SUPPLEMENTAL MATERIAL

Supplementary Table 1. Genotyping platforms for the participating studies

Ancestry	Study	Abbreviation	Study design	Genotyping array	Genotype calling algorithm	Inclusion criteria for SNPs			Inclusion/exclusion criteria		#SNPs that met QC criteria	Analysis software version
						MAF	Call rate	*P* for HWE	Call rate	Exclusions (e.g., IBS clustering, Mendelian checks, excess heterozygosity)		
European ancestry	Age, Gene/Environment Susceptibility Study	AGES[1]	Population-based	Illumina HumanExome v.1.0 BeadChip	GenomeStudio combined with the CHARGE joint calling[2]	≥0%	≥95%	NA	≥95%	Mismatched reference genotypes; sex mismatch	238015	seqMeta v.1.6
	Atherosclerosis Risk in Communities study	ARIC[3]	Population-based	Illumina HumanExome Beadchip v1.0	GenomeStudio combined with the CHARGE joint calling[2]	≥0%	≥95%	N/A	≥89.9%	Plink sex check; relatedness PI_HAT>0.4; genetic cluster check	233,238	seqMeta v1.6.0
	British Genetics of Hypertension	BRIGHT[4]	Hypertensive Cases	Illumina Human Exome BeadChip v1.0	GenCall + Zcall	≥0%	≥99%	$>10^{-4}$	≥95% (GenCall), ≥98% (zCall)	Het: separately <1%, >1% MAF, excl ± 3 SD; IBD: excl. by PI_HAT>0.25; sex mismatch; GWAS discordance	245,322	seqMeta v1.3
	Massachusetts General Hospital Cardiology and Metabolic Patient cohort	CAMP[5]	Population-based	Illumina HumanExome Beadchip v1.0	GeneCall + Zcall	≥0%	≥95%	$>10^{-6}$	≥95%	N/A	235,081	seqMeta v1.6.0
	Cardiovascular Health Study	CHS[6]	Population-based	Illumina HumanExome Beadchip v1.0	GenomeStudio combined with the CHARGE joint calling[2]	≥0%	≥95%	N/A	≥97%	N/A	227,006	seqMeta v1.6.0

Ancestry	Study	Abbreviation	Study design	Genotyping array	Genotype calling algorithm	Inclusion criteria for SNPs			Inclusion/exclusion criteria		#SNPs that met	Analysis software
	Erasmus Rucphen Family Study	ERF[7]	Population-based family	Illumina Human Exome BeadChip v1.1	BeadStudio and zCall	>0%	≥95%	NA	≥95%	Heterozygous haploid genotypes set to missing; SNPs not present in CHARGE recode file	242,848	seqMeta v1.6.0
	Framingham Heart Study	FHS[8]	Population-based	Illumina HumanExome Beadchip v1.0	GenomeStudio combined with the CHARGE joint calling[2]	≥0%	≥95%	N/A	≥97%	N/A	247,501	seqMeta v1.6.0
	Genes for Cerebral Hemorrhage on Anticoagulation	GOCHA[9]	Population-based	Illumina HumanExome Beadchip v1.0_A	GenCall + Zcall	≥0%	≥95%	$>10^{-6}$	≥95%	N/A	240,977	seqMeta v1.5.0
	Genetic Regulation of Arterial Pressure In Humans in the Community	GRAPHIC[10]	Population-based	Illumina Human Exome BeadChip v1.0	GenCall + Zcall	≥ 0%	≥95%	$>10^{-4}$	≥95%	Mismatch reference genotypes, Sex mismatch	246,194	seqMeta v.1.6.0
	INTER99 study	INTER99[11]	Population-based	Illumina HumanExome Beadchip v1.0	GenCall + Zcall	≥0%	≥98%	$>10^{-6}$	≥95%	(1) Heterozygosity was calculated separately for MAF<1% and MAF>1%, and samples were dropped judging by plots; (2) cryptic relatedness (related to ≥20 individuals)	224,872	seqMeta v1.5
	Cooperative Health Research in the Region Augsburg	KORA[12]	Population-based	Illumina HumanExome Beadchip v1.0	GenCall+ChargeCluster File	NA	≥95%	NA	No exclusion	Exclusion of samples with PI_HAT>0.1875	232,832	seqMeta

Ancestry	Study	Abbreviation	Study design	Genotyping array	Genotype calling algorithm	Inclusion criteria for SNPs			Inclusion/exclusion criteria		#SNPs that met	Analysis software
	CROATIA-Korcula	Korcula[13]	Isolate population	Illumina HumanHap 370CNV DUO/QUAD Phase 1	Beadstudio-Gencall v3.0	>0.0001	≥98%	$>10^{-6}$	>95%	N/A	236,308	seqMeta v1.6.0
	LifeLines Cohort Study	LifeLines[14]	Population-based	Illumina HumanExome Beadchip v1.1	GeneCall + Zcall	≥0%	≥95%	$>10^{-6}$	≥95%	Exclusion based on PCA and mean IBS	240888	seqMeta v1.6.0
	Utrecht Health Project	UHP[15]	Population-based	Illumina HumanExome BeadChip v1.1	GenomeStudio + zCall	≥0%	≥95%	$>10^{-3}$	≥95%	Discordant sex; heterozygosity (keeping samples within 4 SD from the mean); related samples (randomly removing one sample until there were no samples with IBD>0.2); samples from non-European descent (based on manual inspection of PCA results that were calculated with Eigensoft).	241,173	seqMeta v1.6.0
	Multi-Ethnic Study of Atherosclerosis	MESA[16]	Population-based	Illumina HumanExome Beadchip v1.0	GeneCall + Zcall	≥0%	≥95%	$>10^{-6}$	≥95%	N/A	235,081	seqMeta v1.6.0
	The Netherlands Epidemiology of Obesity	NEO[17]	Population-based	Illumina HumanCoreExome-24v1-0	GeneCall	≥0%	≥98%	$>10^{-6}$	≥98%	Outlying individuals were excluded on the basis of relatedness; non-European ancestry; sex discrepancy; heterozygosity.	209,874	seqMeta v1.5
	Rotterdam Study	RS[18]	Population-based	Illumina HumanExome BeadChip v1.0	Illumina GenomeStudio2011.1	N/A	≥95%	N/A	≥95%	N/A	236,783	seqMeta v1.6.5

Ancestry	Study	Abbreviation	Study design	Genotyping array	Genotype calling algorithm	Inclusion criteria for SNPs			Inclusion/exclusion criteria		#SNPs that met	Analysis software
	Generation Scotland: Scottish Family Health Study	GS:SFHS[19]	Population-based with enrichment for families	HumanOmniExpressExome8v1-2_A and HumanOmniExpressExome-8v1_A	Beadstudio-Gencall v3.0	>0.0001	≥98%	$>10^{-6}$	≥97%	N/A	234,035	seqMeta v1.6.0
	Study of Health in Pomerania	SHIP[20]	Population-based	Illumina HumanExome Beadchip v1.0	Gencall (Illumina Genome Studio), followed by zCall	≥0%	≥95%	$>10^{-4}$	≥98%	High heterozygosity and/or implausibly high cryptic relatedness; IBS clustering; unexpected duplicates; sex mismatches	247,039	seqMeta v1.3
	TwinsUK	TwinsUK[21]	Twin study	Illumina HumanExome Beadchip HumanExome 12v1.0	Gencall	≥0%	≥95%	$>10^{-6}$	≥97%	Autosomal heterozygosity outliers (+/- 4SD (calculated for variants with MAF <1% and MAF >=1% separately) , gender mismatches, ethnic outliers as determined by combining with 1000 Genomes Project data (PCA), GWAS concordance)	246,001	seqMeta v1.3
	Women's Health Initiative	WHI[22]	Population-based	Illumina HumanExome Beadchip v1.0	GeneCall + Zcall	NA	>95%	NA	NA	First degree relatives	246303	seqMeta
	Young Finns Study	YFS[23]	Population-based	Illumina HumanCoreExome-12 Beadchip v1.0	GenCall	≥0%	≥95%	$>10^{-6}$	≥95%	IBS clustering	238,194	seqMeta v1.3

Ancestry	Study	Abbreviation	Study design	Genotyping array	Genotype calling algorithm	Inclusion criteria for SNPs			Inclusion/exclusion criteria		#SNPs that met	Analysis software
African ancestry	Atherosclerosis Risk in Communities study	ARIC[3]	Population-based	Illumina HumanExome Beadchip v1.0	GenomeStudio combined with the CHARGE joint calling[2]	≥0%	≥95%	N/A	≥89.9%	Plink sex check; relatedness PI_HAT>0.4; genetic cluster check	233,238	seqMeta v1.6.0
	Cardiovascular Health Study	CHS[6]	Population-based	Illumina HumanExome Beadchip v1.0	GenomeStudio combined with the CHARGE joint calling[2]	≥0%	≥95%		≥97%	N/A	227,006	seqMeta v1.6.0
	Jackson Heart Study	JHS[24]	Mixed family and population-based	Illumina HumanExome Beadchip v1.0	GenomeStudio combined with the CHARGE joint calling[2]	≥0%	≥95%	$>10^{-6}$	≥95%	Duplicate samples; sex mismatch; inbreeding coefficient F>0.2 or <0.2	234,937	R (3.1.0), seqMeta (1.6.0)
	MESA	MESA[16]	Population-based	Illumina HumanExome Beadchip v1.0	GeneCall + Zcall	≥0%	≥95%	$>10^{-6}$	≥95%	N/A	235,081	seqMeta v1.6.0
	Women's Health Initiative	WHI[22]	Population-based	Illumina HumanExome Beadchip v1.0	GeneCall + Zcall	NA	>95%	NA	NA	First degree relatives	246303	seqMeta

