-other	<i>MECP2</i>	NM_004992.3	c.1164_1207del	p.Pro389*	heterozygous	XL	Rett syndrome (312750)	de novo	yes	35872528
M-WES-S268	trio	combined-other	<i>MECP2</i>	NM_004992.3	c.502C>T	p.Arg168*	heterozygous	XL	Rett syndrome (312750)	de novo	yes	
M-WES-S269	trio	combined-other	<i>MECR</i>	NM_016011.2	c.553delG	p.Asp185Ilefs*25	compound heterozygous	AR	Dystonia, childhood-onset, with optic atrophy and basal ganglia abnormalities (617282)	AR		33098801

M-WES-S269	trio	combined-other	<i>MECR</i>	NM_016011.2	c.772C>T	p.Arg258Trp	compound heterozygous	AR	Dystonia, childhood-onset, with optic atrophy and basal ganglia abnormalities (617282)	AR		33098801
M-WES-S270	solo	combined-other	<i>MED23</i>	NM_015979.3	c.635T>C	p.Phe212Ser	compound heterozygous	AR	Intellectual developmental disorder, autosomal recessive 18, with or without epilepsy (614249)	AR	yes	33098801
M-WES-S270	solo	combined-other	<i>MED23</i>	NM_015979.3	c.3752dupT	p.Leu1251Phefs*32	compound heterozygous	AR	Intellectual developmental disorder, autosomal recessive 18, with or without epilepsy (614249)	AR	yes	33098801
M-WES-S271	duo	combined-other	<i>MICU1</i>	NM_006077.3	c.741+1G>A	p.?	homozygous	AR	Myopathy with extrapyramidal signs (615673)	AR	yes	
M-WES-S272	trio	combined-other	<i>MMAA</i>	NM_172250.3	c.304G>A	p.Ala102Thr	homozygous	AR	Methylmalonic aciduria, vitamin B12-responsive, cblA type (251100)	AR	yes	
M-WES-S273	trio	combined-other	<i>MORC2</i>	NM_014941.1	c.995A>G	p.Tyr332Cys	heterozygous	AD	Charcot-Marie-Tooth disease, axonal, type 2Z (616688)	de novo	yes	33098801
M-WES-S274	trio	combined-other	<i>MSL3</i>	NM_006800.3	c.816C>A	p.Tyr272*	hemizygous	XL	Basilicata-Akhtar syndrome (301032)	de novo	yes	33098801
M-WES-S275	trio	combined-other	<i>NAA15</i>	NM_057175.5	c.382C>T	p.Arg128*	heterozygous	AD	Intellectual developmental disorder, autosomal dominant 50, with behavioral abnormalities (617787)	de novo	yes	35730864
M-WES-S276	trio	combined-other	<i>NARS2</i>	NM_024678.6	c.418C>T	p.Arg140*	compound heterozygous	AR	Combined oxidative phosphorylation deficiency 24 (616239)	AR	yes	35872528
M-WES-S276	trio	combined-other	<i>NARS2</i>	NM_024678.6	c.749G>A	p.Arg250Gln	compound heterozygous	AR	Combined oxidative phosphorylation deficiency 24 (616239)	AR	yes	35872528
M-WES-S277 ^e	multiplex	combined-other	<i>NAV3</i>	NM_014903.6	c.6809G>A	p.Trp2270*	heterozygous	AD	N/A	dominantly inherited		38977784
M-WES-S278	trio	combined-other	<i>NEFL</i>	NM_006158.4	c.293A>G	p.Asn98Ser	heterozygous	AD	Charcot-Marie-Tooth disease, type 2E (607684)	de novo		35872528
M-WES-S279	trio	combined-other	<i>NFIX</i>	NM_002501.4	c.346C>T	p.Arg116Trp	heterozygous	AD	Malan syndrome (614753)	de novo	yes	
M-WES-S280	trio	combined-other	<i>NGLY1</i>	NM_018297.3	c.1025A>G	p.Tyr342Cys	compound heterozygous	AR	Congenital disorder of deglycosylation (615273)	AR	yes	33098801
M-WES-S280	trio	combined-other	<i>NGLY1</i>	NM_018297.3	c.1533_1536delTCAA	p.Asn511Lysfs*51	compound heterozygous	AR	Congenital disorder of deglycosylation (615273)	AR	yes	33098801
M-WES-S281	solo	combined-other	<i>NKX2-1</i>	NM_003317.3	c.213_229del	p.Ala73Leufs*330	heterozygous	AD	Chorea, hereditary benign/Choreoathetosis, hypothyroidism, and neonatal respiratory distress (118700/610978)	undetermined		33098801
M-WES-S282	trio	combined-other	<i>NKX2-1</i>	NM_003317.4	c.160C>T	p.Gln54*	heterozygous	AD	Chorea, hereditary benign/Choreoathetosis, hypothyroidism, and neonatal respiratory distress (118700/610978)	de novo		
M-WES-S283	trio	combined-other	<i>NPC1</i>	NM_000271.4	c.2196dupT	p.Pro733Serfs*10	compound heterozygous	AR	Niemann-Pick disease, type C1 (257220)	AR		33098801
M-WES-S283	trio	combined-other	<i>NPC1</i>	NM_000271.4	c.2861C>T	p.Ser954Leu	compound heterozygous	AR	Niemann-Pick disease, type C1 (257220)	AR		33098801

M-WES-S284	trio	combined-other	<i>NPC1</i>	NM_000271.4	c.2861C>T	p.Ser954Leu	compound heterozygous	AR	Niemann-Pick disease, type C1 (257220)	AR		33098801
M-WES-S284	trio	combined-other	<i>NPC1</i>	NM_000271.4	c.3027delC	p.Lys1010Serfs*30	compound heterozygous	AR	Niemann-Pick disease, type C1 (257220)	AR		33098801
M-WES-S285 ^f	solo	combined-other	<i>NPC1</i>	NM_000271.4	c.2795+1G>T	p.?	compound heterozygous	AR	Niemann-Pick disease, type C1 (257220)	AR		
M-WES-S285 ^f	solo	combined-other	<i>NPC1</i>	NM_000271.4	c.2974G>C	p.Gly992Arg	compound heterozygous	AR	Niemann-Pick disease, type C1 (257220)	AR		
M-WES-S286	trio	combined-other	<i>NPC1</i>	NM_000271.4	c.506A>T	p.Asn169Ile	homozygous	AR	Niemann-Pick disease, type C1 (257220)	AR		
M-WES-S287	trio	combined-other	<i>NR4A2</i>	NM_006186.3	c.914G>A	p.Cys305Tyr	heterozygous	AD	Intellectual developmental disorder with language impairment and early-onset DOPA-responsive dystonia-parkinsonism (619911)	de novo	yes	33098801
M-WES-S288	trio	combined-other	<i>NR4A2</i>	NM_006186.3	c.863A>G	p.Lys288Arg	heterozygous	AD	Intellectual developmental disorder with language impairment and early-onset DOPA-responsive dystonia-parkinsonism (619911)	de novo	yes	34155693
M-WES-S289 ^g	trio	combined-other	<i>NUP54</i>	NM_017426.4	c.1073T>G	p.Ile358Ser	homozygous	AR	<i>NUP54</i> -related dystonia (620427)	AR		36333996
M-WES-S290	solo	combined-other	<i>OPA1</i>	NM_015560.2	c.575delC	p.Ala192Glyfs*36	heterozygous	AD	Optic atrophy plus syndrome (125250)	undetermined		33098801
M-WES-S291	trio	combined-other	<i>PAK1</i>	NM_002576.4	c.1427T>C	p.Ile476Thr	heterozygous	AD	Intellectual developmental disorder with macrocephaly, seizures, and speech delay (618158)	de novo	yes	33098801
M-WES-S292	solo	combined-other	<i>PANK2</i>	NM_153638.2	CNV (chr20:3888573-3888924, deletion)	CNV (chr20:3888573-3888924, deletion)	homozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	33098801
M-WES-S293	solo	combined-other	<i>PANK2</i>	NM_153638.2	c.1086C>A	p.Tyr362*	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	33098801
M-WES-S293	solo	combined-other	<i>PANK2</i>	NM_153638.2	c.1561G>A	p.Gly521Arg	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	33098801
M-WES-S294	trio	combined-other	<i>PANK2</i>	NM_153638.2	c.791G>A	p.Arg264Gln	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	33098801
M-WES-S294	trio	combined-other	<i>PANK2</i>	NM_153638.2	c.823_824delCT	p.Leu275Valfs*16	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	33098801
M-WES-S295	trio	combined-other	<i>PANK2</i>	NM_153638.2	c.1561G>A	p.Gly521Arg	homozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	33098801
M-WES-S296	solo	combined-other	<i>PANK2</i>	NM_153638.2	c.1583C>T	p.Thr528Met	homozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	33098801
M-WES-S297 ⁱ	solo	combined-other	<i>PANK2</i>	NM_153638.2	c.735dupT	p.Lys246*	homozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	33949708
M-WES-S298	trio	combined-other	<i>PANK2</i>	NM_153638.3	c.1168A>G	p.Ile390Val	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	
M-WES-S298	trio	combined-other	<i>PANK2</i>	NM_153638.3	c.1561G>A	p.Gly521Arg	compound heterozygous	AR	Neurodegeneration with brain iron accumulation 1 (234200)	AR	yes	
M-WES-S299	trio	combined-other	<i>PCDH12</i>	NM_016580.3	c.311G>A	p.Cys104Tyr	compound heterozygous	AR	Diencephalic-mesencephalic junction dysplasia syndrome 1 (251280)	AR	yes	
M-WES-S299	trio	combined-other	<i>PCDH12</i>	NM_016580.3	c.451C>T	p.Arg151*	compound heterozygous	AR	Diencephalic-mesencephalic junction dysplasia syndrome 1	AR	yes	

