INHERITABLE MONOGENIC CHANNELOPATIC ARRHYTMIC SYNDROMES

ECG	Variant	Gene Mutation	Protein	Locus	Channel on chromosome	OMIM NO	I
Congenital Long QT Syndrome (LQTS)							
ECG Broad base T wave. Paradoxical prolongation of the QT interval with infusion of epinephrine	**LQT1** **Frequency** 30-35%	α subunit of the slow delayed rectifier potassium channel (KvLQT1 or **KCNQ1**)	KvLQT1	11p15.5.	Slow delayed rectifier potassium I_{ks} Potassium (I_{Ks})	192500	A (A
ECG Low-amplitude with a notched, bifurcated alternant, biphasic or bifid T appearance due to a very significant slowing of repolarization. KCNH2 on L413P and L559H mutations are associated with bifid T wave Long. QTc > 470ms affected QTc = 450ms to 470ms considered border line QTc < 450ms non affected. With significant dynamic changes during heart rate variations or on exertion	**LQT2** **Frequency** 25-30%	**KCNH2**	(HERG + MiRP1) *human ether-a-go-go related gene* HERG	7q35q36	Rapid delayed rectifier potassium I_{kr} α subunit of the rapid delayed rectifier potassium channel Potassium (I_{Kr})	152.427	A
ECG ST segment prolongation and late T wave.	**LQT3** **Frequency** 5-10%	**SCN5A**	hH1 and $Na_V1.5$	3, 3p 21-24	I_{Na}^+ Prolonged I_{Na}^+ influx in phase 2, plateau or dome	600163	A
Not defined	**LQT4**	KCNJ2	*ANK2, ANKB*	4q25-27	Sodium, potassium	600919	A

					and calcium		
Not defined	**LQT5**	KCNE1	minK		K^+ Efflux	176261	A
Not defined	**LQT6** **Frequency** rare	KCNE2 MiRP1	MiRP1			603796	
Modest prolongation of QT interval, prominent U wave, frequent PVCs, PVT, bidirectional VT.	**LQT7 Andersen Tawil-syndrome** **Frequency** rare	**KCNJ2**	Kir2.1	I_{k1}	Reduction Great reduction in I_{k1} result in the generation of spontaneous APs that are triggered by Na^+-Ca^{2+} exchangers.	170390	A
ECG Fetal bradycardia, remarkably prolonged QT interval often >550 to 600ms, ST prolongation, 2:1 functional AV block(85%), Twave macoralternance(63%) VT	**LQT8** Timothy's syndrome: syndactyly(98%), bald at bird,flat nasal bridge, small upper jaw(94%), autism, recurrent infections(53%), hypoglycemia(20%) **Frequency** rare	**CACNA1C.Ca_v 1.2**	Cav1.2	12p13.3	LTCC Prolonged Ca^{2+} influx.during phase 2	601008	A or AF
ECG: prolonged QT interval and PVT (TdP)	**LQT9 Frequency** rare	**CAV3**	Caveolin-3.An integral membrane protein in trans-Golgi-derived vesicles.	3p25	Prolonged Na^+ influx Late sodium current of the cardiac sodium channel in phase 2	611818	AD
ECG: long isoelectric ST segment,	**LQT10** **Frequency**	**SCN4B**	Na^+ channel beta4 subunit	11q23	Prolonged Na^+ influx	611819	A

