Blueprint Genetics

Retinal Dystrophy Panel

Test code: OP0801

Is a 351 gene panel that includes assessment of non-coding variants.

In addition, it also includes the maternally inherited mitochondrial genome.
Is ideal for patients with a clinical suspicion / diagnosis of an isolated or syndromic retinal dystrophy.

Is not ideal for patients suspected to have blue cone monochromacy, caused by variants in the *OPN1LW* and *OPN1MW* genes.

For patients in the USA with an inherited retinal degenerative disease, please visit the no-cost My Retina Tracker Program for further details.

About Retinal Dystrophy

Retinal dystrophies are a broad group of clinically and genetically heterogenous disorders affecting the retina (Reviewed in PMID: 26835369). Common presentations among these disorders include night or colour blindness, tunnel vision and subsequent progression to complete blindness. Vision loss can occur anywhere from early infancy to late adulthood and both stationary and progressive diseases have been described. The inheritance pattern may be autosomal recessive, autosomal dominant or X-linked. Sporadic cases are also observed. Mutations within the same gene have been shown to cause different disease phenotypes, even among affected individuals within the same family highlighting further levels of complexity. Retinal dystrophy can be nonsyndromic or part of a syndrome in which clinical presentations extend to more than the affected retina. Examples of retinal dystrophies associated with syndromic features are Usher syndrome, Bardet-Biedl syndrome, Joubert syndrome, Senior-Loken syndrome, Cohen syndrome and Alström syndrome. For detailed description of different retinal dystrophies, please see the ophthalmology subpanel descriptions.

Availability

4 weeks

Gene Set Description

Genes in the Retinal Dystrophy Panel and their clinical significance

Gene	Associated phenotypes	Inheritance	ClinVar	HGMD
ABCA4	Stargardt disease, Retinitis pigmentosa, Cone rod dystrophy, Retinal dystrophy, early-onset severe, Fundus flavimaculatus	AR	308	1231
ABCC6*	Pseudoxanthoma elasticum	AR	352	377
ABCD1*	Adrenoleukodystrophy	XL	95	663
ABHD12	Polyneuropathy, hearing loss, ataxia, retinitis pigmentosa, and cataract	AR	16	20
ACO2	Optic atrophy, Infantile cerebellar-retinal degeneration	AR	16	15
ADAM9	Cone rod dystrophy	AR	6	10
ADAMTS18	Knobloch syndrome 2, Microcornea, myopic chorioretinal atrophy, and telecanthus, Retinal dystrophy, early onset, autosomal recessive	AR	4	14
ADGRV1	Usher syndrome, type IIC	AR	71	236

ADIPOR1*	Complement system	AD/AR		4
AGBL5	Retinitis pigmentosa 75	AR	2	9
AHI1	Joubert syndrome	AR	62	93
AIPL1	Retinitis pigmentosa, Cone rod dystrophy, Leber congenital amaurosis	AR	10	79
ALMS1*	Alström syndrome	AR	197	302
AMACR	Alpha-methylacyl-CoA racemase deficiency, Bile acid synthesis defect	AR	3	8
ARHGEF18	Retinitis pigmentosa 78	AR	5	6
ARL13B	Joubert syndrome	AR	11	10
ARL2BP	Retinitis pigmentosa with or without situs inversus	AR	4	4
ARL3	Retinitis pigmentosa, Joubert syndrome	AD/AR		1
ARL6	Bardet-Biedl syndrome, Retinitis pigmentosa	AR	14	21
ARMC9	Joubert syndrome 30	AR	12	11
ARR3			3	3
ARSG	Usher syndrome, type IV	AR	1	1
ATF6	Achromatopsia	AR	13	13
ATOH7	Persistent hyperplastic primary vitreous, autosomal recessive	AR	4	9
B9D1	Meckel syndrome	AR	7	10
B9D2	Meckel syndrome	AR	8	4
BBIP1#	Bardet-Biedl syndrome 18	AR	1	1
BBS1	Bardet-Biedl syndrome	AR	66	103
BBS10	Bardet-Biedl syndrome	AR	90	107
BBS12	Bardet-Biedl syndrome	AR	36	58
BBS2	Bardet-Biedl syndrome, Retinitis pigmentosa	AR	58	91
BBS4	Bardet-Biedl syndrome	AR	25	53
BBS5	Bardet-Biedl syndrome	AR	18	31
BBS7	Bardet-Biedl syndrome	AR	19	43
BBS9	Bardet-Biedl syndrome	AR	27	52

BEST1	Vitreoretinochoroidopathy, Microcornea, Rod-cone dystrophy, Posterior staphyloma, Bestrophinopathy, Vitelliform macular dystrophy, Cataract, Retinitis pigmentosa, Macular dystrophy, vitelliform, adult-onset, Retinitis pigmentosa 50, Macular dystrophy, vitelliform 2, Best macular dystrophy, Bestrophinopathy, autosomal recessive	AD/AR	62	318
C1QTNF5	Late-onset retinal degeneration	AD	27	7
C21ORF2	Retinal dystrophy with or without macular staphyloma (RDMS), Spondylometaphyseal dysplasia, axial (SMDAX)	AR	13	22
C2ORF71	Retinitis pigmentosa	AR	17	51
C5ORF42	Orofaciodigital syndrome, Joubert syndrome	AR	97	103
C8ORF37	Retinitis pigmentosa, Cone rod dystrophy, Bardet-Biedl syndrome 21	AR	8	17
CA4	Retinitis pigmentosa 17	AD	3	10
CABP4	Night blindness, congenital stationary	AR	6	11
CACNA1F	Aland Island eye disease, Cone rod dystrophy, Night blindness, congenital stationary	XL	39	182
CACNA2D4	Retinal cone dystrophy	AR	3	9
CAPN5	Vitreoretinopathy, neovascular inflammatory	AD	3	12
CC2D2A	COACH syndrome, Joubert syndrome, Meckel syndrome	AR	76	91
CDH23	Deafness, Usher syndrome, type 1D	AR	94	358
CDH3	Hypotrichosis, congenital, with juvenile macular dystrophy, Ectodermal dysplasia, ectrodactyly, and macular dystrophy syndrome	AR	7	30
CDHR1	Retinitis pigmentosa, Cone rod dystrophy	AR	12	48
CEP104	Joubert syndrome	AR	7	5
CEP120	Short-rib thoracic dysplasia 13 with or without polydactyly	AR	9	9
CEP164	Nephronophthisis	AR	11	9
CEP19	Morbid obesity and spermatogenic failure, Bardet-Biedl syndrome	AR	2	2
CEP250	Cone rod dystrophy and hearing loss	AR		5
CEP290*	Bardet-Biedl syndrome, Leber congenital amaurosis, Joubert syndrome, Senior-Loken syndrome, Meckel syndrome	AR	130	289
CEP41	Joubert syndrome	AR/Digenic	7	11
CEP78	Cone rod dystrophy and hearing loss	AR	7	9
CEP83	Nephronophthisis	AR	10	10
CERKL	Retinitis pigmentosa	AR	20	37
CHM	Choroideremia	XL	46	284

