

# Supplementary Material

## Primers for Sanger Sequencing

### *ADRA2B*

Forward: 5' - GGTGCGCTTGGAGTTGTA CT - 3'  
Reverse: 5' - GACCACCAGGACCCCTACTC - 3'

### *SCN1A*

Forward 5' - TGTGCCATGCTGGTGTATTT - 3'  
Reverse 5' - GCTGCGAGTTTTCAAGTTGG - 3'

### *SLC9A1*

Forward 5' - TGTCTCCCCTGGAAAATGAG - 3'  
Reverse 5' - TCCTGGACAACCTGCTCTTC - 3'

### *ATP2B3*

Forward 5' - AGGGGTCTCAGGACTCTGGT - 3'  
Reverse 5' - AGATGGGGTTGCTGAAGATG - 3'

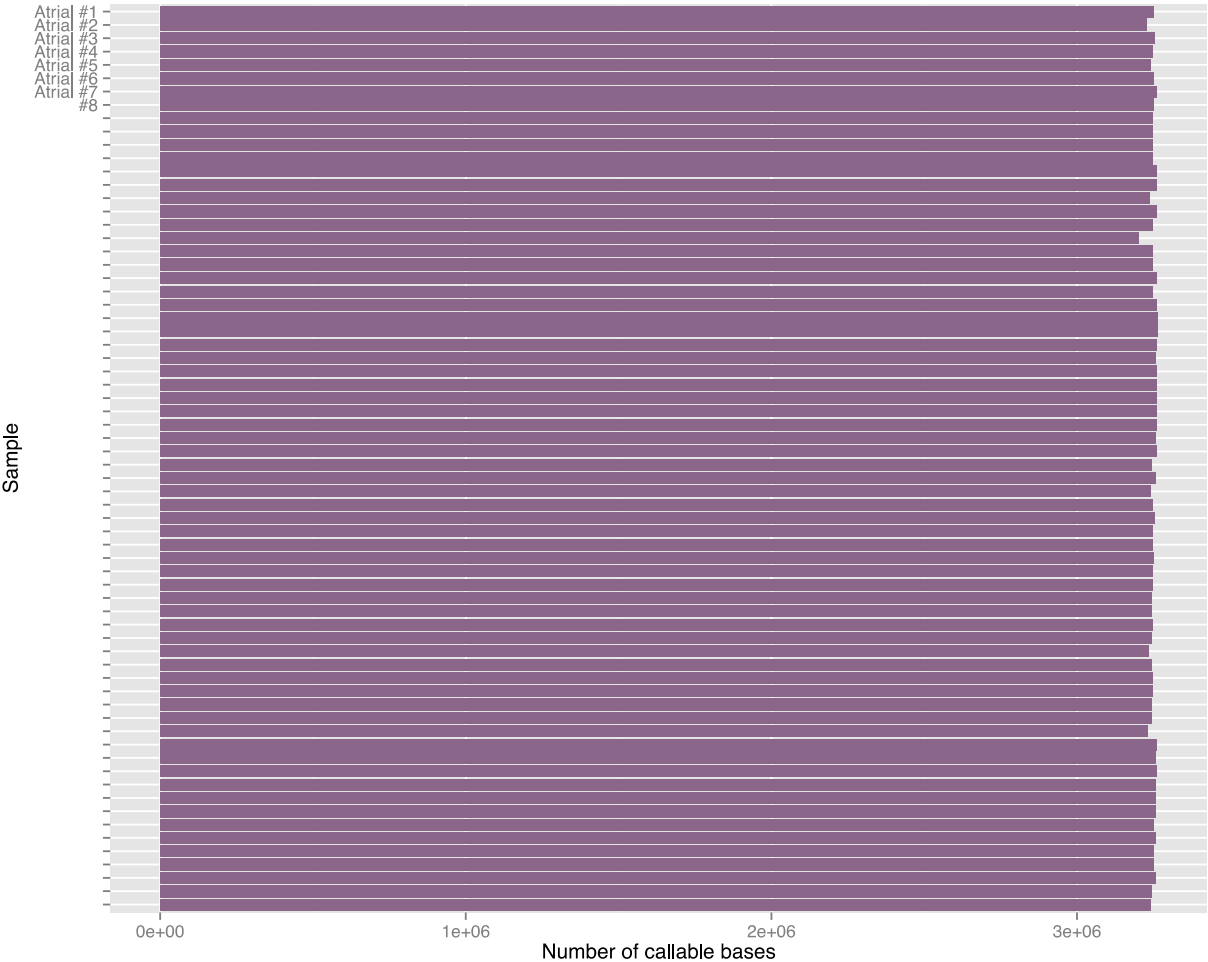
### *CHRN4*

Forward 5' - CTGGTGACGATGGAGAAGGT - 3'  
Reverse 5' - AGTTCCGCTCCTGGACCTAT - 3'

