Rett Syndrome

Precision Panel

Overview

Rett Syndrome (RTT) is a neurodevelopmental disorder that occurs predominantly in females and has a progressive degenerative course resulting in cognitive and physical disabilities. Presentation is clinically heterogeneous ranging from difficulty to ambulate all the way to atrophy, dystonia, scoliosis and intellectual impairment. The hallmark of Rett Syndrome is near constant repetitive hand movements. It is one of the most prevalent causes of intellectual disability in females. Developmental potential for patients with Rett Syndrome is variable and difficult to predict, some individuals achieve functional skills.

The Igenomix Syndrome Precision Panel can serve as an accurate and directed diagnostic tool as well as differential diagnosis of intellectual disability 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 Rett Syndrome Precision Panel is indicated in patients with a clinical suspicion or diagnosis of with or without the following manifestations:

- Gross motor development delay
- Loss of eye contact
- Weight and height growth deceleration
- Head growth deceleration
- Hypotonia
- Hang wringing
- Breathing issues
- Sleep disturbances
- Seizures

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular diagnosis for an accurate clinical diagnosis of a symptomatic patient. Improve diagnostic criteria, natural history studies and novel therapeutic options.
- Early initiation of treatment with a multidisciplinary team in the form of medical care for seizure prevention, dystonia as well as physical and speech therapy.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.
- Improvement of delineation of genotype-phenotype correlation.

Genes & Diseases

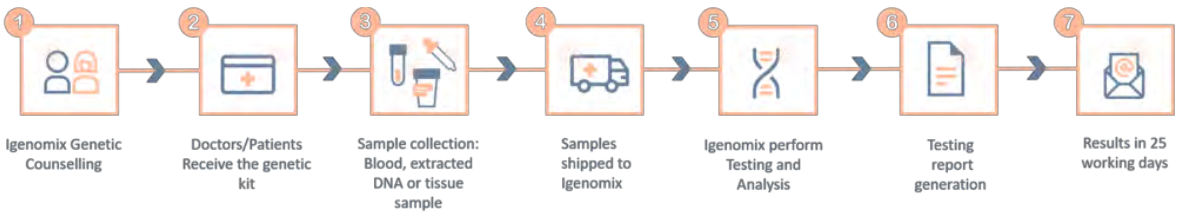
GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
ADSL	Adenylosuccinase Deficiency	AR	100	59 of 59
ALDH5A1	Succinic Semialdehyde Dehydrogenase Deficiency	AR	95.41	65 of 69
ATP1A3	Alternating Hemiplegia Of Childhood, Cerebellar Ataxia, Areflexia, Pes Cavus, Optic Atrophy, And Sensorineural Hearing Loss, Rapid-Onset Dystonia-Parkinsonism	AD	99.94	138 of 138
ATRX	Alpha-thalassemia/Mental Retardation Syndrome, Mental Retardation-Hypotonic Facies Syndrome, Carpenter-Waziri Syndrome, Chudley-Lowry-Hoar Syndrome, Holmes-Gang Syndrome, Juberg-Marsidi Syndrome, Smith-Fineman-Myers Syndrome	X,XR,XD,G	98.5	NA of NA
