Dystonia and Parkinsonism Panel

Panel Gene List:

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ADAR, ADCY5, AFG3L2, ANO3, APTX, ARSA, ATM, ATP13A2, ATP1A2, ATP1A3, ATP6AP2, ATP7B, BCAP31**, C19ORF12, CACNA1A***, CACNA1B, CHCHD2, COASY, CP, CYP27A1, DCAF17, DCTN1, DDC*, DLAT, DNAJC12*, DNAJC5, DNAJC6, ECHS1*, FA2H, FBXO7, FITM2*, FTL, FUCA1*, GBA*, GCDH, GCH1, GLRA1, GNAL, GNAO1*, HEXA, HPCA, HPRT1, KCNJ6*, KCNMA1, KCTD17, KMT2B, LRRK2, MAPT, MARS2, MCOLN1, MECR, MRE11, NKX2-1, NPC1, NPC2, NUBPL*, NUS1*, PANK2, PARK7, PDGFB, PDGFRB, PINK1, PLA2G6, PNKD, PNKP, POLG, POLR3B, PRKN, PRKRA, PRRT2, PTS, RAB39B*, SCP2, SERAC1*, SGCE, SLC16A2, SLC19A3, SLC20A2, SLC2A1, SLC30A10, SLC6A3, SMPD1, SNCA, SPAST, SPR, SQSTM1, SUCLA2*, SYNJ1, TH, THAP1, TIMM8A, TOR1A, TOR1AIP1, TPK1, TPP1*, TRAPPC11, TUBB4A**, TWNK*, VPS13A, VPS35, WDR45, XPR1, ZFYVE26*

* Sequence analysis only of the *ATP1A2, DDC, DNAJC12, ECHS1, FITM2, FUCA1, GBA, GNAO1, KCNJ6, NUBPL, NUS1, RAB39B, SERAC1, SUCLA2, TPP1,* and *TWNK* genes.

**Only whole gene deletions or duplications of *BCAP31* and *TUBB4A* may be detected.

*** The CAG repeat expansion in *CACNA1A* that causes SCA6 may not be detectable by this test.

Dystonia Panel Gene List:

ADAR, ADCY5, AFG3L2, ANO3, APTX, ARSA, ATM, ATP13A2, ATP1A2, ATP1A3, ATP7B, BCAP31**, C19ORF12, CACNA1A, CACNA1B, COASY, CP, CYP27A1, DCAF17, DDC*, DLAT, DNAJC12*, ECHS1*, FA2H, FITM2*, FTL, FUCA1*, GCDH, GCH1, GLRA1, GNAL, GNAO1*, HEXA, HPCA, HPRT1, KCNJ6*, KCNMA1, KCTD17, KMT2B, MARS2, MCOLN1, MECR, MRE11, NKX2-1, NPC1, NPC2, NUBPL*, PANK2, PDGFB, PDGFRB, PLA2G6, PNKD, PNKP, POLR3B, PRKRA, PRRT2, PTS, SCP2, SERAC1*, SGCE, SLC16A2, SLC19A3, SLC20A2, SLC2A1, SLC30A10, SLC6A3, SPAST, SPR, SQSTM1, SUCLA2*, SYNJ1, TH, THAP1, TIMM8A, TOR1A, TOR1AIP1, TPK1, TPP1*, TRAPPC11, TUBB4A**, VPS13A, WDR45, XPR1*

* Sequence analysis only of the *ATP1A2, DDC, DNAJC12, ECHS1, FITM2, FUCA1, GNAO1, KCNJ6, NUBPL, SERAC1, SUCLA2,* and *TPP1* genes.