Supplementary Table 2. Association of top variants with PR interval by random-effect meta-analysis

SNP	Closest gene	SNP call rate in FHS	P-value (Random effect)	P-value (Heterogeneity test)
rs6795970	*SCN10A*	1.000	1.11E-37	<0.0001
rs3922844	*SCN5A*	1.000	7.10E-20	<0.0001
rs3807989	*CAV1*	1.000	5.16E-24	<0.0001
rs7660702	*ARHGAP24*	1.000	3.18E-18	<0.0001
rs17287293	*LINC00477*	1.000	6.65E-12	<0.0001
rs11897119	*MEIS1*	0.997	1.61E-13	2.23E-02
rs1896312	*TBX3*	1.000	2.33E-17	1.46E-01
rs883079	*TBX5*	1.000	7.63E-09	2.20E-03
rs116202356	*DLEC1*	1.000	2.01E-16	2.36E-01
rs251253	*CREBRF*	1.000	1.56E-08	5.30E-03
rs11153730	*SLC35F1*	1.000	1.86E-13	2.10E-01
rs35658696	*PAM*	1.000	3.50E-09	1.15E-01
rs2070492	*SLC22A14*	1.000	7.24E-07	1.53E-02
rs2585897	*XPO4*	1.000	6.44E-13	4.40E-01
rs2042995	*TTN*	1.000	4.34E-11	6.98E-01
rs4399693	*ID2*	1.000	2.43E-07	1.39E-01
rs41306688	*ADPRHL1*	1.000	7.36E-09	5.64E-01
rs4745	*EFNA1*	1.000	1.15E-04	6.09E-02
rs11078078	*LINC00670*	1.000	3.59E-06	1.07E-01
rs60632610	*SYNPO2L*	1.000	4.53E-08	9.34E-01
rs11848785	*SIPA1L1*	0.999	4.58E-08	6.44E-01
rs3733414	*FAT1*	1.000	4.81E-08	6.63E-01
rs17362588	*CCDC141*	1.000	2.01E-05	1.62E-01
rs2296172	*MACF1*	1.000	1.14E-07	8.26E-01
rs9398652	*GJA1*	1.000	1.29E-07	7.26E-01
rs442177	*AFF1*	1.000	1.82E-07	7.20E-01
rs7002002	*PLEC*	1.000	2.06E-07	5.47E-01
rs1768208	*MOBP*	1.000	3.57E-07	7.03E-01
rs2119788	*HAND2*	0.999	5.76E-05	1.82E-01
rs17391905	*C1orf185*	1.000	9.61E-07	6.62E-01
rs524295	*ALDH18A1*	1.000	9.75E-07	7.76E-01

Supplementary Table 3. Biological significance of PR-related genes

Locus number	Gene	Prior GWAS associations	Other disease associations	Biological function	Relation to the heart
1	*SCN10A*	PR interval,[25,26] QRS duration[26,27]	Brugada syndrome,[28] episodic pain syndrome,[29] Pit Hopkins syndrome[30]	Sodium voltage-gated channel alpha subunit 10; mediates upstroke of action potential in neurons.[31]	Present in cardiac ganglia[31]
2	*SCN5A*	PR interval[32,33]	LQT3,[34] BrS,[34] sinus node dysfunction,[34] AF,[35] DCM,[36] familial heart block[37]	Responsible for peak inward Na current that underlies upstroke of the cardiac action potential.[38]	See Biological function
3	*CAV1*	PR interval,[26,39] atrial fibrillation,[40] PR segment[41]	Congenital lipodystrophy type 3,[42] primary pulmonary hypertension 3,[43] LCCNS[44]	CAV1 is a main component of caveolae (plasma membrane "rafts").[45] Caveolins are important for cell cycle progression. CAV1 also plays an important role in insulin receptor stabilization.[46]	See GWAS associations; also has a potential role in vascular remodeling and inflammation[47]
4	*ARHGAP24*	PR interval[26]	Focal segmental glomerulosclerosis[48]	Encodes Rho GTPase-activating protein 24. It antagonizes RAC through binding to filamin A,[49] and has highest expression in podocyte adhesions in the kidney.[48]	Prior GWAS association only.
5	*LINC00477*	Heart rate[50,51]		Long intergenic non-protein coding RNA 477. Linc-RNAs are involved in cell-cycle regulation, transcription and metabolism.[52]	Prior GWAS association only
6	*MEIS1*	PR interval[39]	Restless legs syndrome[53-55]	Encodes a homeodomain containing transcription factor.	Required for normal cardiac development; regulates cardiomyocyte cell cycle[56].
7	*TBX3*	PR interval[39]	Ulnar mammary syndrome[57]	Encodes a T-box containing transcription factor. It specifies sino-atrial node development, and represses the atrial gene program in the region of the AV node.[58]	VSD and WPW reported in a family with TBX3 mutation[57].
8	*TBX5*	QRS duration[59]	Holt-Oram syndrome,[60] atrial fibrillation,[61] tetralogy of Fallot[62]	Encodes a T-box containing transcription factor. It interacts with NKX2.5 and GATA4 to regulate cardiomyocyte differentiation.[63,64] It is required for development of the cardiac conduction system.[65]	See Other disease associations and Biological function
9	*DLEC1*		Lung, esophageal and renal carcinoma[66]	Postulated to be a tumor suppressor.[66]	
10	*CREBRF*	PR interval[39]		Encodes a leucine zipper protein that promotes degradation of *CREB3*, and is involved in the unfolded protein response.[67]	Highest expression in the heart and kidney[67].

Locus number	Gene	Prior GWAS associations	Other disease associations	Biological function	Relation to the heart
11	PLN/*SLC35F1*	QT interval,[68,69] heart rate[50]	Possibly neurodevelopmental disorders[70]	*PLN* encodes phospholamban, which interacts with the cAMP-dependent protein kinase in the heart. The SNP is in strong linkage disequilibrium (R^2=0.87) with SNP rs11153768, which was previously reported to be associated with left ventricle internal diastolic dimension.[71]	Prior GWAS association only
12	*PAM*	Type 2 diabetes[72,73]	*Pam* null mice do not survive gestation.[74]	Encodes a protein that catalyzes the conversion of neuroendocrine peptides into alpha-amidated products[75]	High levels of mRNA in rat heart atria;[76] expression in H9c2 rat cardiac myoblasts displaying developmental regulation[77]
13	*SLC22A14*			May play a role in organic cation transport in various tissues[78]	
14	*XPO4*		Associated with non-alcoholic steatohepatitis;[79] also behaves as a tumor suppressor[80]	Encodes a member of the exportin family, which mediates nuclear export of protein cargoes[81]	*XPO4* variant carriers may have smaller infarcts, due to better glucose uptake by the heart.[82]
15	*TTN*	QT interval[68]	Implicated in a number of cardio- and skeletal-myopathies, including: DCM,[83] HFpEF,[84] arrhythmogenic right ventricular dysplasia,[85] late-onset TMD,[86] limb-girdle muscular dystrophy type 2,[87] hereditary myopathy with early respiratory failure,[88] centronuclear myopathy[89]	Plays a major role within the sarcomere in striated muscle, providing structural support during contraction, and regulating passive tension during stretching; also involved in cellular processes such as biomechanical sensing and signaling[90]	Plays a role in cardiac development, health, and disease (see GWAS and disease associations);[90] major contributor to myocyte passive stiffness[84]
16	*ID2*		Upregulated and/or overexpressed in the development and progression of tumors in prostate,[91] epidermis,[92] colon,[93] and pancreas,[94] as well as neuroblastoma.[95]	Regulates cell growth through inhibition of cell differentiation and stimulation of cell proliferation;[96,97] also negatively regulates basic helix-loop-helix gene products[96]	Expressed in the outflow tract, endocardial cushions, and valves of the developing murine heart[98,99]
17	*ADPRHL1*			Reverses ADP-ribosylation, a posttranslational modification that regulates protein function[100]	mRNA expression induced in hESC differentiation to cardiomyocytes;[101] acts during cardiogenesis in xenopus embryos to modify heart chamber outgrowth and myofibril directionality[102]