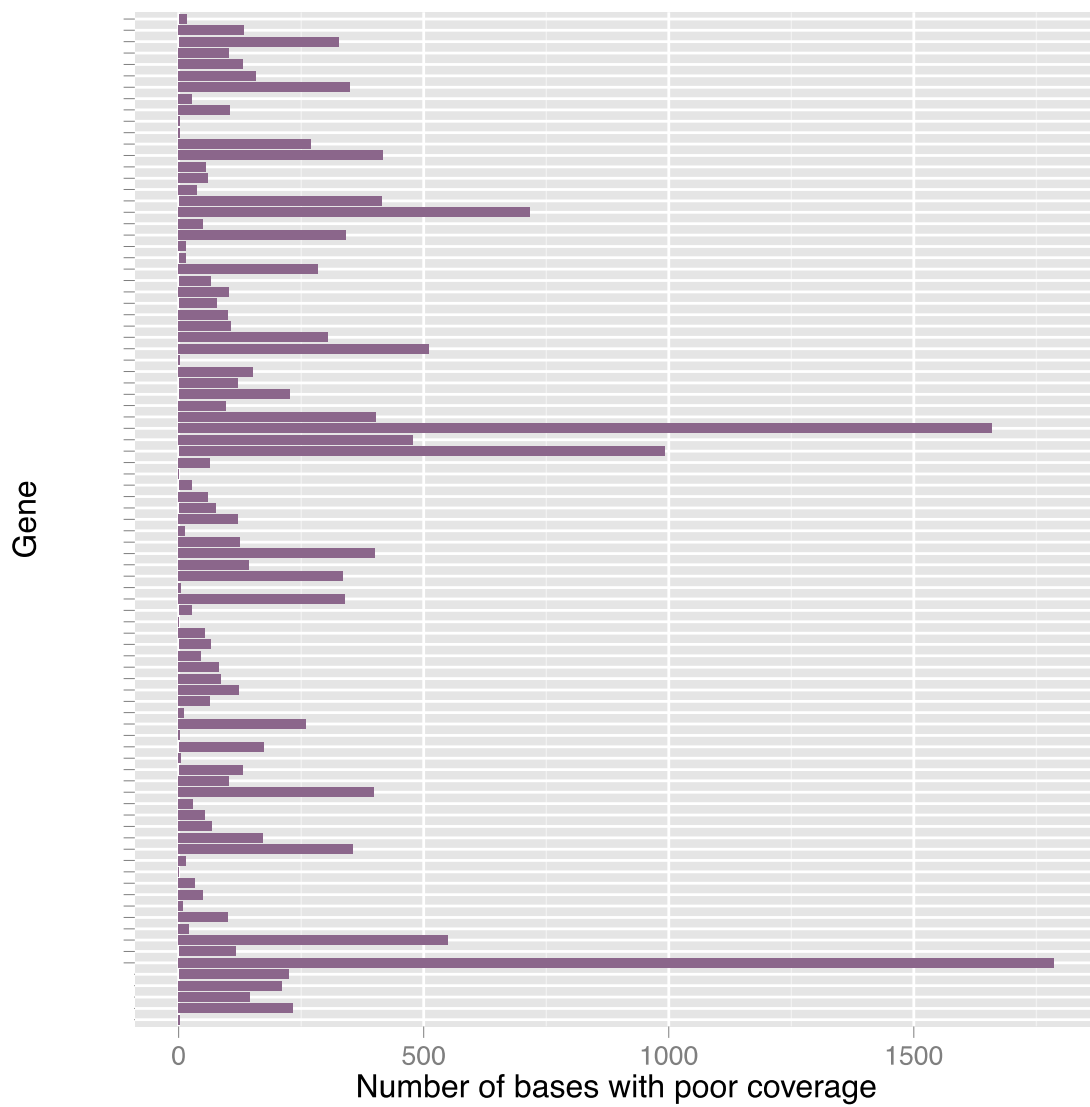
**Supplemental Figure 1: Number of Mapped Bases Per Sample**



