Blueprint Genetics

Comprehensive Cardiology Panel

Test code: CA1301

Is a 260 gene panel that includes assessment of non-coding variants.

In addition, it also includes the maternally inherited mitochondrial genome.
The Comprehensive Cardiology Panel covers known genetic causes of channelopathies and cardiomyopathies. It is ideal for patients in whom the phenotype is complex including features of both channelopathy and cardiomyopathy and for the investigation of sudden cardiac death as this panel includes all of our channelopathy and cardiomyopathy genes.

About Comprehensive Cardiology

When a person dies suddenly and unexpectedly from a suspected cardiovascular cause, the term sudden cardiac death (SCD) is used. SCD is frequently caused by an abrupt change in heart rhythm (arrhythmia), most often ventricular tachycardia or ventricular fibrillation that impairs cardiac pumping, thereby depriving vital organs of oxygenated blood. A brief episode of VT or VF may cause only momentary loss of consciousness (syncope), but death is the inevitable result of sustained VF in the absence of emergent medical care. The differential diagnosis between ion channel disease and cardiomyopathies can be challenging on occasion as severe ventricular arrhythmias can manifest in cardiomyopathy patients with subclinical or no morphological cardiomyopathy.

Availability

4 weeks

Gene Set Description

Genes in the Comprehensive Cardiology Panel and their clinical significance

Gene	Associated phenotypes	Inheritance	ClinVar	HGMD
AARS2	Leukoencephalopathy, progressive, with ovarian failure, Combined oxidative phosphorylation deficiency 8	AR	19	31
ABCC6*	Pseudoxanthoma elasticum	AR	352	377
ABCC9	Atrial fibrillation, Cantu syndrome, Dilated cardiomyopathy (DCM)	AD	27	46
ACAD9	Acyl-CoA dehydrogenase family, deficiency	AR	26	61
ACADVL	Acyl-CoA dehydrogenase, very long chain, deficiency	AR	119	282
ACTA1	Myopathy	AD/AR	68	212
ACTA2	Aortic aneurysm, familial thoracic, Moyamoya disease, Multisystemic smooth muscle dysfunction syndrome	AD	20	76
ACTC1	Left ventricular noncompaction, Hypertrophic cardiomyopathy (HCM), Cardiomyopathy, restrictive, Atrial septal defect, Dilated cardiomyopathy (DCM)	AD	23	63
ACTN2	Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD	11	44
AGK*	Sengers syndrome, Cataract 38	AR	18	27
AGL	Glycogen storage disease	AR	142	245

AGPAT2	Lipodystrophy, congenital generalized	AR	25	39
AKAP9	Long QT syndrome	AD	4	38
ALMS1*	Alström syndrome	AR	197	302
ALPK3	Pediatric cardiomyopathy	AR	12	6
ANK2	Cardiac arrhythmia, Long QT syndrome	AD	6	73
ANO5	Gnathodiaphyseal dysplasia, LGMD2L and distal MMD3 muscular dystrophies	AD/AR	64	121
APOA1	Amyloidosis, systemic nonneuronopathic, Hypoalphalipoproteinemia	AD/AR	28	71
ATPAF2	Mitochondrial complex V (ATP synthase) deficiency, nuclear type 1	AR	3	1
BAG3	Dilated cardiomyopathy (DCM), Myopathy, myofibrillar	AD	39	62
BRAF*	LEOPARD syndrome, Noonan syndrome, Cardiofaciocutaneous syndrome	AD	134	65
CACNA1C*	Brugada syndrome, Timothy syndrome, Neurodevelopmental disorder	AD	19	68
CACNA1D	Primary aldosteronism, seizures, and neurologic abnormalities, Sinoatrial node dysfunction and deafness	AD/AR	7	8
CACNB2	Brugada syndrome	AD	4	22
CALM1*	Ventricular tachycardia, catecholaminergic polymorphic, Recurrent cardiac arrest, infantile, Long QT syndrome	AD	10	10
CALM2	Long QT syndrome	AD	8	10
CALM3	Catecholaminergic polymorphic ventricular tachycardia	AD/AR	4	4
CALR3	Cardiomyopathy, familial hypertrophic, 19	AD		3
CAPN3	Muscular dystrophy, limb-girdle, Eosinophilic myositis	AD/AR	184	437
CASQ2	Ventricular tachycardia, catecholaminergic, polymorphic	AR	24	34
CASZ1	Dilated cardiomyopathy (DCM), Ventricular septal defect	AD	3	2
CAV3	Creatine phosphokinase, elevated serum, Hypertrophic cardiomyopathy (HCM), Long QT syndrome, Muscular dystrophy, limb-girdle, type IC, Myopathy, distal, Tateyama type, Rippling muscle disease 2	AD/AR	23	50
CBL	Noonan syndrome-like disorder with or without juvenile myelomonocytic leukemia	AD	24	43
CDH2	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	AD	1	6
CHKB	Muscular dystrophy, congenital, megaconial	AR	11	27
CHRM2	Dilated cardiomyopathy (DCM)	AD/AR		1
COX15	Leigh syndrome, Cardioencephalomyopathy, fatal infantile, due to cytochrome c oxidase deficiency	AR	7	5

