Combined Cardiac Panel

Panel Gene List: *ABCC9, ACTC1, ACTN2, AKAP9, ALMS1, ALPK3, ANK2, ANKRD1, BAG3, BRAF, CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CALM3, CASQ2, CAV3, CHRM2, CRYAB, CSRP3, CTNNA3, DES, DMD, DOLK, DSC2, DSG2, DSP, DTNA, EMD, EYA4, FHL1, FKRP, FKTN, FLNC, GAA, GATA4, GATA5, GATA6, GATAD1, GJA5, GLA, GNB5, GPD1L, HCN4, HFE, HRAS, ILK, JPH2, JUP, KCNA5, KCND3, KCNE1, KCNE2, KCNE3, KCNE1L (KCNE5), KCNH2 (HERG), KCNJ2, KCNJ5, KCNJ8, KCNQ1, KRAS, LAMA4, LAMP2, LDB3, LMNA, LRRC10, MAP2K1, MAP2K2, MIB1, MTND1, MTND5, MTND6, MTTD, MTTG, MTTH, MTTI, MTTK, MTTL1, MTTL2, MTTM, MTTQ, MTTS1, MTTS2, MURC (CAVIN4), MYBPC3, MYH6, MYH7, MYL2, MYL3, MYL4, MYLK2, MYOZ2, MYPN, NEBL, NEXN, NKX2-5, NRAS, PDLIM3, PKP2, PLN, PPA2, PRDM16, PRKAG2, PTPN11, RAF1, RANGRF, RBM20, RIT1, RYR2, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, SGCD, SHOC2, SNTA1, SOS1, TAZ, TBX20, TCAP, TECRL, TGFB3, TMEM43, TMPO, TNNC1, TNNI3, TNNT2, TOR1AIP1, TPM1, TRDN, TRPM4, TTN, TTR, TXNRD2, VCL*

Additional genes from our cardiology test menu may be added to this panel by selecting test code 935C.

Clinical Features:

Cardiac arrhythmias occur due to disruption of the heart's natural rhythm and cardiomyopathy is defined as disease of the heart muscle. In some individuals or families, the clinical picture may be complex or features of both these conditions may be present, in which case a broader approach to genetic testing may be helpful. Both phenotypes are genetically heterogeneous and have many different clinical presentations.

Several risk factors can predispose an individual to develop an arrhythmia, including genetic disorders, trauma, electrolyte imbalance and structural abnormalities of the heart. There are several different genetic arrhythmia disorders. **Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVC)** affects the cardiac desmosome, which is a protein complex that maintains cell-to-cell connections and provides mechanical attachments between adjacent cells. ARVC is characterized by myocyte death and replacement by fat and fibrous tissue in the right ventricle, predisposing to ventricular tachyarrhythmia and sudden cardiac death.[1,2] **Brugada syndrome (BrS)** is caused by abnormal ion channel function and is characterized by ST segment elevation on ECG (leads V1-3) in the absence of structural heart disease. BrS is associated with increased risk for syncope, entricular tachyarrhythmia and sudden cardiac death.[3-5] **Catecholaminergic polymorphic ventricular tachycardia (CPVT)** is characterized by cardiac calcium channel dysfunction that is precipitated by stress-induced release of catecholamines.[6-8] **Long QT syndrome (LQTS)** is characterized by prolongation of the QT interval on ECG and is associated with increased risk for syncope, ventricular arrhythmia, and sudden cardiac death in individuals with normal heart structure.[9-11] Genetic predisposition to a cardiac arrhythmia may occur as an isolated feature or may be part of a multisystemic disorder, such as Jervell and Lange-

Nielsen syndrome, Timothy syndrome, Andersen-Tawil syndrome, Naxos disease, Carvajal syndrome and muscular dystrophy.[1,12-15]