CIB2	Deafness, Usher syndrome type IJ	AR	5	18
CISD2*	Wolfram syndrome 2	AR	2	4
CLN3	Neuronal ceroid lipofuscinosis, type 3	AR	100	72
CLN5	Neuronal ceroid lipofuscinosis, type 5	AR	62	47
CLN6	Neuronal ceroid lipofuscinosis, type 6	AR	41	83
CLN8	Neuronal ceroid lipofuscinosis, type 8	AR	45	44
CLRN1	Retinitis pigmentosa, Usher sydnrome, type 3A	AR	24	39
CNGA1	Retinitis pigmentosa	AR	14	33
CNGA3	Leber congenital amaurosis, Achromatopsia	AR	32	149
CNGB1	Retinitis pigmentosa	AR	25	61
CNGB3	Macular degeneration, juvenile, Achromatopsia	AR	115	124
CNNM4	Jalili syndrome	AR	11	24
COL11A1	Marshall syndrome, Fibrochondrogenesis, Stickler syndrome type 2	AD/AR	34	94
COL11A2	Weissenbacher-Zweymuller syndrome, Deafness, Otospondylomegaepiphyseal dysplasia, Fibrochondrogenesis, Stickler syndrome type 3 (non-ocular)	AD/AR	29	57
COL18A1	Knobloch syndrome	AR	27	31
COL2A1	Avascular necrosis of femoral head, Rhegmatogenous retinal detachment, Epiphyseal dysplasia, with myopia and deafness, Czech dysplasia, Achondrogenesis type 2, Platyspondylic dysplasia Torrance type, Hypochondrogenesis, Spondyloepiphyseal dysplasia congenital (SEDC), Spondyloepimetaphyseal dysplasia (SEMD) Strudwick type, Kniest dysplasia, Spondyloperipheral dysplasia, Mild SED with premature onset arthrosis, SED with metatarsal shortening, Stickler syndrome type 1	AD	180	561
COL9A1	Multiple epiphyseal dysplasia type 6 (EDM6), Stickler syndrome, type IV	AD/AR	9	6
COL9A2	Stickler syndrome, Multiple epiphyseal dysplasia type 2 (EDM2)	AD/AR	7	12
COL9A3	Multiple epihyseal dysplasia type 3 (EDM3), Stickler syndrome recessive type	AD/AR	10	14
COQ2	Coenzyme Q10 deficiency	AR	16	31
CPE	Obesity, severe, and type II diabetes	AR		2
CRB1	Retinitis pigmentosa, Pigmented paravenous chorioretinal atrophy, Leber congenital amaurosis	AR	54	334
CRX	Cone rod dystrophy, Leber congenital amaurosis	AD/AR	30	106
CSPP1	Jeune asphyxiating thoracic dystrophy, Joubert syndrome	AR	32	27
CTC1	Cerebroretinal microangiopathy with calcifications and cysts	AR	21	33

CTNNA1	Macular dystrophy, patterned 2	AD	6	10
CTNNB1	Exudative vitreoretinopathy 7, Mental retardation, autosomal dominant 19	AD	90	51
CTSD	Ceroid lipofuscinosis, neuronal	AR	12	18
CWC27	Retinitis pigmentosa with or without skeletal anomalies (RPSKA)	AR	5	7
CYP4V2	Retinitis pigmentosa, Bietti crystalline corneoretinal dystrophy	AR	31	94
DFNB31	Usher syndrome, type 2D, Deafness, autosomal recessive 31	AR	12	31
DHDDS	Retinitis pigmentosa, Developmental delay and seizures with or without movement abnormalities (DEDSM)	AD/AR	5	8
DHX38	Retinitis pigmentosa	AR		1
DNAJC5	Kufs disease,, Ceroid lipofuscinosis, neuronal 4, Parry	AD	2	2
DRAM2	Cone-rod dystrophy 21	AR	8	10
DTHD1	Leber congenital amaurosis with muscle dystrophy	AR		1
DYNC2H1	Short -rib thoracic dysplasia with or without polydactyly type 1, Short -rib thoracic dysplasia with or without polydactyly type 3, Asphyxiating thoracic dysplasia (ATD; Jeune), SRPS type 2 (Majewski)	AR/Digenic	148	205
EFEMP1	Doyne honeycomb degeneration of retina, Malattia leventinese	AD	2	8
ELOVL4	Stargardt disease, Icthyosis, spastic quadriplegia, and mental retardation, Spinocerebellar ataxia	AD/AR	13	14
EMC1	Cerebellar atrophy, visual impairment, and psychomotor retardation	AR	3	7
ESPN*	Deafness, Deafness, autosomal recessive 36	AD/AR	12	15
EXOSC2			2	2
EYS*	Retinitis pigmentosa	AR	97	321
FAM161A	Retinitis pigmentosa	AR	14	20
FDXR	Auditory neuropathy and optic atrophy	AR	5	19
FLVCR1	Ataxia, posterior column, with retinitis pigmentosa	AR	9	15
FRMD7	Nystagmus, infantile periodic alternating	XL	15	95
FZD4	Retinopathy of prematurity, Exudative vitreoretinopathy	AD/Digenic	14	90
GNAT1	Night blindness, congenital stationary	AD/AR	5	10
GNAT2	Achromatopsia	AR	7	16
GNB3	Night blindness, congenital stationary, type 1H	AR	3	6
GNPTG	Mucolipidosis	AR	45	46
GPR143	Nystagmus, congenital, Ocular albinism	XL	22	181

GPR179	Night blindness, congenital stationary	AR	13	16
GRK1	Oguchi disease	AR	5	23
GRM6	Night blindness, congenital stationary	AR	11	38
GUCA1A	Cone dystrophy 3/Cone rod dystrophy	AD	7	21
GUCY2D	Cone rod dystrophy, Leber congenital amaurosis	AD/AR	34	235
HARS*	Charcot-Marie-Tooth disease, axonal, type 2W, Usher syndrome, type 3B	AD/AR	6	12
HGSNAT	Mucopolysaccharidosis (Sanfilippo syndrome), Retinitis pigmentosa	AR	43	72
HK1	Hemolytic anemia, nonspherocytic, due to hexokinase deficiency, Retinitis pigmentosa 79, Neuropathy, motor and sensory, Russe type (Charcot-Marie-Tooth disease type 4G)	AD/AR	9	7
HMX1	Oculoauricular syndrome	AR	3	4
IDH3A	Leber congenital amaurosis	AR		7
IDH3B	Retinitis pigmentosa	AR	2	3
IFT140	Short -rib thoracic dysplasia with or without polydactyly, Asphyxiating thoracic dysplasia (ATD; Jeune)	AR	38	63
IFT172	Retinitis pigmentosa, Short -rib thoracic dysplasia with or without polydactyly, Asphyxiating thoracic dysplasia (ATD; Jeune)	AR	22	25
IFT27	Bardet Biedl syndrome 19	AR	1	4
IFT81	Short rib thoracic dysplasia with polydactyly, Cone-Rod dystrophy, autosomal recessive	AR	4	9
IMPDH1	Retinitis pigmentosa, Leber congenital amaurosis	AD	7	23
IMPG1	Macular dystrophy, vitelliform	AD/AR	9	11
IMPG2	Retinitis pigmentosa, Vitelliform macular dystrophy	AD/AR	25	40
INPP5E	Joubert syndrome, Mental retardation, truncal obesity, retinal dystrophy, and micropenis (MORM syndrome)	AR	25	50
INVS	Nephronophthisis	AR	16	34
IQCB1	Senior-Loken syndrome	AR	24	41
ISPD	Muscular dystrophy-dystroglycanopathy	AR	38	53
JAG1	Alagille syndrome	AD	131	610
KCNJ13	Snowflake vitreoretinal degeneration, Leber congenital amaurosis	AD/AR	6	10
KCNV2	Retinal cone dystrophy	AR	16	94
KIAA0556	Joubert syndrome 26	AR	2	2
KIAA0586	Short rib thoracic dysplasia with polydactyly, Joubert syndrome	AR	29	31