Locus number	Gene	Prior GWAS associations	Other disease associations	Biological function	Relation to the heart
18	*EFNA1*	Association with prostate cancer susceptibility was implicated by SNPs, but the association was ultimately mapped to *KCNN3;*[103] obesity related traits[104] (but not at genome wide significance); plasma levels of liver enzymes[105]		Ligand that binds to the EPH group of receptor tyrosine kinases	
19	*LINC00670*	Response to amphetamines (relatively close SNP)[106]		Encodes a long intergenic non-protein coding RNA 670	Associated with torsades de pointes[107]
20	*SYNPO2L*	Susceptibility locus for atrial fibrillation;[40] whole exome sequencing for AF[108]	Susceptibility to AF	Encodes an actin-associated protein that may modulate actin shape	Atrial fibrillation[40,108]
21	*SIPA1L1*	FEV1/FVC in COPD;[109] mitral valve prolapse[110]	COPD; mitral valve prolapse	Stimulates the RAP2A GTPase and promotes reorganization of the actin cytoskeleton; recruits DLG4 to F-actin.	Mitral valve prolapse[110]
22	*FAT1*	Chronotype[111] obesity;[112]-Alzheimer disease (intergenic)[113]	Glomerulotubular nephropathy;[114]-multiple types of cancer[115]	Plays an essential role for cellular polarization, directed cell migration, and modulating cell-cell contact; member of the cadherin family;. plays a role as a tumor suppressor gene	
23	*CCDC141*	Heart rate[50]			
24	*MACF1*	HDL cholesterol[116], type 2 diabetes[117]	Knockdown of *MACF1* caused developmental retardation and embryonic death in mice[118] and failure of oocyte polarization in zebrafish.[119]	Encodes a member of the spectraplakin family,[120] which plays an important role in calcium ion binding and cardiomyocyte microtubule distribution;[121] also involved in the regulation of the cytoskeletal response to environmental signaling cues [122] and directional cell movement[123,124]	Expressed in a variety of tissues, including the heart and lungs[125]

Locus number	Gene	Prior GWAS associations	Other disease associations	Biological function	Relation to the heart
25	*GJA1*	Resting heart rate;[51,126] -heart rate[50]	Genetic variation in *GJA1* mayi affect protein kinase phosphorylation and disrupt cell communication.[127] Reductions in GJA1 have been implicated in arrhythmia predisposition.[128] -Various anomalies were observed in *Gja1* knockout mice, such as conotruncal heart malformation and outflow obstruction.[129] Mutations in *GJA1* may also cause congenital heart disease and visceroatrial heterotaxia.[130]	Encodes a gap junction protein known as connexin 43	Highly expressed in ventricular myocardium -- essential to coronary artery development -- and is involved in electrical conduction and synchronization of heart contraction[131]
26	*AFF1*	Triglycerides[132-134]	Gene associated with leukemia[135]	Encodes a member of the AF4/ lymphoid nuclear family	
27	*PLEC*	Post bronchodilator FEV1;[109] cholesterol;[132] fibrinogen levels[136]		Encodes plectin, a giant, multi-domain protein involved in cell structure and shapethat also regulates a variety of signaling complexes	
28	*MOBP*	Progressive supranuclear palsy[137]		Encodes myelin-associated oligodendrocyte basic protein, which is important for stabilization of the myelin sheath.	
29	*HAND2*		Dysfunction can result in pathological hypertrophy and heart failure[138] and stenosis of the right ventricle.[139] Gene knockdown resulted in extra-embryonic abnormalities.[140]	Encodes a transcription factor that binds to a heart- and neural crest derivatives-expressed proteins	The gene regulates cardiac morphogenesis and ventricular cardiomyocyte expansion during heart development.[141-143] Another gene in the same family, *HAND1*, was associated with QRS interval duration.[59]
30	*C1orf185*	QRS duration;[59] FEV1 in COPD[109]		Encodes an RNA expressed in the testis	
31	*ALDH18A1*	Blood metabolites;[144] *Staphylococcus aureus* carriage[145]	Neurodegeneration;[146] cutis laxa; cataracts; DeBarsy syndrome; spastic paraplegia	Encodes a mitochondrial enzyme that catalyzes a critical step in proline, ornithine, and arginine synthesis	Mutations have been linked to decreased collagens I and III[147]

Supplementary Table 4. Association of PR-related variants with AF and P-wave indices

SNP	Locus	Closest gene	Coding allele	CAF*	PR-interval			AF			P-wave duration			P-wave terminal force		
					Beta	SE	*P* value	Beta	SE	*P* value	Beta	SE	*P* value	Beta	SE	*P* value
rs6795970	3p22.2	*SCN10A*	A	0.37	0.171	0.005	4.0E-240	-0.072	0.016	5.4E-06	1.14	0.089	7.3E-38	-0.1	12.5	1.0E+00
rs3922844	3p22.2	*SCN5A*	A	0.34	-0.107	0.005	9.3E-90	0.048	0.017	5.4E-03	-1.058	0.09	3.1E-32	21.2	12.8	9.8E-02
rs3807989	7q31.2	*CAV1*	A	0.43	0.091	0.005	3.0E-74	-0.086	0.016	6.5E-08	0.538	0.084	1.5E-10	18.5	12	1.2E-01
rs7660702	4q21.23	*ARHGAP24*	C	0.33	-0.092	0.005	1.2E-68	0.004	0.015	8.0E-01	0.09	0.088	3.0E-01	22.3	12.8	8.3E-02
rs17287293	12p12.1	*LINC00477*	G	0.14	-0.108	0.007	1.9E-52	-0.105	0.022	2.1E-06	-0.505	0.12	2.7E-05	17.8	16.9	2.9E-01
rs11897119	2p14	*MEIS1*	C	0.39	0.057	0.006	4.2E-25	0.016	0.017	3.6E-01	0.126	0.087	1.5E-01	-7.5	12.4	5.5E-01
rs1896312	12q24.21	*TBX3*	G	0.28	0.056	0.006	8.7E-25	-0.037	0.014	7.2E-03	0.002	0.093	9.8E-01	-6	13.2	6.5E-01
rs883079	12q24.21	*TBX5*	G	0.29	0.055	0.005	4.5E-24	-0.085	0.018	1.7E-06	0.612	0.094	8.3E-11	-39.4	13.5	3.6E-03
rs116202356	3p22.2	*DLEC1*	A	0.02	-0.195	0.02	1.0E-22	0.079	0.055	1.5E-01	-1.72	0.434	7.3E-05	61.6	60.9	3.1E-01
rs251253	5q35.1	*CREBRF*	G	0.42	-0.044	0.005	4.7E-18	-0.034	0.017	3.8E-02	-0.075	0.088	3.9E-01	-15.5	12.6	2.2E-01
rs11153730	6q22.31	*SLC35F1*	C	0.47	-0.042	0.005	9.5E-18	-0.059	0.014	1.9E-05	0.276	0.083	9.4E-04	8.2	11.9	4.9E-01
rs35658696	5q21.1	*PAM*	G	0.04	0.096	0.012	8.5E-16	0.074	0.037	4.9E-02	-0.046	0.272	8.7E-01	-71.5	38	6.0E-02
rs2070492	3p22.2	*SLC22A14*	T	0.1	0.062	0.008	4.0E-14	-0.023	0.026	3.7E-01	0.864	0.158	4.8E-08	28.3	22.8	2.2E-01
rs2585897	13q12.11	*XPO4*	A	0.17	0.047	0.006	2.8E-13	-0.003	0.021	8.8E-01	-0.207	0.115	7.1E-02	18.6	16.5	2.6E-01
rs2042995	2q31.2	*TTN*	C	0.26	0.038	0.006	4.3E-11	0.059	0.018	1.0E-03	0.308	0.097	1.5E-03	42.9	13.9	2.1E-03
rs4399693	2p25.1	*ID2*	A	0.34	0.037	0.006	9.1E-11	0.004	0.017	8.4E-01	0.095	0.107	3.8E-01	-0.6	14.7	9.7E-01
rs41306688	13q34	*ADPRHL1*	C	0.03	0.1	0.017	7.4E-09	0.057	0.044	2.0E-01	-0.401	0.477	4.0E-01	30.1	67.2	6.5E-01
rs4745	1q22	*EFNA1*	T	0.49	0.03	0.005	1.2E-08	0.023	0.014	1.0E-01	0.042	0.094	6.6E-01	-5	12.8	7.0E-01
rs11078078	17p12	*LINC00670*	A	0.4	0.028	0.005	2.2E-08	-0.022	0.016	1.7E-01	-0.045	0.088	6.1E-01	4.5	12.6	7.2E-01
rs60632610	10q22.2	*SYNPO2L*	T	0.15	-0.037	0.007	4.5E-08	-0.11	0.017	1.5E-10	0.324	0.137	1.8E-02	40.4	19.4	3.7E-02
rs11848785	14q24.2	*SIPA1L1*	G	0.24	0.032	0.006	4.6E-08	0.032	0.018	7.7E-02	-0.018	0.099	8.5E-01	10.4	13.9	4.5E-01
rs3733414	4q35.2	*FAT1*	A	0.38	0.028	0.005	4.8E-08	-0.011	0.016	4.9E-01	-0.098	0.087	2.6E-01	-11.2	12.6	3.7E-01
rs17362588	2q31.2	*CCDC141*	A	0.08	-0.049	0.009	5.5E-08	0.001	0.027	9.8E-01	-0.035	0.153	8.2E-01	-19.4	21.4	3.7E-01
rs2296172	1p34.3	*MACF1*	G	0.2	0.033	0.006	1.1E-07	0.025	0.019	1.8E-01	-0.055	0.107	6.1E-01	20.4	15	1.7E-01
rs9398652	6q22.31	*GJA1*	A	0.14	0.039	0.007	1.3E-07	-0.064	0.017	1.1E-04	-0.033	0.121	7.8E-01	-24.8	17.9	1.7E-01
rs442177	4q22.1	*AFF1*	C	0.42	-0.026	0.005	1.8E-07	-0.01	0.013	4.4E-01	0.072	0.084	3.9E-01	21.5	12.2	7.7E-02
rs7002002	8q24.3	*PLEC*	A	0.38	-0.027	0.005	2.1E-07	-0.016	0.014	2.7E-01	0.07	0.103	5.0E-01	11.4	14.5	4.3E-01
rs1768208	3p22.1	*MOBP*	T	0.25	0.029	0.006	3.6E-07	-0.017	0.014	2.0E-01	0.153	0.102	1.3E-01	-5.4	14.3	7.0E-01
rs2119788	4q34.1	*HAND2*	C	0.52	-0.025	0.005	5.6E-07	0.024	0.015	1.1E-01	-0.145	0.091	1.1E-01	10.8	13.1	4.1E-01
rs17391905[+]	1p32.3	*C1orf185*	G	0.03	-0.069	0.014	9.6E-07	0.123	0.049	1.2E-02	-0.357	0.248	1.5E-01	26.1	37	4.8E-01
rs524295	10q24.1	*ALDH18A1*	A	0.4	-0.026	0.005	9.7E-07	-0.022	0.017	1.9E-01	-0.127	0.089	1.5E-01	-6.3	12.5	6.2E-01