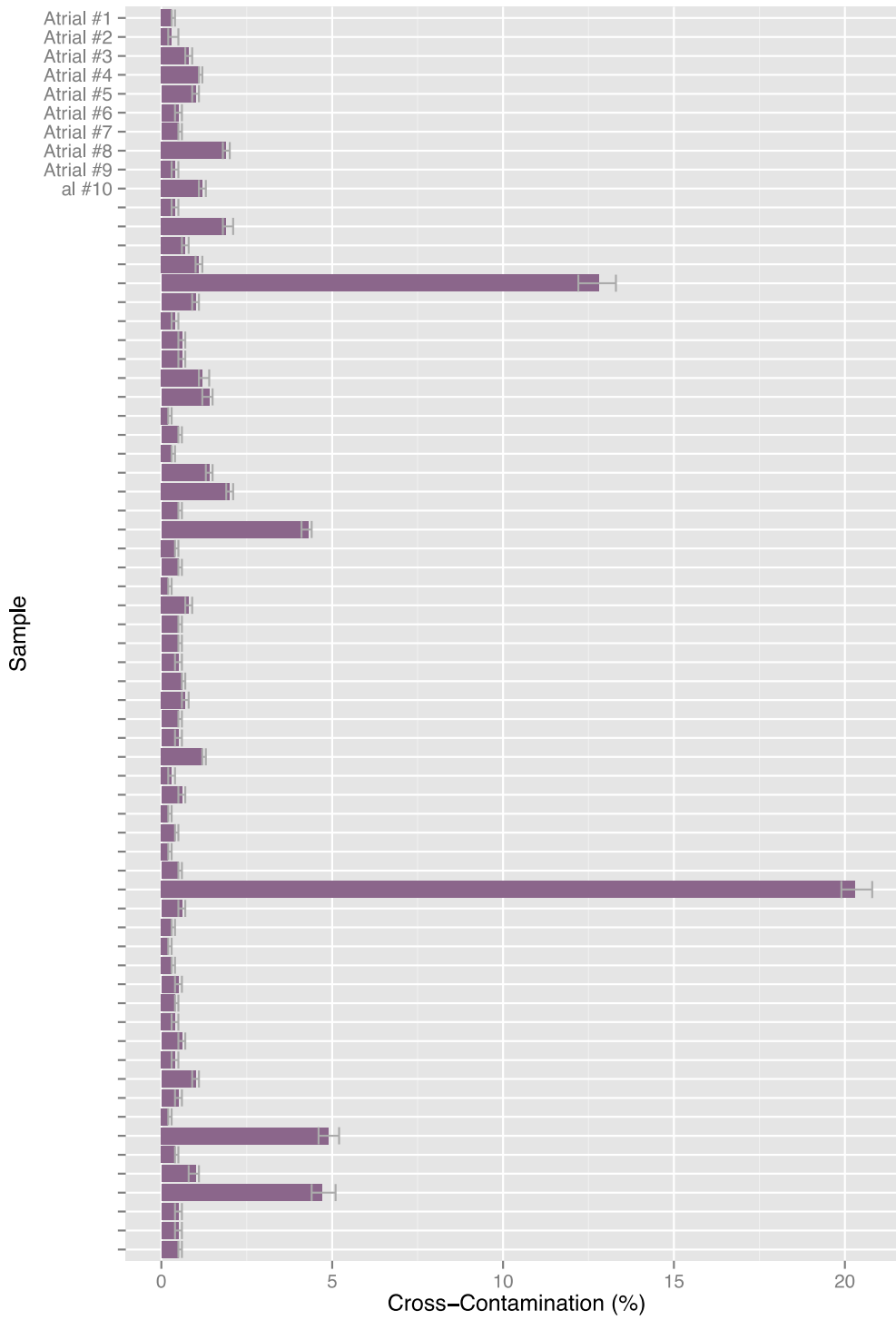
**Supplemental Figure 2: Number of Callable Bases Per Sample**