**Only whole gene deletions or duplications of *BCAP31* and *TUBB4A* may be detected.

Parkinson Disease Panel Gene List:

AFG3L2, ATP13A2, ATP6AP2, C19ORF12, CHCHD2, COASY, CP, CYP27A1, DCTN1, DNAJC5, DNAJC6, FBXO7, FTL, GBA, GCH1, LRRK2, MAPT, NPC1, NPC2, NUS1*, PANK2, PARK7, PDGFB, PDGFRB, PINK1, PLA2G6, POLG, PRKN, PRKRA, PTS, RAB39B*, SLC20A2, SLC30A10, SLC6A3, SMPD1, SNCA, SYNJ1, TH, TWNK*, VPS13A, VPS35, WDR45, XPR1, ZFYVE26*

* Sequence analysis only of the *GBA, NUS1, RAB39B,* and *TWNK* genes.

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Clinical Features:
Dystonia and parkinsonism describe movement disorders that result in abnormal, uncontrolled, movements often caused by inappropriate muscle contractions or nerve signals.[1,2] Some neurodegenerative disorders can have symptoms of both dystonia and parkinsonism. Overlapping features of dystonia and parkinsonism include postural and gait instability, tremor, and speech problems. Treatment is available for some causes of dystonia and parkinsonism.
Neurodegeneration with brain iron accumulation (NBIA) is a group of inherited neurologic disorders characterized by abnormal accumulation of iron in the basal ganglia with clinical features including progressive dystonia and dysarthria, spasticity, parkinsonism, neuropsychiatric abnormalities, and optic atrophy or retinal degeneration.[3]
Primary familial brain calcification (PFBC) is a neurodegenerative disorder with characteristic calcium deposits in the basal ganglia and other brain areas visualized on neuroimaging, which typically presents in the fourth to fifth decade with a gradually progressive movement disorder and neuropsychiatric symptoms.[4]

Dystonia:
Dystonia is characterized by patterned or twisting movements and postures.[1] Dystonias are highly variable and clinically classified by age of onset, affected body part, temporal pattern, or associated features.[1,5] Age of onset ranges from infancy to late adulthood, and almost all parts of the body can be affected. The number and location of affected body parts determine if the dystonia is focal, segmental, multifocal, hemidystonia, or generalized. Although some dystonias are isolated and occur independent of other neurological features, combined and complex forms have been described. Combined dystonias occur when dystonia is observed with other movement disorders including parkinsonism, myoclonus, and paroxysmal dyskinesia, whereas complex dystonias include those that are associated with neurodegenerative or metabolic disorders. Often times, dystonia can be triggered or worsened by nonspecific factors, such as stress, or fatigue.[1] The prevalence of isolated dystonia is estimated to be 16.4:100,000.[6]

Parkinsonism:
Parkinsonism describes all motor dysfunctions that manifest as resting tremor, muscle rigidity, bradykinesia, and postural instability.[7,8] Additional features of Parkinson disease include action or postural tremor, sleep disturbance, mood disorders, dysautonomia, psychosis, and dementia.[7] The neuropathology of Parkinson disease involves the selective loss of dopaminergic neurons and accumulation of inclusions (Lewy bodies) in the brain.[7] The age of onset for disease is generally 60-70 years of age; however, onset can be earlier, especially for monogenic forms.[7,8] Parkinson disease is the second most common neurodegenerative disease and has an age-dependent prevalence that is estimated to be 13.4:100,000, with a prevalence of approximately 1% of individuals over 60 years of age and 4% of individuals over 85 years of age.[2,7]

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Genetics:
Movement disorders such as dystonia and parkinsonism can be either genetic or acquired in nature. Acquired causes include, but are not limited to, brain lesions (resulting from trauma or infection), hypoxic insults, drugs, psychological disorders, and other environmental insults.[1,7] Multifactorial inheritance may also be responsible for some forms of dystonia and parkinsonism.[2,7,8] Genetic forms of dystonia and parkinsonism can be associated with autosomal dominant, autosomal recessive, X-linked, or mitochondrial inheritance.[1,7] Approximately 20% of patients with dystonia are reported to have a positive family history, whereas ~15% of patients with Parkinson disease have a family history and 5-10% have a monogenic form.[2,9] Unfortunately, the etiology of most parkinsonism is unknown.[2,7]