KIAA0753	Orofaciodigital syndrome XV	AR	6	7
KIAA1549	Retinitis pigmentosa	AR	1	6
KIF11	Microcephaly	AD	39	69
KIF7	Acrocallosal syndrome, Hydrolethalus syndrome, Al-Gazali-Bakalinova syndrome, Joubert syndrome	AR/Digenic	24	44
KIZ	Retinitis pigmentosa 69	AR	3	4
KLHL7	Retinitis pigmentosa, Retinitis pigmentosa 42, Cold-induced sweating syndrome 3	AD/AR	12	11
LAMA1	Poretti-Boltshauser syndrome	AR	32	40
LCA5	Leber congenital amaurosis	AR	10	49
LRAT	Retinitis pigmentosa, juvenile, Leber congenital amaurosis, Retinitis punctata albescens, Retinal-dystrophy, early-onset severe	AR	8	23
LRIT3	Night blindness, congenital stationary	AR	4	9
LRP2	Donnai-Barrow syndrome, Facio-oculo-acoustico-renal syndrome	AR	24	38
LRP5*	Van Buchem disease, Osteoporosis-pseudoglioma syndrome, Hyperostosis, endosteal, Osteosclerosis, Exudative vitreoretinopathy, Osteopetrosis late-onset form type 1, LRP5 primary osteoporosis	AD/AR/Digenic	57	196
LZTFL1	Bardet-Biedl syndrome 17	AR	6	3
MAK	Retinitis pigmentosa	AR	11	22
MERTK	Retinitis pigmentosa	AR	25	75
MFN2	Hereditary motor and sensory neuropathy, Charcot-Marie-Tooth disease	AD/AR	70	223
MFRP	Microphthalmia, isolated 5, Nanophthalmos 2, Retinitis pigmentosa, autosomal recessive	AR	27	30
MFSD8	Ceroid lipofuscinosis, neuronal	AR	27	47
MKKS	Bardet-Biedl syndrome, McKusick-Kaufman syndrome	AR	21	59
MKS1	Bardet-Biedl syndrome, Meckel syndrome	AR	50	52
MMACHC	Methylmalonic aciduria and homocystinuria	AR	59	93
MT-ATP6	Neuropathy, ataxia, and retinitis pigmentosa, Leber hereditary optic neuropathy, Ataxia and polyneuropathy, adult-onset, Cardiomyopathy, infantile hypertrophic, Leigh syndrome, Striatonigral degeneration, infantile, mitochondrial	Mitochondrial	19	
MT-ATP8	Cardiomyopathy, apical hypertrophic, and neuropathy, Cardiomyopathy, infantile hypertrophic	Mitochondrial	4	
MT-CO1	Myoglobinuria, recurrent, Leber hereditary optic neuropathy, Sideroblastic anemia, Cytochrome C oxidase deficiency, Deafness, mitochondrial	Mitochondrial	17	

MT-CO2	Cytochrome c oxidase deficiency	Mitochondrial	8
MT-CO3	Cytochrome c oxidase deficiency, Leber hereditary optic neuropathy	Mitochondrial	9
MT-CYB		Mitochondrial	69
MT-ND1	Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes, Leber hereditary optic neuropathy, Leber optic atrophy and dystonia	Mitochondrial	21
MT-ND2	Leber hereditary optic neuropathy, Mitochondrial complex I deficiency	Mitochondrial	6
MT-ND3	Leber optic atrophy and dystonia, Mitochondrial complex I deficiency	Mitochondrial	7
MT-ND4	Leber hereditary optic neuropathy, Leber optic atrophy and dystonia, Mitochondrial complex I deficiency	Mitochondrial	11
MT-ND4L	Leber hereditary optic neuropathy	Mitochondrial	2
MT-ND5	Myoclonic epilepsy with ragged red fibers, Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes, Leber hereditary optic neuropathy, Mitochondrial complex I deficiency	Mitochondrial	19
MT-ND6	Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes, Oncocytoma, Leber hereditary optic neuropathy, Leber optic atrophy and dystonia, Mitochondrial complex I deficiency	Mitochondrial	16
MT-RNR1	Deafness, mitochondrial	Mitochondrial	3
MT-RNR2	Chloramphenicol toxicity/resistance	Mitochondrial	2
MT-TA		Mitochondrial	4
MT-TC	Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes	Mitochondrial	3
MT-TD		Mitochondrial	1
MT-TE	Diabetes-deafness syndrome, Mitochondrial myopathy, infantile, transient, Mitochondrial myopathy with diabetes	Mitochondrial	5
MT-TF	Myoclonic epilepsy with ragged red fibers, Nephropathy, tubulointerstitial, Encephalopathy, mitochondrial, Epilepsy, mitochondrial, Myopathy, mitochondrial, Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	Mitochondrial	7
MT-TG		Mitochondrial	3
MT-TH		Mitochondrial	4
MT-TI		Mitochondrial	7
MT-TK	Myoclonic epilepsy with ragged red fibers, Leigh syndrome	Mitochondrial	5
MT-TL1	Cytochrome c oxidase deficiency, Myoclonic epilepsy with ragged red fibers, Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes, Diabetes-deafness syndrome, Cyclic vomiting syndrome, SIDS, susceptibility to	Mitochondrial	14

MT-TL2	Mitochondrial multisystemic disorder, Progressive external ophthalmoplegia, Mitochondrial Myopathy, Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	Mitochondrial	5	
MT-TM	Leigh syndrome, Mitochondrial multisystemic disorder	Mitochondrial	1	
MT-TN	Progressive external ophthalmoplegia, Mitochondrial multisystemic disorder	Mitochondrial	3	
MT-TP		Mitochondrial	2	
MT-TQ	Mitochondrial multisystemic disorder	Mitochondrial	2	
MT-TR	Encephalopathy, mitochondrial	Mitochondrial	2	
MT-TS1	Myoclonic epilepsy with ragged red fibers, Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes	Mitochondrial	10	
MT-TS2	Mitochondrial multisystemic disorder	Mitochondrial	2	
MT-TT		Mitochondrial	5	
MT-TV	Hypertrophic cardiomyopathy (HCM), Leigh syndrome, Mitochondrial multisystemic disorder, Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	Mitochondrial	3	
MT-TW	Leigh syndrome, Myopathy, mitochondrial	Mitochondrial	8	
MT-TY	Mitochondrial multisystemic disorder	Mitochondrial	4	
MTTP	Abetalipoproteinemia	AR	12	69
MVK	Mevalonic aciduria, Hyper-IgD syndrome, Porokeratosis 3, multiple types	AD/AR	35	181
MYO7A	Deafness, autosomal dominant 11, Usher syndrome, type I, Deafness, autosomal recessive 2	AD/AR	239	515
NAGLU	Mucopolysaccharidosis (Sanfilippo syndrome), Charcot-Marie-Tooth disease, axonal, type 2V	AR	74	171
NDP	Exudative vitreoretinopathy, Norrie disease	XL	31	167
NEK2	Retinitis pigmentosa 67	AR	1	1
NMNAT1	Leber congenital amaurosis	AR	20	74
NPHP1	Nephronophthisis, Joubert syndrome, Senior-Loken syndrome	AR	19	76
NPHP3	Nephronophthisis, Renal-hepatic-pancreatic dysplasia, Meckel syndrome	AR	38	75
NPHP4	Nephronophthisis, Senior-Loken syndrome	AR	20	113
NR2E3	Retinitis pigmentosa, Enhanced S-cone syndrome	AD/AR	19	77
NR2F1	Bosch-Boonstra optic atrophy syndrome	AD	23	34
NRL	Retinitis pigmentosa, Clumped pigmentary retinal degeneration	AD/AR	11	25
NYX	Night blindness, congenital stationary	XL	12	89

OAT	Gyrate atrophy of choroid and retina	AR	67	71
OCA2	Albinism, brown oculocutaneous, Albinism, oculocutaneous, Skin/hair/eye pigmentation	AR	43	310
OFD1	Simpson-Golabi-Behmel syndrome, Retinitis pigmentosa, Orofaciodigital syndrome, Joubert syndrome	XL	153	160
OPA1	Optic atrophy, Optic atrophy 1, Optic atrophy with or without deafness, Ophthalmoplegia, myopathy, ataxia, and neuropathy, Behr synrome, Mitochondrial DNA depletion syndrome 14	AD/AR	96	390
OPA3	Optic atrophy, 3-methylglutaconic aciduria	AD/AR	13	15
OPN1SW	Tritanopia	AD	3	9
OTX2	Microphthalmia, syndromic, Pituitary hormone deficiency, combined, Retinal dystrophy, early-onset, and pituitary dysfunction	AD	23	73
P3H2	Myopia, high, with cataract and vitreoretinal degeneration	AR	7	7
PANK2	Hypoprebetalipoproteinemia, acanthocytosis, retinitis pigmentosa, and pallidal degeneration, Neurodegeneration with brain iron accumulation	AR	37	181
PAX2	Isolated renal hypoplasia, Papillorenal syndrome, Focal segmental glomerulosclerosis 7	AD	30	96
PCDH15	Deafness, Usher syndrome, type 1D	AR/Digenic	113	118
PCYT1A	Spondylometaphyseal dysplasia with cone-rod dystrophy	AR	12	20
PDE6A	Retinitis pigmentosa	AR	16	49
PDE6B	Retinitis pigmentosa, Night blindness, congenital stationary	AD/AR	35	125
PDE6C	Cone dystrophy	AR	31	44
PDE6D	Joubert syndrome 22	AR	3	1
PDE6G	Retinitis pigmentosa	AR	1	2
PDE6H	Retinal cone dystrophy, Achromatopsia	AR	2	2
PDSS1	Coenzyme Q10 deficiency	AR	5	3
PDSS2	Coenzyme Q10 deficiency	AR	8	4
PDZD7	Deafness, autosomal recessive	AR	11	19
PEX1	Heimler syndrome, Peroxisome biogenesis factor disorder 1A, Peroxisome biogenesis factor disorder 1B	AR	112	134
PEX10	Adrenoleukodystrophy, neonatal, Zellweger syndrome, Peroxisome biogenesis disorder, Ataxia	AR	34	29
PEX11B	Zellweger syndrome, Peroxisome biogenesis disorder	AR	5	7
PEX12	Zellweger syndrome, Peroxisome biogenesis disorder	AR	43	37