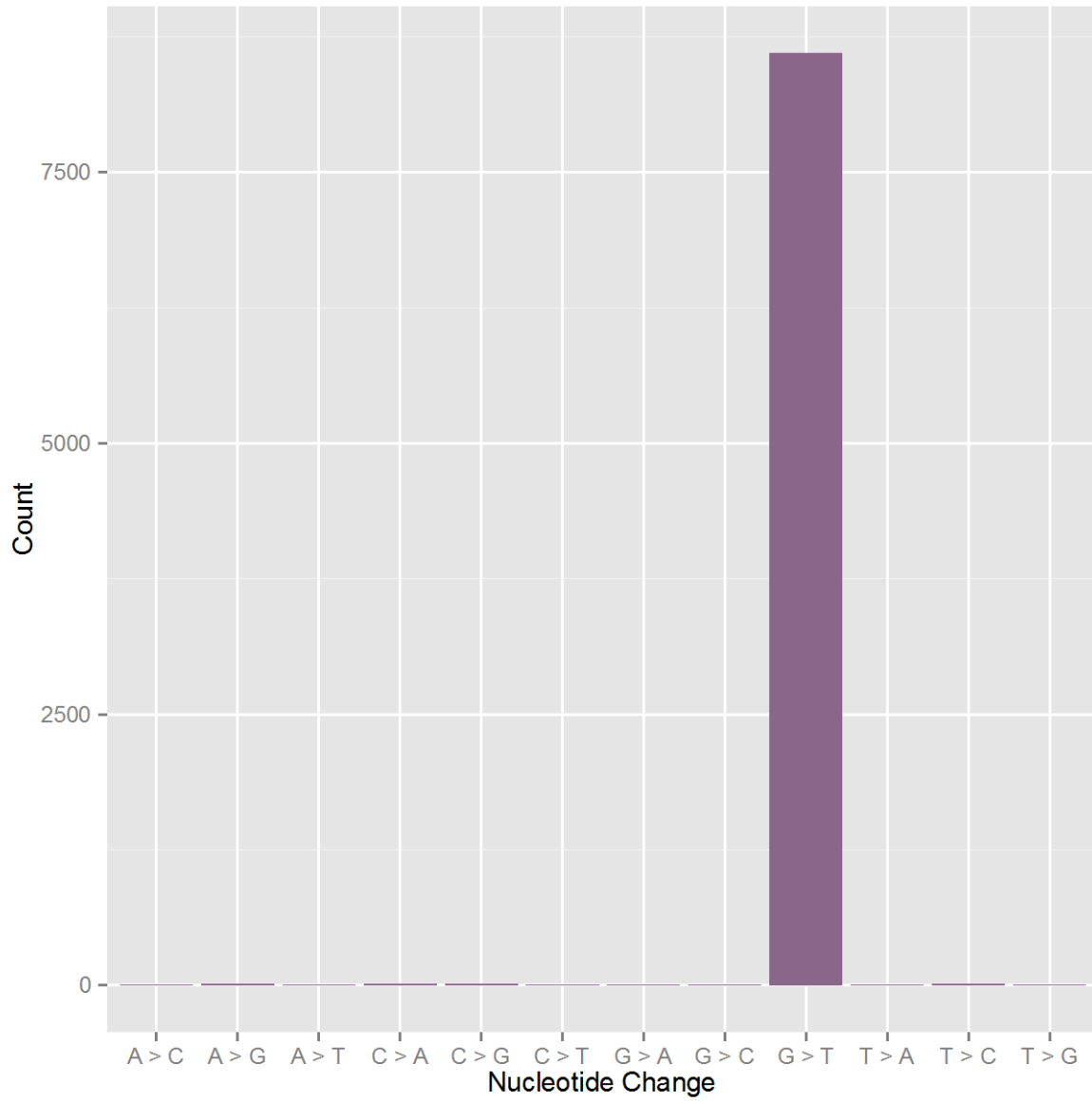
**Supplemental Figure 3: Genes Containing Isolated Base Pair Regions with Inadequate Coverage for Variant Calling**



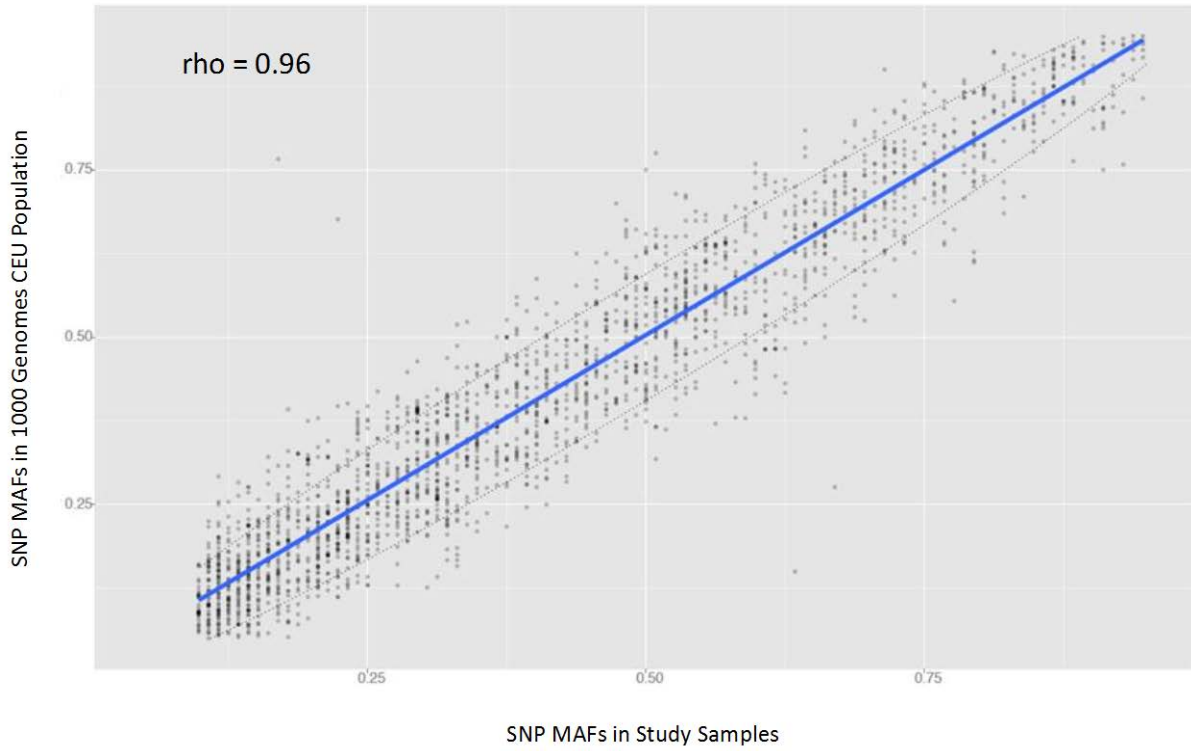
**Supplemental Figure 4:** Estimates of Cross-Contamination Among Samples using ContEst