Supplementary Table 5. Significant common variants associated with PR interval for European ancestry

SNP	Locus	Closest gene	Function	Coding allele	CAF*	Beta	SE	*P* value
rs6795970	3p22.2	*SCN10A*	Missense	A	0.40	0.1699	0.0053	2.1×10^{-228}
rs3807989	7q31.2	*CAV1*	Intronic	A	0.41	0.0940	0.0053	3.4×10^{-71}
rs7660702	4q21.23	*ARHGAP24*	Intronic	C	0.30	-0.0984	0.0056	3.4×10^{-68}
rs3922844	3p22.2	*SCN5A*	Intronic	A	0.31	-0.0987	0.0057	4.8×10^{-67}
rs17287293	12p12.1	*LINC00477*	Intergenic	G	0.15	-0.1110	0.0073	8.0×10^{-53}
rs1896312	12q24.21	*TBX3*	Intergenic	G	0.29	0.0590	0.0058	2.5×10^{-24}
rs11897119	2p14	*MEIS1*	Intronic	C	0.39	0.0559	0.0058	5.1×10^{-22}
rs251253	5q35.1	*CREBRF*	Intergenic	G	0.39	-0.0473	0.0054	1.3×10^{-18}
rs883079	12q24.21	*TBX5*	UTR3	G	0.28	0.0503	0.0058	4.8×10^{-18}
rs11153730	6q22.31	*SLC35F1*	Intergenic	C	0.49	-0.0422	0.0051	2.2×10^{-16}
rs35658696	5q21.1	*PAM*	Missense	G	0.05	0.0936	0.0120	7.7×10^{-15}
rs4399693	2p25.1	*ID2*	Intergenic	A	0.31	0.0453	0.0061	1.6×10^{-13}
rs2585897	13q12.11	*XPO4*	Intronic	A	0.17	0.0475	0.0068	4.0×10^{-12}
rs41306688	13q34	*ADPRHL1*	Missense	C	0.04	0.1040	0.0176	3.3×10^{-9}
rs2042995	2q31.2	*TTN*	Missense	C	0.23	0.0363	0.0062	4.0×10^{-9}
rs4745	1q22	*EFNA1*	Missense	T	0.53	0.0306	0.0055	1.9×10^{-8}
rs3812629	10q22.2	*SYNPO2L*	Missense	A	0.15	-0.0404	0.0073	2.6×10^{-8}
rs3733415	4q35.2	*FAT1*	Missense	A	0.13	0.0465	0.0084	3.2×10^{-8}
rs9398652	6q22.31	*GJA1*	Intergenic	A	0.10	0.0471	0.0085	3.5×10^{-8}
rs2119788	4q34.1	*HAND2*	Intergenic	C	0.54	-0.0281	0.0052	6.0×10^{-8}
rs442177	4q22.1	*AFF1*	Intronic	C	0.41	-0.0289	0.0053	6.3×10^{-8}
rs80238762	3p22.2	*TTC21A*	Missense	A	0.01	0.1186	0.0221	8.6×10^{-8}
rs524295	10q24.1	*ALDH18A1*	Intergenic	A	0.35	-0.0293	0.0055	1.1×10^{-7}
rs2296172	1p34.3	*MACF1*	Missense	G	0.22	0.0327	0.0062	1.6×10^{-7}
rs11848785	14q24.2	*SIPA1L1*	Intronic	G	0.25	0.0309	0.0059	1.9×10^{-7}
rs17362588	2q31.2	*CCDC141*	Missense	A	0.09	-0.0476	0.0092	1.9×10^{-7}
rs11078078	17p12	*FLJ34690*	Intronic	A	0.37	0.0275	0.0053	2.4×10^{-7}
rs1768208	3p22.1	*MOBP*	Intronic	T	0.28	0.0288	0.0058	5.5×10^{-7}
rs33985936	3p22.2	*SCN11A*	Missense	T	0.25	-0.0297	0.0060	6.8×10^{-7}
rs7002002	8q24.3	*PLEC*	Missense	A	0.41	-0.0264	0.0053	7.1×10^{-7}

*Coding allele frequency

Supplementary Table 6. Significant common variants associated with PR interval for African ancestry

SNP	Locus	Closest gene	Function	Coding allele	CAF*	Beta	SE	P value
rs3922844	3p22.2	*SCN5A*	Intron	A	0.58	-0.1620	0.0148	5.5×10^{-28}
rs6795970	3p22.2	*SCN10A*	Missense	A	0.10	0.1834	0.0249	1.8×10^{-13}
rs883079	12q24.21	*TBX5*	3'UTR	G	0.34	0.0878	0.0154	1.1×10^{-8}

*Coding allele frequency

All three top SNPs were also significantly associated with PR interval for European ancestry

Supplementary Table 7. Association with each top variant in individual studies. Z-scores were listed. AA: African ancestry; EA: European ancestry.