PEX13	Adrenoleukodystrophy, neonatal, Zellweger syndrome, Peroxisome biogenesis disorder	AR	9	10
PEX14	Peroxisome biogenesis factor disorder 14, Zellweger syndrome	AR	5	4
PEX16	Zellweger syndrome, Peroxisome biogenesis disorder	AR	8	13
PEX19	Peroxisome biogenesis disorder, 19, Zellweger syndrome	AR	3	4
PEX2	Zellweger syndrome, Peroxisome biogenesis disorder	AR	16	18
PEX26	Adrenoleukodystrophy, neonatal, Zellweger syndrome, Peroxisome biogenesis disorder	AR	13	27
PEX3	Zellweger syndrome, Peroxisome biogenesis disorder	AR	4	10
PEX5	Adrenoleukodystrophy, neonatal, Rhizomelic chondrodysplasia punctata, Zellweger syndrome, Peroxisome biogenesis disorder	AR	8	14
PEX6	Heimler syndrome, Peroxisome biogenesis disorder 4A, Peroxisome biogenesis disorder 4B	AR	58	107
PEX7	Refsum disease, Rhizomelic CDP type 1	AR	44	53
PHYH	Refsum disease	AR	12	36
PISD		AR		
PITPNM3	Cone-rod dystrophy 5	AD	1	5
PLA2G5	Fleck retina, familial benign	AR	1	7
PLK4	Microcephaly and chorioretinopathy, autosomal recessive 2	AR	3	6
PNPLA6	Laurence-Moon syndrome, Boucher-Neuhauser syndrome, Spastic paraplegia 39	AR	26	58
POC1B	Cone-rod dystrophy 20	AR	4	7
POMGNT1	Muscular dystrophy-dystroglycanopathy	AR	96	88
PPT1*	Ceroid lipofuscinosis, neuronal	AR	94	77
PRCD	Retinitis pigmentosa	AR	2	7
PRDM13	Macular dystrophy, retinal 1, North Carolina type	AD		7
PROM1#	Stargardt disease, Retinitis pigmentosa, Cone rod dystrophy, Macular dystrophy, retinal,	AD/AR	22	80
PRPF3	Retinitis pigmentosa	AD	3	7
PRPF31	Retinitis pigmentosa	AD	36	165
PRPF4	Retinitis pigmentosa 70	AD	2	4
PRPF6	Retinitis pigmentosa 60	AD	4	11
PRPF8	Retinitis pigmentosa	AD	13	46

PRPH2	Choriodal dystrophy, central areolar, Macular dystrophy, vitelliform, Retinitis pigmentosa, Retinitis punctata albescens, Macula dystrophy, patterned	AD/AR	48	176
PRPS1*	Phosphoribosylpyrophosphate synthetase I superactivity, Arts syndrome, Charcot-Marie-Tooth disease, X-linked recessive, 5, Deafness, X-linked 1	XL	27	32
RAB28	Cone-rod dystrophy 18	AR	4	5
RAX2	Cone rod dystrophy	AD/AR	5	4
RBP3	Retinitis pigmentosa	AR	5	17
RBP4	Retinal dystrophy, iris coloboma, and comedogenic acne syndrome, Microphthalmia, isolated, with coloboma 10	AD/AR	8	7
RCBTB1	Retinal dystrophy with or without extraocular anomalies (RDEOA), Familial exudative vitreoretinopathy	AR	6	9
RD3	Leber congenital amaurosis	AR	5	13
RDH11	Microphthalmia, isolated, with coloboma 10, Retinal dystrophy, juvenile cataracts, and short stature syndrome	AR	2	2
RDH12	Retinitis pigmentosa, Leber congenital amaurosis	AD/AR	23	102
RDH5	Fundus albipunctatus	AR	11	51
REEP6	Retinitis pigmentosa 77	AR	4	8
RGR	Retinitis pigmentosa	AD/AR	2	11
RGS9	Bradyopsia	AR	2	2
RGS9BP	Bradyopsia	AR	2	7
RHO	Retinitis pigmentosa, Night blindness, congenital stationary, Retinitis punctata albescens	AD/AR	58	212
RIMS1	Cone-rod dystrophy 7	AD	3	12
RLBP1	Newfoundland rod-cone dystrophy, Fundus albipunctatus, Bothnia retinal dystrophy, Retinitis punctata albescens	AR	9	37
ROM1	Retinitis pigmentosa 7, digenic	AD/AR	3	18
RP1	Retinitis pigmentosa	AD/AR	45	181
RP1L1	Occult macular dystrophy, Retinitis pigmentosa	AD/AR	7	48
RP2	Retinitis pigmentosa	XL	26	118
RPE65	Retinitis pigmentosa, Leber congenital amaurosis	AD/AR	31	197
RPGR	Retinitis pigmentosa, Cone-rod dystrophy, X-linked, 1, Macular degeneration, X-linked atrophic, Retinitis pigmentosa 3	XL	79	218
RPGRIP1	Cone rod dystrophy, Leber congenital amaurosis	AR	44	145

RPGRIP1L	COACH syndrome, Joubert syndrome, Meckel syndrome, Retinal degeneration in ciliopathy, modifier	AR	39	49
RS1	Retinoschisis	XL	44	262
RTN4IP1	Optic atrophy 10 with or without ataxia, mental retardation, and seizures	AR	2	12
SAG	Retinitis pigmentosa, Oguchi disease	AD/AR	6	15
SAMD11	Retinitis pigmentosa	AR	2	5
SCAPER	Retinal dystrophy, Retinitis pigmentosa	AR	4	7
SCLT1	Senior-Loken syndrome, Retinal dystrophy	AR		3
SDCCAG8	Bardet-Biedl syndrome, Senior-Loken syndrome	AR	14	18
SEMA4A	Retinitis pigmentosa, Cone rod dystrophy	AR	4	14
SGSH	Mucopolysaccharidosis (Sanfilippo syndrome)	AR	55	148
SLC24A1	Night blindness, congenital stationary, type 1D	AR	7	26
SLC25A46	Neuropathy, hereditary motor and sensory, type VIB	AR	14	17
SLC45A2	Skin/hair/eye pigmentation, Oculocutaneous albinism	AR	16	156
SLC7A14	Retinitis pigmentosa 68	AR	4	8
SNRNP200	Retinitis pigmentosa	AD/AR	6	34
SPATA7	Leber congenital amaurosis, Retitinitis pigmentosa	AR	15	39
SPP2	Retinitis pigmentosa	AD	1	2
SRD5A3*	Kahrizi syndrome, Congenital disorder of glycosylation, Retinal dystrophy	AR	13	16
TCTN1	Joubert syndrome	AR	6	6
TCTN2	Joubert syndrome, Meckel syndrome	AR	20	15
TCTN3	Orofaciodigital syndrome (Mohr-Majewski syndrome), Joubert syndrome	AR	9	12
TEAD1	Sveinsson choreoretinal atrophy	AD	1	2
TIMM8A*	Mohr-Tranebjaerg syndrome, Jensen syndrome, Opticoacoustic nerve atrophy with dementia	XL	11	21
TIMP3	Sorsby fundus dystrophy	AD	6	17
TMEM107	Joubert syndrome	AR	10	3
TMEM126A	Optic atrophy	AR	3	1
TMEM138	Joubert syndrome	AR	6	8
TMEM216	Joubert syndrome, Meckel syndrome	AR	17	8