late-onset T wave, and 2:1 AV block	**Extremely rare, found in 1 family**						
ECG: prolonged QT interval and PVT (TdP)	**LQT11**	**AKAP9**	Yotiao	7q21-q22	I_{ks}	611820	A
Not defined	**LQT12**	**SNTA1**	α-syntrophin	22q11.2	I_{Na+}	601017	A
ECG: markedly prolonged QT interval (corrected QT = 520 ms).	**LQT13**	**KCNJ5**	Kir3.4	11q24	I_{kACTH} I_{K1}	613485	A
ECG: Bradycardia, very prolonged QTc interval (> 550 ms), symptomatic at presentation, younger age at presentation (<1 month) and frequently documented VF. Associated with central deafness (cardioauditory syndrome).	**JLN1**	**KCNQ1**	KvLQT1	11p15.5	Slow delayed rectifier potassium Iks	220400	A
	JLN2	**KCNE1**	minK	21q22.1-q22.2	Slow delayed rectifier potassium Iks	612347	A
Congenital Short QT Syndrome (SQTS)							
ECG: Frequent AF, T waves: Tall peaked, pointed, narrow and symmetrical. QT Interval: Constant and uniform very short QT and QTc interval. ≤ 280 ms and ≤ 300 ms respectively. Without significant dynamic changes during heart rate variations or on exertion. U Wave: Normal. Stress Testing: A slight reduction of	**SQTS1**	**KCNH2**	*human ether-a-go-go related gene* HERG	7q35-q36	I_{kr}	609620	A

the QT interval during physiological increase in heart rate.							
Similar to SQT1	**SQTS2**	**KCNQ1**	KvLQT1	11p15.5	I_{ks}	609621	A
Similar to SQT1	**SQTS3**	**KCNJ2**	Kir 2.1	17q21.1-q36	I_{k1}	#609622	A
ECG: QT Interval between 330 to 370, short ST segment + BrS pattern after procainamide challenge	Overlap Syndrome SQTS + BrS	**CACNB2b**	α1 (*CACNA1C*) and β (*CACNB2b*) subunits of the L-type cardiac calcium channel	10p12.33	L-type Calcium Current LTCC	600003	
Brugada Syndrome (BrS)							
ECG: P wave duration prolongation together with PR and QRS duration prolongation are integrant of depolarization abnormalities. First-degree AV block is observed in ≈ 50% of cases of BrS mainly in presence of SCN5 mutation. Type 1: J point and ST segment elevation ≥ 2mm on right precordial leads followed by negative T wave, frequently PR prolongation, LAFB (9%), aVR sign (final R wave ≥ 3mm in aVR), Supraventricular arrhythmias (30%), PVT-VF	**BrS1**	**SCN5A**	$Na_V1.5$		I_{Na}	**601144**	A
	BrS2	**GPD1L**			I_{Na}	**611778**	A
	BrS3	**CACNA1C.Ca_v 1.2**		12p13.3	LTCC	**114205**	A
	BrS4	**CACNB2b**		*10p12.33*	LTCC	**600003**	A
	BrS5	**SCN1B**	**Navβ.1**	**19q13.1**	I_{Na}	**604433**	A
	BrS6	**KCNE3**			I_{to} transient outward potassium current	**600235**	A
	BrS7	**SCN3B**			I_{Na}	**608214**	A
	BrS8	**HCN4**	GIFtS	15q24-q25	Potassium/sodium hyperpolarization-activated cyclic nucleotide-gated channel 4	**605206**	A

rarely MVT.							
Idiopathic Ventricular Fibrillation							
	VENTRICULAR FIBRILLATION, PAROXYSMAL FAMILIAL, 1 VF1	**SCN5A**	$Na_V1.5$	3p21.	I_{Na}	**600193**	A
ECG rapid PVT PVCs with very short coupling intervals. The PVC (302 +/- 52 msec) within 40 msec of the peak of the preceding Absence of T wave. Pause-dependent	**VENTRICULAR FIBRILLATION, PAROXYSMAL FAMILIAL, 2 VF2**	**DPP6**	Dipeptidyl aminopeptidase-like protein 6	7q26.	Voltage-gated potassium channels	**126141**	A
	IVF	**Akyrin-B mutation**	ANK2	4q25-q27	The Na+/K+ ATPase, the voltage gated Na+ channel and the Na+/Ca2+ exchanger.	**106410**	A
	IVF	**KCNJ8**	$K_{ir}6.1$ protein the K(ATP) channel	12p11.23	inward-rectifier type potassium channel. $K_{ir}6.1$,	**600935**	A
Cardiac Conduction Disease							
ECG Incomplete or complete RBBB, LBBB, LAFB, LPFB, Complete AV block, prolonged intraventricular conduction time.	**CCD1** Progressive Familial heart block, type I, included; PFHB1, 'hereditary bundle branch defect' (HBBD).	**TRPM4**	Trpm4	19q13.2-q13.3	Uncertain	**113900**	A