**Supplemental Figure 5:** Discordant Variants Calls with an Anticipated Overwhelming Predominance of G>T Transversions Secondary to Oxidative DNA Damage

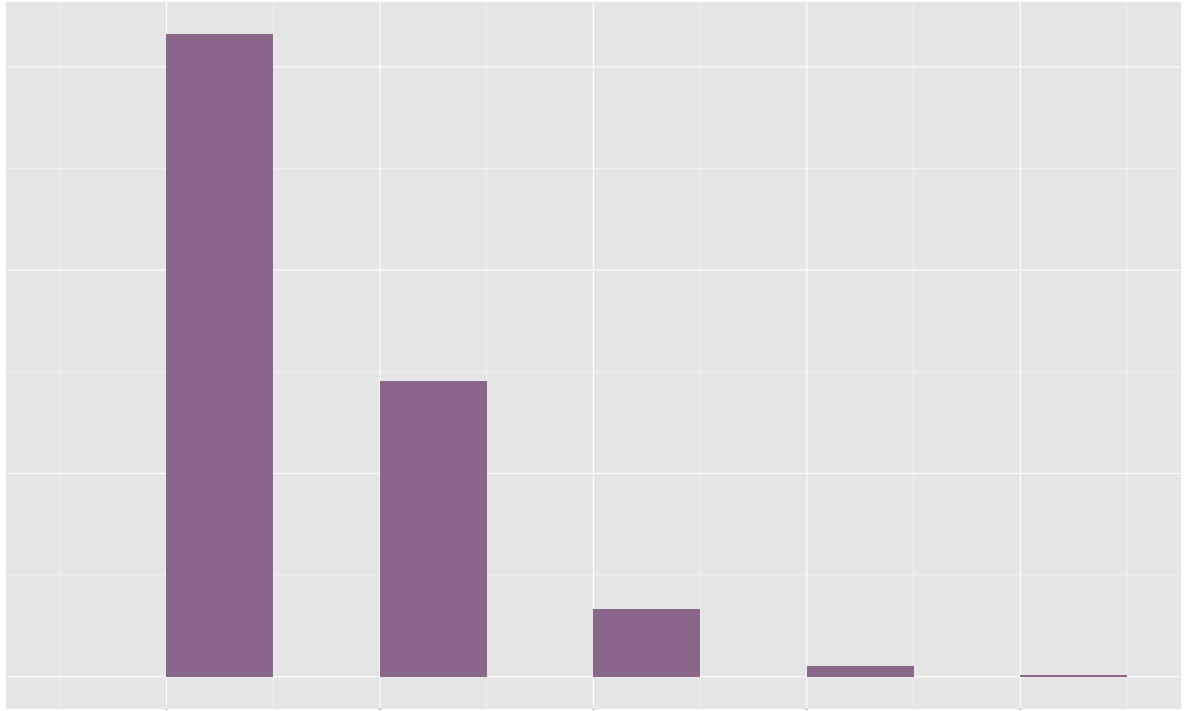


**Supplemental Figure 6:** Correlation of Single Nucleotide Polymorphism Minor Allele Frequencies from our Study Cohort and the 1000 Genomes Project CEU Population.



SNP = single nucleotide polymorphism, MAF = minor allele frequency

**Supplemental Figure 7:** Monte Carlo Simulation Probability Estimate for Missed Somatic Mutations Among Filtered G > T Transversions.





