Spinal Muscular Atrophies

Precision Panel

Overview

Spinal Muscular Atrophies (SMAs) are a group of autosomal recessive inherited disorders characterized by progressive weakness of the lower motor neurons, manifesting as muscle weakness, atrophy and paralysis. It typically presents during infancy or early childhood and the severity of the disease correlates with the age of onset. The clinical and genetic phenotypes incorporate a broad spectrum that is differentiated according to the age of onset, pattern of muscle involvement, and inheritance pattern. There are four types of spinal muscular atrophies, described based on age when accompanying clinical features appear. Type 1 SMA (Werdnig-Hoffman disease) is associated with death within the first two years of life usually due to respiratory failure or aspiration pneumonia.

The Igenomix Spinal Muscular Atrophies Precision Panel can serve as an accurate diagnostic tool ultimately 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 Spinal Muscular Atrophies Precision Panel is indicated in patients with a clinical suspicion or diagnosis of Spinal Muscular Atrophy presenting with the following manifestations:

- Symmetric muscle weakness and hypotonia
- Limb and joint deformities
- Fasciculations of the tongue
- Absent deep tendon reflexes
- Flaccid “frog like” posture
- Restrictive respiratory insufficiency

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 neuroprotective approaches to support muscle strength and function, orthopaedic intervention, appropriate physical therapy and rehabilitation, and prevention of complications.

- Initiation of novel therapeutic strategies including measures to selectively address survival motor neuron protein deficiency with SMN1 gene replacement or modulation of SMN2 encoded protein levels.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.
- Improvement of delineation of genotype-phenotype correlation.