CPT2	Carnitine palmitoyltransferase II deficiency	AR	72	111
CRYAB	Cataract, myofibrillar myopathy and cardiomyopathy, Congenital cataract and cardiomyopathy, Dilated cardiomyopathy (DCM), Myopathy, myofibrillar, Cataract 16, multiple types, Myopathy, myofibrillar, fatal infantile hypertonic, alpha-B crystallin-related	AD	14	28
CSRP3	Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD	4	30
CTNNA3	Arrhythmogenic right ventricular dysplasia	AD	7	46
DBH	Dopamine beta-hydroxylase deficiency	AR	10	11
DES	Dilated cardiomyopathy (DCM), Myopathy, myofibrillar, Scapuloperoneal syndrome, neurogenic, Kaeser type	AD/AR	64	124
DMD	Becker muscular dystrophy, Duchenne muscular dystrophy, Dilated cardiomyopathy (DCM)	XL	832	3915
DNAJC19	3-methylglutaconic aciduria	AR	3	6
DOLK	Congenital disorder of glycosylation	AR	8	11
DPM3	Congenital disorder of glycosylation, Dilated cardiomyopathy (DCM), Limb-girdle muscular dystrophy	AR	3	2
DSC2	Arrhythmogenic right ventricular dysplasia with palmoplantar keratoderma and woolly hair, Arrhythmogenic right ventricular dysplasia	AD/AR	32	87
DSG2	Arrhythmogenic right ventricular dysplasia, Dilated cardiomyopathy (DCM)	AD	44	129
DSP	Cardiomyopathy, dilated, with wooly hair, keratoderma, and tooth agenesis, Arrhythmogenic right ventricular dysplasia, familial, Cardiomyopathy, dilated, with wooly hair and keratoderma, Keratosis palmoplantaris striata II, Epidermolysis bullosa, lethal acantholytic	AD/AR	177	296
DTNA	Left ventricular noncompaction 1	AD	3	7
DYSF	Miyoshi muscular dystrophy, Muscular dystrophy, limb-girdle, Myopathy, distal, with anterior tibial onset	AR	244	529
EEF1A2	Epileptic encephalopathy, early infantile, Mental retardation	AD	17	12
ELAC2	Combined oxidative phosphorylation deficiency 17	AR	11	15
EMD	Emery-Dreifuss muscular dystrophy	XL	48	113
ENPP1	Arterial calcification, Hypophosphatemic rickets	AD/AR	22	72
EPG5	Vici syndrome	AR	36	66
ETFA	Glutaric aciduria, Multiple acyl-CoA dehydrogenase deficiency	AR	8	29
ETFB	Glutaric aciduria, Multiple acyl-CoA dehydrogenase deficiency	AR	6	15
ETFDH	Glutaric aciduria, Multiple acyl-CoA dehydrogenase deficiency	AR	43	190
FAH	Tyrosinemia	AR	53	102

FBXL4	Mitochondrial DNA depletion syndrome	AR	55	47
FBXO32	Dilated cardiomyopathy (DCM)	AD/AR		2
FHL1*	Myopathy with postural muscle atrophy, Emery-Dreifuss muscular dystrophy, Reducing bod myopathy	XL	26	62
FHOD3	Cardiomyopathy, familial hypertrophic	AD		1
FKRP	Muscular dystrophy-dystroglycanopathy	AR	66	140
FKTN	Muscular dystrophy-dystroglycanopathy, Dilated cardiomyopathy (DCM), Muscular dystrophy-dystroglycanopathy (limb-girdle)	AD/AR	45	58
FLNC*	Myopathy	AD	54	109
FOXD4*	Dilated cardiomyopathy (DCM)	AD		1
FOXRED1	Leigh syndrome, Mitochondrial complex I deficiency	AR	15	8
FXN*	Friedreich ataxia	AR	13	63
GAA	Glycogen storage disease	AR	193	573
GATA4	Tetralogy of Fallot, Atrioventricular septal defect, Testicular anomalies with or without congenital heart disease, Ventricular septal defect, Atrial septal defect	AD	37	140
GATA5	Familial atrial fibrillation, Tetralogy of Fallot, Single ventricular septal defect	AD	5	32
GATA6	Heart defects, congenital, and other congenital anomalies, Atrial septal defect 9, atrioventricular septal defect 5, Persistent truncus arteriosus, Tetralogy of Fallot	AD	16	82
GATAD1	Dilated cardiomyopathy (DCM)	AR	31	1
GATC	Cardiomyopathy, fatal	AR	1	
GBE1	Glycogen storage disease	AR	36	70
GFM1	Combined oxidative phosphorylation deficiency	AR	19	19
GLA	Fabry disease	XL	226	937
GLB1	GM1-gangliosidosis, Mucopolysaccharidosis (Morquio syndrome)	AR	90	220
GMPPB	Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), Limb-girdle muscular dystrophy-dystroglycanopathy	AR	19	41
GNB5	Intellectual developmental disorder with cardiac arrhythmia (IDDCA), Language delay and attention deficit-hyperactivity disorder/cognitive impairment with or without cardiac arrhythmia (LADCI)	AR	9	10
GSK3B	Hypertrophic cardiomyopathy, Dilated cardiomyopathy (DCM)		2	
GTPBP3	Combined oxidative phosphorylation deficiency 23	AR	14	15
GUSB*	Mucopolysaccharidosis	AR	27	62