(251280)												
M-WES-S300	solo	combined-other	<i>PDE10A</i>	NM_001130690.2	c.652C>T	p.Arg218Trp	homozygous	AR	Dyskinesia, limb and orofacial, infantile-onset (616921)	AR		33098801
M-WES-S301	trio	combined-other	<i>PDHA1</i>	NM_000284.4	c.640T>G	p.Trp214Gly	heterozygous	XL	Pyruvate dehydrogenase E1-alpha deficiency (312170)	de novo	yes	
M-WES-S302	trio	combined-other	<i>PLA2G6</i>	NM_003560.4	c.2239C>T	p.Arg747Trp	homozygous	AR	Infantile neuroaxonal dystrophy 1/Neurodegeneration with brain iron accumulation 2B/Parkinson disease 14, autosomal recessive (256600/610217/612953)	AR	yes	35872528
M-WES-S303	trio	combined-other	<i>PNPLA6</i>	NM_006702.4	c.2944_2947dupAGCC	p.Arg983Glnfs*38	compound heterozygous	AR	Boucher-Neuhauser syndrome (215470)	AR	yes	33949708
M-WES-S303	trio	combined-other	<i>PNPLA6</i>	NM_006702.4	c.3931C>T	p.Arg1311Trp	compound heterozygous	AR	Boucher-Neuhauser syndrome (215470)	AR	yes	33949708
M-WES-S304	solo	combined-other	<i>POGZ</i>	NM_015100.4	c.1378del	p.Ala460Profs*10	heterozygous	AD	White-Sutton syndrome (616364)	undetermined	yes	
M-WES-S305	trio	combined-other	<i>POLG</i>	NM_002693.2	c.428C>T	p.Ala143Val	compound heterozygous	AR	Mitochondrial DNA depletion syndrome 4A (Alpers type)/Mitochondrial DNA depletion syndrome 4B (MNGIE type)/Mitochondrial recessive ataxia syndrome (includes SANDO and SCAE)/Progressive external ophthalmoplegia, autosomal recessive 1 (203700/613662/607459/258450)	AR	yes	
M-WES-S305	trio	combined-other	<i>POLG</i>	NM_002693.2	c.1399G>A	p.Ala467Thr	compound heterozygous	AR	Mitochondrial DNA depletion syndrome 4A (Alpers type)/Mitochondrial DNA depletion syndrome 4B (MNGIE type)/Mitochondrial recessive ataxia syndrome (includes SANDO and SCAE)/Progressive external ophthalmoplegia, autosomal recessive 1 (203700/613662/607459/258450)	AR	yes	
M-WES-S306	trio	combined-other	<i>POLR3A</i>	NM_007055.3	c.1771-7C>G	p.Gly548_Tyr637del + p.Pro591Metfs*9	homozygous	AR	Leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism (607694)	AR	yes	33098801
M-WES-S307	solo	combined-other	<i>PPP2R5D</i>	NM_006245.3	c.592G>A	p.Glu198Lys	heterozygous	AD	Houge-Janssens syndrome 1 (616355)	de novo	yes	33098801
M-WES-S308	trio	combined-other	<i>PPT1</i>	NM_000310.3	c.169dup	p.Met57Asnfs*45	homozygous	AR	Ceroid lipofuscinosis, neuronal, 1 (256730)	AR	yes	
M-WES-S309	solo	combined-other	<i>PRKCG</i>	NM_002739.3	c.417C>A	p.His139Gln	heterozygous	AD	Spinocerebellar ataxia 14 (605361)	undetermined	yes	33098801
M-WES-S310 ^e	trio	combined-other	<i>PRRT2</i>	NM_145239.3	c.649dup	p.Arg217Profs*8	heterozygous	AD	Convulsions, familial infantile, with paroxysmal choreoathetosis/Episodic kinesigenic dyskinesia 1 (602066/128200)	dominantly inherited	yes	

M-WES-S311	solo	combined-other	<i>PSEN1</i>	NM_000021.3	c.697A>G	p.Met233Val	heterozygous	AD	Alzheimer disease, type 3 (607822)	dominantly inherited		33949708
M-WES-S312 ^f	trio	combined-other	<i>PTS</i>	NM_000317.3	c.366del	p.Pro123Leufs*2	compound heterozygous	AR	Hyperphenylalaninemia, BH4-deficient, A (261640)	AR		
M-WES-S312 ^f	trio	combined-other	<i>PTS</i>	NM_000317.3	c.407A>T	p.Asp136Val	compound heterozygous	AR	Hyperphenylalaninemia, BH4-deficient, A (261640)	AR		
M-WES-S313	solo	combined-other	<i>PURA</i>	NM_005859.5	c.935dup	p.Leu313Thrfs*4	heterozygous	AD	Neurodevelopmental disorder with neonatal respiratory insufficiency, hypotonia, and feeding difficulties (616158)	undetermined	yes	
M-WES-S314 ^f	solo	combined-other	<i>PURA</i>	NM_005859.5	c.668_675dup	p.Val226Profs*2	heterozygous	AD	Neurodevelopmental disorder with neonatal respiratory insufficiency, hypotonia, and feeding difficulties (616158)	undetermined	yes	
M-WES-S298	trio	combined-other	<i>RALA</i>	NM_005402.4	c.472G>A	p.Ala158Thr	heterozygous	AD	Hiatt-Neu-Cooper neurodevelopmental syndrome (619311)	de novo	yes	
M-WES-S315 ^e	trio	combined-other	<i>RARB</i>	NM_000965.4	c.1210C>T	p.Gln404*	heterozygous	AD	Microphthalmia, syndromic 12 (615524)	de novo	yes	37321544
M-WES-S316	solo	combined-other	<i>RERE</i>	NM_012102.4	c.4033G>T	p.Glu1345*	heterozygous	AD	Neurodevelopmental disorder with or without anomalies of the brain, eye, or heart (616975)	undetermined	yes	
M-WES-S317	trio	combined-other	<i>RHOBTB2</i>	NM_001160036.1	c.1448G>A	p.Arg483His	heterozygous	AD	Epileptic encephalopathy, early infantile, 64 (618004)	de novo	yes	33098801
M-WES-S318 ^f	trio	combined-other	<i>RHOBTB2</i>	NM_001160036.1	c.1531C>T	p.Arg511Trp	heterozygous	AD	Epileptic encephalopathy, early infantile, 64 (618004)	de novo	yes	
M-WES-S319	trio	combined-other	<i>SATB1</i>	NM_002971.4	c.1924C>T	p.Arg642*	heterozygous	AD	Developmental delay with dysmorphic facies and dental anomalies (619228)	de novo	yes	34031799
M-WES-S320	solo	combined-other	<i>SCN2A</i>	NM_021007.3	c.1384-2A>G	p.?	heterozygous	AD	Developmental and epileptic encephalopathy 11/Episodic ataxia, type 9 /Seizures, benign familial infantile, 3 (613721 /618924/607745)	undetermined	yes	
M-WES-S321	trio	combined-other	<i>SCO2</i>	NM_005138.2	c.418G>A	p.Glu140Lys	homozygous	AR	Mitochondrial complex IV deficiency, nuclear type 2 (604377)	AR	yes	33098801
M-WES-S322	solo	combined-other	<i>SCO2</i>	NM_005138.2	c.418G>A	p.Glu140Lys	homozygous	AR	Mitochondrial complex IV deficiency, nuclear type 2 (604377)	AR	yes	
M-WES-S323	solo	combined-other	<i>SERAC1</i>	NM_032861.4	c.1211G>A	p.Gly404Glu	homozygous	AR	3-methylglutaconic aciduria with deafness, encephalopathy, and Leigh-like syndrome (614739)	AR	yes	35872528
M-WES-S324 ^f	trio	combined-other	<i>SETX</i>	NM_015046.5	c.5825T>C	p.Ile1942Thr	homozygous	AR	Spinocerebellar ataxia, autosomal recessive, with axonal neuropathy 2 (606002)	AR		33098801
M-WES-S325	solo	combined-other	<i>SETX</i>	NM_015046.5	c.6464T>G	p.Leu2155Trp	compound heterozygous	AR	Spinocerebellar ataxia, autosomal recessive, with axonal neuropathy 2 (606002)	AR		33098801
M-WES-S325	solo	combined-other	<i>SETX</i>	NM_015046.5	c.6620A>T	p.Asp2207Val	compound heterozygous	AR	Spinocerebellar ataxia, autosomal recessive, with axonal neuropathy 2 (606002)	AR		33098801
M-WES-S326	solo	combined-other	<i>SGCE</i> /7q21.3	NM_003919.2	CNV (chr7:93516132-95668732, deletion)	CNV (chr7:93516132-95668732, deletion)	heterozygous	AD	<i>SGCE</i> -related myoclonus-dystonia (159900)	undetermined		33949708

M-WES-S327	trio	combined-other	SHANK3	NM_033517.1	c.3679dupG	p.Ala1227fs	heterozygous	AD	Phelan-McDermid syndrome (606232)	de novo	yes	33098801
M-WES-S328	trio	combined-other	SHANK3	NM_033517.1	CNV (chr22:51123013-51220721, deletion)	CNV (chr22:51123013-51220721, deletion)	heterozygous	AD	Phelan-McDermid syndrome (606232)	de novo	yes	
M-WES-S329 ^e	solo	combined-other	SHQ1	NM_018130.3	c.523G>T	p.Asp175Tyr	compound heterozygous	AR	Neurodevelopmental disorder with dystonia and seizures (619922)	AR	yes	36416405
M-WES-S329 ^e	solo	combined-other	SHQ1	NM_018130.3	c.828_831del	p.Asp277Serfs*27	compound heterozygous	AR	Neurodevelopmental disorder with dystonia and seizures (619922)	AR	yes	36416405
M-WES-S330	solo	combined-other	SLC16A2	NM_006517.5	c.731del	p.Met244Serfs*23	hemizygous	XL	Allan-Herndon-Dudley syndrome (300523)	undetermined	yes	35872528
M-WES-S331	solo	combined-other	SLC19A3	NM_025243.4	c.952G>A	p.Ala318Thr	homozygous	AR	Thiamine metabolism dysfunction syndrome 2 (biotin/thiamine-responsive basal ganglia disease type) (607483)	AR		31036918
M-WES-S332	trio	combined-other	SLC2A1	NM_006516.2	c.732delG	p.Met244Ilefs*8	heterozygous	AD	SLC2A1-related dystonia /GLUT1 deficiency syndrome 2, childhood onset (601042/612126)	de novo	yes	33098801
M-WES-S333	trio	combined-other	SLC2A1	NM_006516.2	c.1199_1200insGAG	p.Arg400_Pro401insSer	heterozygous	AD	SLC2A1-related dystonia /GLUT1 deficiency syndrome 2, childhood onset (601042/612126)	de novo	yes	33098801
M-WES-S334	solo	combined-other	SLC6A1	NM_003042.3	c.1079-1G>A	p.?	heterozygous	AD	Myoclonic-atonic epilepsy (616421)	undetermined	yes	33098801
M-WES-S335 ^f	solo	combined-other	SLC6A3	NM_001044.4	c.178C>T	p.Arg60Trp	homozygous	AR	Parkinsonism-dystonia, infantile, 1 (613135)	AR	yes	33098801
M-WES-S336	trio	combined-other	SLC9A6	NM_006359.2	c.1569_1573delAAGGA	p.Arg524Asnfs*17	hemizygous	XL	Intellectual developmental disorder, X-linked syndromic, Christianson type (300243)	de novo	yes	33098801
M-WES-S337	solo	combined-other	SNAP25	NM_001322902.1	c.601A>T	p.Lys201*	heterozygous	AD	N/A	undetermined	yes	
M-WES-S338	quartet	combined-other	SNX14	NM_153816.6	CNV (chr6:86235844-86253477, deletion)	CNV (chr6:86235844-86253477, deletion)	homozygous	AR	Spinocerebellar ataxia, autosomal recessive 20 (616354)	AR	yes	
M-WES-S339	solo	combined-other	SON	NM_032195.2	c.5753_5756delTTAG	p.Val1918Glufs*87	heterozygous	AD	ZTTK syndrome (617140)	de novo	yes	33949708
M-WES-S340	solo	combined-other	SOX2	NM_003106.4	c.59dup	p.Gly21Argfs*75	heterozygous	AD	Optic nerve hypoplasia and abnormalities of the central nervous system (206900)	undetermined	yes	35872528
M-WES-S341	trio	combined-other	SOX6	NM_017508.3	c.1996C>T	p.Arg666*	heterozygous	AD	Tolchin-Le Caignec syndrome (618971)	de novo	yes	38141365
M-WES-S342	trio	combined-other	SPAST	NM_014946.3	c.1360G>A	p.Glu454Lys	heterozygous	AD	Spastic paraplegia 4, autosomal dominant (182601)	de novo		33098801
M-WES-S343	trio	combined-other	SPAST	NM_014946.3	c.1496G>A	p.Arg499His	heterozygous	AD	Spastic paraplegia 4, autosomal dominant (182601)	de novo		33098801
M-WES-S344	solo	combined-other	SPAST	NM_014946.3	c.1169T>A	p.Met390Lys	heterozygous	AD	Spastic paraplegia 4, autosomal dominant (182601)	de novo		33098801
M-WES-S345	solo	combined-other	SPAST	NM_014946.3	c.1484C>T	p.Ala495Val	heterozygous	AD	Spastic paraplegia 4, autosomal dominant (182601)	de novo		33098801
M-WES-S346	solo	combined-other	SPAST	NM_014946.3	c.1496G>A	p.Arg499His	heterozygous	AD	Spastic paraplegia 4, autosomal dominant (182601)	de novo		33098801