SNP	AA: ARIC	AA: CHS	AA: JHS	AA: MESA	AA: WHI	EA: AGES	EA: ARIC	EA: BRIGHT	EA: CHS	EA: ERF	EA: FHS	EA: GOCHA	EA: GRAPHIC	EA: INTER99	EA: KORA	EA: KORCULA	EA: Lifelines	EA: LRGP	EA: MESA	EA: CAMP	EA: NEO	EA: RS	EA: SCOTLAND	EA: SHIP	EA: TwinsUK	EA: WHI	EA: YFS
rs6795970	3.60	1.73	5.22	0.04	5.39	6.12	12.02	3.81	6.83	1.67	7.54	0.59	3.56	9.23	6.05	-0.09	4.90	4.65	0.51	5.73	11.37	7.06	9.83	8.80	2.29	14.79	7.47
rs3922844	-7.11	-2.89	-7.76	-0.26	-5.10	-2.33	-5.94	-3.18	-3.49	-2.06	-5.86	-2.19	-1.47	-4.86	-1.15	-3.10	-3.38	-1.70	0.80	NA	-4.90	-3.55	-7.35	-6.08	-2.59	-8.07	-2.84
rs3807989	2.03	2.32	1.09	0.85	3.49	4.69	7.47	1.53	3.60	1.76	5.43	0.19	2.50	4.75	3.03	0.90	1.52	3.50	-0.08	3.04	5.65	3.73	7.05	6.29	-0.17	6.15	3.06
rs7660702	-2.91	-0.08	-1.39	-0.51	-1.83	-3.05	-4.74	0.30	-3.67	-2.33	-4.76	0.63	-3.61	-5.91	-4.59	0.31	-3.56	-1.63	0.51	-3.05	-5.08	-3.66	-5.23	-6.79	-1.70	-8.79	-1.74
rs17287293	-0.24	-4.33	-0.01	0.71	-0.55	-3.04	-5.91	-2.06	-3.36	-2.50	-4.33	-1.06	-1.14	-3.50	-3.79	0.51	-0.63	-4.78	1.19	-1.81	-3.69	-0.90	-5.11	-4.34	-1.67	-8.56	-4.71
rs11897119	2.85	-0.20	2.95	0.93	NA	1.53	3.22	0.98	2.47	1.96	2.71	0.97	2.31	3.93	4.01	-1.17	2.64	0.82	-1.34	1.69	3.22	2.93	4.88	1.98	0.03	NA	0.03
rs1896312	2.08	1.36	1.08	0.36	-0.62	1.74	4.20	1.68	1.38	1.31	3.44	-0.33	2.27	3.22	2.49	0.29	1.11	3.00	-0.34	NA	2.24	3.22	2.72	3.36	2.18	3.93	2.18
rs883079	3.32	3.06	3.09	0.40	3.00	1.31	3.38	-0.26	2.52	0.47	1.85	1.60	1.46	2.74	0.51	-0.20	0.85	0.89	-1.38	NA	1.02	0.23	3.58	2.17	0.09	7.45	0.25
rs116202356	-0.60	-0.10	-1.49	-2.10	-0.69	-1.38	-4.02	1.21	-1.78	-1.23	-2.08	-2.02	-2.06	-3.15	-2.10	-0.66	-1.27	-1.76	0.74	-3.20	-3.15	-3.02	-1.71	-2.23	0.12	-5.00	-0.63
rs251253	0.62	-1.63	-1.92	0.28	-0.49	-0.68	-4.06	-0.97	-2.27	-0.86	-4.32	0.85	-1.60	-4.88	-1.93	-0.45	-3.17	-1.02	0.29	NA	-2.59	-1.73	-2.88	-2.06	-1.07	-2.22	-1.30
rs11153730	-1.83	-1.90	-1.31	-0.43	-0.24	-3.14	-2.00	-1.92	-0.82	-1.44	-0.74	0.36	-2.48	-2.08	-2.01	1.08	-1.41	0.77	0.18	-3.66	-3.94	-1.46	-1.60	-2.15	-1.41	-3.92	-1.17
rs35658696	1.69	-0.69	1.04	1.14	1.52	0.51	2.68	0.64	2.21	3.24	1.21	1.41	-0.32	2.68	0.87	-2.29	0.00	-0.56	-0.29	0.22	1.98	1.01	3.62	2.35	2.29	4.11	2.36
rs2070492	2.08	-0.23	0.44	-0.95	0.46	0.44	1.22	-0.20	2.71	-1.38	1.07	0.79	1.53	2.05	2.36	1.95	3.09	2.27	-1.35	0.36	3.02	2.03	2.54	1.64	2.70	4.50	-0.51
rs2585897	2.48	2.13	1.34	-0.44	-0.48	0.20	4.59	1.38	1.55	0.41	0.89	1.58	-0.33	2.54	1.02	0.80	1.12	1.74	0.65	1.92	1.22	0.89	1.74	1.03	2.23	1.92	2.50
rs2042995	1.57	1.47	3.04	-0.93	1.52	1.58	3.39	-0.28	2.13	0.95	1.00	0.01	1.31	1.83	0.89	0.28	2.27	1.18	0.06	-0.72	1.35	0.26	2.04	1.83	-0.53	1.82	1.32
rs4399693	-0.78	0.68	-2.08	0.14	NA	1.10	4.18	-0.24	1.64	0.61	1.76	1.10	1.78	2.47	1.79	1.05	1.52	1.59	-0.70	1.94	2.48	0.71	2.97	1.91	0.35	NA	0.23
rs41306688	0.79	NA	-0.21	-0.75	-0.66	2.93	3.79	1.53	NA	0.52	0.39	0.13	0.62	NA	1.47	1.08	1.48	0.69	-1.16	1.50	NA	2.10	1.93	1.31	2.04	NA	1.14
rs4745	0.06	1.25	0.71	0.40	0.38	1.49	3.32	-0.14	0.69	-0.62	1.82	-0.74	2.95	1.47	0.93	-0.06	2.49	-0.24	0.20	0.38	NA	-1.86	1.64	2.37	2.75	3.33	0.49
rs11078078	0.12	-0.15	1.44	0.68	2.84	2.92	0.97	1.53	0.76	1.59	1.53	-0.03	0.02	1.49	1.80	0.43	-0.65	-1.22	-0.37	0.90	1.90	0.87	1.52	2.55	3.20	1.86	1.82

rs60632610	-0.53	-1.70	-0.46	-0.91	0.46	-0.43	-1.28	-0.09	-0.85	-0.93	-0.23	0.91	-1.57	-0.81	0.15	0.59	-0.94	-1.72	-1.05	-1.92	-1.65	-2.52	-1.44	-1.14	-0.15	-3.39	-1.09
rs11848785	1.67	-0.25	1.14	0.20	0.68	0.33	3.52	-0.29	-0.40	0.01	1.39	-1.13	1.94	2.11	1.22	0.28	0.50	2.15	0.91	0.21	1.57	2.54	1.25	-0.19	-0.13	2.08	1.31
rs3733414	0.71	-0.22	0.51	-0.35	3.69	1.05	0.66	0.83	1.06	1.83	1.45	1.45	1.46	1.87	-0.72	1.24	0.09	1.03	0.62	0.99	1.32	0.87	1.97	1.82	0.94	2.15	1.21
rs17362588	-1.78	0.82	-1.84	0.34	-0.88	-2.71	-0.73	1.02	-0.34	-2.80	-1.35	0.74	-1.19	-1.60	-0.59	1.48	0.32	-0.64	-0.96	-0.55	-1.28	0.90	-1.73	-2.18	-0.48	-3.40	-2.23
rs2296172	1.44	1.45	-0.07	-0.08	-0.74	0.74	1.38	1.50	0.92	2.11	-0.93	0.14	-0.58	2.54	0.79	0.82	0.20	1.89	1.39	2.34	0.85	1.35	2.19	1.88	-0.49	0.85	0.92
rs9398652	1.62	0.48	-0.60	0.43	0.09	0.94	1.74	-0.23	1.66	-0.08	0.75	1.21	0.58	1.93	2.17	0.87	-0.01	0.90	1.48	NA	2.11	-0.50	1.51	-0.10	1.90	3.47	0.95
rs442177	0.84	-0.97	-0.56	0.32	-1.20	-0.32	-3.98	-0.77	-0.16	-1.27	-0.41	0.32	-1.33	-2.05	-2.40	0.60	-0.34	0.33	-1.21	NA	-1.24	0.17	-1.32	-0.52	-0.93	-2.73	-0.31
rs7002002	0.20	NA	-0.93	-1.79	-1.23	-0.91	-1.92	-1.66	NA	-1.27	0.43	-1.86	-0.36	-4.32	-1.16	-0.06	0.09	-0.19	-1.42	0.37	-0.93	0.33	-2.07	-0.71	-0.53	-1.68	-0.41
rs1768208	2.08	-1.59	0.97	-0.65	0.15	1.14	1.84	0.53	1.62	0.25	1.04	-0.22	1.26	2.72	1.11	0.67	1.23	-0.94	-0.77	0.28	1.68	1.88	0.32	2.08	-0.18	2.09	1.31
rs2119788	2.29	-1.35	0.44	-1.47	-0.60	-1.12	-1.38	-1.65	-1.68	-0.23	-1.33	1.04	-0.34	-0.56	-0.32	0.65	-2.08	-0.51	-0.45	-0.68	-2.40	-0.05	-3.97	-1.41	0.34	-1.73	-1.77
rs17391905	-1.96	-1.01	0.26	-1.11	0.06	-2.88	-3.15	-0.52	-0.65	1.56	-0.24	-0.49	0.16	-2.37	-0.64	-0.01	-0.09	-0.10	-0.27	-1.82	-0.02	-1.61	-1.57	-0.60	0.48	-1.89	-0.20
rs524295	1.90	-0.23	0.58	-0.58	-0.66	-1.15	-3.36	-0.83	-1.23	-0.63	-0.16	-1.29	-0.15	0.01	-2.50	-0.05	-0.68	-0.79	-0.33	NA	-2.30	-0.22	-1.77	-0.78	-0.78	-1.89	-0.97