Several risk factors may also contribute towards development of a cardiomyopathy, including genetic disorders, hypertension, ischemic heart disease and infection. There are several different genetic cardiomyopathies. **Hypertrophic cardiomyopathy (HCM)** is characterized by myocardial hypertrophy and myocyte disarray in the absence of other cardiac or systemic causes.[16-18] **Dilated cardiomyopathy (DCM)** usually presents with one or more of the following: i) heart failure with symptoms of congestion (edema, orthopnea or paroxysmal dyspnea), ii) reduced cardiac output resulting in fatigue or dyspnea on exertion, arrhythmias and/or conduction system disease and iii) thromboembolic disease or stroke, mainly from left ventricular mural thrombus. However, some individuals with a DCM pathogenic variant may also be asymptomatic.[15,19] **Left ventricular non-compaction (LVNC)** is characterized by abnormal trabeculations in the left ventricle, most frequently at the apex, and can share the same clinical presentation as DCM, ranging from asymptomatic disease to progressive deterioration of cardiac function, arrhythmias, thromboembolic events, or sudden cardiac death.[19,20] **Noonan syndrome (NS)** is a relatively common multi-system disorder that may include HCM, facial dysmorphism, congenital heart defects, short stature, skeletal malformations, motor delay, learning disabilities, and impaired blood clotting ability.[21] Cardiomyopathy can also be a presenting feature of other inherited disorders, such as Danon disease, Fabry disease, mitochondrial myopathy, or muscular dystrophy[15-19].

Inheritance Pattern/Genetics: Autosomal Dominant, Autosomal Recessive, X-linked, or Mitochondrial

Test Methods:

Using genomic DNA extracted from the submitted specimen, the complete coding regions and splice site junctions of the genes tested are enriched using a proprietary targeted capture system developed by GeneDx for next-generation sequencing with CNV calling (NGS-CNV) (Only exons 1-44 for *CACNA1C*, only the *KCNQ1*-binding domains including Ser1570 residue for *AKAP9*, excluding exon 6 of the *PKP2* gene and the following genomic regions of the *TTN* gene: chr2:179527692-179527782,179523898-179523982, 179523731-179523815). The enriched targets are simultaneously sequenced with paired-end reads on an Illumina platform. Bi-directional sequence reads are assembled and aligned to reference sequences based on NCBI RefSeq transcripts and human genome build GRCh37/UCSC hg19. After gene specific filtering, data are analyzed to identify sequence variants and most deletions and duplications involving coding exons; however, technical limitations and inherent sequence properties effectively reduce this resolution for some genes. Alternative sequencing or copy number detection methods are used to analyze or confirm regions with inadequate sequence or copy number data by NGS. Reportable variants include pathogenic variants, likely pathogenic variants and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported but are available upon request.

Test Sensitivity:

The technical sensitivity of sequencing is estimated to be >99% at detecting single nucleotide events. It will not reliably detect deletions greater than 20 base pairs, insertions or rearrangements greater than 10 base pairs, or low-level mosaicism. The copy number assessment methods used with this test cannot reliably detect copy number variants of less than 500 base pairs or mosaicism and cannot identify balanced chromosome aberrations. Assessment of exon-level copy number events is dependent on the inherent sequence properties of the targeted regions, including shared homology and exon size. For the HRAS gene, FKRP gene and the mitochondrial genes, sequencing but not deletion/duplication analysis, is performed. Gene specific exclusions for exon-level deletion/duplication testing for this panel are: CALM1, GATA5, SCN1B, TAZ and TBX20 genes only whole gene deletions or duplications may be detected.