Pathogenic variants in a single gene may be associated with a wide range of phenotypes (clinical heterogeneity), and conversely, pathogenic variants in different genes can cause the same phenotype (genetic heterogeneity). Clinical evaluation alone may not be sufficient to distinguish the various genetic causes of dystonia and parkinsonism given their phenotypic and genetic heterogeneity. The Dystonia and Parkinsonism panel at GeneDx can assist in confirming a clinical diagnosis or aid in the development of a comprehensive medical plan including symptom management and recurrence risk assessment. In some instances, molecular confirmation of a clinical diagnosis of dystonia and/or parkinsonism may have implications for treatment and management of the specific form of disease.

The Dystonia and Parkinsonism Panel at GeneDx includes sequencing and deletion/duplication analysis of genes associated with Mendelian forms of dystonia and parkinsonism. The complete list of genes and associated disorders is included in the table below.

Test Methods:
Using genomic DNA from the submitted specimen, the complete coding regions and splice site junctions of the genes on this panel are enriched using a proprietary targeted capture system developed by GeneDx for next-generation sequencing with CNV calling (NGS-CNV). The enriched targets are simultaneously sequenced with paired-end reads on an Illumina platform. Bi-directional sequence reads are assembled and aligned to reference sequences based on NCBI RefSeq transcripts and human genome build GRCh37/UCSC hg19. After gene specific filtering, data are analyzed to identify sequence variants and most deletions and duplications involving coding exons. Alternative sequencing or copy number detection methods are used to analyze regions with inadequate sequence or copy number data and to evaluate the GBA gene. Reportable variants include pathogenic variants, likely pathogenic variants and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported but are available upon request.

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The technical sensitivity of sequencing is estimated to be > 99% at detecting single nucleotide events. It will not reliably detect deletions greater than 20 base pairs, insertions or rearrangements greater than 10 base pairs, or low-level mosaicism. The copy number assessment methods used with this test cannot reliably detect copy number variants of less than 500 base pairs or mosaicism and cannot identify balanced chromosome aberrations. Assessment of exon-level copy number events is dependent on the inherent sequence properties of the targeted regions, including shared homology and exon size. Gene specific exclusions for exon-level deletion/duplication testing for this panel are: *ATP1A2, DDC, DNAJC12, ECHS1, FITM2, FUCA1, GBA, GNAO1, KCNJ6, NUBPL, NUS1, RAB39B, SERAC1, SUCLA2, TPP1,* and *TWNK* genes, no copy number testing; *BCAP31* and *TUBB4A* genes, only whole gene deletions or duplications may be detected.

Clinical Sensitivity:

The clinical sensitivity of sequencing and deletion/duplication analysis of the genes included in this panel depends in part on the patient's clinical phenotype. Specific information about the diagnostic yield for each gene in selected populations is summarized in the table below.

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Dystonia and Parkinsonism Panel

