Supplemental Materials for

AF Genetics: Is There a Practical Clinical Value Now or In The Future?

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Supplemental Table S1. Rare variants associated with AF

Gene	Gene product	Presumed mechanism of action	Reference
Potassium Channels			
KCNQ1	α–subunit of K_v7.1 channel	Increased I_{Ks}	1-8
KCNE1	β-subunit of K_v7.1 channel (minK)	Increased I_{Ks}	9, 10
KCNE2	β-subunit of K_v7.1 channel (MiRP1)	Increased I_{Ks}	11,12
KCNE5	β-subunit of K_v7.1 channel	Increased I_{Ks}	13
KCNJ2	β-subunit of K_{ir}2.1 channel	Increased I_{K1}	14-16
KCNA5	α-subunit of $K_{v1.5}$ channel	Modulation of I_{Kur}	11, 17, 18
KCNH2	α–subunit of K_v11.1 channel (HERG)	Modulation of I_{Kr}	19, 20
KCND3	α-subunit of $K_{v4.3}$ channel	Increased I_{to} current	21
KCNJ8	α-subunit of K_{ir}6.1 channel	Increased I_{KATP}	22
KCNN3	Ca activated K channel KCa2.3	Modulation of SK_{Ca} current	23, 24
HCN4	Hyperpolarization activated cyclic nucleotide gated K channel 4	Modulation of the pacemaking I_f current	25
ABCC9	SUR2A subunit of K_{ATP} channel	Decreased I_{KATP}	26
Sodium Channels			
SCN5A	α-subunit of Na_v1.5	Modulation of I_{Na}	27-29 30, 31
SCN1B	β-subunit of Na_v1.5	Reduced I_{Na}	32 33
SCN2B	β-subunit of Na_v1.5	Reduced I_{Na}	32
SCN3B	β-subunit of Na_v1.5	Reduced I_{Na}	27, 34
SCN4B	β-subunit of Nav1.5	Not characterized	35
SCN10A	α-subunit of Na_v1.5	Modulation of Na_v1.5	36, 37
Other Candidate Genes			
NUP155	Nucleoporin	Reduced nuclear membrane permeability	38

GJA1	Connexin-43 (Cx43)	Reduced intercellular electrical coupling	39
GJA5	Connexin-40 (Cx40)	Impaired intercellular electrical coupling	40-42
NPPA	Naturetic peptide precursor A	Altered ANP signaling	43-45
ZFHX3	Transcription Factor ATBF-1	Altered binding activity	46
SYNE2	Neseprin-2	Altered expression	46, 47
C9orf3	Aminopeptidase-O	Altered expression	46, 47
GATA4	Transcription Factor: cardiogenesis	Decreased activity	48-50
GATA5	Transcription Factor: cardiogenesis	Decreased activity	51-53
GATA6	Transcription Factor: cardiogenesis	Decreased activity	54-56
NKX2-5	Transcription Factor: cardiogenesis	Decreased activity	57-59
JPH2	Junctophilin-2: modulation of RyR activity	Decreased RyR stabilization	60
CAV1	Caveolin 1/2	Altered ion channel signaling	61, 62
PITX2	Transcription Factor: cardiogenesis	decreased activity	46, 63-65
RYR2	Ryanodine Receptor	Increased activity	66, 67

Supplemental Table S2. Genetic loci associated with AF in Genome Wide Association Studies.

SNP	Chromosome	Closest Gene	Relative Position	Gene Function	Reference(s)
rs13376333	1q21	*KCNN3*	Intronic	Ca-activated K channel	[68]
rs3903239	1q24	*PRRX1*	46kb Upstream	Transcription Factor	[69]
rs6817105	4q25	*PITX2*	150kb Upstream	Transcription Factor	[69, 70]
rs3807989	7q31	*CAV1/2*	Intronic	Cell membrane protein Caveolin 1/2	[69]
rs10821415	9q22	*C9orf3*	Intronic	Aminopeptidase-O	[69]
rs10824026	10q22	*MYOZ1/ SYNPO2L*	5kb Upstream	Z-disk protein Myozenin-1	[69]
rs1152591	14q23	*SYNE2*	Intronic	Sarcomeric protein Neseprin-2	[69]
rs7164883	15q24	*HCN4*	Intronic	Funny current channel	[69]
rs2106261	16q22	*ZFHX3*	Intronic	Transcription Factor	[71]
rs6584555	10q24	*NEURL*	Intronic	E3 Ubiquitin Ligase	[72]
rs10507248	12q24	*TBX5*	Intronic	Transcription Factor	[72]
rs4642101	3p25	*CAND2*	Intronic	Ubiquination scaffold	[72]
rs13216675	6q22	*GJA1*	670 kb Upstream	Gap junction protein Connexin 43	[72]
rs6490029	12q24	*CUX2*	Intronic	Transcription Factor	[72]

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