M-WES-S347	trio	combined-other	<i>SPAST</i>	NM_014946.3	c.1496G>A	p.Arg499His	heterozygous	AD	Spastic paraplegia 4, autosomal dominant (182601)	de novo		33949708
M-WES-S348	solo	combined-other	<i>SPAST</i>	NM_014946.3	c.1456A>G	p.Thr486Ala	heterozygous	AD	Spastic paraplegia 4, autosomal dominant (182601)	undetermined		
M-WES-S349	solo	combined-other	<i>SPG11</i>	NM_025137.3	c.5381T>C	p.Leu1794Pro	homozygous	AR	Spastic paraplegia 11, autosomal recessive (604360)	AR	yes	33098801
M-WES-S350	trio	combined-other	<i>SPG11</i>	NM_025137.3	c.4307_4308delAA	p.Gln1436Argfs*7	homozygous	AR	Spastic paraplegia 11, autosomal recessive (604360)	AR	yes	33098801
M-WES-S351	quartet	combined-other	<i>SPR</i>	NM_003124.4	c.524C>A	p.Ala175Asp	homozygous	AR	Dystonia, dopa-responsive, due to sepiapterin reductase deficiency (612716)	AR	yes	33098801
M-WES-S352	trio	combined-other	<i>SPR</i>	NM_003124.5	c.381C>G	p.Asn127Lys	homozygous	AR	Dystonia, dopa-responsive, due to sepiapterin reductase deficiency (612716)	AR	yes	
M-WES-S353	trio	combined-other	<i>SPR</i>	NM_003124.5	c.381C>G	p.Asn127Lys	homozygous	AR	Dystonia, dopa-responsive, due to sepiapterin reductase deficiency (612716)	AR	yes	
M-WES-S354 ^e	trio	combined-other	<i>SPTBN1</i>	NM_003128.3	c.5961+2T>C	p.?	heterozygous	AD	Developmental delay, impaired speech, and behavioral abnormalities (619475)	de novo	yes	34211179
M-WES-S355 ^e	solo	combined-other	<i>SRRM2</i>	NM_016333.4	c.1156_1157dup	p.Leu386Phefs*2	heterozygous	AD	Intellectual developmental disorder, autosomal dominant 72 (620439)	undetermined	yes	
M-WES-S356 ^f	solo	combined-other	<i>SUCLG1</i>	NM_003849.4	c.137C>T	p.Ser46Phe	compound heterozygous	AR	Mitochondrial DNA depletion syndrome 9 (encephalomyopathic type with methylmalonic aciduria) (245400)	AR		
M-WES-S356 ^f	solo	combined-other	<i>SUCLG1</i>	NM_003849.4	c.152A>T	p.Tyr51Phe	compound heterozygous	AR	Mitochondrial DNA depletion syndrome 9 (encephalomyopathic type with methylmalonic aciduria) (245400)	AR		
M-WES-S357	trio	combined-other	<i>SUOX</i>	NM_000456.2	c.1097G>A	p.Arg366His	homozygous	AR	Sulfite oxidase deficiency (272300)	AR	yes	33098801
M-WES-S358 ^f	solo	combined-other	<i>TBC1D24</i>	NM_020705.3	c.1061G>T	p.Arg354Leu	homozygous	AR	Developmental and epileptic encephalopathy 16/DOORS syndrome/Epilepsy, rolandic, with proxysmal exercise-induce dystonia and writer's cramp (615338/220500/608105)	AR	yes	35872528
M-WES-S359 ^f	trio	combined-other	<i>TBC1D24</i>	NM_020705.3	c.686T>C	p.Phe229Ser	compound heterozygous	AR	Developmental and epileptic encephalopathy 16/DOORS syndrome/Epilepsy, rolandic, with proxysmal exercise-induce dystonia and writer's cramp (615338/220500/608105)	AR	yes	
M-WES-S359 ^f	trio	combined-other	<i>TBC1D24</i>	NM_020705.3	c.1507G>A	p.Gly503Arg	compound heterozygous	AR	Developmental and epileptic encephalopathy 16/DOORS syndrome/Epilepsy, rolandic, with proxysmal exercise-induce dystonia and writer's cramp (615338/220500/608105)	AR	yes	
M-WES-S360	trio	combined-other	<i>TBCD</i>	NM_005993.5	c.230A>G	p.His77Arg	compound heterozygous	AR	Encephalopathy, progressive, early-onset, with brain atrophy and thin corpus callosum (617193)	AR	yes	

M-WES-S360	trio	combined-other	<i>TBCD</i>	NM_005993.5	c.2380-1G>A	p.?	compound heterozygous	AR	Encephalopathy, progressive, early-onset, with brain atrophy and thin corpus callosum (617193)	AR	yes	
M-WES-S361 ^e	trio	combined-other	<i>TBX1/22q11.21</i>	NM_080647.1	CNV (chr22:18893888-21386100, deletion)	CNV (chr22:18893888-21386100, deletion)	heterozygous	AD	DiGeorge syndrome (188400)	de novo		
M-WES-S362	solo	combined-other	<i>TCF20</i>	NM_005650.3	c.3943_3944del	p.Asp1315Phefs*10	heterozygous	AD	Developmental delay with variable intellectual impairment and behavioral abnormalities (618430)	undetermined	yes	35872528
M-WES-S363	solo	combined-other	<i>TCF20</i>	NM_005650.3	c.1707dup	p.Arg570Glnfs*5	heterozygous	AD	Developmental delay with variable intellectual impairment and behavioral abnormalities (618430)	undetermined	yes	35977450
M-WES-S364	trio	combined-other	<i>TECPR2</i>	NM_014844.3	c.715G>A	p.Gly239Arg	compound heterozygous	AR	Spastic paraplegia 49, autosomal recessive (615031)	AR	yes	33098801
M-WES-S364	trio	combined-other	<i>TECPR2</i>	NM_014844.3	c.4033G>C	p.Ala1345Pro	compound heterozygous	AR	Spastic paraplegia 49, autosomal recessive (615031)	AR	yes	33098801
M-WES-S365	trio	combined-other	<i>TFE3</i>	NM_006521.6	c.374_379del	p.Ala125_Gln126del	heterozygous	XL	Intellectual developmental disorder, X-linked, syndromic, with pigmentary mosaicism and coarse facies (301066)	de novo	yes	35872528
M-WES-S366	solo	combined-other	<i>TUBB4A</i>	NM_006087.2	c.1228G>A	p.Glu410Lys	heterozygous	AD	<i>TUBB4A</i> -related dystonia /Leukodystrophy, hypomyelinating, 6 (128101/612438)	undetermined	yes	33098801
M-WES-S367	solo	combined-other	<i>TUBB4A</i>	NM_006087.2	c.1054G>T	p.Ala352Ser	heterozygous	AD	<i>TUBB4A</i> -related dystonia /Leukodystrophy, hypomyelinating, 6 (128101/612438)	undetermined	yes	33098801
M-WES-S368	solo	combined-other	<i>TUBB4A</i>	NM_006087.2	c.1065C>A	p.Asp355Glu	heterozygous	AD	<i>TUBB4A</i> -related dystonia /Leukodystrophy, hypomyelinating, 6 (128101/612438)	undetermined	yes	33098801
M-WES-S369	solo	combined-other	<i>TUBB4A</i>	NM_006087.2	c.1228G>A	p.Glu410Lys	heterozygous	AD	<i>TUBB4A</i> -related dystonia /Leukodystrophy, hypomyelinating, 6 (128101/612438)	de novo	yes	33098801
M-WES-S370	trio	combined-other	<i>UBE3A/15q11.2-q13</i>	NM_130838.1	CNV (chr15:23684690-28544661, deletion)	CNV (chr15:23684690-28544661, deletion)	heterozygous	AD	Angelman syndrome (105830)	de novo	yes	33098801
M-WES-S371	solo	combined-other	<i>UBE3A/15q11.2-q13</i>	NM_130838.1	CNV (chr15:23684689-32450807, deletion)	CNV (chr15:23684689-32450807, deletion)	heterozygous	AD	Angelman syndrome (105830)	undetermined	yes	35872528
M-WES-S372	trio	combined-other	<i>UBE3A/15q11.2-q13</i>	NM_130838.1	CNV (chr15:22708983-28566578, deletion)	CNV (chr15:22708983-28566578, deletion)	heterozygous	AD	Angelman syndrome (105830)	de novo	yes	
M-WES-S373	trio	combined-other	<i>UBTF</i>	NM_014233.4	c.628G>A	p.Glu210Lys	heterozygous	AD	Neurodegeneration, childhood-onset, with brain atrophy (617672)	de novo	yes	
M-WES-S184	trio	combined-other	<i>VLDLR</i>	NM_003383.5	c.1962+1G>C	p.?	compound heterozygous	AR	Cerebellar hypoplasia, impaired intellectual development, and dysequilibrium syndrome 1 (224050)	AR	yes	
M-WES-S184	trio	combined-other	<i>VLDLR</i>	NM_003383.5	CNV (chr9:2635453-2653867, deletion)	CNV (chr9:2635453-2653867, deletion)	compound heterozygous	AR	Cerebellar hypoplasia, impaired intellectual development, and dysequilibrium syndrome 1 (224050)	AR	yes	