Gene	Protein	Inheritance	Disease Association(s)
ABCC9	ATP-BINDING CASSETTE, SUBFAMILY C, MEMBER 9	AD	DCM, BrS, Cantu syndrome and related disorders
ACTC1	ACTIN, ALPHA, CARDIAC MUSCLE	AD	CHD, DCM, HCM, LVNC
ACTN2	ACTININ, ALPHA-2	AD	DCM, HCM
AKAP9	A-KINASE ANCHOR PROTEIN 9	AD	LQTS, Cardiomyopathy
ALMS1	CENTROSOME AND BASAL BODY ASSOCIATED PROTEIN	AR	Alstrom syndrome, infantile DCM, mitogenic cardiomyopathy
ALPK3	ALPHA-KINASE 3	AR	Pediatric Cardiomyopathy
ANK2	ANKYRIN 2	AD	Arrhythmia, LQTS
ANKRD1	ANKYRIN REPEAT DOMAIN-CONTAINING PROTEIN 1	AD	DCM
BAG3	BCL2-ASSOCIATED ATHANOGENE 3	AD	DCM, myofibrillar myopathy
BRAF	V-RAF MURINE SARCOMA VIRAL ONCOGENE HOMOLOG B1	AD	Noonan/CFC/Costello syndromes
CACNA1C	CALCIUM CHANNEL, VOLTAGE-DEPENDENT, L TYPE, ALPHA-1C SUBUNIT	AD	BrS, Timothy syndrome, LQTS
CACNA2D1	CALCIUM CHANNEL, VOLTSGE-DEPENDENT ALPHA-2/DELTA SUBUNIT 1	AD	BrS
CACNB2	CALCIUM CHANNEL, VOLTAGE-DEPENDENT, BETA-2 SUBUNIT	AD	BrS
CALM1	CALMODULIN 1	AD	LQTS,CPVT
CALM2	CALMODULIN 2	AD	LQTS, CPVT
CALM3	CALMODULIN 3	AD	LQTS, CPVT
CASQ2	CALSEQUESTRIN 2	AR	CPVT
CAV3	CAVEOLIN 3	AD	HCM, LQTS, LGMD, Tateyama-type distal myopathy, SIDS, rippling muscle disease
CHRM2	M2-MUSCARINIC ACETYLCHOLINE RECEPTOR	AD	DCM
CRYAB	CRYSTALLIN, ALPHA-B	AD, AR	DCM, myofibrillar myopathy
CSRP3	CYSTEINE- AND GLYCINE-RICH PROTEIN 3	AD	HCM, DCM
CTNNA3	CATENIN ALPHA 3	AD, AR	ARVC, Autism
DES	DESMIN	AD, AR	DCM, ARVC, myopathy, AV block, LGMD
DMD	DYSTROPHIN	XL	DMD, BMD, DCM
DOLK	DOLICHOL KINASE	AR	DCM, congenital disorder of glycosylation type LM
DSC2	DESMOCOLLIN	AD, AR	ARVC, ARVC+skin and hair findings , DCM
DSG2	DESMOGLEIN	AD	ARVC, DCM
DSP	DESMOPLAKIN	AD, AR	ARVC, DCM, Carvajal syndrome and related