HADHA	Trifunctional protein deficiency, Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency	AR	65	71
HAND1	Congenital heart defects, Dilated cardiomyopathy	AD		9
HAND2	Dilated cardiomyopathy (DCM), Congenital heart malformations	AD	2	5
HCN4	Sick sinus syndrome, Brugada syndrome, Left ventricular non-compaction cardiomyopathy (LVNC)	AD	8	34
HFE	Hemochromatosis	AR/Digenic	11	56
HRAS	Costello syndrome, Congenital myopathy with excess of muscle spindles	AD	43	31
IDUA	Mucopolysaccharidosis	AR	105	282
ILK	Dilated cardiomyopathy (DCM)	AD		10
ISPD	Muscular dystrophy-dystroglycanopathy	AR	38	53
JPH2	Hypertrophic cardiomyopathy (HCM)	AD	3	13
JUP	Arrhythmogenic right ventricular dysplasia, Naxos disease	AD/AR	8	46
KCNA5	Atrial fibrillation	AD	4	25
KCNE1	Long QT syndrome, Jervell and Lange-Nielsen syndrome	AD/AR/Digenic	11	46
KCNE2	Long QT syndrome, Atrial fibrillation, familial	AD	5	24
KCNH2	Short QT syndrome, Long QT syndrome	AD	371	933
KCNJ2	Short QT syndrome, Andersen syndrome, Long QT syndrome, Atrial fibrillation	AD	41	93
KCNJ5	Long QT syndrome, Hyperaldosteronism, familial	AD	7	15
KCNQ1	Short QT syndrome, Long QT syndrome, Atrial fibrillation, Jervell and Lange-Nielsen syndrome	AD/AR/Digenic	298	631
KLHL24	Epidermolysis bullosa simplex, generalized, with scarring and hair loss, Dilated cardiomyopathy (DCM), Hypertrophic cardiomyopathy (HCM)	AD/AR	5	5
KRAS*	Noonan syndrome, Cardiofaciocutaneous syndrome	AD	63	35
LAMA2	Muscular dystrophy, congenital merosin-deficient	AR	199	301
LAMP2	Danon disease	XL	62	101
LARGE	Muscular dystrophy-dystroglycanopathy	AR	19	27
LDB3	Dilated cardiomyopathy (DCM), Myopathy, myofibrillar	AD	9	14
LEMD2	Cataract 46, juvenile onset, Arrhythmogenic right ventricular cardiomyopathy (ARVC), Dilated cardiomyopathy (DCM)	AR	1	1

LMNA	Heart-hand syndrome, Slovenian, Limb-girdle muscular dystrophy, Muscular dystrophy, congenital, LMNA-related, Lipodystrophy (Dunnigan), Emery-Dreiffus muscular dystrophy, Malouf syndrome, Dilated cardiomyopathy (DCM), Mandibuloacral dysplasia type A, Progeria Hutchinson-Gilford type	AD/AR	250	564
LMOD2	Familial dilated cardiomyopathy	AR		
LRRC10	Dilated cardiomyopathy (DCM)	AD/AR		4
LZTR1	Schwannomatosis, Noonan syndrome	AD/AR	34	71
MAP2K1	Cardiofaciocutaneous syndrome	AD	45	23
MAP2K2	Cardiofaciocutaneous syndrome	AD	21	35
MAP3K8	Noonan syndrome	AD		1
MIPEP	Combined oxidative phosphorylation deficiency 31	AR	5	8
MLYCD	Malonyl-CoA decarboxylase deficiency	AR	14	38
MRPL3	Combined oxidative phosphorylation deficiency 9	AR	2	4
MRPL44	Combined oxidative phosphorylation deficiency 16	AR	2	2
MRPS22	Combined oxidative phosphorylation deficiency 5	AR	7	9
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	
MTO1	Combined oxidative phosphorylation deficiency	AR	16	24
MYBPC3	Left ventricular noncompaction, Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD	482	1048
MYBPHL	Dilated cardiomyopathy (DCM)	AD		3
MYH6	Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM), Atrial septal defect 3	AD	14	123
MYH7	Hypertrophic cardiomyopathy (HCM), Myopathy, myosin storage, Myopathy, distal, Dilated cardiomyopathy (DCM)	AD	305	986
MYL2	Hypertrophic cardiomyopathy (HCM), Infantile type I muscle fibre disease and cardiomyopathy	AD	21	67
MYL3	Hypertrophic cardiomyopathy (HCM)	AD/AR	12	41
MYL4	Atrial fibrillation, familial, 18	AD	2	2
MYO18B	Klippel-Feil syndrome 4, autosomal recessive, with myopathy and facial dysmorphism	AR	2	4
MYOT	Myopathy, myofibrillar, Muscular dystrophy, limb-girdle, 1A, Myopathy, spheroid body	AD	6	16
MYPN	Hypertrophic cardiomyopathy (HCM), Cardiomyopathy, restrictive, Dilated cardiomyopathy (DCM), Nemaline myopathy 11, autosomal recessive	AD	6	44
MYRF	Congenital heart malformations, Congenital abnormalities of the kidney and urinary tract	AD	1	1
NDUFAF2	Mitochondrial complex I deficiency, Leigh syndrome	AR	9	8
NDUFB11	Linear skin defects with multiple congenital anomalies 3	AD	4	6
NEXN	Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD	6	43
NF1*	Watson syndrome, Neurofibromatosis, Neurofibromatosis-Noonan syndrome	AD	1157	2901
NKX2-5	Conotruncal heart malformations, Hypothyroidism, congenital nongoitrous,, Atrial septal defect, Ventricular septal defect 3, Conotruncal heart malformations, variable, Tetralogy of Fallot	AD	45	108
NONO	Mental retardation, X-linked, syndrome 34, Left ventricular non-compaction cardiomyopathy (LVNC)	XL	10	4
NOS1AP	Romano-Ward syndrome	AD/AR		4
NRAP	Dilated cardiomyopathy (DCM)	AR	1	6