CACNA1A	Early Infantile Epileptic Encephalopathy, Episodic Ataxia Type 2, Spinocerebellar Ataxia, Benign Paroxysmal Torticollis Of Infancy, Familial Or Sporadic Hemiplegic Migraine	AD	96.13	249 of 266
CASK	X-linked Mental Retardation With Or Without Nystagmus, Mental Retardation And Microcephaly With Pontine And Cerebellar Hypoplasia, Early Infantile Epileptic Encephalopathy	X,XR,XD,G	99.98	NA of NA
CDKL5	Early Infantile Epileptic Encephalopathy, Atypical Rett Syndrome, West Syndrome	X,XD,G	99.92	NA of NA
CHD2	Childhood-Onset Epileptic Encephalopathy, Lennox-Gastaut Syndrome, Myoclonic-Astastic Epilepsy	AD	98.91	103 of 103
CHRNA2	Epilepsy, Nocturnal Frontal Lobe	AD	99.91	8 of 8
CHRNA4	Epilepsy, Nocturnal Frontal Lobe	AD	99.8	24 of 24
CHRNA7	15q13.3 Microdeletion Syndrome	AD	82.09	2 of 2
CHRNB2	Epilepsy, Nocturnal Frontal Lobe	AD	100	13 of 13
CLCN4	X-linked Intellectual Disability Syndrome	X,XR,XD,G	99.69	NA of NA
CLN3	Neuronal Ceroid Lipofuscinosis	AR	99.93	73 of 75
CLN5	Neuronal Ceroid Lipofuscinosis	AR	99.56	52 of 55
CLN6	Neuronal Ceroid Lipofuscinosis	AR	99.94	98 of 99
CLN8	Neuronal Ceroid Lipofuscinosis, Progressive Epilepsy-Intellectual Disability Syndrome	AR	100	44 of 45
CNTNAP2	Pitt-Hopkins-like Syndrome	AR	99.91	39 of 41
CSTB	Myoclonic Epilepsy Of Unverricht And Lundborg, Autosomal Recessive Hypohidrotic Ectodermal Dysplasia	AR	100	14 of 14
CTSD	Neuronal Ceroid Lipofuscinosis	AR	100	18 of 18
DDX3X	X-linked Intellectual Disability-Hypotonia-Movement Disorder Syndrome	X,XR,XD,G	99.03	NA of NA
DEPDC5	Familial Focal Epilepsy	AD	100	127 of 127
DYRK1A	Intellectual Disability Syndrome	AD	99.85	78 of 81
EEF1A2	Early Infantile Epileptic Encephalopathy, Undetermined Early-Onset Epileptic Encephalopathy	AD	100	14 of 14
EHMT1	Kleefstra Syndrome	AD	98.58	58 of 75
EPM2A	Myoclonic Epilepsy Of Lafora	AR	89.2	63 of 70
FOLR1	Neurodegeneration Due To Cerebral Folate Transport Deficiency	AR	100	19 of 23
FOXG1	Rett Syndrome, 14q12 Microdeletion Syndrome, Foxg1 Syndrome	AD	88.71	93 of 109
GABBR2	Early Infantile Epileptic Encephalopathy, Neurodevelopmental Disorder With Poor Language And Loss Of Hand Skills, Atypical Rett Syndrome	AD	95.98	7 of 7