M-WES-S374 ^f	solo	combined-other	VPS16	NM_022575.2	c.559C>T	p.Arg187*	heterozygous	AD	VPS16-related dystonia (619291)	undetermined	yes	33949708
M-WES-S375 ^f	solo	combined-other	VPS16	NM_022575.2	c.559C>T	p.Arg187*	heterozygous	AD	VPS16-related dystonia (619291)	undetermined	yes	33949708
M-WES-S376 ^f	trio	combined-other	VPS16	NM_022575.2	c.559C>T	p.Arg187*	heterozygous	AD	VPS16-related dystonia (619291)	dominantly inherited	yes	33949708
M-WES-S377 ^e	trio	combined-other	VPS16	NM_022575.2	c.1335T>G	p.Tyr445*	heterozygous	AD	VPS16-related dystonia (619291)	dominantly inherited	yes	32808683
M-WES-S378	solo	combined-other	VPS16	NM_022575.4	c.1389C>G	p.Tyr463*	heterozygous	AD	VPS16-related dystonia (619291)	dominantly inherited	yes	38291845
M-WES-S379 ^f	solo	combined-other	VPS16	NM_022575.4	c.1818+2T>G	p.?	heterozygous	AD	VPS16-related dystonia (619291)	undetermined	yes	
M-WES-S380 ^f	solo	combined-other	WAC	NM_016628.5	c.381+1G>T	p.?	heterozygous	AD	Desanto-Shinawi syndrome (616708)	undetermined	yes	
M-WES-S381	solo	combined-other	WARS2	NM_015836.3	c.1045G>C	p.Val349Leu	homozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	33098801
M-WES-S382	duo	combined-other	WARS2	NM_015836.3	c.37T>G	p.Trp13Gly	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	33949708
M-WES-S382	duo	combined-other	WARS2	NM_015836.3	CNV (chr1:119618973-119619229, deletion)	CNV (chr1:119618973-119619229, deletion)	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	33949708
M-WES-S383	quartet	combined-other	WARS2	NM_015836.3	c.37T>G	p.Trp13Gly	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	33949708
M-WES-S383	quartet	combined-other	WARS2	NM_015836.3	c.298_300delCTT	p.Leu100del	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	33949708
M-WES-S384	trio	combined-other	WARS2	NM_015836.3	c.37T>G	p.Trp13Gly	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	
M-WES-S384	trio	combined-other	WARS2	NM_015836.3	CNV (chr1:119618973-119619229, deletion)	CNV (chr1:119618973-119619229, deletion)	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	
M-WES-S385	trio	combined-other	WARS2	NM_015836.3	c.37T>G	p.Trp13Gly	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	
M-WES-S385	trio	combined-other	WARS2	NM_015836.3	c.535G>A	p.Gly179Arg	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	
M-WES-S386 ^f	trio	combined-other	WARS2	NM_015836.3	c.37T>G	p.Trp13Gly	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	

M-WES-S386 ^f	trio	combined-other	WARS2	NM_015836.3	c.143A>G	p.His48Arg	compound heterozygous	AR	Neurodevelopmental disorder, mitochondrial, with abnormal movements and lactic acidosis, with or without seizures (617710)	AR	yes	
M-WES-S387	trio	combined-other	WASHC5	NM_014846.4	c.1256A>G	p.Gln419Arg	heterozygous	AD	Spastic paraplegia 8, autosomal dominant (603563)	de novo	yes	
M-WES-S388	solo	combined-other	WDR45	NM_007075.3	CNV (chrX:48919573-48935753, deletion)	CNV (chrX:48919573-48935753, deletion)	heterozygous	XL	Neurodegeneration with brain iron accumulation 5 (300894)	undetermined	yes	33098801
M-WES-S389	solo	combined-other	WDR73	NM_032856.4	c.706_719dup	p.Ser240Argfs*28	compound heterozygous	AR	Galloway-Mowat syndrome 1 (251300)	AR	yes	
M-WES-S389	solo	combined-other	WDR73	NM_032856.4	c.766dup	p.Arg256Profs*18	compound heterozygous	AR	Galloway-Mowat syndrome 1 (251300)	AR	yes	
M-WES-S390	solo	combined-other	WFS1	NM_006005.3	c.2051C>T	p.Ala684Val	heterozygous	AD	Wolfram-like syndrome, autosomal dominant (614296)	undetermined		33098801
M-WES-S391	solo	combined-other	YY1	NM_003403.4	c.1118A>G	p.His373Arg	heterozygous	AD	Gabriele-de Vries syndrome (617557)	undetermined	yes	33949708
M-WES-S392	trio	combined-other	ZC4H2	NM_018684.4	c.172G>T	p.Glu58*	heterozygous	XL	Wieacker-Wolff syndrome, female-restricted (301041)	de novo	yes	35872528
M-WES-S393	trio	combined-other	ZEB2	NM_014795.3	c.899A>G	p.His300Arg	heterozygous	AD	Mowat-Wilson syndrome (235730)	de novo	yes	33098801
M-WES-S328	trio	combined-other	ZEB2	NM_014795.3	c.3616G>A	p.Glu1206Lys	heterozygous	AD	Mowat-Wilson syndrome (235730)	de novo	yes	
M-WES-S394	trio	combined-other	ZMYND11	NM_006624.5	c.1798C>T	p.Arg600Trp	heterozygous	AD	Intellectual developmental disorder, autosomal dominant 30 (616083)	de novo	yes	33098801
M-WES-S331	solo	combined-other	ZNF142	NM_001105537.2	c.3175C>T	p.Arg1059*	homozygous	AR	Neurodevelopmental disorder with impaired speech and hyperkinetic movements (618425)	AR	yes	31036918
M-WES-S395	quartet	combined-other	ZNF142	NM_001105537.2	c.817_818delAA	p.Lys273Glufs*32	compound heterozygous	AR	Neurodevelopmental disorder with impaired speech and hyperkinetic movements (618425)	AR	yes	33098801
M-WES-S395	quartet	combined-other	ZNF142	NM_001105537.2	c.1292delG	p.Cys431Leufs*11	compound heterozygous	AR	Neurodevelopmental disorder with impaired speech and hyperkinetic movements (618425)	AR	yes	33098801
M-WES-S396 ^f	solo	combined-other	ZNF335	NM_022095.4	c.1603C>T	p.Arg535Trp	compound heterozygous	AR	Microcephaly 10, primary, autosomal recessive (615095)	AR	yes	
M-WES-S396 ^f	solo	combined-other	ZNF335	NM_022095.4	c.3486_3487del	p.Thr1163Cysfs*83	compound heterozygous	AR	Microcephaly 10, primary, autosomal recessive (615095)	AR	yes	

^aDual diagnoses identified in nine cases: M-WES-S59, *AOPEP* and *CHD8*; M-WES-S166, *CACNA1A* and *IRF2BPL*; M-WES-S167, *CACNA1E* and *KIF5A*; M-WES-S184, *CUX1* and *VLDLR*; M-WES-S222, *GJC2* and *LIG4*; M-WES-S298, *PANK2* and *RALA*; M-WES-S319, *SATB1* and trisomy X; M-WES-S328, *SHANK3* and *ZEB2*; M-WES-S331, *SLC19A3* and *ZNF142*.

^bSolo, exome analysis of the index patient only; duo, exome analysis of the index patient and 1 affected family member (affected parent or affected sibling); trio, exome analysis of the index patient and the parents; quartet, exome analysis of the index patient and the parents plus 1 affected sibling; multiplex, exome analysis of the index patient and 2 affected family members (first/second degree relatives).

^cIsolated, isolated dystonia; combined-MD, dystonia combined with additional movement disorder(s); combined-other, dystonia combined with other neurologic and/or systemic features (with or without additional movement disorder/s).

^dBased on WES data and Sanger evaluation of all available family members.

^eSolved by re-analysis.

^fIndex patient from underrepresented population.

Abbreviations: NDD, neurodevelopmental disorder; OMIM, Online Mendelian Inheritance in Man database; PMID, PubMed identifier; WES, whole-exome sequencing.