NRAS	Noonan syndrome	AD	31	14
NUP155	Atrial fibrillation 15	AR	2	1
PARS2	Alpers syndrome	AR	3	6
PCCA	Propionic acidemia	AR	66	125
PCCB	Propionic acidemia	AR	68	115
PKP2*	Arrhythmogenic right ventricular dysplasia	AD	150	289
PLEC	Muscular dystrophy, limb-girdle, Epidermolysis bullosa	AD/AR	36	103
PLEKHM2	Dilated cardiomyopathy (DCM), left ventricular noncompaction	AR	1	1
PLN	Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD/AR	8	30
PNPLA2	Neutral lipid storage disease with myopathy	AR	13	35
POMT1	Muscular dystrophy-dystroglycanopathy	AR	47	96
PPA2	Sudden cardiac failure, infantile	AR	8	8
PPCS	Dilated cardiomyopathy (DCM)	AR		4
PPP1CB#	Noonan syndrome-like disorder with loose anagen hair 2	AD	8	11
PRDM16	Left ventricular noncompaction, Dilated cardiomyopathy (DCM)	AD	17	20
PRKAG2#	Hypertrophic cardiomyopathy (HCM), Wolff-Parkinson-White syndrome, Glycogen storage disease of heart, lethal congenital	AD	19	57
PTPN11	Noonan syndrome, Metachondromatosis	AD	135	140
QRSL1	Mitochondrial multisystemic disorder	AR	4	2
RAF1	LEOPARD syndrome, Noonan syndrome, Dilated cardiomyopathy (DCM)	AD	45	53
RASA2#	Noonan syndrome	AD	1	3
RBCK1	Polyglucosan body myopathy	AR	11	14
RBM20	Dilated cardiomyopathy (DCM)	AD	19	47
RIT1	Noonan syndrome	AD	23	26
RMND1*	Combined oxidative phosphorylation deficiency	AR	17	15
RRAS	Noonan-syndrome like phenotype	AD/AR		2
RYR2	Ventricular tachycardia, catecholaminergic polymorphic, Arrhythmogenic right ventricular dysplasia	AD	124	372
SALL4	Acro-renal-ocular syndrome, Duane-radial ray/Okihiro syndrome	AD	21	56
SCN10A	Paroxysmal extreme pain disorder, Channelopathy-associated congenital insensitivity to pain, Primary erythermalgia, Sodium channelopathy-related small fiber neuropathy, Brugada syndrome	AD/AR	2	76

SCN1B	Atrial fibrillation, Brugada syndrome, Generalized epilepsy with febrile seizures plus, Epilepsy, generalized, with febrile seizures plus, type 1, Epileptic encephalopathy, early infantile, 52	AD	16	31
SCN3B	Atrial fibrillation, familial, Brugada syndrome	AD	3	7
SCN5A	Heart block, nonprogressive, Heart block, progressive, Long QT syndrome, Ventricular fibrillation, Atrial fibrillation, Sick sinus syndrome, Brugada syndrome, Dilated cardiomyopathy (DCM)	AD/AR/Digenic	234	899
SCNN1B	Liddle syndrome, Pseudohypoaldosteronism, Bronchiectasis with or without elevated sweat chloride	AD/AR	19	47
SCNN1G	Liddle syndrome, Pseudohypoaldosteronism, Bronchiectasis with or without elevated sweat chloride	AD/AR	8	20
SCO1	Mitochondrial complex IV deficiency	AR	6	5
SCO2	Leigh syndrome, Hypertrophic cardiomyopathy (HCM), Cardioencephalomyopathy, fatal infantile, due to cytochrome c oxidase deficiency, Myopia	AR	42	37
SDHA*	Leigh syndrome/Mitochondrial respiratory chain complex II deficiency, Gastrointestinal stromal tumor, Paragangliomas, Dilated cardiomyopathy (DCM), Cardiomyopathy, dilated, 1GG	AD/AR	54	87
SELENON	Muscular dystrophy, rigid spine, Myopathy, congenital, with fiber-disproportion	AR	38	63
SGCA	Muscular dystrophy, limb-girdle	AR	60	100
SGCB	Muscular dystrophy, limb-girdle	AR	37	64
SGCD	Muscular dystrophy, limb-girdle, Dilated cardiomyopathy (DCM)	AR	21	27
SGCG	Muscular dystrophy, limb-girdle	AR	33	63
SHOC2	Noonan-like syndrome with loose anagen hair	AD	2	4
SLC12A3	Gitelman syndrome	AR	49	489
SLC22A5	Carnitine deficiency, systemic primary	AR	98	151
SLC25A20	Carnitine-acylcarnitine translocase deficiency	AR	15	42
SLC25A3	Micochondrial phosphate carrier deficiency	AR	2	5
SLC25A4	Progressive external ophthalmoplegia with mitochondrial DNA deletions, Mitochondrial DNA depletion syndrome	AD/AR	12	14
SMCHD1	Facioscapulohumeral muscular dystrophy, Facioscapulohumeral muscular dystrophy, type 2	AD	51	79
SOS1	Noonan syndrome	AD	44	71
SOS2	Noonan syndrome 9	AD	4	6
SPEG	Centronuclear myopathy 5	AR	5	11
SPRED1	Legius syndrome	AD	38	71