GABRA1	Early Infantile Epileptic Encephalopathy, Childhood Absence Epilepsy, Dravet Syndrome, Juvenile Myoclonic Epilepsy	AD	100	45 of 46
GABRB2	Early Infantile Epileptic Encephalopathy	AD	99.19	16 of 19
GABRB3	Early Infantile Epileptic Encephalopathy, Childhood Absence Epilepsy, Lennox-Gastaut Syndrome	AD	100	54 of 62
GABRG2	Early Epilepsy, Childhood Absence, 2 , Epileptic Encephalopathy, Early Infantile, 74; Eiee74 , Childhood Absence Epilepsy , Dravet Syndrome , Generalized Epilepsy With Febrile Seizures-plus , Rolandic Epilepsy , Undetermined Early-onset Epileptic Encephalopathy	AD	99.67	53 of 53
GAMT	Cerebral Creatine Deficiency Syndrome, Guanidinoacetate Methyltransferase Deficiency	AR	99.92	60 of 60
GATM	Cerebral Creatine Deficiency Syndrome, Fanconi Renotubular Syndrome	AD,AR	99.98	21 of 21
GNAO1	Early Infantile Epileptic Encephalopathy, Neurodevelopmental Disorder With Involuntary Movements	AD	100	47 of 47
GOSR2	Progressive Myoclonic Epilepsy	AR	88.39	6 of 6
GRIN1	Neurodevelopmental Disorder With Or Without Hyperkinetic Movements And Seizures	AD,AR	100	43 of 43
GRIN2A	Focal Epilepsy, With Speech Disorder And With Or Without Mental Retardation, Rolandic Epilepsy-Speech Dyspraxia Syndrome	AD	100	143 of 143
HDC	Gilles De La Tourette Syndrome	AD	100	4 of 4
IQSEC2	X-linked Mental Retardation, Microduplication Xp11.22p11.23 Syndrome, Severe Intellectual Disability-Progressive Postnatal Microcephaly-Midline Stereotypic Hand Movements Syndrome, Smith-Magenis Syndrome	X,XR,XD,G	99.73	NA of NA
KANSL1	Koolen-de Vries Syndrome	AD	96.03	22 of 27
KCNA2	Early Infantile Epileptic Encephalopathy	AD	99.86	23 of 23
KCNC1	Progressive Myoclonic Epilepsy	AD	99.87	10 of 10
KCNMA1	Cerebellar Atrophy, Developmental Delay, And Seizures, Epilepsy, Generalized Epilepsy And Paroxysmal Dyskinesia, Liang-Wang Syndrome	AD,AR	99.98	24 of 26
KCNT1	Nocturnal Frontal Lobe Epilepsy, Early Infantile Epileptic Encephalopathy	AD	95.98	64 of 64
KCTD7	Progressive Myoclonic Epilepsy With Or Without Intracellular Inclusions	AR	99.99	40 of 40
KDM6A	Kabuki Syndrome	AD,X,XD,G	99.98	NA of NA
LAMA1	Poretti-Boltshauser Syndrome, Ataxia-Intellectual Disability-Oculomotor Apraxia-Cerebellar Cysts Syndrome	AR	100	43 of 43
LGI1	Autosomal Dominant Lateral Temporal Lobe Epilepsy	AD	99.94	54 of 54
MAGI2	Nephrotic Syndrome	AR	93.82	7 of 9
MBD5	Autosomal Dominant Mental Retardation, 2q23.1 Microdeletion Syndrome	AD	99.99	33 of 35
MECP2	X-linked Autism, Severe Neonatal Encephalopathy, Lubs X-linked Mental Retardation Syndrome, Rett Syndrome, Atypical Rett Syndrome	X,XR,XD,MU,G	99.81	NA of NA
MEF2C	Mental Retardation, Stereotypic Movements, Epilepsy, And/Or Cerebralmalformations, 5q14.3 Microdeletion Syndrome	AD	99.91	43 of 46
MFSD8	Neuronal Ceroid Lipofuscinosis, Macular Dystrophy With Central Cone Involvement	AR	100	63 of 63
NALCN	Congenital Contractures Of The Limbs And Face, Hypotonia, And Developmental Delay, Digitotalar Dysmorphism, Freeman-Sheldon Syndrome, Hypotonia-Speech Impairment-Severe Cognitive Delay Syndrome, Sheldon-Hall Syndrome	AD,AR	99.97	69 of 69
NEXMIF	X-linked Mental Retardation	X,XR,XD,G	99.74	NA of NA
NGLY1	Congenital Disorder Of Glycosylation Type IV, Alacrimia-Choreoathetosis-Liver Dysfunction Syndrome	AR	99.8	28 of 28
NHLRC1	Myoclonic Epilepsy Of Lafora	AR	100	71 of 71
NPRL3	Familial Focal Epilepsy With Variable Foci	AD	99.61	18 of 18
NRXN1	Pitt-Hopkins-like Syndrome	AR	97.42	33 of 74
NTNG1	Atypical Rett Syndrome, Non-Specific Syndromic Intellectual Disability		99.96	2 of 2
OCLN	Pseudo-Torch Syndrome, Congenital Intrauterine Infection-like Syndrome	AR	86.89	15 of 17
PACS1	Autosomal Dominant Mental Retardation, Intellectual Disability-Craniofacial Dysmorphism-Cryptorchidism Syndrome	AD	97.98	3 of 3
PCDH19	Epilepsy, Female-Restricted, With Mental Retardation, Dravet Syndrome	X,G	99.99	NA of NA
PIGN	Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome, Fryns Syndrome	AR	93.97	36 of 39
PNKP	Ataxia-Oculomotor Apraxia, Charcot-Marie-Tooth Disease, Axonal, Type 2b2, Early Infantile Epileptic Encephalopathy, Early Infantile Epileptic Encephalopathy	AR	100	36 of 36
POLG	Mitochondrial DNA Depletion Syndrome, Progressive External Ophthalmoplegia With Mitochondrial DNA Deletions, Alpers-	AD,AR	99.92	325 of 326