Suppl. Table 3 WGS summary metrics for 305 dystonia index patients and 259 sequenced relatives

Average number of reads	Average number of mapped reads	Average mapped reads in %	Average mapping yield (Gb)	Average read length	Average read depth	Average bases covered >20x in %
7.93x10 ⁸	7.88x10 ⁸	99.31	118.92	150.5	40.06	96.10

Suppl. Table 4 Summary of 44 index patients solved by WGS or WGS combined with proteomics

Index patient study ID (cohort)	Sex, age, origin	Age at dystonia onset, distribution; comorbid (extra-) neurologic symptoms (if present)	WGS design	Gene(s)/ locus	Genomic variant(s) (hg19); zygosity, variant category, variant size	IP	OMIM diagnosis	Published evidence supporting variant pathogenicity	Findings from fibroblast-based proteomics (+/- RNA-seq) ^s	Variant(s) likely pathogenic/ pathogenic (ACMG)	Comment: why missed in WES study/ barrier overcome by WGS or WGS plus proteomics
New variant or gene evidence (coding SNVs/indels)											
G096 (M-WES)	F, 12y, Eur	childhood-onset dystonia, segmental; spasticity, DD, ID, epilepsy	solo	<i>DNM1L</i>	NM_012062.5: c.176C>T, p.Thr59Ile; het, SNV, 1bp	AD (dn) ^a	encephalopathy, lethal, due to defective mitochondrial peroxisomal fission 1 (MIM:614388)	NA (novel variant)	NA	yes	new ClinVar evidence (02/2022) not available at the time of WES analysis
G114 (M-WES)	F, 51y, Eur	adult-onset dystonia, generalized; parkinsonism	solo	<i>ANO3</i>	NM_031418.4: c.1699G>A, p.Gly567Arg; het, SNV, 1bp ^b	AD (mat) ^a	<i>ANO3</i> -related dystonia (MIM:615034)	ClinVar: 1700707, PMID: 36228993	NA	yes	new ClinVar evidence (08/2022) not available at the time of WES analysis
G125 (EXT)	M, 12y, Eur	childhood-onset dystonia, generalized	trio	<i>VPS16</i>	NM_022575.4: c.639del, p.Gly214Alafs*6; het, indel, 1bp	AD (dn)	<i>VPS16</i> -related dystonia (MIM:619291)	NA (novel variant)	NA	yes	novel disease gene not considered in external routine WES analysis in 2020
G162 ^x (M-WES)	F, 17y, Eur	childhood-onset dystonia, generalized; myoclonus, DD, epilepsy	solo	<i>ATP6V1A</i>	NM_001690.4: c.955C>T, p.Pro319Ser; het, SNV, 1bp	AD (dn) ^a	developmental and epileptic encephalopathy 93 (MIM:618012)	ClinVar: 1512702	NA	yes	new ClinVar evidence (03/2022) not available at the time of WES analysis
G191 (EXT)	M, 54y, Eur	adult-onset dystonia, segmental; ataxia, chorea, myoclonus, cognitive decline	solo	<i>XPA</i>	NM_000380.3: c.772_785del, p.Arg258Tyrfs*5; hom, indel, 14bp	AR	xeroderma pigmentosum, group A (MIM:278700)	ClinVar: 523608, PMID: 35699229	NA	yes	new gene-phenotype link established in 2022 (PMID: 35699229), not reported by WES in external laboratory in 2021
G227 (M-WES)	M, 33y, Eur	childhood-onset dystonia, generalized; myoclonus, DD, ID, epilepsy	solo	<i>DNM1L</i>	NM_012062.5: c.176C>T, p.Thr59Ile; het, SNV, 1bp	AD (dn) ^a	encephalopathy, lethal, due to defective mitochondrial peroxisomal fission 1 (MIM:614388)	NA (novel variant)	Prot: no expression alteration	yes	new ClinVar evidence (02/2022) not available at the time of WES analysis
G281 (M-WES)	M, 7y, Eur	childhood-onset dystonia, segmental; DD, ID, dysmorphia	solo	<i>KMT5B</i> ^c & <i>SRRM2</i> ^{c,d}	NM_017635.5: c.391_394del, p.Lys131Glufs*6; het, indel, 4bp & NM_016333.4: c.205C>T, p.Arg69*; het, SNV, 1bp	AD (mat) ^a & AD (non-mat) ^a	intellectual developmental disorder, autosomal dominant 51 (MIM:617788) & intellectual developmental disorder, autosomal dominant 72 (MIM:620439)	NA (novel variants)	NA	yes & yes ^d	novel disease genes with no (well-)established phenotype links at the time of WES analysis in 2021, interpretation complicated by blended phenotype

Known pathogenic intronic variants

G110 (EXT)	F, 28y, Eur	childhood-onset dystonia, generalized; cognitive decline, neuropsychiatric issues	duo	<i>POLR3A</i>	NM_007055.4: c.1771-6C>G; hom, SNV, 1bp ^e	AR	leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism (MIM:607694)	ClinVar: 976718, PMID: 33134517	Prot: no expression alteration RNA-seq: reduced expression (~30%), exon 14 skipping	yes	-6 variant not retained in external routine WES analysis of coding and +/-5bp splice-site regions
G172 (EXT)	F, 16y, Eur	adolescence-onset dystonia, segmental; myoclonus	solo	<i>POLR3A</i>	NM_007055.4: c.1909+22G>A/ c.3243-2A; het/het, SNV/SNV, 1bp/1bp	AR	leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism (MIM:607694)	ClinVar: 445922/619038, PMID: 38700104/ 25339210	NA	yes/yes	+22 variant not retained in external routine WES analysis of coding and +/-5bp splice-site regions

Coding variants not (sufficiently) covered by WES

G043 (M-WES)	M, 20y, Eur	infantile-onset dystonia, generalized; DD, microcephaly	trio	<i>KMT2B</i>	NM_014727.2: c.17_23dup, p.Ser9Argfs*109; het, indel, 7bp	AD (dn)	<i>KMT2B</i> -related dystonia (MIM:617284)	ClinVar: 1995855	NA	yes	variant in region with WES read depth <10, missed by WES pipeline
G113* (M-WES)	F, 5y, Eur	childhood-onset dystonia, focal; ataxia, myoclonus, DD	solo	<i>SHANK1</i> ^{c,f}	NM_016148.5: c.3142C>T, p.Arg1048*; het, SNV, 1bp	AD (pat) ^a	NA (PMID: 34113010)	ClinVar: 1678865	NA	yes	variant in region with WES read depth <10, missed by WES pipeline
G132 (EXT)	F, 13, Eur	childhood-onset dystonia, generalized; spasticity, epilepsy, leukoencephalopathy	solo	<i>SNORD118</i>	NR_033294.2: n.61A>T/n.84T>A; het/het, SNV/SNV, 1bp/1bp	AR	leukoencephalopathy, brain calcifications, and cysts (MIM:614561)	PMID: 28177126/NA (novel variant)	Prot: SNORD118 not assayable	yes/yes	non-coding RNA not assessed in routine WES analysis of protein-coding regions

Mitochondrial DNA mutations^g

G055 (M-WES)	M, 14y, Eur	childhood-onset dystonia, segmental; ataxia, neuropathy, DD	trio	<i>MT-ATP6</i>	NC_012920.1: m.8993T>C, p.Leu156Pro; 96% mutational load, MT variant, 1bp	MT (dn)	mitochondrial complex V deficiency, mitochondrial type 1 (MIM:500015)	MITOMAP: "Cfrm" status, ClinVar: 9642, PMID: 8190310	NA	yes	mitochondrial genome not included in regular WES design
G085 (M-WES)	M, 8y, Eur	childhood-onset dystonia, generalized; bilateral basal ganglia lesions	trio	<i>MT-ND3</i>	NC_012920.1: m.10197G>A, p.Ala47Thr; 97% mutational load, MT variant, 1bp	MT (mat, 20%)	mitochondrial complex I deficiency, mitochondrial type 1 (MIM:500014)	MITOMAP: "Cfrm" status, ClinVar: 9715, PMID: 17152068	NA	yes	mitochondrial genome not included in regular WES design
G139 (M-WES)	F, 38y, Eur	childhood-onset dystonia, generalized	trio	<i>MT-ND6</i>	NC_012920.1: m.14459G>A, p.Ala72Val; 25% mutational load, MT variant, 1bp	MT (dn)	Leber optic atrophy and dystonia (MIM:500001)	MITOMAP: "Cfrm" status, ClinVar: 9689, PMID: 7654063	NA	yes	mitochondrial genome not included in regular WES design
G254 (M-WES)	M, 16y, Eur	adolescence-onset dystonia, generalized; cognitive decline,	solo	<i>MT-TL1</i>	NC_012920.1: m.3243A>G; 12% mutational load, MT variant, 1bp	MT (nk)	MELAS syndrome (MIM:540000)	MITOMAP: "Cfrm" status, ClinVar: 9589, PMID:	NA	yes	mitochondrial genome not included in regular WES design

neuropsychiatric issues											
38553553											
CNVs/SVs ^a											
G059* (M-WES)	M, 2y, Eur	infantile-onset dystonia, generalized; DD	solo	<i>SLC16A2</i>	chrX:73740304-73743410, del (Xq13.2) exon 2 (NM_006517.5); hem, CNV, 3.1kb	XL (nk)	Allan-Herndon- Dudley syndrome (MIM:300523) neurodevelopmental disorder with nonspecific brain abnormalities and with or without seizures (MIM:618709) <i>CACNA1A</i> -related disorder (MIM:617106/108500 /141500)	NA ⁱ	NA	yes	single-exon deletion difficult to detect in WES analysis
G120 (EXT)	M, 31y, Eur	adolescence-onset dystonia, focal; DD, ID, dysmorphia, ventriculomegaly	trio	<i>DLL1</i>	chr6:170551811-171040023, del (6q27) whole gene (NM_005618.4); het, CNV, 488.2kb	AD (dn)		PMID: 36935482	NA	yes	CNV analysis not performed by WES in external laboratory
G173 (M- WES)	F, 29y, Eur	adult-onset dystonia, segmental; ataxia, drowsiness, vertigo	trio	<i>CACNA1A</i>	chr19:13361500-13364807, del (19p13.2) exon 30 (NM_000068.4); het, CNV, 3.3kb	AD (mat)		ClinVar: 2498799	NA	yes	single-exon deletion difficult to detect in WES analysis
G174* (M- WES)	F, 20y, Mid	childhood-onset dystonia, generalized; ataxia, neuropathy, ID	solo	<i>TTC19^f</i>	chr17:15909581-15909828, del (17p12) part of exon 7 (NM_017775.4); hom, CNV, 248bp	AR	mitochondrial complex III deficiency, nuclear type 2 (MIM:615157) Mohr-Tranebjaerg syndrome (MIM:304700) ^j	NA ⁱ	NA	yes	partial-exon deletion difficult to detect in WES analysis
G201 (EXT)	F, 50y, Eur	adolescence-onset dystonia, focal	solo	<i>TIMM8A</i>	chrX:100582499-100607872, del (Xq22.1) whole gene (NM_004085.4); het, CNV, 25.4kb	XL (nk)		ClinVar: 1312518	NA	yes	CNV analysis not performed by WES in external laboratory
G204 (M- WES)	F, 40y, Eur	adolescence-onset dystonia, generalized; parkinsonism	trio	<i>PRKN</i>	chr6:162641656-162927750, del (6q26) exons 2-3 (NM_004562.3) /chr6:162411702-162718522, del (6q26) exons 3-5 (NM_004562.3); het/het, CNV/CNV, 286.1kb/306.8kb	AR	Parkinson disease, juvenile, type 2 (MIM:600116)	PMID: 29644727	NA	yes/yes	overlapping compound heterozygous deletions missed by WES pipeline
G205 (M- WES)	M, 59y, Eur	infantile-onset dystonia, generalized; chorea (dyskinetic CP)	solo	<i>ATM</i>	chr11:108231094-108248156, del (11q22.3) exons 62-63 plus 3'-UTR (NM_000051.3)/ NM_000051.3: c.8147T>C, p.Val2716Ala; het/het, CNV/SNV, 17.1kb/1bp	AR	ataxia-telangiectasia (MIM:208900)	PMID: 37438524/ClinVar: 142700	NA	yes/yes ^l	deletion of last two exons missed by WES pipeline
G222 (M- WES)	M, 29y, Eur	childhood-onset dystonia, generalized; myoclonus	solo	<i>SGCE</i>	chr7:94251073-94261239, dup (7q21.3) exons 2-4 (NM_003919.3); het, CNV, 10.2kb	AD (nk)	<i>SGCE</i> -related myoclonus-dystonia (MIM: 159900)	NA ⁱ	NA	yes	intragenic tandem duplication missed by WES pipeline
G225 (EXT)	M, 48y, Eur	childhood-onset dystonia, focal	solo	<i>THAP1</i>	chr8:42541312-42695674, del (8p11.21) exons 2-3 plus 3'-UTR (NM_018105.3); het, CNV, 154.4kb	AD (nk)	<i>THAP1</i> -related dystonia (MIM:602629) intellectual developmental disorder with dysmorphic facies, speech delay, and T- cell abnormalities	ClinVar: 547123	NA	yes	CNV analysis not performed by WES in external laboratory
G226* (M-WES)	F, 22y, Eur	adolescence-onset dystonia, generalized; borderline ID	duo	<i>BCL11B</i>	chr14:99642203-99642420, del (14q32.2) intra-exonic exon 4 (NM_138576.4); het, CNV, 218bp ^k	AD (nk)		NA ⁱ	Prot: BCL11B not assayable	yes	new gene-phenotype link established in 2022-24 (PMIDs: 36202297, 38801144), not prioritized in WES analysis