STAG2	Congenital heart defects, dysmorphic facial features, and intellectual developmental disorder	XL	6	14
TAB2	Congenital heart defects, multiple types, 2	AD	13	31
TANGO2	Metabolic encephalomyopathic crises, recurrent, with rhabdomyolysis, cardiac arrhythmias, and neurodegeneration (MECRCN)	AR	13	9
TAZ	3-Methylglutaconic aciduria, (Barth syndrome)	XL	45	158
TBX20*	Atrial septal defect 4	AD	4	28
TBX5	Holt-Oram syndrome	AD	61	127
TCAP	Muscular dystrophy, limb-girdle, Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD/AR	12	28
TECRL	Ventricular tachycardia, catecholaminergic polymorphic, 3	AR	2	3
TGFB3	Loeys-Dietz syndrome (Reinhoff syndrome), Arrhythmogenic right ventricular dysplasia	AD	19	26
TMEM43	Arrhythmogenic right ventricular dysplasia, Emery-Dreifuss muscular dystrophy	AD	4	24
TMEM70	Mitochondrial complex V (ATP synthase) deficiency	AR	12	18
TNNC1	Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD	9	24
TNNI3	Hypertrophic cardiomyopathy (HCM), Cardiomyopathy, restrictive, Dilated cardiomyopathy (DCM)	AD/AR	56	129
TNNI3K	Cardiac conduction disease with or without dilated cardiomyopathy	AD	1	3
TNNT2	Left ventricular noncompaction, Hypertrophic cardiomyopathy (HCM), Cardiomyopathy, restrictive, Dilated cardiomyopathy (DCM)	AD	61	148
TOR1AIP1	Muscular dystrophy with progressive weakness, distal contractures and rigid spine	AD/AR	3	5
TPM1	Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD	34	98
TRDN	Ventricular tachycardia, catecholaminergic polymorphic	AR	19	6
TRIM32	Bardet-Biedl syndrome, Muscular dystrophy, limb-girdle	AR	13	16
TRPM4	Progressive familial heart block	AD	5	32
TSFM	Combined oxidative phosphorylation deficiency	AR	6	6
TTN*	Dilated cardiomyopathy (DCM), Tibial muscular dystrophy, Limb-girdle muscular dystrophy, Hereditary myopathy with early respiratory failure, Myopathy, early-onset, with fatal cardiomyopathy (Salih myopathy), Muscular dystrophy, limb-girdle, type 2J	AD	818	327
TTR	Dystransthyretinemic hyperthyroxinemia, Amyloidosis, hereditary, transthyretin-related	AD	52	148
VARS2	Combined oxidative phosphorylation deficiency 20	AR	7	10

VCL	Hypertrophic cardiomyopathy (HCM), Dilated cardiomyopathy (DCM)	AD	8	30
VCP	Amyotrophic lateral sclerosis, Inclusion body myopathy with early-onset Paget disease, Charcot-Marie-Tooth disease	AD	17	61
VPS13A	Choreoacanthocytosis	AR	19	115
XK	McLeod syndrome	XL	10	41

*

Some, or all, of the gene is duplicated in the genome. Read more.

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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
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
ACADVL	Chr17:7123160	c.-144_-132delCCCAGCATGCCCCinsT	NM_000018.3	
ACADVL	Chr17:7125469	c.822-27C>T	NM_001270447.1	rs374911841
ACADVL	Chr17:7125485	c.822-11T>G	NM_001270447.1	
ACADVL	Chr17:7126199	c.1146+15C>T	NM_001270447.1	rs202237278
ACADVL	Chr17:7126948	c.1252-15A>G	NM_001270447.1	rs765390290
ACADVL	Chr17:7127894	c.1747+23C>T	NM_001270447.1	rs147546456
ACTC1	Chr15:35080829	c.*1784T>C	NM_005159.4	
AGL	Chr1:100381954	c.4260-12A>G	NM_000028.2	rs369973784

APOA1	Chr11:116708299	c.-21+22G>A	NM_000039.1	
APOA1	Chr11:116708365	c.-65A>C	NM_000039.1	
CAPN3	Chr15:42678352	c.380-13T>A	NM_000070.2	
CAPN3	Chr15:42695919	c.1746-20C>T	NM_000070.2	
CAPN3	Chr15:42697047	c.-188G>C	NM_173089.1	
CAPN3	Chr15:42702715	c.2184+21G>A	NM_000070.2	rs763572829
CAPN3	Chr15:42702770	c.2185-16A>G	NM_000070.2	
DMD	ChrX:31165653	c.10554-18C>G	NM_004006.2	
DMD	ChrX:31200680	c.9974+175T>A	NM_004006.2	
DMD	ChrX:31224814	c.9564-30A>T	NM_004006.2	
DMD	ChrX:31225211	c.9564-427T>G	NM_004006.2	
DMD	ChrX:31226400	c.9563+1215A>G	NM_004006.2	
DMD	ChrX:31229031	c.9362-1215A>G	NM_004006.2	
DMD	ChrX:31241047	c.9361+117A>G	NM_004006.2	
DMD	ChrX:31279293	c.9225-160A>G	NM_004006.2	
DMD	ChrX:31279418	c.9225-285A>G	NM_004006.2	
DMD	ChrX:31279420	c.9225-287C>A	NM_004006.2	
DMD	ChrX:31279780	c.9225-647A>G	NM_004006.2	rs398124091
DMD	ChrX:31279781	c.9225-648A>G	NM_004006.2	rs398124084
DMD	ChrX:31332523	c.9224+9192C>A	NM_004006.2	
DMD	ChrX:31382270	c.9085-15519G>T	NM_004006.2	
DMD	ChrX:31613687	c.8217+32103G>T	NM_004006.2	
DMD	ChrX:31627738	c.8217+18052A>G	NM_004006.2	
DMD	ChrX:31697714	c.7661-11T>C	NM_004006.2	
DMD	ChrX:31897527	c.6913-4037T>G	NM_004006.2	
DMD	ChrX:31983146	c.6614+3310G>T	NM_004006.2	rs797045526
DMD	ChrX:32274692	c.6290+30954C>T	NM_004006.2	
DMD	ChrX:32305833	c.6118-15A>G	NM_004006.2	
DMD	ChrX:32360414	c.5740-15G>T	NM_004006.2	
DMD	ChrX:32366860	c.5326-215T>G	NM_004006.2	
DMD	ChrX:32379144	c.5325+1743_5325+1760delTATTAAAAAATGGGTAGA	NM_004006.2	
DMD	ChrX:32398808	c.4675-11A>G	NM_004006.2	
DMD	ChrX:32460274	c.3787-843C>A	NM_004006.2	
DMD	ChrX:32470726	c.3603+2053G>C	NM_004006.2	
DMD	ChrX:32479316	c.3432+2240A>G	NM_004006.2	
DMD	ChrX:32479520	c.3432+2036A>G	NM_004006.2	

