Dystonia

Precision Panel

Overview

Dystonia is a heterogeneous movement disorder featuring sustained or intermittent muscle contractions causing abnormal, often repetitive movements, postures or both. Dystonic movements are typically patterned and twisting, even tremulous. It is generally initiated or worsened by voluntary action and associated with overflow muscle activation. Out of the different types of dystonia, focal dystonia, more specifically cervical dystonia is the most common and is approximately 10 times more frequent than generalized dystonia. Their clinical heterogeneity accounts for a profound effect on the personal, vocational, and emotional life of a patient and can impact greatly his/her ability to live independently. Dystonia may be inherited, acquired, or idiopathic. A strong genetic component has been identified in familial dystonia syndromes.

The Igenomix Dystonia Precision Panel can serve as an accurate and directed diagnostic tool ultimately as well as a differential diagnosis of muscle cramps leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved.

Indications

The Igenomix Dystonia Precision Panel is indicated in patients with a clinical suspicion or diagnosis presenting with or without the following manifestations:

- Uncontrolled muscle cramps and spasms
- Body twisting and unusual positions
- Shanking (tremors)
- Uncontrolled blinking

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular diagnosis for an accurate clinical diagnosis of a symptomatic patient.
- Early initiation of treatment with a multidisciplinary team in the form of pharmacologic therapy with anticholinergics, intramuscular botulinum toxin injection and/or deep brain stimulation.

- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.
- Improvement of delineation of genotype-phenotype correlation.

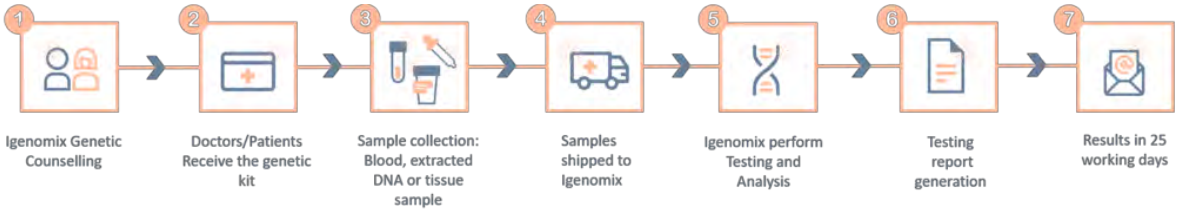
Genes & Diseases

GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
ACTB	Baraitser-Winter Syndrome, Dystonia, Becker Nevus Syndrome, Developmental Malformations, Deafness	AD	100	40 of 40
ADCY5	Dyskinesia, Facial Myokymia, Chorea	AD	94.14	30 of 30
ANO3	Dystonia	AD	99.95	30 of 30
ATP1A3	Alternating Hemiplegia Of Childhood, Cerebellar Ataxia, Pes Cavus, Optic Atrophy, Sensorineuralhearing Loss, Dystonia, Parkinson Disease	AD	99.94	138 of 138
ATP7B	Wilson Disease	AR	99.97	989 of 1000
BCAP31	Deafness, Dystonia, Cerebral Hypomyelination, Motor And Intellectual Disabilities	X,XR,G	100	-
CACNA1B	Neurodevelopmental Disorder, Seizures, Hyperkinetic Movements, Epileptic Encephalopathy	AR	95.83	7 of 7
CACNA1G	Spinocerebellar Ataxia, Neurodevelopmental Deficits	AD	99.52	16 of 16
CIZ1	Cervical Dystonia	-	100	3 of 3
COL6A3	Bethlem Myopathy, Dystonia, Ullrich Congenital Muscular Dystrophy	AD,AR	99.63	232 of 232
CYP27A1	Cerebrotendinous Xanthomatosis	AR	100	118 of 118
DCAF17	Woodhouse-Sakati Syndrome	AR	98.77	21 of 21
DDC	Aromatic L-Amino Acid Decarboxylase Deficiency	AR	100	59 of 59
DNAJC12	Hyperphenylalaninemia	AR	81.82	10 of 10
DRD2	Myoclonus-Dystonia Syndrome	-	100	4 of 4
DRD5	Attention Deficit-Hyperactivity Disorder, Blepharospasm	AD	98.8	-
FA2H	Spastic Paraplegia, Fatty Acid Hydroxylase-Associated Neurodegeneration	AR	88.77	60 of 62
FITM2	Siddiqi Syndrome	AR	99.97	3 of 3
GCH1	Dystonia, Gtp Cyclohydrolase I Deficiency	AD,AR	99.41	225 of 244
GNAL	Dystonia	AD	90.85	34 of 35
GNAO1	Epileptic Encephalopathy, Neurodevelopmental Disorder	AD	100	47 of 47
HEXA	Tay-Sachs Disease	AR	100	205 of 206
HPCA	Dystonia	AR	99.98	6 of 6
KCNMA1	Cerebellar Atrophy, Developmental Delay, Seizures, Epilepsy, Paroxysmal Dyskinesia, Liang-Wang Syndrome	AD,AR	99.98	24 of 26
KCTD17	Dystonia	AD	93.61	3 of 3
KMT2B	Dystonia	AD	95.88	61 of 62
MECR	Dystonia, Optic Atrophy, Basal Ganglia Abnormalities	AR	100	8 of 8
MED20	Waardenburg Syndrome	-	99.98	2 of 2
MIPEP	Oxidative Phosphorylation Deficiency	AR	99.84	7 of 8
PANK2	Hypoprebetalipoproteinemia, Acanthocytosis, Retinitis Pigmentosa, Pallidal Degeneration, Neurodegeneration, Brain Iron Accumulation	AR	98.92	177 of 182
PDE10A	Dyskinesia, Striatal Degeneration, Chorea	AD,AR	100	8 of 8
PDGFB	Basal Ganglia Calcification, Meningioma, Bilateral Striopallidodentate Calcinosis, Dermatofibrosarcoma Protuberans	AD	100	22 of 22
PDGFRB	Basal Ganglia Calcification, Kosaki Overgrowth Syndrome, Myeloproliferative Disorder, Myofibromatosis, Premature Aging Syndrome, Bilateral Striopallidodentate Calcinosis	AD	99.64	28 of 28