TMEM231	Joubert syndrome, Meckel syndrome	AR	12	19
TMEM237	Joubert syndrome	AR	7	11
TMEM67	Nephronophthisis, COACH syndrome, Joubert syndrome, Meckel syndrome	AR	87	170
TOPORS	Retinitis pigmentosa	AD	7	22
TPP1	Spinocerebellar ataxia, Neuronal ceroid lipofuscinosis type 2	AR	75	112
TRAF3IP1	Senior-Loken syndrome 9	AR	11	15
TREX1	Vasculopathy, retinal, with cerebral leukodystrophy, Chilblain lupus, Aicardi-Goutières syndrome	AD/AR	30	71
TRIM32	Bardet-Biedl syndrome, Muscular dystrophy, limb-girdle	AR	13	16
TRPM1	Night blindness, congenital stationary	AR	21	82
TSPAN12	Exudative vitreoretinopathy, Retinal dysplasia and severe familial exudative vitreoretinopathy	AD/AR	16	51
TTC21B	Short-rib thoracic dysplasia, Nephronophthisis, Asphyxiating thoracic dysplasia (ATD; Jeune)	AR	23	63
TTC8	Bardet-Biedl syndrome, Retinitis pigmentosa	AR	5	16
TTLL5	Cone-rod dystrophy 19	AR	13	12
TTPA	Ataxia with isolated vitamin E deficiency	AR	29	30
TUB	Retinal dystrophy and obesity	AR	1	2
TUBB4B	Leber congenital amaurosis, Hearing loss	AD	2	3
TUBGCP4	Microcephaly and chorioretinopathy, autosomal recessive 3	AR	7	6
TUBGCP6	Microcephaly and chorioretinopathy, autosomal recessive 1	AR	16	7
TULP1	Retinitis pigmentosa, Leber congenital amaurosis	AR	24	74
TYR*	Albinism, oculocutaneous	AR	77	441
TYRP1	Albinism, oculocutaneous	AR	10	55
USH1C	Deafness, Usher syndrome, type IC	AR	45	51
USH1G	Usher syndrome, type 1G	AR	13	32
USH2A	Retinitis pigmentosa 39, Usher syndrome, type 2A	AR	401	1169
VCAN	Wagner disease	AD	11	19
VPS13B	Cohen syndrome	AR	351	203
WDPCP	Meckel-Gruber syndrome, modifier, Bardet-Biedl syndrome, Congenital heart defects, hamartomas of tongue, and polysyndactyly	AR	6	8

WDR19	Retinitis pigmentosa, Nephronophthisis, Short -rib thoracic dysplasia with or without polydactyly, Senior-Loken syndrome, Cranioectodermal dysplasia (Levin-Sensenbrenner) type 1, Cranioectodermal dysplasia (Levin-Sensenbrenner) type 2, Asphyxiating thoracic dysplasia (ATD; Jeune)	AR	33	43
WFS1	Wolfram syndrome, Wolfram-like syndrome, autosomal dominant, Deafness, autosomal dominant 6/14/38, Cataract 41	AD/AR	69	362
YME1L1	Optic atrophy 11		1	1
ZNF408	Exudative vitreoretinopathy 6, Retinitis pigmentosa 72	AD/AR	3	9
ZNF423	Nephronophthisis, Joubert syndrome	AD/AR	10	7
ZNF513	Retinitis pigmentosa	AR	1	3

*Some regions of the gene are duplicated in the genome. Read more.

The gene has suboptimal coverage (means <90% of the gene's target nucleotides are covered at >20x with mapping quality score (MQ>20) reads), and/or the gene has exons listed under Test limitations section that are not included in the panel as they are not sufficiently covered with high quality sequence reads.

The sensitivity to detect variants may be limited in genes marked with an asterisk (*) or number sign (#). Due to possible limitations these genes may not be available as single gene tests.

Gene refers to the HGNC approved gene symbol; Inheritance refers to inheritance patterns such as autosomal dominant (AD), autosomal recessive (AR), mitochondrial (mi), X-linked (XL), X-linked dominant (XLD) and X-linked recessive (XLR); ClinVar refers to the number of variants in the gene classified as pathogenic or likely pathogenic in this database (ClinVar); HGMD refers to the number of variants with possible disease association in the gene listed in Human Gene Mutation Database (HGMD). The list of associated, gene specific phenotypes are generated from CGD or Mitomap databases.

Non-coding disease causing variants covered by the panel

Gene	Genomic location HG19	HGVS	RefSeq	RS-number
ABCA4	Chr1:94461770	c.6730-19G>A	NM_000350.2	rs375179475
ABCA4	Chr1:94468019	c.6148-471C>T	NM_000350.2	
ABCA4	Chr1:94481967	c.5197–557G>T	NM_000350.2	
ABCA4	Chr1:94484001	c.5196+1137G>A	NM_000350.2	rs778234759
ABCA4	Chr1:94484001	c.5196+1137G>T	NM_000350.2	
ABCA4	Chr1:94484082	c.5196+1056A>G	NM_000350.2	
ABCA4	Chr1:94492936	c.4539+2065C>G	NM_000350.2	
ABCA4	Chr1:94492937	c.4539+2064C>T	NM_000350.2	
ABCA4	Chr1:94492973	c.4539+2028C>T	NM_000350.2	rs869320785
ABCA4	Chr1:94493000	c.4539+2001G>A	NM_000350.2	
ABCA4	Chr1:94493073	c.4539+1928C>T	NM_000350.2	

ABCA4	Chr1:94493272	c.4539+1729G>T	NM_000350.2	
ABCA4	Chr1:94493895	c.4539 +1106C>T	NM_000350.2	
ABCA4	Chr1:94493901	c.4539+1100A>G	NM_000350.2	
ABCA4	Chr1:94496509	c.4253+43G>A	NM_000350.2	
ABCA4	Chr1:94508465	c.3191–11T>A	NM_000350.2	
ABCA4	Chr1:94509047	c.3051-16T>A	NM_000350.2	
ABCA4	Chr1:94509799	c.3050+370C>T	NM_000350.2	
ABCA4	Chr1:94510683	c.2919-383C>T	NM_000350.2	
ABCA4	Chr1:94525509	c.2160+584A>G	NM_000350.2	
ABCA4	Chr1:94526934	c.1938-619A>G	NM_000350.2	
ABCA4	Chr1:94527698	c.1937+435C>G	NM_000350.2	
ABCA4	Chr1:94528120	c.1937+13T>G	NM_000350.2	
ABCA4	Chr1:94546780	c.859-506G>C	NM_000350.2	
ABCA4	Chr1:94546814	c.859–540C>G	NM_000350.2	
ABCA4	Chr1:94549781	c.769–784C>T	NM_000350.2	
ABCA4	Chr1:94561127	c.768+3223C>T	NM_000350.2	
ABCA4	Chr1:94566773	c.570+1798A>G	NM_000350.2	
ABCA4	Chr1:94576926	c.302+68C>T	NM_000350.2	rs761188244
ABCA4	Chr1:94577158	c.161–23T>G	NM_000350.2	
ABCA4	Chr1:94578638	c.67-16T>A	NM_000350.2	
ABCC6	Chr16:16244424	c.4403+11C>G	NM_001171.5	rs72664215
ABCC6	Chr16:16256835	c.3506+15G>A	NM_001171.5	rs72664302
ABCC6	Chr16:16281097	c.1780-29T>A	NM_001171.5	rs72664206
ABCC6	Chr16:16284246	c.1432-22C>A	NM_001171.5	rs72664297
BBS1	Chr11:66291105	c.951+58C>T	NM_024649.4	
BBS4	Chr15:73001820	c.77-216delA	NM_033028.4	rs113994189
BBS5	Chr2:170354110	c.619-27T>G	NM_152384.2	
BEST1	Chr11:61717900	c.-29+1G>T	NM_001139443.1	
BEST1	Chr11:61717904	c.-29+5G>A	NM_001139443.1	
C21ORF2	Chr21:45750232	c.1000-23A>T	NM_001271441.1	
CEP290	Chr12:88462434	c.6012-12T>A	NM_025114.3	rs752197734