DMD	ChrX:32669100	c.961-5831C>T	NM_004006.2	rs398124099
DMD	ChrX:32669194	c.961-5925A>C	NM_004006.2	
DMD	ChrX:32716130	c.832-15A>G	NM_004006.2	rs72470513
DMD	ChrX:32756908	c.650-39498A>G	NM_004006.2	
DMD	ChrX:32827744	c.531-16T>A/G	NM_004006.2	
DMD	ChrX:32827744	c.531-16T>A	NM_004006.2	
DMD	ChrX:32827744	c.531-16T>G	NM_004006.2	
DMD	ChrX:32841967	c.265-463A>G	NM_004006.2	
DMD	ChrX:33032666	c.93+5590T>A	NM_004006.2	
DMD	ChrX:33192452	c.31+36947G>A	NM_004006.2	
DMD	ChrX:33229483	c.-54T>A	NM_004006.2	
DSC2	Chr18:28683379	c.-1445G>C	NM_024422.4	rs75494355
DYSF	Chr2:71817308	c.3443-33A>G	NM_003494.3	rs786205083
DYSF	Chr2:71840553	c.4410+13T>G	NM_003494.3	
DYSF	Chr2:71889030	c.4886+1249G>T	NM_003494.3	
DYSF	Chr2:71900503	c.5668-824C>T	NM_003494.3	
DYSF	Chr2:71913729	c.*107T>A	NM_003494.3	rs11903223
EMD	ChrX:153608559	c.266-27_266-10delTCTGCTACCGCTGCCCCC	NM_000117.2	
ETFDH	Chr4:159593534	c.-75A>G	NM_004453.2	
ETFDH	Chr4:159602711	c.176-636C>G	NM_004453.2	
FKRP	Chr19:47249328	c.-272G>A	NM_024301.4	
FKTN	Chr9:108368857	c.648-1243G>T	NM_006731.2	
GAA	Chr17:78078341	c.-32-13T>G	NM_000152.3	rs386834236
GAA	Chr17:78078341	c.-32-13T>A	NM_000152.3	
GAA	Chr17:78078351	c.-32-3C>A/G	NM_000152.3	
GAA	Chr17:78078352	c.-32-2A>G	NM_000152.3	
GAA	Chr17:78078353	c.-32-1G>C	NM_000152.3	
GAA	Chr17:78078369	c.-17C>T	NM_000152.3	
GAA	Chr17:78082266	c.1076-22T>G	NM_000152.3	rs762260678
GAA	Chr17:78090422	c.2190-345A>G	NM_000152.3	
GAA	Chr17:78092432	c.2647-20T>G	NM_000152.3	
GATA4	Chr8:11561282	c.-989C>T	NM_002052.3	
GATA4	Chr8:11561369	c.-902G>T	NM_002052.3	
GATA4	Chr8:11561399		NM_002052.3	rs1195641788
GATA4	Chr8:11612500	c.910-55T>C	NM_002052.3	
GATA4	Chr8:11612745	c.997+103G>T	NM_002052.3	rs113049875