## **Supplemental Table 1: Cardiac Arrhythmia Genetic Panel**

### **Genes Implicated with AF (rare variants)**

*KCNQ1*

*KCNJ2*

*KCNE2*

*KCNE5*

*KCNA5*

*KCNH2*

*GJA5*

*GJA1*

*SCN5A*

*SCN1B*

*SCN1Bb*

*SCN2B*

*SCN3B*

*NPPA*

*ANK2*

*GATA4*

*NUP155*

### **Genes implicated with AF (common variants) - restricted to studies involving >1000 subjects**

*KCNH2*

*GJA1*

*IL6*

### **Loci implicated with AF - restricted to studies involving >1000 subjects**

4q25 - *PITX2*, *ENPEP*

16q22 - *ZFHX3*

1q21 - *KCNN3*, *PMVK*

1q24 - *PRRX1*

7q31 - *CAV1*, *CAV2*

9q22 - *C9orf3*, *FBP1*, *FBP2*

10q22 - *SYNPO2L*, *MYOZ1*

14q23 - *SYNE2*, *ESR2*

15q24 - *HCN4*

12p12 - *SOX5*

6p21 - *CDKN1A*, *PXT1*

3p22 - *SCN10A*, *SCN11A*

5q34 - *NKX2-5*

12q24 - *TBX5*

1q21 - *IL6R*

**Other Genes Implicated with Primary Arrhythmic Disorders That Are Not Ion Channels**

**Long QT Syndrome**

*CAV3*

*AKAP9*

*SNTA1*

**Brugada Syndrome**

*GPD1L*

*MOG1*

*SLMAP*

**CPVT**

*CALM1*

**Idiopathic Ventricular Fibrillation**

*DPP6*

**Autonomic**

**Adrenergic Receptors**

*ADRA1D*

*ADRA1B*

*ADRA1A*

*ADRA2A*

*ADRA2B*

*ADRA2C*

*ADRB1*

*ADRB2*

*ADRB3*

**Inflammation/Fibrosis**

*TGFBR1*

*TGFBR2*

*TGFBR3*

*PDGFA*

*PDGFB*

*PDGFC*

*PDGFD*

*PDGFRA*

*PDGFRB*

*CRP*  
*TNF*  
*NFKB1*  
*NFKB2*  
*IFNG*  
*CTGF*

**RAAS Genes**

*ACE*  
*ACE2*  
*ACE3*  
*REN*  
*AGT*  
*AGTR1*  
*CYP11B2*

**Natriuretic Hormones/Receptors**

*NPPA*  
*NPPB*  
*NPPC*  
*NPR1*  
*NPR2*  
*NPR3*

**MMPs/TIMPs**

*MMP1*  
*MMP2*  
*MMP3*  
*MMP9*  
*MMP13*  
*TIMP1*  
*TIMP2*  
*TIMP3*  
*TIMP4*

**Cardiomyopathies** (DCM = Dilated Cardiomyopathy, HCM = Hypertrophic Cardiomyopathy, RCM = Restrictive Cardiomyopathy, LVNC = Left Ventricular Non-Compaction, Mito = Mitochondrial Myopathy, ARVC = Arrhythmogenic Right Ventricular Cardiomyopathy)

**Cardiomyopathies**

BAG3	DCM
RBM20	DCM

RBM24	DCM
<i>MYH7</i>	DCM,HCM,RCM,LVNC
<i>TNNT2</i>	DCM,HCM,RCM
TPM1	DCM,HCM
MYBPC3	DCM,HCM
<i>MYL3</i>	HCM
<i>MYL2</i>	HCM
PSEN1	DCM
<i>PSEN2</i>	DCM
<i>MYOZ2</i>	HCM
<i>TNNI3</i>	DCM,HCM,RCM
<i>ACTC1</i>	DCM,HCM,LVNC
<i>TTN</i>	DCM,HCM
<i>TNNC1</i>	DCM,HCM
<i>MYH6</i>	HCM
<i>CSRP3</i>	DCM,HCM
TCAP	DCM,HCM
VCL	DCM,HCM
<i>JPH2</i>	HCM
<i>OBSCN</i>	HCM
<i>DES</i>	DCM,RCM
<i>LMNA</i>	DCM
<i>SGCD</i>	DCM
<i>PLN</i>	DCM
<i>ACTN2</i>	DCM
LDB3	DCM,LVNC
<i>CRYAB</i>	DCM,HCM
FHL2	DCM
ILK	DCM
LAMA4	DCM
MYPN	DCM
DMD	DCM
EMD	DCM
TAZ	DCM,LVNC,Mito
FKTN	DCM
DSP	DCM,ARVC
JUP	DCM,ARVC
PKP2	ARVC
TMEM43	ARVC
TGFB3	ARVC
DSG2	ARVC
DSC2	ARVC
DTNA	LVNC

PRKAG2	HCM
GLA	HCM (Fabry)
GAA	HCM (Pompe)
LAMP2	HCM (Danon)
AARS2	Mito
MRPL3	Mito
SLC25A3	Mito
SLC25A4	Mito
COX15	Mito
SCO2	Mito
AGK	Mito
NDUFS2	Mito
NDUFAF1	Mito
TMEM70	Mito
FLNC	DCM
SVIL	DCM
HSPB7	DCM
HSPB2	DCM
HSPB8	DCM
HSPB6	DCM
LMOD2	DCM
TMOD1	DCM
TRIM63	HCM
XIRP1	DCM
HRC	DCM
MYOM1	DCM
CMYA5	DCM
ACTA1	HCM
EYA4	DCM

**Sodium Channel Genes**

*NALCN*  
*SCN10A*  
*SCN11A*  
*SCN1A*  
*SCN1B*  
*SCN2A*  
*SCN2B*  
*SCN3A*  
*SCN3B*  
*SCN4A*  
*SCN4B*  
*SCN5A*  
*SCN7A*

*SCN8A*  
*SCN9A*  
*SCNN1A*  
*SCNN1B*  
*SCNN1D*  
*SCNN1G*

**Potassium Channel Genes**

*ABCC8*  
*ABCC9*  
*KCNA1*  
*KCNA10*  
*KCNA2*  
*KCNA3*  
*KCNA4*  
*KCNA5*  
*KCNA6*  
*KCNA7*  
*KCNAB1*  
*KCNAB2*  
*KCNAB3*  
*KCNB1*  
*KCNB2*  
*KCNC1*  
*KCNC2*  
*KCNC3*  
*KCNC4*  
*KCND1*  
*KCND2*  
*KCND3*  
*KCNE1*  
*KCNE2*  
*KCNE3*  
*KCNE4*  
*KCNE5*  
*KCNF1*  
*KCNG1*  
*KCNG2*  
*KCNG3*  
*KCNG4*  
*KCNH1*  
*KCNH2*  
*KCNH3*