(MIM:618092)											
G234 (M-WES)	F, 55y, Eur	adult-onset dystonia, generalized; cognitive decline	solo	<i>TNRC6B</i> ^c	chr22:40706970-40780192, del (22q13.1) exons 17-23 plus 3'-UTR (NM_001162501.2); het, CNV, 73.2kb	AD (nk)	global developmental delay with speech and behavioral abnormalities (MIM:619243)	NA ⁱ	NA	yes	novel disease gene with no (well-)established phenotype link at the time of WES analysis in 2020, initially discounted
G266 (M-WES)	F, 3y, Eur	infantile-onset dystonia, generalized	trio	22q11.2	22q11.21, dup; het, CNV, ~1.3Mb	AD (dn)	chromosome 22q11.2 duplication syndrome (MIM:608363)	PMID: 38196101	NA	yes	new gene-phenotype link established in 2024 (PMID: 38196101), not prioritized in WES analysis
G274 (M-WES)	M, 3y, Eur	infantile-onset dystonia, generalized; spasticity, DD, dysmorphia (spastic-dystonic CP)	trio	<i>ASXL3</i>	chr18:31319263-31319614, dup (18q12.1) part of exon 11 (NM_030632.3) and chr18:31319615-31322822, inv (18q12.1) part of exon 11 (NM_030632.3) and chr18:31322823-31325397, del (18q12.1) part of exon 12 (NM_030632.3); het, complex rearrangement, 352bp (dup) and 3.2kb (inv) and 2.6kb (del)	AD (dn)	Bainbridge-Ropers syndrome (MIM:615485)	NA ⁱ	NA	yes	complex rearrangement undetectable by WES
G275 (M-WES)	M, 47y, Eur	adult-onset dystonia segmental; ataxia, spasticity	solo	<i>SPG7</i>	chr16:89596808-89597521, del (16q24.3) exon 7 (NM_003119.4); hom, CNV, 714bp	AR	spastic paraplegia 7, autosomal recessive (MIM:607259)	NA ⁱ	NA	yes	single-exon deletion difficult to detect in WES analysis
STR diagnoses											
G014 (M-WES)	M, 58y, Eur	adult-onset dystonia, generalized; chorea, basal ganglia signal changes	solo	<i>HTT</i>	chr4:3076603[40] (NM_001388492.1); het, STR, 40 CAG units	AD (nk)	Huntington disease (MIM:143100)	PMID: 20301482	NA	NA ^m	STR analysis not completed using WES
G075 (M-WES)	M, 63y, Eur	adult-onset dystonia, generalized; chorea, cognitive decline, dysphagia, muscle weakness/wasting	multi	<i>PABPN1</i>	chr14:23790681[7] (NM_004643.4); het, STR, 4 GCG and 3 GCA units ⁿ	AD (nk)	oculopharyngeal muscular dystrophy-1 (MIM:164300)	PMID: 20301305, 24878479	NA	NA ^m	STR analysis not completed using WES
G079 (M-WES)	M, 24y, Eur	adolescence-onset dystonia, segmental; ataxia	solo	<i>FXN</i>	chr9:71652203[128] (NM_000144.5); hom, STR, CI: 108-216 GAA units (allele 1) and 87-181 GAA units (allele 2) ^p	AR	Friedreich ataxia (MIM:229300)	PMID: 20301458	NA	NA ^m / NA ^m	STR analysis not completed using WES, STRs in non-coding region
G236 (M-WES)	F, 19y, Eur	childhood-onset dystonia, focal; ataxia, myoclonus, epilepsy	quad	<i>CSTB</i>	chr21:45196349[38] (NM_000100.4); hom, STR, CI: 27-51 CCCC GCCCGCG units (allele 1) and 22-42 CCCC GCCCGCG units (allele 2) ^{p,p}	AR	epilepsy, progressive myoclonic 1A, Unverricht and Lundborg (MIM:254800)	PMID: 20301321, 30363394	Prot: reduced expression (~80%) RNA-seq: reduced expression (~70%)	NA ^m	STR analysis not completed using WES, STRs in non-coding region

G258 (M-WES)	M, 14y, Eur	childhood-onset dystonia, focal; ataxia, DD, ID	multi	<i>GLS</i> ^{c,f}	chr2:191745598GCA[138] (NM_014905.5)/ NM_014905.5: c.1197+2T>C; het/het, STR/SNV, CI: 115-195 GCA units°/1bp ^q	AR	global developmental delay, progressive ataxia, and elevated glutamine (MIM:618412)	PMID: 30970188/ NA (novel variant)	Prot: GLS not assayable (reduced protein expression demonstrated by immunoblotting) RNA-seq: exon 10 extension	NA ^m /yes ^r	STR analysis not completed using WES, STR in non-coding region
G293 (M-WES)	F, 18y, Eur	adolescence-onset dystonia, segmental; ataxia, myoclonus, epilepsy	solo	<i>CSTB</i>	chr21:45196349[53] (NM_000100.4); hom, STR, CI: 29-70 CCCC GCCCGCG units (allele 1) and 23-56 CCCC GCCCGCG units (allele 2) ^o	AR	epilepsy, progressive myoclonic 1A, Unverricht and Lundborg (MIM:254800)	PMID: 20301321, 30363394	NA	NA ^m	STR analysis not completed using WES, STRs in non-coding region
G299 (EXT)	M, 27y, Eur	adolescence-onset dystonia, generalized; ataxia	solo	<i>FXN</i>	chr9:71652203[137] (NM_000144.5); hom, STR, CI: 107-228 GAA units (allele 1) and 86-189 GAA units (allele 2) ^o	AR	Friedreich ataxia (MIM:229300)	PMID: 20301458	NA	NA ^m / NA ^m	STR analysis not completed using WES, STRs in non-coding region
Diagnoses enabled by integrative multi-omic analysis*											
G052 (M-WES)	M, 11y, Eur	infantile-onset dystonia, generalized; neuroregression, ID, epilepsy	trio	<i>IRF2BPL</i>	NM_024496.4: c.189_211dup, p.Gly71Alafs*89; het, indel, 23bp	AD (dn)	neurodevelopmental disorder with regression, abnormal movements, loss of speech, and seizures (MIM:618088)	NA (novel variant)	Prot: reduced expression (~60%)	yes	technically challenging variant missed by WES pipeline, low-quality call in WGS data, confirmed to affect protein expression
G161 (M-WES)	F, 7y, Eur	infantile-onset dystonia, generalized; ataxia, spasticity, ID, epilepsy, microcephaly	trio	<i>MECP2</i>	NM_004992.4: c.1146_1193delinsC, p.Leu383Profs*6; het, indel, 47bp	XL (dn)	Rett syndrome (MIM:312750)	NA (novel variant)	Prot: reduced expression (~50%)	yes	technically challenging variant missed by WES pipeline, low-quality call in WGS data, confirmed to affect protein expression
G168 (M-WES)	F, 21y, Eur	childhood-onset dystonia, segmental; ataxia, myoclonus, DD, ID	trio	<i>SLC16A2</i>	NM_006517.5: c.1025T>C, p.Leu342Pro; het, SNV, 1bp	XL (dn)	Allan-Herndon-Dudley syndrome (MIM:300523) ⁱ	NA (novel variant)	Prot: reduced expression (~70%)	yes ^u	initially classified as VUS and not reported, confirmed to affect protein expression
G196 (M-WES)	M, 25y, Eur	adolescence-onset dystonia, segmental; spasticity	solo	<i>SPG11</i>	NM_025137.4: c.1235C>G, p.Ser412*/c.3454-28A>G; het/het, SNV/SNV, 1bp/1bp	AR	spastic paraplegia 11, autosomal recessive (MIM:604360)	ClinVar: 41269/ NA (novel variant)	Prot: reduced expression (near 100%) RNA-seq: reduced expression (~80%), exon 20 skipping plus intron retention	yes/yes	intronic variant not identified/retained in WES/WGS analyses, confirmed to affect protein/RNA expression and splicing
G245 (M-WES)	M, 16y, Eur	infantile-onset dystonia, generalized; spasticity, DD, epilepsy, microcephaly	solo	<i>UFC1</i> ^{c,f}	NM_016406.4: c.244_255del, p.Glu83_Ile86del/c.255+17G>A; het/het, indel/SNV, 12bp/1bp ^v	AR	neurodevelopmental disorder with spasticity and poor growth (MIM:618076)	NA (novel variants)	Prot: reduced expression (~80%) RNA-seq: reduced	yes/yes	intronic variant not identified/retained in WES/WGS analyses, confirmed to affect protein/RNA expression and splicing

		(spastic-dystonic CP)							expression (~40%), exon 3 skipping		
G269* (EXT)	F, 10y, Eur	infantile-onset dystonia, segmental; spasticity, DD (spastic-dystonic CP)	solo	<i>UFC1</i> ^{c,f}	NM_016406.4: c.141del, p.Asn48Metfs*29/c.255+17G>A; het/het, indel/SNV, 1bp/1bp	AR	neurodevelopmental disorder with spasticity and poor growth (MIM:618076)	NA (novel variants)	NA ^w	yes/yes	intronic variant not identified/retained in WES/WGS analyses, diagnosis established by reanalysis of WGS data based on results in G245
G277 (M-WES)	F, 23y, Eur	adolescence-onset dystonia, segmental	trio	<i>ATM</i>	NM_000051.3: c.3284+695G>T; c.3284+699A>C; hom, MNV, 2bp	AR	ataxia-telangiectasia (MIM:208900)	NA (novel variants)	Prot: reduced expression (~70%) RNA-seq: reduced expression (~60%), pseudoexon splicing-in	yes ^l	deep intronic variants not identified/retained in WES/WGS analyses, confirmed to affect protein/RNA expression and splicing

^aInheritance determined by follow-up targeted Sanger sequencing.