Supplementary Table 8. Association with rare variants in *MYH6* with PR interval

Marker name	dbSNP ID	Chr	Position	Coding allele	Non-coding allele	Coding allele frequency	Beta	SE	P-value	Function
exm1090339	rs201199853	14	23851739	C	G	5.75E-05	-0.340	0.326	2.97E-01	Missense
exm1090343	rs201919534	14	23852468	C	T	7.44E-05	-0.536	0.315	8.90E-02	Missense
exm1090381	rs151324358	14	23854213	A	G	9.16E-05	0.835	0.243	5.92E-04	Missense
exm1090429	rs34330111	14	23856793	A	C	2.05E-04	0.294	0.162	7.03E-02	Missense
exm1090430	rs201827489	14	23856794	A	G	4.31E-05	0.479	0.379	2.07E-01	Missense
exm1090436	rs199936506	14	23856987	T	C	1.72E-04	0.331	0.209	1.13E-01	Missense
exm1809071	rs201016285	14	23857430	T	C	1.08E-05	0.642	0.707	3.64E-01	Missense
exm1090461	rs150815925	14	23857530	T	C	6.77E-04	-0.071	0.095	4.57E-01	Missense
exm1090474	rs145611185	14	23858107	A	G	3.77E-04	0.359	0.121	2.93E-03	Missense
exm1090522	rs145508517	14	23862173	C	T	8.08E-05	0.174	0.257	4.97E-01	Missense
exm1090530	rs143978652	14	23862646	A	C	1.05E-03	-0.120	0.078	1.22E-01	Missense
exm1090537	rs144907522	14	23862913	A	C	4.85E-04	0.179	0.106	8.99E-02	Missense
exm1090541	rs199838024	14	23862996	A	G	1.40E-04	0.529	0.205	9.72E-03	Missense
exm1090542	rs141704264	14	23862997	A	C	2.85E-03	0.110	0.044	1.32E-02	Missense
exm1090555	rs201193346	14	23863348	A	G	4.69E-04	0.002	0.116	9.87E-01	Missense
exm1090559	rs143284278	14	23863362	C	T	3.26E-05	-0.088	0.408	8.30E-01	Missense
exm1090560	rs115845031	14	23863383	T	C	2.11E-03	-0.014	0.051	7.89E-01	Missense
exm1090567	rs202120238	14	23865539	A	G	2.14E-04	0.245	0.178	1.69E-01	Missense
exm1090599	rs142992009	14	23868065	G	T	2.69E-03	0.357	0.046	1.03E-14	Missense
exm1090600	rs150415679	14	23868075	T	C	1.02E-04	0.098	0.249	6.94E-01	Missense
exm1090629	rs200359124	14	23870067	T	C	5.94E-05	0.169	0.302	5.76E-01	Missense
exm1090630	rs147606900	14	23870076	T	C	4.85E-05	0.073	0.333	8.27E-01	Missense
exm1090652	rs138572790	14	23871807	C	G	1.12E-04	0.018	0.277	9.48E-01	Missense
exm1090664	rs140660481	14	23872624	A	C	2.83E-04	-0.229	0.163	1.61E-01	Missense
exm1090665	rs201327273	14	23872631	T	A	1.49E-04	0.347	0.236	1.41E-01	Missense
exm1090674	NA	14	23873927	A	G	4.40E-05	0.298	0.386	4.41E-01	Missense
exm1090675	rs142027794	14	23873940	T	C	6.74E-03	-0.078	0.030	9.54E-03	Missense
exm1090676	rs200623022	14	23873951	T	C	2.16E-05	-0.077	0.500	8.78E-01	Missense
exm1090695	rs141187241	14	23874590	C	T	3.77E-05	-0.176	0.376	6.40E-01	Splicing site
exm1090701	rs140596256	14	23874889	T	C	5.34E-04	0.393	0.112	4.46E-04	Missense
exm1090710	rs142850511	14	23876318	T	C	1.29E-04	0.475	0.242	4.98E-02	Missense
exm1090712	rs150574114	14	23876347	T	C	1.45E-03	0.156	0.061	1.06E-02	Missense

Supplementary Table 9. Association with rare variants in *SCN5A* with PR interval

Marker name	dbSNP ID	Chr	Position	Coding allele	Non-coding allele	Coding allele frequency	Beta	SE	P-value	Function
exm301106	rs7626962	3	38620907	T	G	8.30E-03	-0.11	0.029	1.55E-04	Missense
exm301170	rs41313691	3	38645522	T	G	3.86E-03	-0.02	0.038	5.98E-01	Missense
exm301004	rs41311117	3	38591853	G	A	3.69E-03	0.132	0.042	1.75E-03	Missense
exm301003	rs45489199	3	38591847	C	G	1.75E-03	-0.204	0.06	6.09E-04	Missense
exm301177	rs41313697	3	38646357	C	A	1.29E-03	-0.173	0.067	1.01E-02	Missense
exm301174	rs144511230	3	38646297	A	G	1.14E-03	-0.027	0.070	6.97E-01	Missense
exm301095	rs41261344	3	38616876	T	C	1.11E-03	0.119	0.072	1.01E-01	Missense
exm301214	rs41276525	3	38655290	A	G	8.84E-04	0.311	0.083	1.63E-04	Missense
exm301213	rs45620037	3	38655278	A	G	7.87E-04	0.324	0.086	1.64E-04	Missense
exm301155	rs12720452	3	38645249	T	C	6.95E-04	0.099	0.107	3.55E-01	Missense
exm301154	rs45488304	3	38645241	A	G	6.61E-04	-0.170	0.091	6.20E-02	Missense
exm301081	rs41313031	3	38603947	A	G	6.45E-04	0.237	0.103	2.16E-02	Missense
exm301039	rs199473316	3	38592503	T	C	5.44E-04	0.151	0.106	1.54E-01	Missense
exm301082	rs199473603	3	38603958	A	G	4.85E-04	0.123	0.114	2.79E-01	Missense
exm301207	rs61746118	3	38651303	A	C	3.77E-04	-0.021	0.120	8.61E-01	Missense
exm301149	rs41313681	3	38640465	A	G	3.45E-04	-0.081	0.125	5.19E-01	Missense
exm301085	rs41311127	3	38603991	G	A	3.13E-04	0.197	0.138	1.53E-01	Missense
exm301108	rs1805125	3	38620946	A	G	3.09E-04	-0.163	0.161	3.12E-01	Missense
exm301030	rs45563942	3	38592356	G	A	2.21E-04	-0.06	0.156	7.02E-01	Missense
exm301203	rs199473087	3	38651264	T	A	2.07E-04	-0.145	0.167	3.84E-01	Missense
exm301090	rs199473600	3	38607989	T	C	1.51E-04	-0.15	0.189	4.26E-01	Missense
exm2050823	rs192113333	3	38662392	T	C	1.40E-04	0.017	0.215	9.37E-01	Missense
exm301143	rs199473140	3	38640418	T	C	1.35E-04	0.279	0.305	3.60E-01	Missense
exm301022	rs150264233	3	38592152	A	G	1.19E-04	0.401	0.218	6.54E-02	Missense
exm301061	rs199473618	3	38595989	T	C	1.19E-04	-0.692	0.215	1.27E-03	Missense
exm301152	rs199473577	3	38645235	A	G	1.17E-04	0.002	0.402	9.96E-01	Missense
exm301107	rs199473192	3	38620916	A	G	1.13E-04	-0.216	0.454	6.34E-01	Missense
exm301026	rs45465995	3	38592174	A	G	1.04E-04	0.095	0.250	7.05E-01	Missense
exm301223	rs201232332	3	38662449	T	C	9.17E-05	0.127	0.243	6.02E-01	Missense
exm301220	rs201002736	3	38655522	A	G	8.08E-05	0.175	0.267	5.13E-01	Missense
exm301183	rs199473111	3	38647498	T	C	3.77E-05	-0.205	0.389	5.98E-01	Missense
exm301141	rs199473146	3	38639411	T	C	2.69E-05	0.631	0.447	1.58E-01	Missense
exm301232	rs202114798	3	38671914	C	T	2.16E-05	0.552	0.563	3.27E-01	Missense
exm2239463	rs199473061	3	38663937	T	C	1.18E-05	0.095	0.709	8.94E-01	Missense
exm2050754	rs192379242	3	38616877	A	G	1.08E-05	0.280	0.709	6.92E-01	Missense

Supplementary Table 10. Top gene regions associated with PR interval by the SKAT test that included only damaging variants

Gene	*P* value	Qmeta	CMAF*	#Variants
GORASP1	**1.1E-05**	**14066507**	**0.0262**	**11**
NEBL	**1.9E-05**	**10818563**	**0.0237**	**22**
SCN5A	**2.2E-05**	**10335754**	**0.0184**	**22**
PLEC	1.9E-04	9000047	0.0283	70
CD36	2.8E-04	7951469	0.0132	22
MTRF1	2.9E-04	7671348	0.0150	8
TTN	7.8E-04	51687919	0.3652	435
PRKDC	1.1E-03	3978379	0.0115	22
SDR42E1	1.1E-03	5721052	0.0125	16
AFP	1.1E-03	7479080	0.0175	10

*CMAF: Cumulative minor allele frequency

The significance level threshold for gene-based tests after Bonferroni correction was $P<0.05/2030=2.5x10^{-5}$. The three genes that reached this significance cutoff were highlighted by bold.

Supplementary Table 11. Association of PR-related SNPs with gene expression in the heart and vascular tissues from GTEx database[148]

PR-related SNP[+]	eSNP*	r^2	eGene[$]	*P*-value[&]	Tissue
rs11153730	rs56399949	0.84	*SSXP10*	1.3E-07	Artery Aorta
rs11153730	rs78757409	0.84	*SSXP10*	3.5E-07	Heart Atrial Appendage
rs1768208	rs1768208	1.00	*RPSA*	2.1E-07	Heart Atrial Appendage
rs1768208	rs1768234	0.80	*RPSA*	6.1E-07	Artery Aorta
rs2042995	rs6723399	0.63	*FKBP7*	9.1E-11	Artery Aorta
rs2296172	rs61779310	0.74	*OXCT2P1*	1.7E-10	Artery Aorta
rs2296172	rs1775654	0.61	*RP11-69E11.4*	5.6E-08	Artery Aorta
rs2296172	rs4617393	0.61	*RP11-69E11.4*	1.8E-07	Heart Left Ventricle
rs2296172	rs61779277	1.00	*PABPC4*	2.2E-06	Artery Aorta
rs2296172	rs613511	0.62	*BMP8A*	2.9E-06	Heart Atrial Appendage
rs2296172	rs61779314	0.52	*OXCT2*	4.4E-06	Artery Aorta
rs2296172	rs17264866	0.59	*BMP8A*	5.3E-06	Heart Left Ventricle
rs2296172	rs598415	0.62	*OXCT2P1*	6.4E-06	Heart Atrial Appendage
rs4745	rs370545	0.57	*GBAP1*	3.0E-28	Artery Aorta
rs4745	rs2066981	0.56	*GBAP1*	4.1E-20	Heart Left Ventricle
rs4745	rs914615	0.57	*GBAP1*	3.3E-10	Heart Atrial Appendage
rs4745	rs370545	0.57	*GBAP1*	1.6E-07	Artery Coronary
rs60632610	rs60632610	1.00	*MYOZ1*	4.7E-23	Heart Atrial Appendage
rs7002002	rs11777239	0.86	*PLEC*	1.8E-13	Artery Aorta
rs7002002	rs12543539	0.88	*PLEC*	5.1E-06	Heart Atrial Appendage
rs883079	rs2891503	0.73	*TBX5*	3.8E-06	Heart Left Ventricle

[+] Each variant listed is the top SNP associated with PR-interval at the indicated locus (from Table 2).