*KCNH4*  
*KCNH5*  
*KCNH6*  
*KCNH7*  
*KCNH8*  
*KCNIP1*  
*KCNIP2*  
*KCNIP3*  
*KCNIP4*  
*KCNJ1*  
*KCNJ10*  
*KCNJ11*  
*KCNJ12*  
*KCNJ13*  
*KCNJ14*  
*KCNJ15*  
*KCNJ16*  
*KCNJ18*  
*KCNJ2*  
*KCNJ3*  
*KCNJ4*  
*KCNJ5*  
*KCNJ6*  
*KCNJ8*  
*KCNJ9*  
*KCNK1*  
*KCNK10*  
*KCNK12*  
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*KCNK15*  
*KCNK16*  
*KCNK17*  
*KCNK18*  
*KCNK2*  
*KCNK3*  
*KCNK4*  
*KCNK5*  
*KCNK6*  
*KCNK7*  
*KCNK9*  
*KCNMA1*  
*KCNMB1*  
*KCNMB2*

*KCNMB3*  
*KCNMB4*  
*KCNN1*  
*KCNN2*  
*KCNN3*  
*KCNN4*  
*KCNQ1*  
*KCNQ2*  
*KCNQ3*  
*KCNQ4*  
*KCNQ5*  
*KCNS1*  
*KCNS2*  
*KCNS3*  
*KCNT1*  
*KCNT2*  
*KCNU1*  
*KCNV1*  
*KCNV2*

**Calcium Channel Genes**

*ATP2A1*  
*ATP2A2*  
*ATP2A3*  
*ATP2B1*  
*ATP2B2*  
*ATP2B3*  
*ATP2B4*  
*ATP2C1*  
*CACFD1*  
*CACNA1A*  
*CACNA1B*  
*CACNA1C*  
*CACNA1D*  
*CACNA1E*  
*CACNA1F*  
*CACNA1G*  
*CACNA1H*  
*CACNA1I*  
*CACNA1S*  
*CACNA2D1*  
*CACNA2D2*  
*CACNA2D3*



*CACNA2D4*  
*CACNB1*  
*CACNB2*  
*CACNB2b*  
*CACNB3*  
*CACNB4*  
*CACNG1*  
*CACNG2*  
*CACNG3*  
*CACNG4*  
*CACNG5*  
*CACNG6*  
*CACNG7*  
*CACNG8*  
*CALHM1*  
*CATSPER1*  
*CATSPER2*  
*CATSPER3*  
*CATSPER4*  
*CATSPERB*  
*CATSPERD*  
*CATSPERG*  
*ITPR1*  
*ITPR2*  
*ITPR3*  
*MCU*  
*ORAI1*  
*ORAI2*  
*ORAI3*  
*PKD1*  
*PKD1L2*  
*PKD1L3*  
*PKD2*  
*PKD2L1*  
*PKD2L2*  
*TPCN1*  
*TPCN2*

**Acid Sensing Ion Channel Genes**

*ASIC1*  
*ASIC2*  
*ASIC3*  
*ASIC4*

*ASIC5*

**Ion Exchanger Genes**

*SLC11A2*

*SLC17A3*

*SLC24A2*

*SLC26A7*

*SLC26A8*

*SLC26A9*

*SLC30A1*

*SLC35F1*

*SLC4A11*

*SLC4A7*

*SLC8A1*

*SLC8A3*

*SLC9A1*

*SLC9C2*

**Ammonium Ion Transporting Genes**

*RHAG*

*RHCG*

**Transient Receptor Potential Cation Channel Genes**

*MCOLN1*

*MCOLN2*

*MCOLN3*

*TRPA1*

*TRPC1*

*TRPC3*

*TRPC4*

*TRPC5*

*TRPC6*

*TRPC7*

*TRPM1*

*TRPM2*

*TRPM3*

*TRPM4*

*TRPM5*

*TRPM6*

*TRPM7*

*TRPM8*

*TRPV1*

*TRPV2*

*TRPV3*  
*TRPV4*  
*TRPV5*  
*TRPV6*

**Bestrophin Ion Channel Genes**

*BEST1*  
*BEST2*  
*BEST3*  
*BEST4*

**Cyclic Nucleotide-gated Cation Channel Genes**

*CNGA1*  
*CNGA2*  
*CNGA3*  
*CNGA4*  
*CNGB1*  
*CNGB3*  
*HCN1*  
*HCN2*  
*HCN3*  
*HCN4*

**GABA-gated Ion Channel Genes**

*GABRA1*  
*GABRA2*  
*GABRA3*  
*GABRA4*  
*GABRA5*  
*GABRA6*  
*GABRB1*  
*GABRB2*  
*GABRB3*  
*GABRD*  
*GABRE*  
*GABRG1*  
*GABRG2*  
*GABRG3*  
*GABRP*  
*GABRQ*  
*GABRR1*  
*GABRR2*  
*GABRR3*