	Huttenlocher Syndrome, Progressive External Ophthalmoplegia, Sensory Ataxic Neuropathy-Dysarthria-Ophthalmoparesis Syndrome			
PPP2R5D	Autosomal Dominant Mental Retardation, Intellectual Disability-Macrocephaly-Hypotonia-Behavioral Abnormalities Syndrome	AD	100	11 of 11
PPT1	Neuronal Ceroid Lipofuscinosis	AR	100	81 of 81
PURA	Autosomal Dominant Mental Retardation	AD	85.36	59 of 65
SCN1A	Early Infantile Epileptic Encephalopathy, Familial Febrile Convulsions, Dravet Syndrome, Familial Or Sporadic Hemiplegic Migraine, Lennox-Gastaut Syndrome	AD	99.8	1776 of 1797
SCN1B	Early Infantile Epileptic Encephalopathy, Generalized Epilepsy With Febrile Seizures Plus, Dravet Syndrome	AD,AR	99.67	46 of 48
SCN2A	Early Infantile Epileptic Encephalopathy, Episodic Ataxia, Seizures, Benign Familial Neonatal-Infantile, Dravet Syndrome, West Syndrome	AD	100	351 of 351
SLC19A3	Infantile Spasms-Psychomotor Retardation-Progressive Brain Atrophy-Basal Ganglia Disease Syndrome, Leigh Syndrome With Leukodystrophy	AR	100	38 of 39
SLC2A1	Episodic Epilepsy Choreoathetosis/Spasticity, Glut1 Deficiency Syndrome, Stomatin-Deficient Cryohydrocytosis With Neurologic Defects, Childhood Absence Epilepsy, Paroxysmal Exertion-Induced Dyskinesia	AD,AR	99.99	301 of 304
SLC6A1	Myoclonic-Astastic Epilepsy	AD	100	55 of 55
SLC6A8	X-linked Creatine Transporter Deficiency	X,XR,G	99.87	NA of NA
SLC9A6	X-linked Mental Retardation, Christianson Syndrome	X,XD,G	98.87	NA of NA
SLITRK1	Gilles De La Tourette Syndrome	AD,MU	100	10 of 12
SMC1A	Cornelia De Lange Syndrome, Semilobar Holoprosencephaly, Wiedemann-Steiner Syndrome	X,XR,XD,G	100	NA of NA
SPATA5	Epilepsy, Hearing Loss, And Mental Retardation Syndrome, Microcephaly-Intellectual Disability-Sensorineural Hearing Loss-Epilepsy-Abnormal Muscle Tone Syndrome	AR	99.83	30 of 30
STX1B	Generalized Epilepsy With Febrile Seizures Plus	AD	100	24 of 24
STXBP1	Early Infantile Epileptic Encephalopathy, Atypical Rett Syndrome, Dravet Syndrome, West Syndrome	AD	100	209 of 215
SYNGAP1	Autosomal Dominant Mental Retardation, Syngap1-Related Developmental And Epileptic Encephalopathy	AD	99.46	168 of 171
TBC1D24	Autosomal Dominant Deafness, Autosomal Recessive Deafness, Doors Syndrome, Rolandic Epilepsy With Paroxysmal Exercise-Induced Dystonia And Writer's Cramp, Early Infantile Epileptic Encephalopathy, Familial Infantile Myoclonic Epilepsy, Progressive Myoclonic Epilepsy With Dystonia	AD,AR	100	80 of 80
TCF4	Fuchs Endothelial Corneal Dystrophy, Pitt-Hopkins Syndrome, Primary Sclerosing Cholangitis	AD	98.91	124 of 124
TPP1	Neuronal Ceroid Lipofuscinosis, Spinocerebellar Ataxia	AR	100	147 of 147
UBE3A	Angelman Syndrome	AD	99.98	208 of 211
WDR45	Neurodegeneration With Brain Iron Accumulation, West Syndrome	X,XD,G	100	NA of NA
ZEB2	Mowat-Wilson Syndrome	AD	98.95	253 of 254

*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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