Gene	Disease Associations	Inheritance	Diagnostic Yield in Selected Population(s)
ADAR	Aicardi-Goutières syndrome (AGS); dyschromatosis symmetrica hereditaria 1 (DSH)	AD/AR	7% of AGS, AGS is a rare contribution to dystonia[1]
ADCY5	Familial dyskinesia with facial myokymia (FDFM)	AD/AR	Rare contribution to dystonia[2]
AFG3L2	Spinocerebellar ataxia, type 28 (SCA28); spastic ataxia 5 (SPAX5)	AD/AR	~1.5% of autosomal dominant cerebellar ataxia, rare contribution to dystonia[3,4]
ANO3	Dystonia 24 (adult-onset focal or segmental dystonia)	AD	1% of dystonia[5,6]
APTX	Ataxia with oculomotor apraxia type I (AOA1)	AR	3.6-9.1% of autosomal recessive ataxias, rare contribution to dystonia[7]
ARSA	Metachromatic leukodystrophy (MLD); also known as arylsulfatase A deficiency	AR	Rare contribution to dystonia[8]
ATM	Ataxia-telangiectasia	AD/AR	Rare contribution to dystonia[9]
ATP13A2	Kufor-Rakeb syndrome	AR	Rare contribution to NBIA, NBIA is commonly associated with dystonia and parkinsonism[10]
*ATP1A2**	Alternating hemiplegia of childhood 1 (AHC1); familial basilar migraine or sporadic hemiplegic migraine (SHM); familial hemiplegic migraine type 2 (FHM2); ATP1A2-related disorder	AD/AR	Rare contribution to dystonia[93]
ATP1A3	Rapid-onset dystonia-parkinsonism; alternating hemiplegia of childhood; CAPOS syndrome	AD	Rare overall[11]
ATP6AP2	X-linked parkinsonism with spasticity (XPDS); X-linked intellectual disability and epilepsy	XL	Rare overall[12,13]
ATP7B	Wilson disease	AR	Commonly associated with dystonia and parkinsonism[14]
*BCAP31***	Deafness, dystonia, and cerebral hypomyelination (DDCH) syndrome	XL	Rare contribution of dystonia[94,95]
C19orf12	Mitochondrial membrane protein-associated neurodegeneration (MPAN, AKA NBIA4)	AD/AR	5-10% of NBIA, NBIA is commonly associated with dystonia and parkinsonism[10,16,17]
*CACNA1A****	Episodic ataxia type 2 (EA2); familial hemiplegic migraine (FHM); spinocerebellar ataxia type 6 (SCA6)*	AD	EA2 is rare[18] 7% of FHM[19,20]
CACNA1B	Neurodevelopmental disorder with seizures and nonepileptic hyperkinetic movements	AR	Rare contribution to dystonia[96]
CHCHD2	Parkinson disease 22 (PARK22)	AD	Rare cause of parkinsonism. Both disease-associated and risk variants have been reported[97]
COASY	COASY protein-associated neurodegeneration (CoPAN) (AKA NBIA6); pontocerebellar hypoplasia, type 12	AR	Rare contribution to NBIA, NBIA is commonly associated with dystonia and parkinsonism[10,21]
CP	Aceruloplasminemia	AR	Rare contribution to NBIA, NBIA is commonly associated with dystonia and parkinsonism[10]
CYP27A1	Cerebrotendinous xanthomatosis (CTX)	AR	~98% of CTX, rare contribution to dystonia[22]