Gene	Protein	Inheritance	Disease Association(s)
			disroders
DTNA	DYSTROBREVIN, ALPHA	AD	LVNC, CHD
EMD	EMERIN	XL	EMD
FHL1	FOUR-AND-A-HALF LIM DOMAINS 1	XL	HCM, EMD, Myofibrillar myopathy
FKRP	FUKUTIN RELATED PROTEIN	AR	Muscular dystrophy
FKTN	FUKUTIN	AR	DCM, LGMD, Fukuyama Congenital Muscular Dystrophy
FLNC	FILAMIN C	AD	RCM, HCM, ARVC, DCM, myopathy
GAA	GLUCOSIDASE, ALPHA, ACID	AR	Pompe Disease (Glycogen storage disease II)
GATA4	GATA-BINDING PROTEIN 4	AD	AF, CHD, cardiomyopathy, SUDS
GATA5	GATA-BINDING PROTEIN 5	AD	AF, congenital heart defects, cardiomyopathy
GATA6	GATA-BINDING PROTEIN 5	AD	AF, CHD, pancreatic agenesis, diaphragmatic hernia, diabetes, cardiomyopathy
GATAD1	GATA ZINC FINGER DOMAIN-CONTAINING PROTEIN 1	AR	DCM
GJA5	GAP JUNCTION PROTEIN, ALPHA-5	AD	AF, HB, SADS, SIDS, congenital heart defects
GLA	GALACTOSIDASE, ALPHA	XL	Fabry disease
GNB5	GUANINE NUCLEOTIDE-BINDING PROTEIN, BETA-5	AR	Intellectual developmental disorder with cardiac arrhythmia
GDPIL	GLYCEROL-3-PHOSPHATE DEHYDROGENASE 1-LIKE	AD	BrS
HCN4	HYPERPOLARIZATION-ACTIVATED CYCLIC NUCLEOTIDE-GATED POTASSIUM CHANNEL 4	AD	BrS, SSS, tachycardia, LVNC, AF, AV block, bradycardia
HFE	HUMAN HEMOCHROMATOSIS PROTEIN (HFE)	AR	Hereditary Hemochromatosis, cardiomyopathy
HRAS	V-HA-RAS HARVEY RAT SARCOMA VIRAL ONCOGENE HOMOLOG	AD	Costello syndrome
ILK	INTEGRIN-LINKED KINASE	AD	DCM
JPH2	JUNCTOPHILIN 2	AD	HCM
JUP	JUNCTION PLAKOGLOBIN	AD, AR	ARVC, Naxos Disease and related disorders
KCNA5	POTASSIUM CHANNEL, VOLTAGE-GATED, SHAKER-RELATED SUBFAMILY, MEMBER 5	AD	AF
KCND3	POTASSIUM CHANNEL, VOLTAGE-GATED, SHAL-RELATED SUBFAMILY, MEMBER 3	AD	BrS, SIDS, Spinocerebellar ataxia
KCNE1	POTASSIUM CHANNEL, VOLTAGE-GATED, ISK-RELATED SUBFAMILY, MEMBER 1	AD, AR	LQTS, JLNS
KCNE2	POTASSIUM CHANNEL, VOLTAGE-GATED, ISK-RELATED SUBFAMILY, MEMBER 2	AD	LQTS
KCNE3	POTASSIUM CHANNEL, VOLTAGE-GATED, ISK-RELATED SUBFAMILY, MEMBER 3	AD	BrS
KCNE1L (KCNE5)	POTASSIUM CHANNEL, VOLTAGE-GATED, ISK-RELATED FAMILY, MEMBER 1-LIKE	XL	BrS, AF, VF
KCNH2 (HERG)	POTASSIUM CHANNEL, VOLTAGE-GATED, SUBFAMILY H, MEMBER 2	AD	LQTS, SQTS
KCNJ2	POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 2	AD	Andersen-Tawil syndrome, SQTS
KCNJ5	POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 5	AD	LQTS
KCNJ8	POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 8	AD	ERS, SIDS
KCNQ1	POTASSIUM CHANNEL, VOLTAGE-GATED, KQT-LIKE SUBFAMILY, MEMBER 1	AD, AR	JLNS, LQTS, SQTS
KRAS	V-KI-RAS2 KIRSTEN RAT SARCOMA VIRAL ONCOGENE HOMOLOG	AD	Noonan/CFC/Costello
LAMA4	LAMININ, ALPHA-4	AD	DCM
LAMP2	LYSOSOME-ASSOCIATED MEMBRANE PROTEIN 2	XL	Danon disease
LDB3	LIM DOMAIN-BINDING 3	AD	DCM, LVNC, ARVC, LDB3-related myopathy