CEP290	Chr12:88494960	c.2991+1655A>G	NM_025114.3	rs281865192
CEP290	Chr12:88508350	c.1910-11T>G	NM_025114.3	
CEP290	Chr12:88534822	c.103-18_103-13delGCTTTT	NM_025114.3	
CHM	ChrX:85220593	c.315-1536A>G	NM_000390.2	
CHM	ChrX:85223644	c.315-4587T>A	NM_000390.2	
CHM	ChrX:85302626		NM_000390.2	
CHM	ChrX:85302634		NM_000390.2	
CHM	ChrX:85302634		NM_000390.2	
CHM	ChrX:85302644		NM_000390.2	
CLN3	Chr16:28493392	c.1056+34C>A	NM_000086.2	
CLN3	Chr16:28497984	c.461-13G>C	NM_000086.2	rs386833721
CLN6	Chr15:68506515	c.297+113G>C	NM_017882.2	
CLRN1	Chr3:150660197	c.254-649T>G	NM_001195794.1	rs976853535
CNGA3	Chr2:98986401	c.-37-1G>C	NM_001298.2	
COL11A1	Chr1:103386637	c.3744+437T>G	NM_080629.2	
COL11A1	Chr1:103488576	c.1027-24A>G	NM_080629.2	
COL11A1	Chr1:103491958	c.781-450T>G	NM_080629.2	rs587782990
COL2A1	Chr12:48379984	c.1527+135G>A	NM_001844.4	
DHDDS	Chr1:26774026	c.441-24A>G	NM_024887.3	rs764831063
DYNC2H1	Chr11:103019205	c.2819-14A>G	NM_001080463.1	rs781091611
DYNC2H1	Chr11:103055609	c.6478-16G>A	NM_001080463.1	rs376892534
EYS	Chr6:66417023	c.-448+5G>A	NM_001142800.1	
FRMD7	ChrX:131228285	c.285-118C>T	NM_194277.2	
GNAT2	Chr1:110151229	c.461+24G>A	NM_005272.3	rs397515384
GNPTG	Chr16:1412562	c.610-16_609+28del	NM_032520.4	rs193302853
GPR143	ChrX:9708630	c.885+748G>A	NM_000273.2	
GPR143	ChrX:9711844	c.659-131T>G	NM_000273.2	
GUCY2D	Chr17:7906220	c.-9-137T>C	NM_000180.3	
HGSNAT	Chr8:43028824	c.821-28_821-10delTTGCTTATGCTTTGTACTT	NM_152419.2	
HK1	Chr10:71038447	c.-390-3838G>C	NM_033500.2	rs797044964
HK1	Chr10:71038467	c.-390-3818G>C	NM_033500.2	rs397514654

HK1	Chr10:71075518	c.27+14901A>G	NM_033500.2	rs187500777
IFT140	Chr16:1576595	c.2577+25G>A	NM_014714.3	rs1423102192
JAG1	Chr20:10629767	c.1349-12T>G	NM_000214.2	
LRAT	Chr4:155670121	c.541-15T>G	NM_004744.3	rs779487944
MTTP	Chr4:100512792	c.619-5_619-2delTTTA	NM_000253.2	rs755155385
MTTP	Chr4:100522736	c.1237-28A>G	NM_000253.2	
MVK	Chr12:110029032	c.769-7dupT	NM_000431.2	rs104895348
MYO7A	Chr11:76839534	c.-48A>G	NM_000260.3	
MYO7A	Chr11:76893448	c.3109-21G>A	NM_000260.3	
MYO7A	Chr11:76915107	c.5327-14T>G	NM_000260.3	
MYO7A	Chr11:76915110	c.5327-11A>G	NM_000260.3	rs397516316
MYO7A	Chr11:76919448	c.5857-27_5857-26insTTGAG	NM_000260.3	
NDP	ChrX:43818099	c.-207-1G>A	NM_000266.3	
NDP	ChrX:43832545	c.-208+5G>A	NM_000266.3	
NDP	ChrX:43832548	c.-208+2T>G	NM_000266.3	
NDP	ChrX:43832549	c.-208+1G>A	NM_000266.3	
NDP	ChrX:43832685	c.-343A>G	NM_000266.3	rs895911086
NDP	ChrX:43832722	c.-391_-380delCTCTCTCTCCCTinsGTCTCTC	NM_000266.3	
NDP	ChrX:43832724	c.-396_-383delTCCCTCTCTCTCTC	NM_000266.3	rs770996360
NMNAT1	Chr1:10003560	c.-70A>T	NM_022787.3	
NMNAT1	Chr1:10003561	c.-69C>T	NM_022787.3	
NMNAT1	Chr1:10003580	c.-57+7T>G	NM_022787.3	
OCA2	Chr15:28234823	c.1117-11T>A	NM_000275.2	
OCA2	Chr15:28234829	c.1117-17T>C	NM_000275.2	rs200081580
OCA2	Chr15:28235808	c.1045-15T>G	NM_000275.2	rs779461179
OCA2	Chr15:28267738	c.574-19A>G	NM_000275.2	rs145242923
OFD1	ChrX:13768358	c.935+706A>G	NM_003611.2	rs730880283
OFD1	ChrX:13773245	c.1130-22_1130-19delAATT	NM_003611.2	rs312262865
OFD1	ChrX:13773249	c.1130-20_1130-16delTTGGT	NM_003611.2	
OPA1	Chr3:193334932	c.449-34dupA	NM_130837.2	
OPA1	Chr3:193374829	c.2179-40G>C	NM_130837.2	

PANK2	Chr20:3903981	c.*40G>C	NM_153638.2	
PCDH15	Chr10:56560684	c.-29+1G>C	NM_001142763.1	
PDE6C	Chr10:95380377	c.481-12T>A	NM_006204.3	rs786200909
PEX6	Chr6:42933858	c.2301-15C>G	NM_000287.3	rs267608236
PEX6	Chr6:42933952	c.2300+28G>A	NM_000287.3	rs267608237
PEX7	Chr6:137143759	c.-45C>T	NM_000288.3	rs267608252
PPT1	Chr1:40539203	c.*526_*529delATCA	NM_000310.3	rs386833624
PPT1	Chr1:40558194	c.125-15T>G	NM_000310.3	rs386833629
PRDM13	Chr6:100040906	c.-14005G>T	.	
PRDM13	Chr6:100040987	c.-13924G>C	.	
PRDM13	Chr6:100041040	c.-13871C>T	.	
PRDM13	Chr6:100046783	c.-8128A>C	NM_021620.3	
PRDM13	Chr6:100046804	c.-8107T>C	NM_021620.3	
PROM1	Chr4:15989860	c.2077-521A>G	NM_006017.2	rs796051882
PRPF31	Chr19:54631586	c.1073+20_1073+36delCGGTAGGCATGGGGGTC	NM_015629.3	
PRPF31	Chr19:54633399	c.1374+654C>G	NM_015629.3	
PRPF4	Chr9:116037909		NM_004697.4	rs541873609
RDH5	Chr12:56114302	c.-33+2dupT	NM_002905.3	
RPE65	Chr1:68910577	c.246-11A>G	NM_000329.2	
RPGR	ChrX:38128234		NM_000328.2	
RPGR	ChrX:38160137	c.1059+363G>A	NM_001034853.1	
RPGRIP1	Chr14:21789155	c.1468-263G>C	NM_020366.3	
RPGRIP1	Chr14:21789588	c.1611+27G>A	NM_020366.3	
RPGRIP1	Chr14:21793563	c.2367+23delG	NM_020366.3	rs781728563
RPGRIP1	Chr14:21793564	c.2367+23delG	NM_020366.3	
RPGRIP1	Chr14:21795769	c.2711-13G>T	NM_020366.3	rs369991630
SGSH	Chr17:78190802	c.249+27_249+28delGG	NM_000199.3	
SLC45A2	Chr5:33985176		NM_016180.3	rs984225803
SLC45A2	Chr5:33985764		NM_016180.3	rs199972025
TIMM8A	ChrX:100601671	c.133-23A>C	NM_004085.3	rs869320666
TMEM231	Chr16:75575364	c.824-11T>C	NM_001077416.2	