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Gene	Disease Associations	Inheritance	Diagnostic Yield in Selected Population(s)
DCAF17	Woodhouse-Sakati syndrome (WSS)	AR	Rare contribution to NBIA, NBIA is commonly associated with dystonia and parkinsonism[10]
DCTN1	Perry syndrome	AD	Rare contribution to parkinsonism[98]
*DDC**	Aromatic L-amino acid decarboxylase (AADC) deficiency	AR	Rare contribution to dystonia[99,100]
DLAT	Pyruvate dehydrogenase E2 deficiency	AR	Rare contribution to dystonia[23]
DNAJC5	Kufs disease (AKA adult neuronal ceroid lipofuscinoses 4, Parry type)	AD	25% of Kufs disease [24,25]
DNAJC6	Juvenile-onset Parkinson disease	AR	Rare cause of parkinsonism[26,27]
*DNAJC12**	Mild non-BH4-deficient hyperphenylalaninemia	AR	Rare cause of dystonia[101]
*ECHS1**	Mitochondrial short-chain enoyl-CoA hydratase 1 deficiency	AR	Rare contribution to dystonia[102]
FA2H	Fatty acid hydroxylase-associated neurodegeneration (FAHN); spastic paraplegia type 35 (SPG35)	AR	Rare contribution to NBIA, NBIA is commonly associated with dystonia[10]
FBXO7	Parkinsonian-pyramidal syndrome (PARK15)	AR	Rare cause of parkinsonism[28,29]
*FITM2**	Siddiqi syndrome	AR	Rare contribution to dystonia[103,104]
FTL	Neuroferritinopathy	AD/AR	Rare contribution to NBIA, NBIA is commonly associated with dystonia and parkinsonism[10]
*FUCA1**	Fucosidosis	AR	Rare contribution to dystonia[5], dystonia in 12% of cases of fucosidosis[106]
*GBA**	Gaucher disease; late-onset Parkinson disease	AD/AR	3-7% of adult Parkinson disease[28,30]
GCDH	Glutaric aciduria type I (GA I)	AR	Rare contribution to dystonia[31]
GCH1	Dopa-responsive dystonia (DRD); tetrahydrobiopterin (BH4)-deficient hyperphenylalaninemia type B	AD/AR	Common cause of dystonia[32]; Rare cause of parkinsonism[32]
GLRA1	Hereditary hyperekplexia 1 (HKPX1)	AD/AR	80% of hyperekplexia, rare contribution to dystonia[33]
GNAL	Dystonia 25	AD	Rare cause of dystonia[34]
*GNAO1**	Movement disorder with neurodevelopmental features; epileptic encephalopathy, early infantile, 17	AD	Rare contribution to dystonia[93]
HEXA	GM2-gangliosidosis/Tay-Sachs disease (TSD)	AR	Rare contribution to dystonia[107]; rare contribution to parkinsonism[108]
HPCA	Torsion dystonia 2	AR	Rare cause of dystonia[109,110]
HPRT1	Lesch-Nyhan syndrome; HPRT-related hyperuricemia	XL	Rare contribution to dystonia[111]
*KCNJ6**	Keppen-Lubinsky syndrome	AD	Rare contribution to dystonia[112]
KCNMA1	Paroxysmal nonkinesigenic dyskinesia, 3, with or without generalized epilepsy; Liang-Wang syndrome; autosomal recessive KCNMA1-related disorder	AD/AR	Rare contribution to dystonia[35]
KCTD17	KCTD17-related dystonia	AD	Rare cause of dystonia[113,114]
KMT2B	Dystonia 28; KMT2B-related disorder	AD/AR	Rare cause of dystonia[36]
LRRK2	Parkinson disease 8	AD	1-2% of Parkinson disease[28,37]
MAPT	Frontotemporal dementia, with or without parkinsonism; Pick disease; progressive supranuclear palsy	AD	Rare contribution to parkinsonism[115,116]