*KCTD12*

**Chloride Channel Genes**

*ANO1*

*ANO10*

*ANO2*

*ANO3*

*ANO4*

*ANO5*

*ANO6*

*ANO7*

*ANO8*

*ANO9*

*BSND*

*CACA3P*

*CFTR*

*CLCA1*

*CLCA2*

*CLCA4*

*CLCC1*

*CLCN1*

*CLCN2*

*CLCN3*

*CLCN4*

*CLCN5*

*CLCN6*

*CLCN7*

*CLCNKA*

*CLCNKB*

*CLIC1*

*CLIC2*

*CLIC3*

*CLIC4*

*CLIC5*

*CLIC6*

*CLNS1A*

*TTYH1*

*TTYH2*

*TTYH3*

**Glutamate-gated Ion Channel Genes**

*GRIA1*

*GRIA2*

*GRIA3*  
*GRIA4*  
*GRID1*  
*GRID2*  
*GRIK1*  
*GRIK2*  
*GRIK3*  
*GRIK4*  
*GRIK5*  
*GRIN1*  
*GRIN2A*  
*GRIN2B*  
*GRIN2C*  
*GRIN2D*  
*GRIN3A*  
*GRIN3B*  
*GRINA*

**Gap Junction Ion Channel Genes**

*GJA1*  
*GJA3*  
*GJA4*  
*GJA5*  
*GJC1*  
*GJD3*  
*PANX1*  
*PANX2*  
*PANX3*

**Nicotinic-gated Cholinergic Ion Channel Genes**

*CHRFAM7A*  
*CHRNA1*  
*CHRNA10*  
*CHRNA2*  
*CHRNA3*  
*CHRNA4*  
*CHRNA5*  
*CHRNA6*  
*CHRNA7*  
*CHRNA9*  
*CHRNB1*  
*CHRNB2*  
*CHRNB3*

*CHRNA4*  
*CHRND*  
*CHRNE*  
*CHRNA3*

**FXRD Ion Transport Regulator Genes**

*FXRD1*  
*FXRD2*  
*FXRD3*  
*FXRD4*  
*FXRD5*  
*FXRD6*  
*FXRD7*

**Hydrogen Ion Channel Genes**

*ATP1B1*  
*ATP5A1*  
*ATP5B*  
*ATP5C1*  
*ATP5D*  
*ATP5E*  
*ATP5EP2*  
*ATP5F1*  
*ATP5G1*  
*ATP5G2*  
*ATP5G3*  
*ATP5H*  
*ATP5I*  
*ATP5J*  
*ATP5J2*  
*ATP5L*  
*ATP5L2*  
*ATP5O*  
*ATP5S*  
*ATP6*  
*ATP6V0C*  
*ATP6VOA2*  
*ATP6VOA4*  
*ATP8*  
*HVCN1*  
*TCIRG1*

**Glycine-gated Ion Channel Genes**

*GLRA1*  
*GLRA2*  
*GLRA3*  
*GLRA4*  
*GLRB*

**Golgi pH Regulator Ion Channel Genes**

*GPR89A*  
*GPR89B*

**Mitochondrial Voltage Dependent Anion Channel Genes**

*VDAC1*  
*VDAC2*  
*VDAC3*

**Ryanodine Receptor & Related Genes**

*CASQ1*  
*CASQ2*  
*JPH1*  
*JPH2*  
*JPH3*  
*JPH4*  
*RYR1*  
*RYR2*  
*RYR3*  
*TRDN*  
*ASPH*

**Piezo-type Mechanosensitive Ion Channel Genes**

*PIEZO1*  
*PIEZO2*

**Serotonin-gated Ion Channel Receptor Genes**

*HTR3A*  
*HTR3B*  
*HTR3C*  
*HTR3D*  
*HTR3E*

**Transmembrane Channel-like Genes**

*TMC4*  
*TMC5*

*TMC7*

**Trimeric Intracellular Cation Channel Genes**

*TMEM37*

*TMEM38A*

*TMEM38B*

**Zinc Activated Ligand Gated Ion Channel Genes**

*ZACN*

**Purinergic Receptor Genes**

*P2RX1*

*P2RX2*

*P2RX3*

*P2RX4*

*P2RX5*

*P2RX6*

*P2RX7*

**Other Calcium Genes**

*CALM2*

*CALM3*

*CAMK2D*

**Phosphodiesterase Genes**

*PDE4A*

*PDE4B*

*PDE4C*

*PDE4D*

**Other**

*NOS1AP* (QT-interval)