* The most significant eSNP at the locus, which is in LD with PR-related SNP ($r^2 \geq 0.5$)

[$] The most significant eGene at the locus

[&] For the association between the eSNP and the eGene from GTEx with FDR<0.05

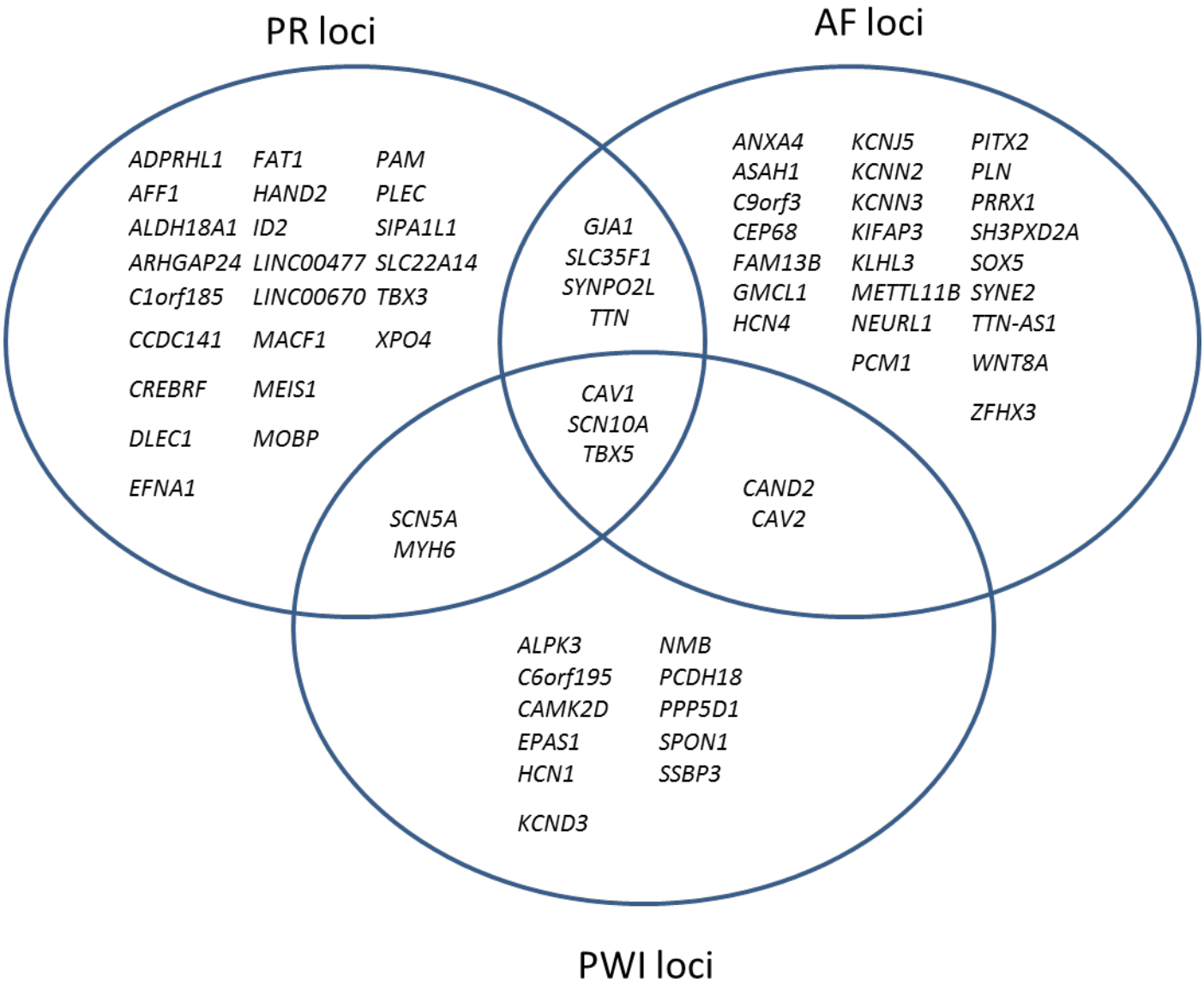
Supplementary Table 12. Most significantly enriched biological pathways

Database	Get set	Original get set size	Effective gene set size	Expected number of genes above 95% cutoff	Observed number of genes above 95% cutoff	Nominal *P*-value	FDR
GO Process	Heart morphogenesis	124	69	3	13	3.6E-05	0.049
GO Process	Regulation of microtubule cytoskeleton organization	52	32	2	7	1.0E-03	0.082
GO Process	Vesicle coating	25	13	1	4	2.9E-03	0.085
REACTOME	Phospholipase C mediated cascade	23	11	1	4	1.6E-03	0.089
GO Process	Actomyosin structure organization	32	20	1	5	2.0E-03	0.092
GO Process	Regulation of heart contraction	83	54	3	9	1.1E-03	0.094
GO Process	Myofibril assembly	26	17	1	5	1.4E-03	0.095
GO Process	Ventricular septum development	23	12	1	4	2.5E-03	0.096

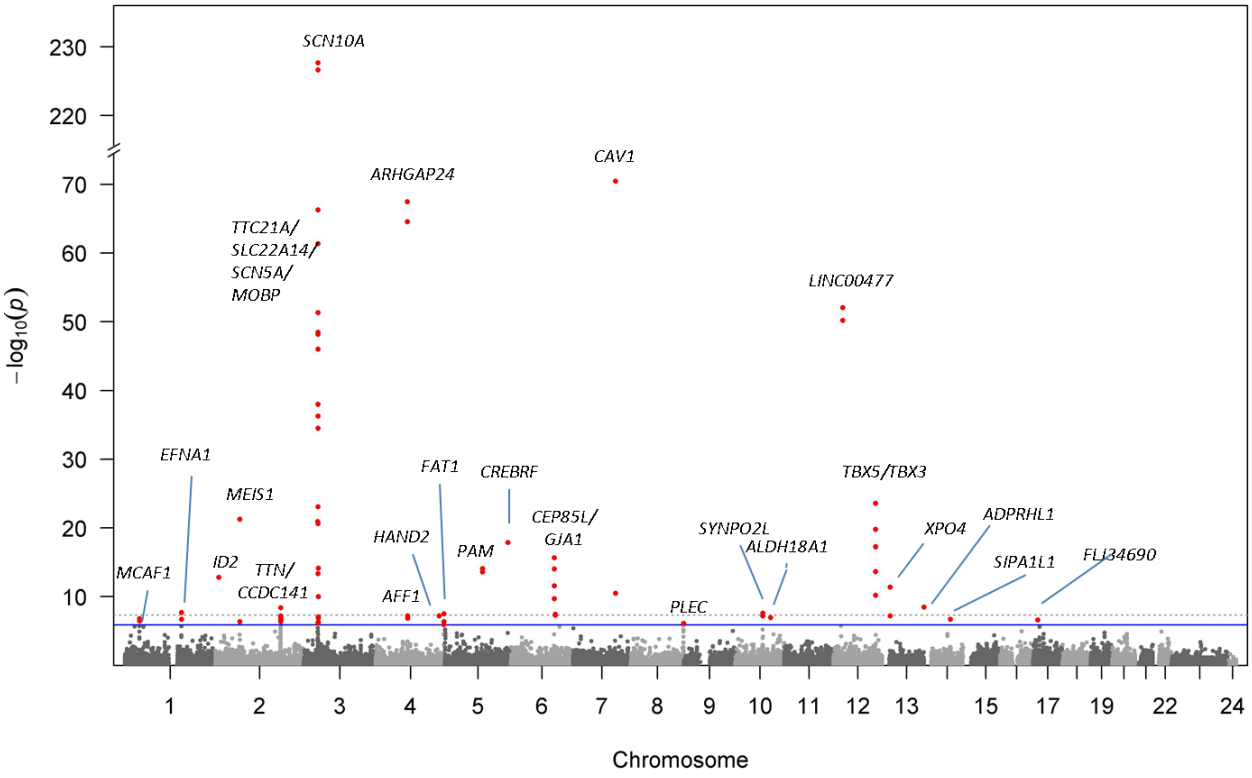
Supplementary Table 13. Percentile of expression compared to all other genes in the same tissue in the GTEx database[148].