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MARS2	Autosomal recessive spastic ataxia with leukoencephalopathy (ARSAL)	AR	Rare contribution to dystonia[38]
MCOLN1	Mucolipidosis type IV	AR	Rare overall; founder mutations in the Ashkenazi Jewish population[39]
MECR	Childhood-onset dystonia with optic atrophy and basal ganglia abnormalities	AR	Rare cause of dystonia[117]
MRE11	Ataxia-telangiectasia-like disorder (ATLD)	AR	Rare contribution to dystonia[40]
NKX2-1	Benign hereditary chorea (BHC); choreoathetosis, hypothyroidism, and neonatal respiratory distress	AD	Rare contribution to dystonia[41,42]
NPC1	Niemann-Pick disease type C1 (NPC1)	AR	Rare contribution to dystonia[43]
NPC2	Niemann-Pick disease type C2 (NPC2)	AR	Rare contribution to dystonia[43]
*NUBPL**	Mitochondrial complex I deficiency, nuclear type 21	AR	Rare cause of dystonia[118]
*NUS1**	Intellectual disability with seizures; early onset Parkinson disease candidate	AD	Rare association with parkinsonism[119]
PANK2	Pantothenate kinase-associated neurodegeneration (PKAN)	AR	30-35% of NBIA, NBIA is commonly associated with dystonia and parkinsonism[10,44,45]
PARK7	Early-onset Parkinson disease 7	AR	Rare in Parkinson disease; 1-2% of early-onset Parkinson disease[28,47]
PDGFB	Primary familial brain calcification (PFBC)	AD	Rare overall; ~11% of primary familial brain calcification; PFBC is a rare cause of dystonia[48,49]
PDGFRB	Primary familial brain calcification (PFBC)	AD	Rare overall; ~2% of primary familial brain calcification; PFBC is a rare cause of dystonia[49,120]
PINK1	Early-onset Parkinson disease 6	AR	Rare in Parkinson disease; 1-8% of early-onset Parkinson disease[28,47]
PLA2G6	PLA2G6-associated neurodegeneration (PLAN)	AR	10-15% of NBIA, NBIA is commonly associated with dystonia[10,50]
PNKD	Paroxysmal nonkinesigenic dyskinesia (PNKD)	AD	Rare contribution to parkinsonism[51]
PNKP	Microcephaly, seizures, and developmental delay (MCSZ); Ataxia-oculomotor apraxia 4	AR	Rare contribution to parkinsonism[52]
POLG	POLG-related disorders	AD/AR	Rare in parkinsonism[53,54]
POLR3B	4H leukodystrophy: hypomyelination, hypodontia, and hypogonadotropic hypogonadism	AD/AR	Rare association with dystonia[55]
PRKN	Juvenile Parkinson disease	AR	~1% of Parkinson disease; Up to 50% of early-onset Parkinson disease[28,46,47]
PRKRA	Dystonia 16	AR	Rare contribution to dystonia[56]
PRRT2	PRRT2-Associated Paroxysmal Movement Disorders (PRRT2-PxMD)	AD	62-96% of familial PKD/IC; 36% sporadic PKD/IC[57,58] 83% familial and 30% sporadic BFIS[57,59,60]
PTS	BH4-deficient hyperphenylalaninemia A	AR	Rare contribution to dystonia[121,122]
*RAB39B**	Early-onset parkinsonism-intellectual disability syndrome	XL	Rare cause of parkinsonism[123,124]
SCP2	Leukoencephalopathy with dystonia and motor neuropathy	AR	Rare in NBIA, NBIA is commonly associated with dystonia[61]