TPP1	Chr11:6637752	c.887-18A>G	NM_000391.3	
TYR	Chr11:88960973	c.1037-18T>G	NM_000372.4	
USH2A	Chr1:215821092	c.14583-20C>G	NM_206933.2	
USH2A	Chr1:215967783	c.9959-4159A>G	NM_206933.2	
USH2A	Chr1:216039721	c.8845+628C>T	NM_206933.2	
USH2A	Chr1:216064540	c.7595-2144A>G	NM_206933.2	rs786200928
USH2A	Chr1:216247476	c.5573-834A>G	NM_206933.2	
USH2A	Chr1:216592035	c.486-14G>A	NM_206933.2	rs374536346
USH2A	Chr1:216596610	c.-259G>T	NM_206933.2	
WFS1	Chr4:6271704	c.-43G>T	NM_006005.3	

Test Strengths

The majority of the X-linked RP is caused by mutations in the*RPGR* gene, which contains a mutational hotspot at a unique 567-aa exon called ORF15 accounting for two-thirds of all disease-causing mutations. The exon ORF15, however, includes a highly repetitive, purine-rich sequence, which generally performs poorly in NGS-based assays. Blueprint Genetics custom assay has good coverage (>20x) with high mapping rates (mapping quality >20) for 100.0% of the target regions in *RPGR* gene. Our validation showed high mean coverage of 139X for the *RPGR* gene. Thus, our NGS Panel is not expected to have major limitations in detecting variants in *RPGR* gene including ORF15 exon.

The strengths of this test include:

- CAP accredited laboratory
- CLIA-certified personnel performing clinical testing in a CLIA-certified laboratory
- Powerful sequencing technologies, advanced target enrichment methods and precision bioinformatics pipelines ensure superior analytical performance
- Careful construction of clinically effective and scientifically justified gene panels
- Some of the panels include the whole mitochondrial genome (please see the Panel Content section)
- Our Nucleus online portal providing transparent and easy access to quality and performance data at the patient level
- Our publicly available analytic validation demonstrating complete details of test performance
- ~2,000 non-coding disease causing variants in our clinical grade NGS assay for panels (please see 'Non-coding disease causing variants covered by this panel' in the Panel Content section)
- Our rigorous variant classification scheme
- Our systematic clinical interpretation workflow using proprietary software enabling accurate and traceable processing of NGS data
- Our comprehensive clinical statements

Test Limitations

The following exons are not included in the panel as they are not sufficiently covered with high quality sequence reads: *CC2D2A* (NM_020785:7), *CHM* (NM_001145414:5), *CNGA1* (NM_001142564:2), *HK1* (NM_001322365:5), *IFT81* (NM_031473:12), *KIAA0586* (NM_001244189:6, 33), *NEK2* (NM_001204182:8), *NMNAT1* (NM_001297779:5), *PDSS1* (NM_014317:2), *PDZD7* (NM_024895:10), *RPGRIP1L* (NM_015272:23), *SCLT1* (NM_001300898:6), *TCTN1* (NM_001173976:2;NM_024549:6). Genes with suboptimal coverage in our assay are marked with number sign (#) and genes with partial, or whole gene, segmental

duplications in the human genome are marked with an asterisk (*) if they overlap with the UCSC pseudogene regions. Gene is considered to have suboptimal coverage when >90% of the gene's target nucleotides are not covered at >20x with mapping quality score (MQ>20) reads. The technology may have limited sensitivity to detect variants in genes marked with these symbols (please see the Panel content table above).

This test does not d etect the following:

- Complex inversions
- Gene conversions
- Balanced translocations
- Some of the panels include the whole mitochondrial genome (please see the Panel Content section)
- Repeat expansion disorders unless specifically mentioned
- Non-coding variants deeper than ±20 base pairs from exon-intron boundary unless otherwise indicated (please see above Panel Content / non-coding variants covered by the panel).

This test may not reliably detect the following:

- Low level mosaicism in nuclear genes (variant with a minor allele fraction of 14.6% is detected with 90% probability)
- Stretches of mononucleotide repeats
- Low level heteroplasmy in mtDNA (>90% are detected at 5% level)
- Indels larger than 50bp
- Single exon deletions or duplications
- Variants within pseudogene regions/duplicated segments
- Some disease causing variants present in mtDNA are not detectable from blood, thus post-mitotic tissue such as skeletal muscle may be required for establishing molecular diagnosis.

The sensitivity of this test may be reduced if DNA is extracted by a laboratory other than Blueprint Genetics.

For additional information, please refer to the Test performance section and see our Analytic Validation.

Test Performance

The genes on the panel have been carefully selected based on scientific literature, mutation databases and our experience.

Our panels are sectioned from our high-quality, clinical grade NGS assay. Please see our sequencing and detection performance table for details regarding our ability to detect different types of alterations (Table).

Assays have been validated for various sample types including EDTA-blood, isolated DNA (excluding from formalin fixed paraffin embedded tissue), saliva and dry blood spots (filter cards). These sample types were selected in order to maximize the likelihood for high-quality DNA yield. The diagnostic yield varies depending on the assay used, referring healthcare professional, hospital and country. Plus analysis increases the likelihood of finding a genetic diagnosis for your patient, as large deletions and duplications cannot be detected using sequence analysis alone. Blueprint Genetics' Plus Analysis is a combination of both sequencing and deletion/duplication (copy number variant (CNV)) analysis.

The performance metrics listed below are from an initial validation performed at our main laboratory in Finland. The performance metrics of our laboratory in Seattle, WA, are equivalent.

Performance of Blueprint Genetics high-quality, clinical grade NGS sequencing assay for panels.

	Sensitivity % (TP/(TP+FN)	Specificity %
Single nucleotide variants	99.89% (99,153/99,266)	>99.9999%
Insertions, deletions and indels by sequence analysis		
1-10 bps	99.2% (7,745/7,806)	>99.9999%
11-50 bps	99.13% (2,524/2,546)	>99.9999%

Copy number variants (exon level dels/dups)		
1 exon level deletion (heterozygous)	100% (20/20)	NA
1 exon level deletion (homozygous)	100% (5/5)	NA
1 exon level deletion (het or homo)	100% (25/25)	NA
2-7 exon level deletion (het or homo)	100% (44/44)	NA
1-9 exon level duplication (het or homo)	75% (6/8)	NA
Simulated CNV detection		
5 exons level deletion/duplication	98.7%	100.00%
Microdeletion/-duplication sdrs (large CNVs, n=37))		
Size range (0.1-47 Mb)	100% (25/25)	

The performance presented above reached by Blueprint Genetics high-quality, clinical grade NGS sequencing assay with the following coverage metrics

Mean sequencing depth	143X
Nucleotides with >20x sequencing coverage (%)	99.86%

Performance of Blueprint Genetics Mitochondrial Sequencing Assay.