PLA2G6	Neuroaxonal Dystrophy, Neurodegeneration, Brain Iron Accumulation, Parkinson Disease, Dystonia, Parkinson Disease	AR	99.94	190 of 191
PNKD	Paroxysmal Nonkinesigenic Dyskinesia	AD	99.98	6 of 6
PRKN	Lung Cancer, Parkinson Disease	AD,AR	100	-
PRKRA	Dystonia	AR	100	9 of 9
PRRT2	Convulsions, Paroxysmal Choreoathetosis, Kinesigenic Dyskinesia, Epilepsy, Hemiplegic Migraine	AD	99.93	111 of 111
SCP2	Leukoencephalopathy, Dystonia, Motor Neuropathy	AR	100	5 of 5
SGCE	Myoclonic Dystonia	AD	99.46	94 of 98
SLC2A1	Choreoathetosis, Spasticity, Epilepsy, Glucose Transport Defect, Glut1 Deficiency Syndrome, Stomatin-Deficient Cryohydrocytosis, Childhood Absence Epilepsy, Dyskinesia	AD,AR	99.99	301 of 304
SLC30A10	Hypermanganesemia, Dystonia, Polycythemia, Cirrhosis	AR	100	19 of 19
SLC39A14	Hypermanganesemia, Dystonia, Hyperostosis Cranialis Interna, Parkinson Disease	AD,AR	100	9 of 9
SLC6A3	Parkinson Disease, Dystonia	AR	100	31 of 31
SPR	Dystonia, Sepiapterin Reductase Deficiency	AD,AR	99.89	27 of 27
TAF1	Dystonia, Mental Retardation, Parkinson Disease, Global Development Delay, Facial Dysmorphism	X,XR,G	99.74	-
TH	Segawa Syndrome, Dystonia	AR	100	71 of 71
THAP1	Dystonia	AD	99.94	96 of 98
TOR1A	Arthrogryposis Multiplex Congenita, Dystonia	AD,AR	100	17 of 18
TOR1AIP1	Limb Girdle Muscular Dystrophy	AR	97.5	5 of 6
TUBB4A	Dystonia Musculorum Deformans, Leukodystrophy	AD	89.81	44 of 44
UBTF	Neurodegeneration, Brain Atrophy, Motor And Cognitive Regression Syndrome	AD	99.99	2 of 2
VAC14	Striatonigral Degeneration, Yunis-Varon Syndrome	AR	100	11 of 11
VPS13A	Choreoacanthocytosis	AR	99.37	120 of 122
VPS13D	Spinocerebellar Ataxia	AR	99.97	19 of 19
XPR1	Basal Ganglia Calcification, Bilateral Striopallidodentate Calcinosis	AD	99.88	14 of 14

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology



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References

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