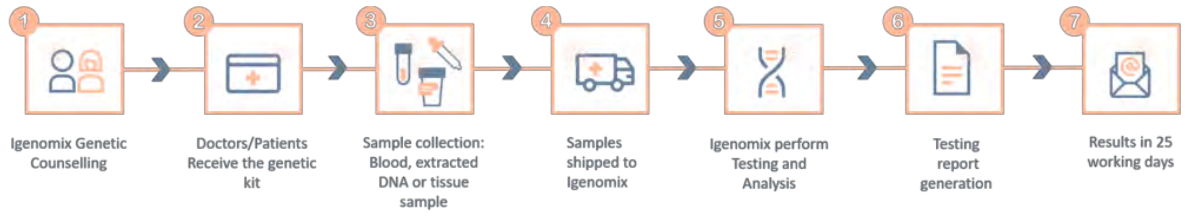
Genes & Diseases

GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
AARS1	Charcot-Marie-Tooth Disease, Axonal Type 2n, Early Infantile Epileptic Encephalopathy	AD,AR	99.07	30 of 30
AR	Reifenstein Syndrome, X-linked Spinal And Bulbar Muscular Atrophy, Kennedy Disease	AD,X,XR,G	97.96	NA of NA
ASAH1	Farber Lipogranulomatosis, Spinal Muscular Atrophy With Progressive Myoclonic Epilepsy, Farber Disease	AR	99.98	69 of 70
ASCC1	Spinal Muscular Atrophy With Congenital Bone Fractures	AR	99.97	6 of 6
ATP7A	X-linked Cutis Laxa, Menkes Disease, X-linked Spinal Muscular Atrophy, Menkes Disease, Occipital Horn Syndrome	X,XR,G	99.83	NA of NA
BICD2	Spinal Muscular Atrophy Lower Extremity-Predominant, BICD2-Related Autosomal Dominant Childhood-Onset Proximal Spinal Muscular Atrophy	AD	99.94	39 of 39
BSCL2	Progressive Encephalopathy With Or Without Lipodystrophy, Distal Hereditary Motor Neuronopathy Type V, Spastic Paraplegia, Distal Hereditary Motor Neuropathy Type 5, Severe Neurodegenerative Syndrome With Lipodystrophy	AD,AR	99.83	60 of 61
CHCHD10	Frontotemporal Dementia And/Or Amyotrophic Lateral Sclerosis, Autosomal Dominant Isolated Mitochondrial Myopathy, Spinal Muscular Atrophy Jokela Type, Autosomal Dominant Amyotrophic Lateral Sclerosis	AD	95.3	22 of 30
DCTN1	Amyotrophic Lateral Sclerosis, Distal Hereditary Motor Neuronopathy Type VIIb, Perry Syndrome	AD,AR	100	56 of 56
DNAJB2	Autosomal Recessive Distal Spinal Muscular Atrophy	AR	99.97	4 of 5
DYNC1H1	Charcot-Marie-Tooth Disease Axonal Type 2o, Autosomal Dominant Spinal Muscular Atrophy Lower Extremity	AD	100	104 of 104
EXOSC3	Pontocerebellar Hypoplasia Type 1b	AR	100	19 of 20
EXOSC8	Pontocerebellar Hypoplasia Type 1c	AR	99.98	3 of 3
FBXO38	Distal Hereditary Motor Neuronopathy Type IId	AD	99.87	6 of 6
GARS1	Charcot-Marie-Tooth Disease Axonal Type 2d, Distal Hereditary Motor Neuronopathy Type V	AD	100	46 of 46
HEXA	Tay-Sachs Disease	AR	100	205 of 206
HSPB1	Charcot-Marie-Tooth Disease Axonal Type 2f, Distal Hereditary Motor Neuronopathy, Type IIb, Autosomal Dominant Charcot-Marie-Tooth Disease Type 2f	AD	99.96	45 of 46
HSPB3	Distal Hereditary Motor Neuronopathy, Type IIc	AD	100	5 of 5
HSPB8	Charcot-Marie-Tooth Disease Axonal Type 2l , Distal Hereditary Motor Neuronopathy Type IIa	AD	97.59	9 of 9
IGHMBP2	Charcot-Marie-Tooth Disease Axonal Type 2, Autosomal Recessive Distal Spinal Muscular Atrophy	AR	99.94	141 of 142
KCNK9	Birk-Barel Mental Retardation Dysmorphism Syndrome	AD	100	3 of 3
LAS1L	Wilson-Turner Syndrome	X,XR,G	92.67	NA of NA
MORC2	Charcot-Marie-Tooth Disease Axonal Type 2z	AD	100	20 of 20
PLEKHG5	Charcot-Marie-Tooth Disease, Autosomal Recessive Distal Spinal Muscular Atrophy	AR	99.98	14 of 14
REEP1	Distal Hereditary Motor Neuronopathy Type Vb, Autosomal Dominant Spastic Paraplegia Type 31, Distal Hereditary Motor Neuropathy Type 5	AD	100	62 of 62
SCO2	Fatal Infantile Cardioencephalomyopathy, Autosomal Recessive Axonal Charcot-Marie-Tooth Disease Due To Copper Metabolism Defect, Leigh Syndrome With Cardiomyopathy	AD,AR	100	38 of 38
SIGMAR1	Juvenile Amyotrophic Lateral Sclerosis, Autosomal Recessive Distal Spinal Muscular Atrophy	AR	100	20 of 20

SLC5A7	Presynaptic Congenital Myasthenic Syndrome, Distal Hereditary Motor Neuronopathy Type VIIa	AD,AR	99.92	21 of 21
SMN1	Spinal Muscular Atrophy Type I, Spinal Muscular Atrophy Type II, Spinal Muscular Atrophy Type III, Spinal Muscular Atrophy Type IV	AR	5.2	17 of 91
SMN2	Spinal Muscular Atrophy Type III	AR	7.6	0 of 3
TBCE	Progressive Encephalopathy With Amyotrophy And Optic Atrophy, Hypoparathyroidism-Retardation-Dysmorphism Syndrome, Kenny-Caffey Syndrome Type 1, Early-Onset Progressive Encephalopathy-Spastic Ataxia-Distal Spinal Muscular Atrophy Syndrome, Sanjad-Sakati Syndrome	AR	100	8 of 8
TK2	Autosomal Recessive Progressive External Ophthalmoplegia, Mitochondrial DNA Depletion Syndrome Myopathic Form	AR	97.08	64 of 65
TRIP4	Congenital Muscular Dystrophy Davignon-Chauveau Type, Spinal Muscular Atrophy With Congenital Bone Fractures, Congenital Muscular Dystrophy-Respiratory Failure-Skin Abnormalities-Joint Hyperlaxity Syndrome	AR	99.92	3 of 3
TRPV4	Brachyrachia, Familial Digital Arthropathy-Brachydactyly, Hereditary Motor And Sensory Neuropathy Type IIc, Metatropic Dysplasia, Parastremmatic Dwarfism, Scapuloperoneal Spinal Muscular Atrophy, Spinal Muscular Atrophy, Spondyloepiphyseal Dysplasia, Spondylometaphyseal Dysplasia, Autosomal Dominant Brachyolmia, Autosomal Dominant Congenital Benign Spinal Muscular Atrophy	AD	100	88 of 88
UBA1	X-linked Spinal Muscular Atrophy, Infantile-Onset X-linked Spinal Muscular Atrophy	X,XR,G	99.58	NA of NA
VAPB	Amyotrophic Lateral Sclerosis, Autosomal Dominant Adult Spinal Muscular Atrophy	AD	100	9 of 9
VRK1	Pontocerebellar Hypoplasia Type 1	AR	99.64	15 of 15

*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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