Gene	Protein	Inheritance	Disease Association(s)
LMNA	LAMIN A/C	AD, AR	DCM, LVNC, ARVC, LDB3-related myopathy
LRRC10	LEUCINE-RICH REPEAT-CONTAINING PROTEIN 10	AD, AR	DCM
MAP2K1	MITOGEN-ACTIVATED PROTEIN KINASE KINASE 1	AD	Noonan/CFC/Costello
MAP2K2	MITOGEN-ACTIVATED PROTEIN KINASE KINASE 2	AD	Noonan/CFC/Costello
MIB1	MINDBOMB E3 UBIQUITIN PROTEIN LIGASE 1	AD	LVNC
MTND1	mtDNA ENCODED COMPLEX I, SUBUNIT ND1	MITO	Cardiomyopathy, myopathy
MTND5	mtDNA ENCODED COMPLEX I, SUBUNIT ND5	MITO	Cardiomyopathy, myopathy
MTND6	mtDNA ENCODED COMPLEX I, SUBUNIT ND6	MITO	Cardiomyopathy, myopathy
MTTD	MITOCHONDRIAL tRNA FOR ASPARTIC ACID	MITO	Cardiomyopathy, myopathy
MTTG	MITOCHONDRIAL tRNA FOR GLYCINE	MITO	Cardiomyopathy, myopathy
MTTH	MITOCHONDRIAL tRNA FOR HISTIDINE	MITO	Cardiomyopathy, myopathy
MTTI	MITOCHONDRIAL tRNA FOR ISOLEUCINE	MITO	Cardiomyopathy, myopathy
MTTK	MITOCHONDRIAL tRNA FOR LYSINE	MITO	Cardiomyopathy, myopathy
MTTL1	MITOCHONDRIAL tRNA FOR LEUCINE 1	MITO	Cardiomyopathy, myopathy
MTTL2	MITOCHONDRIAL tRNA FOR LEUCINE 2	MITO	Cardiomyopathy, myopathy
MTTM	MITOCHONDRIAL tRNA FOR METHIONINE	MITO	Cardiomyopathy, myopathy
MTTQ	MITOCHONDRIAL tRNA FOR GLUTAMINE	MITO	Cardiomyopathy, myopathy
MTTS1	MITOCHONDRIAL tRNA FOR SERINE 1	MITO	Cardiomyopathy, myopathy
MTTS2	MITOCHONDRIAL tRNA FOR SERINE 2	MITO	Cardiomyopathy, myopathy
MURC	MUSCLE-RELATED COILED-COIL PROTEIN	AD	DCM
MYBPC3	MYOSIN-BINDING PROTEIN C, CARDIAC	AD	HCM, DCM
MYH6	MYOSIN, HEAVY CHAIN 6, CARDIAC MUSCLE, ALPHA	AD	CHD, DCM, HCM, SSS
MYH7	MYOSIN, HEAVY CHAIN 7, CARDIAC MUSCLE, BETA	AD	DCM, HCM, myopathy
MYL2	MYOSIN, LIGHT CHAIN 2, REGULATORY, CARDIAC, SLOW	AD, AR	HCM, muscle fiber disease
MYL3	MYOSIN, LIGHT CHAIN 3, ALKALI, VENTRICULAR, SKELETAL, SLOW	AD, AR	HCM
MYL4	MYOSIN, LIGHT CHAIN 4, ALKALI, ATRIAL, EMBRYONIC	AD, AR	AF
MYLK2	MYOSIN LIGHT CHAIN KINASE 2	AD	HCM
MYOZ2	MYOZENIN 2	AD	HCM
MYPN	MYOPALLADIN	AD	DCM, RCM, HCM
NEBL	NEBULETTE	AD	DCM, endocardial fibroelastosis
NEXN	NEXILIN	AD	DCM, HCM
NKX2-5	NK2 HOMEOBOX 5	AD	CHD, CCD, cardiomyopathy
NRAS	NEUROBLASTOMA RAS VIRAL ONCOGENE HOMOLOG	AD	Noonan/CFC/Costello syndromes
PDLIM3	PDZ AND LIM DOMAIN PROTEIN 3	AD	HCM, DCM
PKP2	PLAKOPHILIN 2	AD	ARVC, BrS
PLN	PHOSPHOLAMBAN	AD	DCM, HCM, ARVC
PPA2	PYROPHOSPHATASE, INORGANIC, 2	AR	Cardiomyopathy, infantile cardiac arrest
PRDM16	PR DOMAIN CONTAINING 16	AD	DCM, LVNC
PRKAG2	PROTEIN KINASE, AMP-ACTIVATED, NONCATALYTIC, GAMMA2	AD	HCM, Wolff-Parkinson-White syndrome
PTPN11	PROTEIN-TYROSINE PHOSPHATASE, NONRECEPTOR-TYPE 11	AD	Noonan/CFC/Costello syndromes
RAF1	V-RAF-1 MURINE LEUKEMIA VIRAL ONCOGENE HOMOLOG 1	AD	Noonan/CFC/Costello syndromes
RBM20	RNA-BINDING MOTIF PROTEIN 20	AD	DCM
RIT1	RAS-LIKE WITHOUT CAAX 1	AD	Noonan syndrome
RANGRF	RAN GUANINE NUCLEOTIDE RELEASE FACTOR	AD	BrS
RYR2	RYANODINE RECEPTOR 2	AD	ARVC, CPVT, DCM
SCN10A	SODIUM CHANNEL, VOLTAGE-GATED, TYPE X, ALPHA SUBUNIT	AD	BrS