GATA4	Chr8:11614418	c.998-26G>A	NM_002052.3	
GATA5	Chr20:61051165	c.-201A>G	NM_080473.4	
GATA5	Chr20:61051462		NM_080473.4	rs1193866928
GATA6	Chr18:19749151	c.-530A>T	NM_005257.4	
GATA6	Chr18:19749272	c.-409C>G	NM_005257.4	
GBE1	Chr3:81542964	c.2053-3358_2053-3350delGTGTGGTGGinsTGTTTTTTACATGACAGGT	NM_000158.3	rs869320698
GLA	ChrX:100653945	c.640-11T>A	NM_000169.2	
GLA	ChrX:100654735	c.640-801G>A	NM_000169.2	rs199473684
GLA	ChrX:100654793	c.640-859C>T	NM_000169.2	rs869312374
GLA	ChrX:100656225	c.547+395G>C	NM_000169.2	
GMPPB	Chr3:49761246	c.-87C>T	NM_013334.3	rs780961444
HFE	Chr6:26087649	c.-20G>A	NM_000410.3	rs138378000
KCNH2	Chr7:150646165	c.2399-28A>G	NM_000238.3	
KCNQ1	Chr11:2484803			rs2074238
LAMA2	Chr6:129633984	c.3175-22G>A	NM_000426.3	rs777129293
LAMA2	Chr6:129636608	c.3556-13T>A	NM_000426.3	rs775278003
LAMA2	Chr6:129714172	c.5235-18G>A	NM_000426.3	rs188365084
LAMA2	Chr6:129835506	c.8989-12C>G	NM_000426.3	rs144860334
LMNA	Chr1:156100609	c.513+45T>G	NM_170707.3	
LMNA	Chr1:156105681	c.937-11C>G	NM_170707.3	rs267607645
LMNA	Chr1:156107037	c.1608+14G>A	NM_170707.3	
LMNA	Chr1:156107433	c.1609-12T>G	NM_170707.3	rs267607582
LZTR1	Chr22:21336623	c.-38T>A	NM_006767.3	
LZTR1	Chr22:21350968	c.2220-17C>A	NM_006767.3	rs1249726034
MLYCD	Chr16:83948547	c.949-14A>G	NM_012213.2	rs761146008
MYBPC3	Chr11:47353394	c.*26+2T>C	NM_000256.3	
MYBPC3	Chr11:47353821	c.3628-12C>G	NM_000256.3	rs371428751
MYBPC3	Chr11:47359371	c.2309-26A>G	NM_000256.3	
MYBPC3	Chr11:47360310	c.2149-80G>A	NM_000256.3	
MYBPC3	Chr11:47364709	c.1227-13G>A	NM_000256.3	rs397515893
MYBPC3	Chr11:47364832	c.1224-19G>A	NM_000256.3	rs587776699
MYBPC3	Chr11:47364865	c.1224-52G>A	NM_000256.3	rs786204336
MYBPC3	Chr11:47365750	c.1091-575A>C	NM_000256.3	
MYBPC3	Chr11:47367305	c.1090+453C>T	NM_000256.3	
MYBPC3	Chr11:47368602	c.906-22G>A	NM_000256.3	rs756267771
MYBPC3	Chr11:47368616	c.906-36G>A	NM_000256.3	rs864622197

NEXN	Chr1:78381662	c.-52-78C>A	NM_144573.3	
NF1	Chr17:29422055	c.-273A>C	NM_001042492.2	
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NF1	Chr17:29431417	c.60+9031_60+9035delAAGTT	NM_001042492.2	
NF1	Chr17:29475515	c.61-7486G>T	NM_001042492.2	
NF1	Chr17:29488136	c.288+2025T>G	NM_001042492.2	
NF1	Chr17:29508426	c.587-14T>A	NM_001042492.2	
NF1	Chr17:29508428	c.587-12T>A	NM_001042492.2	
NF1	Chr17:29510334	c.888+651T>A	NM_001042492.2	
NF1	Chr17:29510427	c.888+744A>G	NM_001042492.2	
NF1	Chr17:29510472	c.888+789A>G	NM_001042492.2	
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NF1	Chr17:29542762	c.1527+1159C>T	NM_001042492.2	
NF1	Chr17:29548419	c.1642-449A>G	NM_001042492.2	rs863224655
NF1	Chr17:29549489	c.*481A>G	NM_001128147.2	
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NF1	Chr17:29556027	c.2410-16A>G	NM_001042492.2	
NF1	Chr17:29556028	c.2410-15A>G	NM_001042492.2	
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NF1	Chr17:29557267	c.2991-11T>G	NM_001042492.2	
NF1	Chr17:29558777	c.3198-314G>A	NM_001042492.2	
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NF1	Chr17:29580296	c.4173+278A>G	NM_001042492.2	
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NF1	Chr17:29588715	c.4578-14T>G	NM_001042492.2	
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NF1	Chr17:29656858	c.5610-456G>T	NM_001042492.2	
NF1	Chr17:29657848	c.5812+332A>G	NM_001042492.2	rs863224491

NF1	Chr17:29661577	c.5813-279A>G	NM_001042492.2	
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NF1	Chr17:29676127	c.7190-11_7190-10insGTTT	NM_001042492.2	
NF1	Chr17:29685177	c.7971-321C>G	NM_001042492.2	
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NKX2-5	Chr5:172662741		NM_004387.3	
NKX2-5	Chr5:172672291	c.-10205G>A	.	
NKX2-5	Chr5:172672303	c.-10217G>C	.	
PCCA	Chr13:100958030	c.1285-1416A>G	NM_000282.3	
PCCB	Chr3:136003251	c.714+462A>G	NM_001178014.1	
PLN	Chr6:118869382	c.-271A>G	NM_002667.4	
PLN	Chr6:118869417	c.-236C>G	NM_002667.4	rs188578681
POMT1	Chr9:134379574	c.-30-2A>G	NM_007171.3	
PTPN11	Chr12:112915602	c.934-59T>A	NM_002834.3	
RYR2	Chr1:237730106	c.3423+32dupG	NM_001035.2	
SCN5A	Chr3:38639469	c.2024-11T>A	NM_198056.2	rs777987317
SCN5A	Chr3:38691021	c.-53+1G>A	NM_198056.2	
SELENON	Chr1:26143316	c.*1107T>C	NM_020451.2	
SGCA	Chr17:48246419	c.585-31_585-23delTCTGCTGAC	NM_000023.2	
SGCA	Chr17:48246421	c.585-31_585-24delTCTGCTGA	NM_000023.2	
SGCA	Chr17:48247492	c.748-12_748-11delCTinsAA	NM_000023.2	
SGCG	Chr13:23755086	c.-127_-121delACAGTTG	NM_000231.2	rs1422849467
SGCG	Chr13:23755215	c.-1+1G>T	NM_000231.2	
SLC12A3	Chr16:56903992	c.602-16G>A	NM_000339.2	rs750901478
SLC12A3	Chr16:56914462	c.1567+297T>G	NM_000339.2	
SLC12A3	Chr16:56917770	c.1670-191C>T	NM_000339.2	rs374182921
SLC12A3	Chr16:56927219	c.2548+253C>T	NM_000339.2	
SLC22A5	Chr5:131714054	c.394-16T>A	NM_003060.3	rs775097754
SLC22A5	Chr5:131722665	c.825-52G>A	NM_003060.3	
SMCHD1	Chr18:2701019	c.1647+103A>G	NM_015295.2	
SMCHD1	Chr18:2705677	c.1843-15A>G	NM_015295.2	
SMCHD1	Chr18:2743740	c.3634-19A>G	NM_015295.2	
TAZ	ChrX:153641699	n.694+4G>A	NR_024048.1	