^b*ANO3* variant also detected in three affected maternal relatives by Sanger sequencing.

^cNeurologic disease gene not previously associated with dystonia (as of April 2024).

^dDual diagnosis; mother affected by ID without dystonia.

^e*POLR3A* homozygous variant also detected in affected sibling by WGS.

^fUltra-rare condition with fewer than approximately 20 families reported in the original literature to date (as of April 2024).

^g*De novo* MT variants defined as absent or present in <5% in maternal mtDNA (PMID: 36368308).

^hDefined as DNA segments ≥50bp.

ⁱNo identical or similar CNVs/SVs in ClinVar or DECIPHER.

^jManifesting heterozygous female carrier (PMID: 20301395).

^k*BCL11B* CNV also detected in affected sibling by WGS (see Fig.3E).

^lPathologically elevated AFP levels in blood.

^mACMG guidelines currently not applicable to the interpretation of STRs.

ⁿ*PABPN1* STR expansion also detected in two affected siblings by ExpansionHunter (see Fig.4B): sister II-1: chr14:23790681[7]; brother II-4: chr14:23790681[7].

^oExpansionHunter estimates the repeat size within a confidence interval (CI) for STRs that are longer than the WGS read length (>150bp) (PMID: 31134279).

^p*CSTB* STR expansions also detected in affected sibling by ExpansionHunter (see Fig.4C): sister II-2: chr21:45196349[32], CI: 22-45 CCCC GCCCGCG units (allele 1) and 17-36 CCCC GCCCGCG units (allele 2)^o.

^q*GLS* STR expansion also detected in two affected siblings by ExpansionHunter (see Fig.4D): brother II-1: chr2:191745598GCA[89], CI: 82-137 GCA units^o; sister II-2: chr2:191745598GCA[119], CI: 106-173 GCA units^o; both affected siblings also positive for the splice-disrupting SNV c.1197+2T>C.

^rPathologically elevated glutamine levels in blood.

^sProteomics was performed to facilitate interpretation of variants of uncertain significance or variants in technically challenging regions and to guide variant prioritization in unresolved cases.

Additional RNA-seq was performed for patients with variants that were suspected to have a potential effect on splicing and/or transcript integrity.

^tManifesting heterozygous female carrier (PMID: 18398436, 35782622).

^uThyroid function test abnormalities with elevated free T3 levels and high free T3/T4 ratio (see Fig.5C) (PMID: 31410843).

^v*UFC1* variants also detected in two affected siblings by Sanger sequencing (see Fig.6B).

^wDiagnosis indirectly enabled by multi-omic analysis: reanalysis of the WGS cohort for other carriers of the *UFC1* c.255+17G>A variant characterized in G245 allowed to solve this additional case.

^xIndex patient from underrepresented population.

Abbreviations: ACMG, American College of Medical Genetics and Genomics; AD, autosomal dominant; AFP, alpha-fetoprotein; AR, autosomal recessive; bp, base pair(s); “Cfrm”, “confirmed” (strong evidence of pathogenicity for the MT variant; PMID: 15608272); CI, confidence interval (ExpansionHunter); CNVs, copy-number variants; CP, cerebral palsy; DD, developmental delay; del, deletion; dn, *de novo*; dup, duplication; Eur, European; EXT, individual from the externally recruited subcohort with ‘negative’ commercial whole-exome sequencing; F, female; hem, hemizygous; het, heterozygous; hom, homozygous; ID, intellectual disability; indel, short insertion/deletion (<50bp); inv, inversion; IP, inheritance pattern; M, male; mat, maternally inherited; Mid, Middle Eastern; MNV, multinucleotide variation; MT variant, mitochondrial variant; multi, multiplex pedigree; M-WES, individual from the here-described whole-exome sequencing cohort (Munich, Germany); NA, not applicable/not available; nk, inheritance not known; OMIM, Online Mendelian Inheritance in Man; pat, paternally inherited; PMID, PubMed identifier; Prot, proteomics; quad, quartet; RNA-seq, RNA sequencing; SNV, single-nucleotide variant; STR, short tandem repeat; SVs, structural variants; UTR, untranslated region; VUS, variant of uncertain significance; WES, whole-exome sequencing; WGS, whole-genome sequencing; XL, X-linked; y, years.

Suppl. Table 5 Novel disease gene candidates prioritized by WGS

Index patient study ID (cohort)	Sex, age	Age at dystonia onset, distribution; comorbid (extra-) neurologic symptoms (if present)	WGS designation	Gene; variant(s) (hg19); zygosity	IP	Evidence
G035 (EXT)	F, 9y	infantile-onset dystonia, generalized; DD, epilepsy	trio	<i>SRRM4</i> ; NM_194286.4: c.464+2T>C; heterozygous	AD (<i>dn</i>)	<i>de novo</i> essential splice-site variant, identical variant listed as <i>de novo</i> event in database (ClinVar: 493125)
G131 (M-WES)	F, 13y	childhood-onset dystonia, segmental; chorea, DD, leukodystrophy	solo	<i>TMEFF1</i> ; NM_003692.5: c.1059-2A>G; homozygous	AR	homozygous pLoF variant predicted to inactivate both gene copies (knockout)
G138 (M-WES)	F, 4y	infantile-onset dystonia, generalized; chorea, ataxia, DD, epilepsy	trio	<i>TXLNG</i> ; NM_018360.3: c.515_519del, p.Ser172Thrfs*24; heterozygous	XL (<i>dn</i>)	<i>de novo</i> pLoF variant in gene with high loss-of-function constraint (gnomAD v2.1.1: pLI score = 1.0; pLI score in v4.1.0 not available for the gene)
G147 (EXT)	M, 13y	infantile-onset dystonia, generalized; DD, ID, hearing impairment (dystonic CP)	trio	<i>PRMT1</i> ; NM_001536.5: c.1033C>T, p.Arg345Trp; heterozygous	AD (<i>dn</i>)	<i>de novo</i> missense variant in gene with high missense constraint (gnomAD v4.1.0: missense z score = 4.43)
G199 (EXT)	F, 5y	infantile-onset dystonia, generalized; DD	solo	<i>ETV1</i> ; NM_004956.5: c.988C>T, p.Gln330*; homozygous	AR	homozygous pLoF variant predicted to inactivate both gene copies (knockout)
G282 (M-WES)	F, 30y	adolescence-onset dystonia, segmental; parkinsonism, ID, epilepsy	solo	<i>MYO16</i> ; NM_015011.3: c.1687del p.Glu563Argfs*6; homozygous	AR ^a	homozygous pLoF variant predicted to inactivate both gene copies (knockout)
G292 (M-WES)	M, 3y	infantile-onset dystonia, segmental	trio	<i>ADCY1</i> ; NM_021116.4: c.265G>T, p.Gly89Cys; heterozygous	AD (<i>dn</i>)	<i>de novo</i> missense variant in gene with high missense constraint (gnomAD v4.1.0: missense z score = 4.71)

^a*MYO16* variant detected in heterozygous state in three unaffected siblings by Sanger sequencing.

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; DD, developmental delay; *dn*, *de novo*; EXT, individual from the externally recruited subcohort with 'negative' commercial whole-exome sequencing; F, female; gnomAD, The Genome Aggregation Database; ID, intellectual disability; IP, inheritance pattern; M, male; M-WES, individual from the here-described whole-exome sequencing cohort (Munich, Germany); pLI, probability of being loss-of-function intolerant; pLoF, predicted loss-of-function; WES, whole-exome sequencing; WGS, whole-genome sequencing; XL, X-linked; y, years.

Suppl. Table 6 Molecular and clinical features of identified patients with *de novo* *PRMT1* variants

Index patient study ID (cohort)	G147 (EXT) ^a	PRMT1-GM-A ^b	PRMT1-GM-B ^b	PRMT1-GM-C ^b
Sex, age	M, 13y	F, 17y	F, 13y	F, 8y
Genomic testing	Trio-WES, trio-WGS	Trio-WES	Trio-WES	Trio-WES
<i>PRMT1</i> variant details				
Chromosomal position (hg19)	chr19:50,191,419	chr19:50,188,280	chr19:50,189,461	chr19:50,189,461
cDNA variant (NM_001536.5)	c.1033C>T	c.745G>T	c.871G>A	c.871G>A
Protein variant (NP_001527.3)	p.Arg345Trp	p.Ala249Ser	p.Glu291Lys	p.Glu291Lys
CADD v1.7 score	33	20	24	24
gnomAD v4.1.0/in-house controls	Not found	Not found	Not found	Not found
Zygosity	Heterozygous	Heterozygous	Heterozygous	Heterozygous
Inheritance	<i>de novo</i>	<i>de novo</i>	<i>de novo</i>	<i>de novo</i>
Dystonia and other movement-disorder features				
Dystonia	+ (infantile-onset generalized dystonia, dystonic CP)	+ (infantile-onset generalized dystonia)	-	-
Tremor	+	-	-	-
Myoclonus	-	-	+	-
Ataxia	+	-	-	-
Independent ambulation	- (walking only with bilateral support, wheelchair use)	-	+	+
Neurodevelopmental and other comorbidities				
First symptoms	first months of life (motor delay)	7 months	first months of life (motor delay)	first months of life (motor delay)
Developmental motor delay	+	+ (and transient regression)	+	+
Hypotonia	+ (during infancy)	+ (during infancy)	+	+ (during infancy)
Intellectual impairment	+ (mild-moderate)	-	+ (severe)	+ (borderline-mild)
Impaired expressive speech development	+ (severe)	+ (severe)	+ (severe)	+ (mild)
Dysarthria	+	+	-	-
Dysphagia	+	-	-	-
Hearing impairment	+	-	-	-
Dysmorphic features	-	-	+ (short philtrum, thin upper lip)	+ (enophthalmia, thin upper lip)
Behavioral deficits	+ (hyperactivity)	-	+ (hyperactivity, stereotypies)	+ (autistic features, stereotypies)
Seizures	-	-	+	-
Other features	-	+ (episodes of ketoacidosis, dehydration, moderate hyperammonemia)	+ (hemorrhagic colitis)	+ (sleep disorder, microcephaly)
Brain MRI abnormality	-	+ (basal ganglia signal changes)	-	-

^aG147, dystonia WGS-cohort case.