Gene	Protein	Inheritance	Disease Association(s)
SCN1B	SODIUM CHANNEL, VOLTAGE-GATED, TYPE I, BETA SUBUNIT	AD, AR	BrS, Cardiac conduction disease
SCN2B	SODIUM CHANNEL, VOLTAGE-GATED, TYPE II, BETA SUBUNIT	AD	BrS, AF
SCN3B	SODIUM CHANNEL, VOLTAGE-GATED, TYPE III, BETA SUBUNIT	AD	BrS, AF, VF, SIDS
SCN4B	SODIUM CHANNEL, VOLTAGE-GATED, TYPE IV, BETA SUBUNIT	AD	LQTS
SCN5A	SODIUM CHANNEL, VOLTAGE-GATED, TYPE V, ALPHA SUBUNIT	AD	BrS, DCM, Heart block, LQTS, SSS, SIDS, ARVC, ARVC-like disease
SGCD	SARCOGLYCAN, DELTA	AD, AR	DCM, LGMD
SHOC2	SOC-2 HOMOLOG	AD	Noonan-like syndrome with loose Anagen Hair 1
SNTA1	ALPHA SYNTROPHIN	AD	LQTS
SOS1	SON OF SEVENLESS, DROSOPHILA, HOMOLOG 1	AD	Noonan/CFC/Costello syndromes
TAZ	TAFAZZIN	XL	DCM, LVNC, Barth syndrome
TBX20	T-BOX 20	AD	CHD, DCM, LVNC
TCAP	TITIN-CAP (TELETHONIN)	AD, AR	HCM, DCM, LGMD
TECRL	TRANS-2,3-ENOYL-CoA REDUCTASE-LIKE PROTEIN	AR	CPVT3
TGFB3	TRANSFORMING GROWTH FACTOR BETA 3	AD	ARVC, Loeys-Dietz syndrome, TAAD
TMEM43	TRANSMEMBRANE PROTEIN 43	AD	ARVC, EMD
TMPO	THYMOPOIETIN	AD	DCM
TNNC1	TROPONIN C, SLOW	AD	DCM, HCM
TNNI3	TROPONIN I, CARDIAC	AD	DCM, HCM, RCM
TNNT2	TROPONIN T2, CARDIAC	AD	DCM, HCM, RCM, LVNC
TOR1AIP1	TORSIN-1A-INTERACTING PROTEIN 1	AR	LGMD, Contractures, DCM
TPM1	TROPOMYOSIN 1	AD	DCM, HCM
TRDN	TRIADIN	AR	CPVT, LQTS
TRPM4	TRANSIENT RECEPTOR POTENTIAL CATION CHANNEL, SUBFAMILY M, MEMBER 4	AD	HB, BrS
TTN	TITIN	AD, AR	DCM, ARVC, TTN-related myopathies and muscular dystrophies
TTR	TRANSTHYRETIN	AD	TTR-related amyloidosis
TXNRD2	THIOREDOXIN REDUCTASE 2	AD, AR	DCM
VCL	VINCULIN	AD	HCM, DCM, LVNC