	Sensitivity %	**Specificity %**
ANALYTIC VALIDATION (NA samples; n=4)		
Single nucleotide variants		
Heteroplasmic (45-100%)	100.0% (50/50)	100.0%
Heteroplasmic (35-45%)	100.0% (87/87)	100.0%
Heteroplasmic (25-35%)	100.0% (73/73)	100.0%
Heteroplasmic (15-25%)	100.0% (77/77)	100.0%
Heteroplasmic (10-15%)	100.0% (74/74)	100.0%
Heteroplasmic (5-10%)	100.0% (3/3)	100.0%
Heteroplasmic (<5%)	50.0% (2/4)	100.0%
CLINICAL VALIDATION (n=76 samples)		
All types		
Single nucleotide variants n=2026 SNVs		
Heteroplasmic (45-100%)	100.0% (1940/1940)	100.0%

Heteroplasmic (35-45%)	100.0% (4/4)	100.0%
Heteroplasmic (25-35%)	100.0% (3/3)	100.0%
Heteroplasmic (15-25%)	100.0% (3/3)	100.0%
Heteroplasmic (10-15%)	100.0% (9/9)	100.0%
Heteroplasmic (5-10%)	92.3% (12/13)	99.98%
Heteroplasmic (<5%)	88.9% (48/54)	99.93%
Insertions and deletions by sequence analysis n=40 indels		
Heteroplasmic (45-100%) 1-10bp	100.0% (32/32)	100.0%
Heteroplasmic (5-45%) 1-10bp	100.0% (3/3)	100.0%
Heteroplasmic (<5%) 1-10bp	100.0% (5/5)	99,997%
SIMULATION DATA /(mitomap mutations)		
Insertions, and deletions 1-24 bps by sequence analysis; n=17		
Homoplasmic (100%) 1-24bp	100.0% (17/17)	99.98%
Heteroplasmic (50%)	100.0% (17/17)	99.99%
Heteroplasmic (25%)	100.0% (17/17)	100.0%
Heteroplasmic (20%)	100.0% (17/17)	100.0%
Heteroplasmic (15%)	100.0% (17/17)	100.0%
Heteroplasmic (10%)	94.1% (16/17)	100.0%
Heteroplasmic (5%)	94.1% (16/17)	100.0%
Copy number variants (separate artifical mutations; n=1500)		
Homoplasmic (100%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (50%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (30%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (20%) 500 bp, 1kb, 5 kb	99.7%	100.0%
Heteroplasmic (10%) 500 bp, 1kb, 5 kb	99.0%	100.0%
The performance presented above reached by following coverage metrics at assay level (n=66)		
	Mean of medians	Median of medians
Mean sequencing depth MQ0 (clinical)	18224X	17366X
Nucleotides with >1000x MQ0 sequencing coverage (%) (clinical)	100%	
rho zero cell line (=no mtDNA), mean sequencing depth	12X	

Bioinformatics

The target region for each gene includes coding exons and ±20 base pairs from the exon-intron boundary. In addition, the panel includes non-coding variants if listed above (Non-coding variants covered by the panel). Some regions of the gene(s) may be removed from the panel if specifically mentioned in the 'Test limitations" section above. The sequencing data generated in our laboratory is analyzed with our proprietary data analysis and annotation pipeline, integrating state-of-the art algorithms and industry-standard software solutions. Incorporation of rigorous quality control steps throughout the workflow of the pipeline ensures the consistency, validity and accuracy of results. Our pipeline is streamlined to maximize sensitivity without sacrificing specificity. We have incorporated a number of reference population databases and mutation databases such as, but not limited, to 1000 Genomes Project, gnomAD, ClinVar and HGMD into our clinical interpretation software to make the process effective and efficient. For missense variants, *in silico* variant prediction tools such as SIFT, PolyPhen, MutationTaster are used to assist with variant classification. Through our online ordering and statement reporting system, Nucleus, the customer has an access to details of the analysis, including patient specific sequencing metrics, a gene level coverage plot and a list of regions with inadequate coverage if present. This reflects our mission to build fully transparent diagnostics where customers have easy access to crucial details of the analysis process.

Clinical Interpretation

We provide customers with the most comprehensive clinical report available on the market. Clinical interpretation requires a fundamental understanding of clinical genetics and genetic principles. At Blueprint Genetics, our PhD molecular geneticists, medical geneticists and clinical consultants prepare the clinical statement together by evaluating the identified variants in the context of the phenotypic information provided in the requisition form. Our goal is to provide clinically meaningful statements that are understandable for all medical professionals regardless of whether they have formal training in genetics.

Variant classification is the corner stone of clinical interpretation and resulting patient management decisions. Our classifications follow the ACMG guideline 2015.

The final step in the analysis of sequence variants is confirmation of variants classified as pathogenic or likely pathogenic using bi-directional Sanger sequencing. Variant(s) fulfilling the following criteria are not Sanger confirmed: the variant quality score is above the internal threshold for a true positive call, and visual check-up of the variant at IGV is in-line with the variant call. Reported variants of uncertain significance are confirmed with bi-directional Sanger sequencing only if the quality score is below our internally defined quality score for true positive call. Reported copy number variations with a size <10 exons are confirmed by orthogonal methods such as qPCR if the specific CNV has been seen less than three times at Blueprint Genetics.

Our clinical statement includes tables for sequencing and copy number variants that include basic variant information (genomic coordinates, HGVS nomenclature, zygosity, allele frequencies, in silico predictions, OMIM phenotypes and classification of the variant). In addition, the statement includes detailed descriptions of the variant, gene and phenotype(s) including the role of the specific gene in human disease, the mutation profile, information about the gene's variation in population cohorts and detailed information about related phenotypes. We also provide links to the references used, congress abstracts and mutation variant databases used to help our customers further evaluate the reported findings if desired. The conclusion summarizes all of the existing information and provides our rationale for the classification of the variant.

Identification of pathogenic or likely pathogenic variants in dominant disorders or their combinations in different alleles in recessive disorders are considered molecular confirmation of the clinical diagnosis. In these cases, family member testing can be used for risk stratification within the family. In the case of variants of uncertain significance (VUS), we do not recommend family member risk stratification based on the VUS result. Furthermore, in the case of VUS, we do not recommend the use of genetic information in patient management or genetic counseling.

Our interpretation team analyzes millions of variants from thousands of individuals with rare diseases. Thus, our database, and our understanding of variants and related phenotypes, is growing by leaps and bounds. Our laboratory is therefore well positioned to re-classify previously reported variants as new information becomes available. If a variant previously reported by Blueprint Genetics is re-classified, our laboratory will issue a follow-up statement to the original ordering health care provider at no additional cost.

Blueprint Genetics

Reference information

Recommendations on Clinical Assessment of Patients with Inherited Retinal Degenerations – 2016

CPT code(s) *

81434, 81460, 81465

* The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

ICD Codes

Refer to the most current version of ICD-10-CM manual for a complete list of ICD-10 codes.

Sample Requirements

- Blood (min. 1ml) in an EDTA tube
- Extracted DNA, min. 2 µg in TE buffer or equivalent
- Saliva (Please see Sample Requirements for accepted saliva kits)

Label the sample tube with your patient's name, date of birth and the date of sample collection.

We do not accept DNA samples isolated from formalin-fixed paraffin-embedded (FFPE) tissue. In addition, if the patient is affected with a hematological malignancy, DNA extracted from a non-hematological source (e.g. skin fibroblasts) is strongly recommended.

Please note that, in rare cases, mitochondrial genome (mtDNA) variants may not be detectable in blood or saliva in which case DNA extracted from post-mitotic tissue such as skeletal muscle may be a better option.

Read more about our sample requirements here.

For Patients

Other

- American Academy of Ophthalmology. Guideline. 2016. Recommendations of Clinical Assessment of Patients with Inherited Retinal Degeneration - 2016.
- Cohen Syndrome Association
- European Leukodystrophies Association
- Fighting Blindness - Cone Rod Dystrophies
- Fighting Blindness - Stargardts Disease
- Foundation Fighting Blindness - Retinitis Pigmentosa
- Foundation Fighting Blindness - Stargardt Disease
- GARD - CSNB
- GeneReviews - Bardet-Biedl Syndrome
- GeneReviews - Congenital Stationary Night Blindness
- GeneReviews - Familial Exudative Vitreoretinopathy
- GeneReviews - Stickler Syndrome
- GeneReviews - Usher Syndrome Type II
- GeneReviews - X-linked Retinoschisis

- GeneReviews - X-linked retinoschisis
- Joubert Syndrome & Related Disorders Foundation
- NORD - Bardet-Biedl Syndrome
- NORD - Refsum Disease
- NORD - Retinitis Pigmentosa
- NORD - Senior-Loken Syndrome
- NORD - Usher Syndrome
- NORD - X-linked retinoschisis
- Norrie Disease Association
- Patient information UK
- RetNet - Retinal Information Network
- Royal National Institute of Blind People - Retinitis Pigmentosa
- Stone EM et al. 2017. Clinically Focused Molecular Investigation of 1000 Consecutive Families with Inherited Retinal Disease. Ophthalmology. 2017 Sep;124(9):1314-1331.
- The Vision Institut
- The Vision Institut - FEVR
- Usher Syndrome Coalition