TAZ	ChrX:153649161	c.778-63_778-51delCTCCCAGGGCACC	NM_000116.3	rs782249471
TBX20	Chr7:35293780	c.-549G>A	NM_001077653.2	rs571512677
TBX5	Chr12:114704515	c.*88822C>A	NM_000192.3	rs141875471
TGFB3	Chr14:76425035	c.*495C>T	NM_003239.2	rs387906514
TGFB3	Chr14:76447266	c.-30G>A	NM_003239.2	rs770828281
TPM1	Chr15:63349172	c.241-12_241-11delCTinsTG	NM_001018005.1	rs199476309
TRDN	Chr6:123957870	c.22+29A>G	NM_006073.3	rs774068079
VCP	Chr9:35072710	c.-360G>C	NM_007126.3	

Test Strengths

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
- ~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

Variants in the *KCNE1* gene should not be used for risk assessment at the moment. Specifically, *KCNE1* c.253G>A, p.(Asp85Asn) variant has been considered to be a mild risk factor for acquired long QT syndrome. However, in the newest version of the reference genome GRCh38, a gene KCNE1B, nearly identical to *KCNE1* has appeared. By using standard NGS technologies, as well as Sanger sequencing, it is not possible to get reliable region-specific sequences for these genes. It is likely that reads that have been earlier mapped to *KCNE1* actually belong to *KCNE1B*. Moreover, it is currently unclear whether *KCNE1B* produces a protein product, and if a protein is produced, whether the gene is expressed in heart. More independent data characterizing *KCNE1B* and its function are needed. Currently, all *KCNE1* sequence data and the literature related to *KCNE1* variants should be interpreted with caution. The following exons are not included in the panel as they are not sufficiently covered with high quality sequence reads: *MTO1* (NM_133645:7;NM_001123226:8), *PCCB* (NM_001178014:4), *PKP2* (NM_001254727:6), *SELENON* (NM_020451:3), *TSFM* (NM_001172696:5). 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 detect the following:

- Complex inversions
- Gene conversions
- Balanced translocations

- Some of the panels include the whole mitochondrial genome but not all (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.

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 and regulatory 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. If the test includes the mitochondrial genome the target region gene list contains the mitochondrial genes. 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 including, 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, ordering providers have access to the details of the analysis, including patient specific sequencing metrics, a gene level coverage plot and a list of regions with suboptimal coverage (<20X for nuclear genes and <1000X for mtDNA) if applicable. This reflects our mission to build fully transparent diagnostics where ordering providers can easily visualize the 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 is orthogonal confirmation. Sequence and copy number variants classified as pathogenic, likely pathogenic and variants of uncertain significance (VUS) are confirmed using bi-directional Sanger sequencing or by orthogonal methods such as qPCR/ddPCR when they do not meet our stringent NGS quality metrics for a true positive call.

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, abstracts and variant databases used to help ordering providers 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. We do not recommend using variants of uncertain significance (VUS) for family member risk stratification or patient management. Genetic counseling is recommended.

Our interpretation team analyzes millions of variants from thousands of individuals with rare diseases. Our internal database and our understanding of variants and related phenotypes increases with every case analyzed. 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.

CPT code(s) *

81439, 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

- Al-Khatib SM et al. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. Circulation. 2017 Oct 30 [Epub ahead of print].
- American Foundation for Cardiomyopathy
- Bozkurt B et al. Current Diagnostic and Treatment Strategies for Specific Dilated Cardiomyopathies: A Scientific Statement From the American Heart Association. Circulation. 2016 Dec 6;134(23):e579-e646.
- British Heart Foundation
- Cardiomyopathy Association Australia
- Cardiomyopathy UK
- Children´s Cardiomyopathy Association
- GeneReviews - ARVC
- GeneReviews - Brugada Syndrome
- GeneReviews - CPVT
- GeneReviews - DCM
- GeneReviews - HCM
- GeneReviews - LQTS
- GeneReviews - Noonan Syndrome
- Genetic and Rare Diseases Information Center - LVNC
- Genetics Home Reference - SQTS
- Gersh BJ et al. 2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy. J Am Coll Cardiol. 2011 Dec 13;58(25):e212-60.
- Hypertrophic Cardiomyopathy Association
- Ingles J et al. Genetic testing for inherited heart diseases: longitudinal impact on health-related quality of life. Genet Med. 2012 May 3.
- NORD - ARVC
- NORD - Brugada
- NORD - Brugada Syndrome
- NORD - Noonan Syndrome
- NORD - Pediatric Cardiomyopathy
- Noonan Syndrome Association - UK
- Philips B et al. 2015 update on the diagnosis and management of arrhythmogenic right ventricular cardiomyopathy. Curr Opin Cardiol. 2016 Jan;31(1):46-56.
- SADS Foundation
- Sudden Cardiac Arrest Foundation
- The Noonan Syndrome Foundation - USA