Abbreviations: AD- Autosomal dominant; AF- Atrial Fibrillation; AR- Autosomal recessive; ARVC – Arrhythmogenic Right Ventricular Cardiomyopathy; BMD – Becker Muscular Dystrophy; BrS – Brugada Syndrome; CHD – Congenital Heart Defects; CPVT – Catecholaminergic Polymorphic Ventricular Tachycardia; DCM – Dilated Cardiomyopathy; DMD- Duchenne Muscular Dystrophy; EMD – Emery Dreifuss Muscular Dystrophy; ERS-Early repolarization syndrome; HB- Heart Block; HCM – Hypertrophic Cardiomyopathy; JLNS – Jervell and Lange-Nielsen Syndrome; LGMD – Limb Girdle Muscular Dystrophy; LQTS – Long QT Syndrome; LVNC – Left Ventricular Non-Compaction; RCM – Restrictive Cardiomyopathy; SIDS – Sudden Infant Death Syndrome; SSS – Sick Sinus Syndrome; VF-Ventricular fibrillation; XL- X-linked

References:

1. McNally E, MacLeod H, Dellefave-Castillo L. Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy. 2005 Apr 18 [Updated 2014 Jan 9]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews®[Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1131/
2. Nava et al. (2000) Journal of the American College of Cardiology 36 (7):2226-33 (PMID: 11127465)
3. Fowler et al. (2009) Current Opinion In Cardiology 24 (1):74-81 (PMID: 19102039)
4. Hedley et al. (2009) Human mutation 30 (9):1256-66 (PMID: 19606473)
5. Brugada, Campuzano, Brugada, et al. Brugada Syndrome. 2005 Mar 31 [Updated 2014 Apr 10]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2014. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1517/
6. de et al. (2008) Pacing And Clinical Electrophysiology : Pace 31 (7):916-9 (PMID: 18684293)
7. Napolitano C, Priori SG, Bloise R. Catecholaminergic Polymorphic Ventricular Tachycardia. 2004 Oct 14 [Updated 2014 Mar 6]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1289/
8. Priori et al. (2002) Circulation 106 (1):69-74 (PMID: 12093772)
9. Goldenberg et al. (2008) Current problems in cardiology 33 (11):629-94 (PMID: 18835466)

10. Priori et al. (2004) Annals of the New York Academy of Sciences 1015:96-110 (PMID: 15201152)
11. Alders M, Christiaans I. Long QT Syndrome. 2003 Feb 20 [Updated 2015 Jun 18]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1129/
12. Tranebjærg L, Samson RA, Green GE. Jervell and Lange-Nielsen Syndrome. 2002 Jul 29 [Updated 2014 Nov 20]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1405/
13. Napolitano C, Splawski I, Timothy KW, et al. Timothy Syndrome. 2006 Feb 15 [Updated 2015 Jul 16]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1403/
14. Statland JM, Tawil R, Venance SL. Andersen-Tawil Syndrome. 2004 Nov 22 [Updated 2015 Sep 3]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1264/
15. Hershberger RE, Morales A. Dilated Cardiomyopathy Overview. 2007 Jul 27 [Updated 2015 Sep 24]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1309/
16. Marian et al. (1995) Annual Review Of Medicine 46 :213-22 (PMID: 7598458)
17. Maron et al. (2002) JAMA : the journal of the American Medical Association 287 (10):1308-20 (PMID: 11886323)
18. Cirino AL, Ho C. Hypertrophic Cardiomyopathy Overview. 2008 Aug 5 [Updated 2014 Jan 16]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1768/
19. Callis et al. (2010) Expert Review of Molecular Diagnostics 10(3):329-51 (PMID: 20370590)
20. Towbin JA et al. (2015) Lancet 386(9995):813-25 (PMID: 25865865)
21. Allanson J and Roberts A. (Updated 2016 Feb 25). Noonan Syndrome. In: GeneReviews at GeneTests Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle.1997-2012. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1124/