^bPRMT1-GM-A/B/C, additional patients ascertained via international collaboration¹².

Abbreviations: CADD, Combined Annotation Dependent Depletion; CP, cerebral palsy; EXT, individual from the externally recruited subcohort with 'negative' commercial whole-exome sequencing; F, female; gnomAD, The Genome Aggregation Database; M, male; minus (-) feature absent or not reported; MRI, magnetic resonance imaging; plus (+), feature present; WES, whole-exome sequencing; WGS, whole-genome sequencing; y, years.

Suppl. Table 7 Actionable genetic diagnoses enabled by WGS and WGS combined with proteomics

Index patient study ID (cohort)	Gene/locus	OMIM diagnosis	Reference(s)	Genetic diagnosis-informed new clinical care or management option(s)
G096 (M-WES)	<i>DNM1L</i>	encephalopathy, lethal, due to defective mitochondrial peroxisomal fission 1 (MIM:614388)	PMID: 38341530	levocarnitine/coenzyme Q10
G114 (M-WES)	<i>ANO3</i>	dystonia 24 (MIM:615034)	PMID: 38341631	DBS
G125 (EXT)	<i>VPS16</i>	dystonia 30 (MIM:619291)	PMID: 35644611	DBS
G191 (EXT)	<i>XPA</i>	xeroderma pigmentosum, group A (MIM:278700)	PMID: 20301571	malignancy surveillance, avoidance of UV radiation
G227 (M-WES)	<i>DNM1L</i>	encephalopathy, lethal, due to defective mitochondrial peroxisomal fission 1 (MIM:614388)	PMID: 38341530	levocarnitine/coenzyme Q10
G110 (EXT)	<i>POLR3A</i>	leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism (MIM:607694)	PMID: 28459997	monitoring for dental/endocrine abnormalities
G172 (EXT)	<i>POLR3A</i>	leukodystrophy, hypomyelinating, 7, with or without oligodontia and/or hypogonadotropic hypogonadism (MIM:607694)	PMID: 28459997	monitoring for dental/endocrine abnormalities
G043 (M-WES)	<i>KMT2B</i>	dystonia 28, childhood-onset (MIM:617284)	PMID: 29697234	DBS
G132 (EXT)	<i>SNORD118</i>	leukoencephalopathy, brain calcifications, and cysts (MIM:614561)	PMIDs: 37761957, 32911264	bevacizumab
G055 (M-WES)	<i>MT-ATP6</i>	mitochondrial complex V deficiency, mitochondrial type 1 (MIM:500015)	PMID: 20301352	mitochondrial disease monitoring (multisystem involvement)
G085 (M-WES)	<i>MT-ND3</i>	mitochondrial complex I deficiency, mitochondrial type 1 (MIM:500014)	PMID: 20301352	mitochondrial disease monitoring (multisystem involvement)
G139 (M-WES)	<i>MT-ND6</i>	Leber optic atrophy and dystonia (MIM:500001)	PMID: 20301352	mitochondrial disease monitoring (multisystem involvement)
G254 (M-WES)	<i>MT-TL1</i>	MELAS syndrome (MIM:540000)	PMID: 20301352	mitochondrial disease monitoring (multisystem involvement)
G059 (M-WES)	<i>SLC16A2</i>	Allan-Herndon-Dudley syndrome (MIM:300523)	PMID: 20301789	TRIAC
G173 (M-WES)	<i>CACNA1A</i>	<i>CACNA1A</i> -related disorder (MIM:617106/108500/141500)	PMID: 20301562	acetazolamide
G201 (EXT)	<i>TIMM8A</i>	Mohr-Tranebjaerg syndrome (MIM:304700)	PMID: 20301395	monitoring for hearing abnormalities
G204 (M-WES)	<i>PRKN</i>	Parkinson disease, juvenile, type 2 (MIM:600116)	PMID: 20301651	levodopa

G205 (M-WES)	<i>ATM</i>	ataxia-telangiectasia (MIM:208900)	PMID: 20301790	malignancy surveillance, avoidance of ionizing radiation
G222 (M-WES)	<i>SGCE</i>	dystonia-11, myoclonic intellectual	PMID: 20301587	DBS, zonisamide
G226 (M-WES)	<i>BCL11B</i>	developmental disorder with dysmorphic facies, speech delay, and T-cell abnormalities (MIM:618092)	PMID: 37860968	monitoring for systemic abnormalities (immune system dysfunction)
G266 (M-WES)	22q11.2 microduplication	chromosome 22q11.2 duplication syndrome (MIM:608363)	PMID: 38196101	DBS
G079 (M-WES)	<i>FXN</i>	Friedreich ataxia (MIM:229300)	PMIDs: 20301458, 36444905	monitoring for systemic abnormalities (cardiac involvement, diabetes mellitus); omaveloxolone
G236 (M-WES)	<i>CSTB</i>	epilepsy, progressive myoclonic 1A, Unverricht and Lundborg (MIM:254800)	PMID: 20301321	avoidance of phenytoin
G293 (M-WES)	<i>CSTB</i>	epilepsy, progressive myoclonic 1A, Unverricht and Lundborg (MIM:254800)	PMID: 20301321	avoidance of phenytoin
G299 (EXT)	<i>FXN</i>	Friedreich ataxia (MIM:229300)	PMIDs: 20301458, 36444905	monitoring for systemic abnormalities (cardiac involvement, diabetes mellitus); omaveloxolone
G161 (M-WES)	<i>MECP2</i>	Rett syndrome (MIM:312750)	PMID: 20301670	cardiac monitoring (QTc monitoring)
G168 (M-WES)	<i>SLC16A2</i>	Allan-Herndon-Dudley syndrome (MIM:300523)	PMID: 20301789	TRIAC
G196 (M-WES)	<i>SPG11</i>	spastic paraplegia 11, autosomal recessive (MIM:604360)	PMID: 32355960	levodopa
G277 (M-WES)	<i>ATM</i>	ataxia-telangiectasia (MIM:208900)	PMID: 20301790	malignancy surveillance, avoidance of ionizing radiation
Individualized variant mechanism-directed therapy under development				
G196 (M-WES)	<i>SPG11</i>	spastic paraplegia 11, autosomal recessive (MIM:604360)	PMID: 36669889	antisense oligonucleotide therapy for <i>SPG11</i> intronic mutations under development
G277 (M-WES)	<i>ATM</i>	ataxia-telangiectasia (MIM:208900)	PMIDs: 36669889, 37438524	antisense oligonucleotide therapy for <i>ATM</i> intronic mutations under development

Abbreviations: DBS, deep brain stimulation; EXT, individual from the externally recruited subcohort with 'negative' commercial whole-exome sequencing; M-WES, individual from the here-described whole-exome sequencing cohort (Munich, Germany); OMIM, Online Mendelian Inheritance in Man; PMID, PubMed identifier; TRIAC, T₃ analog acide 3,3',5-triiodothyroacetique; WGS, whole-genome sequencing.

Supplemental References

1. Robinson JT, Thorvaldsdottir H, Winckler W, *et al.* Integrative genomics viewer. *Nat Biotechnol.* Jan 2011;29(1):24-6. doi:10.1038/nbt.1754
2. Jenkinson EM, Rodero MP, Kasher PR, *et al.* Mutations in SNORD118 cause the cerebral microangiopathy leukoencephalopathy with calcifications and cysts. *Nat Genet.* Oct 2016;48(10):1185-92. doi:10.1038/ng.3661
3. Kodama K, Aoyama H, Murakami Y, *et al.* A case of early-infantile onset, rapidly progressive leukoencephalopathy with calcifications and cysts caused by biallelic SNORD118 variants. *Radiol Case Rep.* Mar 2023;18(3):1217-1220. doi:10.1016/j.radcr.2022.11.033
4. Brandon MC, Lott MT, Nguyen KC, *et al.* MITOMAP: a human mitochondrial genome database--2004 update. *Nucleic Acids Res.* Jan 1 2005;33(Database issue):D611-3. doi:10.1093/nar/gki079
5. AlGethami HJ, Breitbart S, Warsi NM, Fasano A, Ibrahim GM, Gorodetsky C. Severe Pediatric Dystonia Responding to Deep Brain Stimulation in 22q11.2 Microduplication Syndrome: Rare Clinical Presentation. *Mov Disord Clin Pract.* Mar 2024;11(3):309-311. doi:10.1002/mdc3.13955
6. Dolzhenko E, Deshpande V, Schlesinger F, *et al.* ExpansionHunter: a sequence-graph-based tool to analyze variation in short tandem repeat regions. *Bioinformatics.* Nov 1 2019;35(22):4754-4756. doi:10.1093/bioinformatics/btz431
7. Kaplanis J, Samocha KE, Wiel L, *et al.* Evidence for 28 genetic disorders discovered by combining healthcare and research data. *Nature.* Oct 2020;586(7831):757-762. doi:10.1038/s41586-020-2832-5
8. Karczewski KJ, Francioli LC, Tiao G, *et al.* The mutational constraint spectrum quantified from variation in 141,456 humans. *Nature.* May 2020;581(7809):434-443. doi:10.1038/s41586-020-2308-7
9. Richards S, Aziz N, Bale S, *et al.* Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* May 2015;17(5):405-24. doi:10.1038/gim.2015.30
10. Riggs ER, Andersen EF, Cherry AM, *et al.* Technical standards for the interpretation and reporting of constitutional copy-number variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics (ACMG) and the Clinical Genome Resource (ClinGen). *Genet Med.* Feb 2020;22(2):245-257. doi:10.1038/s41436-019-0686-8
11. Kochinke K, Zweier C, Nijhof B, *et al.* Systematic Phenomics Analysis Deconvolutes Genes Mutated in Intellectual Disability into Biologically Coherent Modules. *Am J Hum Genet.* Jan 7 2016;98(1):149-64. doi:10.1016/j.ajhg.2015.11.024
12. Sobreira N, Schiettecatte F, Valle D, Hamosh A. GeneMatcher: a matching tool for connecting investigators with an interest in the same gene. *Hum Mutat.* Oct 2015;36(10):928-30. doi:10.1002/humu.22844