ECG BBB, VT, AVB, BrS type 1, LQT3	**CCD2** Progressive familial heart block type II (PFHBII) **associated with** DCM,	**SCN5A**	$Na_V1.5$	3p21 And 1q32.2-q32.3.	I_{Na}		
	CCD3	**Unknown**	NA	16q23-q24	NA		
	CCD4	**unknown**	NA	1q32.2-q32.3	NA		
Progressive Cardiac Conduction Defect Susceptibility Gene							
	Timothy Syndrome	**CACNAC1C**	$Ca_V1.2$, L-type calcium channel				
	Atrial Standstill	**GJAS**	Connexins				
	Myotonic dystrophy 1	**DAMPK**	Serine-threonine protein kinase				
	SSS	**HCN4**	Pacemaker I_f channel				
	LQT2, SQT1	**KCNH2**	I_{Kr}				
	Andersen-Tawil syndrome, SQT3, CPVT	**KCNJ2**	Kir2.1 channel				
	Danon Disease	**LAMP2**	Lysosomal-associated membrane protein 2				
	Emery-Dreifuss and limb-girdle muscular dystrophy, Werner's syndrome, Charcot-Marie-Tooth syndrome type 2	**LMNA**	Lamin A/C				
	Atrial Septal defect, tetralogy of Fallot	**NKX2.5**	Homeobox transcription factor				
	Glycogen storage disease	**PRKAG2**	AMPK □2 subunit				
	LQT3, Brugada syndrome type 1, PCCD	**SCN5A**	$Na_V1.5$ channel				
	Holt-Oram Disease	**TBX5**	T-box transcription factor				

CPVT							
Stress-induced **PVT**, Bidirectional VT.	**CPVT1**	**RyR2 Cardiac** Ryanodine Receptor	Ryanodine receptor Ryr Tetrameric protein	1q42.1-q43	Abnormal diastolic Ca^{+2} release from sarcoplasmatic reticulumfacilitating the delopment of afterdepolarization and triggered activity.	**180902**	A
	CPVT2 3%	**CASQ2** Calsequestrin	Casq2 Calsequestrin	1p23.21	NA	**114251**	A
QT interval prolongation 485ms	**CPVT3**	**Unknown**		7p14-22			A
CPVT-Related Phenotypes							
QT prolongation, stress-induced bidirectional VT	**LQT4**	**ANK2**		4q25-26		600919	A
U waves, bidirectional VT	**ATS**	**KCNJ2**		17q23.1-q24.2		**601379**	A
Stress-induced VT	**CPVT/DCM**	**RYR2**		1q42-43		180902	A
Sick Sinus Syndrome (SSS)							
	SSS1	**SCN5A**	$Na_V1.5$	3p21	I_{Na}^+		
	SSS2	**HCN4**	Hcn4	15q24-q25	I_f		
Familial Atrial Fibrillation							
ECG: chronic AF and paroxysmal FA	**AF, Familial 1**	**ATFB1**	Slow voltage-gated potassium channel alpha subunit	10q22-q24	I_{ks}	**%608583**	A
	AF, Familial 2	**ATFB2**	Cardiac sodium channel alpha subunit (Nav 1.5)	6q14-q16	I_{Na}	**608988**	A
	AF, Familial 3	**ATFB3 KCNQ1**	Potassium voltage-gated channel, I_{ks}-related family, member 2	11p15.5	Potassium voltage-gated channel I_{Ks}	**607542**	A
	AF, Familial 4	**KCNE2**	minK-related peptide-1	21q22.12	Potassium voltage-gated channel	**603796**	A