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Gene	Disease Associations	Inheritance	Diagnostic Yield in Selected Population(s)
*SERAC1**	3-methylglutaconic aciduria with deafness, encephalopathy, and Leigh-like syndrome	AR	Rare cause of dystonia; 81% of patients with SERAC1 deficiency present with early onset dystonia[125]
SGCE	Myoclonic dystonia 11 (DYT11)	AD	~40-65% of myoclonic dystonia[62]
SLC16A2	MCT8-specific thyroid hormone cell-membrane transporter deficiency (Allan-Herndon-Dudley syndrome)	XL	Rare contribution to dystonia[63]
SLC19A3	Thiamine metabolism dysfunction syndrome 2 (biotin- or thiamine-responsive encephalopathy type 2)	AR	Rare cause of dystonia[5,126]
SLC20A2	Primary familial brain calcification (PFBC)	AD	~40% of primary familial brain calcification (PFBC), PFBC is a rare cause of dystonia[49,64,65]
SLC2A1	Glucose transporter type 1 deficiency syndrome (Glut1-DS)	AD	91% of GLUT1 deficiency commonly associated with dystonia[66,67]
SLC30A10	hypermanganesemia with dystonia, polycythemia and cirrhosis (HMDPC)	AR	Rare[68] overall
SLC6A3	Hereditary dopamine transporter deficiency syndrome	AR	Rare contribution to parkinsonism and dystonia[28,69]
SMPD1	Acid sphingomyelinase (ASM) deficiency (Niemann-Pick disease types A and B)	AR	>95% of ASM deficiency, rare contribution to dystonia[70]
SNCA	Parkinson disease; lewy body dementia	AD	Rare cause of Parkinson disease[28]
SPAST	Hereditary spastic paraplegia 4	AD	Rare cause of dystonia[64]; 40% of HSP cases[127]
SPR	Dopa responsive dystonia due to sepiapterin reductase deficiency	AR	Rare contribution to dystonia[71]
SQSTM1	Neurodegeneration with ataxia, dystonia, and gaze palsy, childhood-onset; myopathy, distal, with rimmed vacuoles; frontotemporal dementia and/or amyotrophic lateral sclerosis 3; Paget disease of bone 3	AD/AR	Rare contribution to dystonia[128,129]
*SUCLA2**	Mitochondrial DNA depletion syndrome 5 (encephalomyopathic with or without methylmalonic aciduria)	AR	Rare contribution to dystonia; dystonia in 86% cases of SUCLA2 deficiency[130]
SYNJ1	Early-onset Parkinson disease 20; early infantile epileptic encephalopathy 53	AR	Rare cause of Parkinson disease[72,73,74]
TH	Tyrosine hydroxylase deficiency	AR	Rare contribution to dystonia[75]
THAP1	Torsion dystonia type 6	AD	Founder mutation in the Amish-Mennonite population[76]; ~1-4% of isolated dystonia[77]
TIMM8A	Deafness-dystonia-optic neuronopathy (DDON) syndrome (Mohr-Tranebjaerg syndrome)	XL	Rare contribution to dystonia[78]
TOR1A	Early-onset isolated dystonia; TOR1A-related arthrogryposis syndrome	AD/AR	Founder mutation accounts for 80-90% of cases of early-onset dystonia in the Ashkenazi Jewish population and 16-53% of cases in non-Jewish population[79]
TOR1AIP1	Early-onset dystonia, limb-girdle muscular dystrophy, and cardiomyopathy	AR	Rare contribution to dystonia[80,81]
*TPP1**	Neuronal ceroid lipofuscinosis 2; Spinocerebellar ataxia 7	AR	Rare contribution to dystonia[131] and parkinsonism[132]

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TPK1	Thiamine pyrophosphokinase deficiency	AR	Rare contribution to dystonia[82]
TRAPPC11	Limb-girdle muscular dystrophy, type R18	AR	Rare contribution to dystonia[83,84]
*TUBB4A***	Torsion dystonia-4 (DYT4); hypomyelinating leukodystrophy-6 (HLD6)	AD	Rare cause of dystonia[85,86]
*TWNK**	Chronic progressive external ophthalmoplegia (CPEO)	AD/AR	Rare contribution to dystonia[15]
VPS13A	Choreoacanthocytosis	AR	Rare contribution to dystonia[87,88]
VPS35	Late-onset levodopa-responsive Parkinson disease (PARK17)	AD	Rare cause of Parkinson disease[28,89]
WDR45	Beta-propeller protein-associated neurodegeneration (BPAN)	XL	40-45% of NBIA, NBIA is commonly associated with dystonia and parkinsonism[10,90]
XPR1	Primary familial brain calcification (PFBC)	AD	8% of cases negative for other forms of PFBC; PFBC is a rare cause of dystonia[49,91,92]
ZFYVE26	Spastic paraplegia 15 (SPG15)	AR	Rare contribution to parkinsonism[105,133], SPG15 represents 2-4% of HSP[133]

** Sequence analysis only for the *ATP1A2, DDC, DNAJC12, ECHS1, FITM2, FUCA1, GBA, GNAO1, KCNJ6, NUBPL, NUS1, RAB39B, SERAC1, SUCLA2, TPP1*, and *TWNK* genes.
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*** The CAG repeat expansion in *CACNA1A* that causes SCA6 is not be detectable by this test.

Table References:

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