	AF, Familial 5	**ATFB5**	ankyrinB	4q25	First non-ion channel involved in LQTS	**611494**	A
	AF, Familial 6	**ATFB6**	**NPPA**	1p36.2	Non-ion channel	**108780**	A
	AF, Familial 7	**ATFB7 KCNA5**	Potassium channel protein	12p13	Potassium voltage-gated channel	**176267**	A
	AF, Familial 8 Cardioembolic Stroke	**ATFB 8**		16q22		**613055**	A
Sudden Infant Death Syndrome (SIDS) Is the sudden unexpected death of an infant before the age of 1 yo for which no cause is apparent. Incidence: 0.1 to 2 infants per 1000 live births. With the peak incidence between the ages of 2 and 5 months.							
MELAS SYNDROME which stands for mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke		MTTL1	TRANSFER RNA, MITOCHONDRIAL, LEUCINE			**272120**	
		MTND1	NADH-UBIQUINONE OXIDOREDUCTASE			**516000**	
		SCN5A					
SQTS		KCNQ1			$\mathbf{I_{Ks}}$		
LQTS		CAV3					
		SLC6A4				**182138**	
		GPD1L					
		KCNH2			$\mathbf{I_{Kr}}$		
		KCNE2			$\mathbf{I_{Na}}$		
		RYR2					

AD: autosomal dominant or **AR:** autosomal recessive.; **AVB:** Atrioventricular Block **BrS:** Brugada Syndrome; **CCD:** Cardiac Conduction Disease, Progressive Cardiac Conduction Disease (PCCD) or Lenègre disease; **CE:** Current Effect.; **CPVT:** Catecholaminergic Polymorphic Ventricular Tachycardia.; **G**: Gain **GIFtS:** Gene Cards Inferred Functionality Scores (GIFtS) Gene Cards Inferred Functionality Scores.; **HCN:** hyperpolarization activated cyclic nucleotide-gated potassium channel/ potassium/sodium hyperpolarization-activated cyclic nucleotide-gated channel; **HERG:** the **h**uman *Ether-à-go-go* **R**elated **G**ene **IP:** Inheritance Pattern: **IVF:** Idiopathic Ventricular Fibrillation.; **L**: Loss.; **LQTS:** Long QT Syndrome.; **LTCC:** L-type Calcium Channel; **OMIM** ® Online Mendelian Inheritance in Man ® . OMIM is a comprehensive, authoritative, and timely compendium of human genes and genetic phenotypes. The full-text, referenced overviews in OMIM contain information on all known mendelian disorders and over 12,000 genes.

OMIM focuses on the relationship between phenotype and genotype. It is updated daily, and the entries contain copious links to other genetics resources. This database was initiated in the early 1960s by Dr. Victor A. McKusick as a catalog of mendelian traits and disorders, entitled Mendelian Inheritance in Man (MIM). Twelve book editions of MIM were published between 1966 and 1998. The online version, OMIM, was created in 1985 by a collaboration between the National Library of Medicine and the William H. Welch Medical Library at Johns Hopkins. It was made generally available on the internet starting in 1987. In 1995, OMIM was developed for the World Wide Web by NCBI, the National Center for Biotechnology Information. OMIM is authored and edited at the McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, under the direction of Dr. Ada Hamosh.; **PVT**: Polymorphci Ventricular Tachycardia.; **SCN5A:** "sodium channel, voltage-gated, type V, alpha subunit." **SIDS:** Sudden Infant Death Syndrome **SQTS:** Short QT Syndrome.; **SSS:** Sick Sinus Syndrome; **VF1** and **VF2:** Paroxysmal Familial Ventricular Fibrillation.