Gene	Heart - Atrial Appendage	Heart - Left Ventricle
ADPRHL1	99%	99%
AFF1	93%	92%
ALDH18A1	89%	89%
ARHGAP24	84%	85%
C1orf185	23%	26%
CAV1	99%	99%
CCDC141	84%	86%
CREBRF	83%	85%
DLEC1	60%	58%
EFNA1	95%	93%
FAT1	88%	89%
GJA1	98%	97%
HAND2	96%	95%
ID2	99%	99%
LINC00477	21%	23%
LINC00670	56%	52%
MACF1	93%	92%
MEIS1	83%	83%
MOBP	33%	36%
PAM	100%	99%
PLEC	96%	95%
SCN10A	38%	42%
SCN5A	96%	97%
SIPA1L1	75%	77%
SLC22A14	43%	50%
SLC35F1	73%	75%
SYNPO2L	99%	99%
TBX3	85%	86%
TBX5	98%	99%
TTN	98%	98%
XPO4	80%	79%

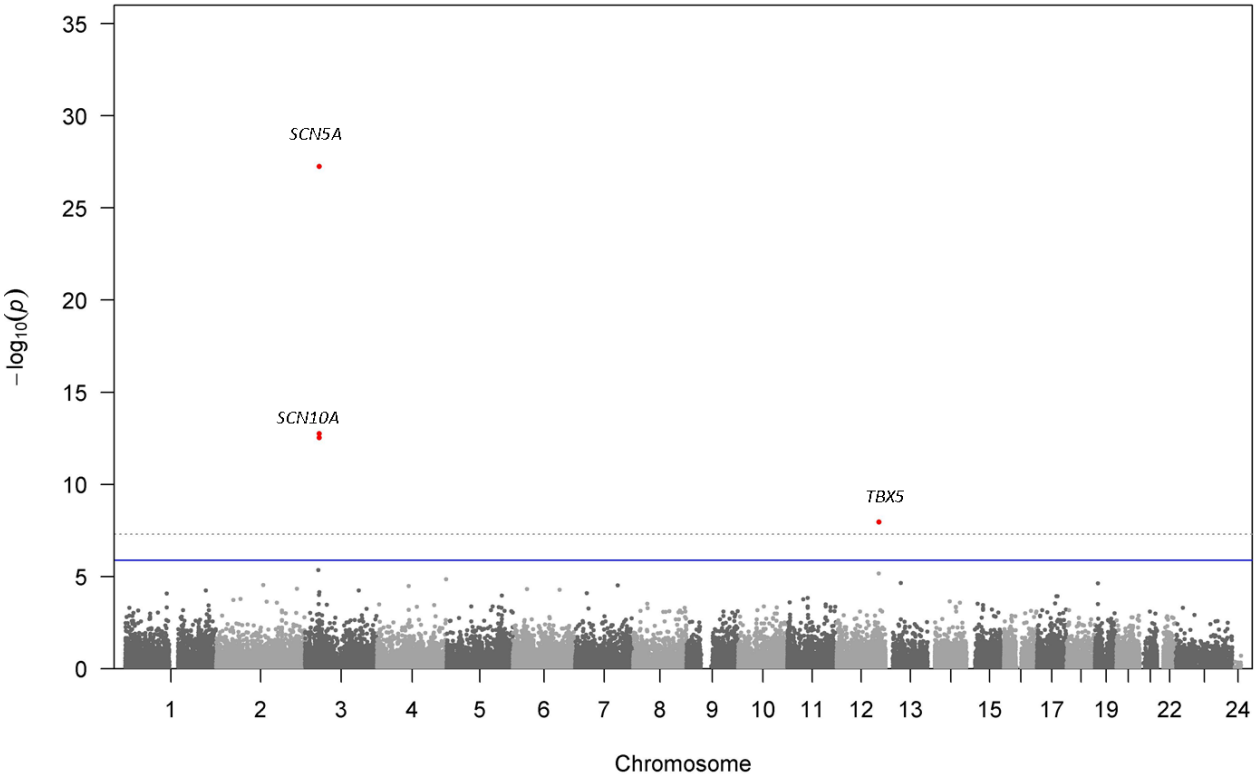
Supplementary Figure 1. Overlap between PR loci with loci associated with AF or P-wave Indices (PWI). "PR loci" represents the top loci from the current study. "AF loci" are the top loci that were recently reported from a large-scale GWAS study of AF(*Nat Genet*, *in press*). "PWI loci" are the top loci that were recently reported from a large-scale GWAS study of PWI (manuscript under review).



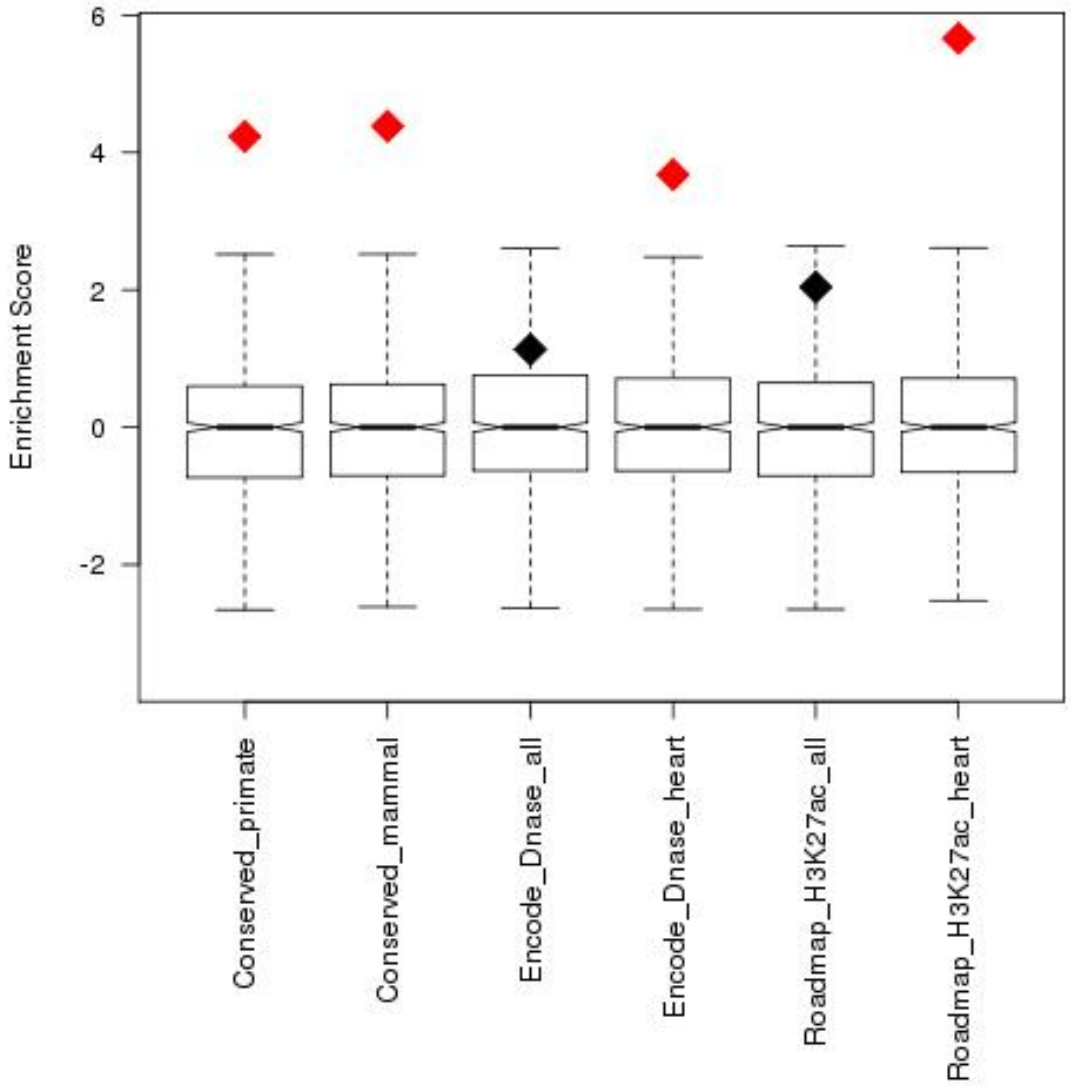
Supplementary Figure 2. Manhattan plot for samples of European ancestry. The x-axis represents the chromosomal position for each SNP, and the y-axis represents the $-\log_{10}$(*P*-value) of the association with PR interval. The dashed line represents the genome-wide significance cutoff of 5×10^{-8}, and the blue line represents the Bonferroni *P*-value cutoff of 1.3×10^{-6}.



Supplementary Figure 3. Manhattan plot for samples of African ancestry. The x-axis represents the chromosomal position for each SNP, and the y-axis represents the –log10(*P*-value) of the association with PR interval. The dashed line represents the genome-wide significance cutoff of $5x10^{-8}$, and blue line represents the Bonferroni *P*-value cutoff of $1.3x10^{-6}$.



Supplementary Figure 4. Enrichment of PR-related variants in regulatory regions. For comparison, 1000 random variant sets were generated, each with MAF values and LD structures similar to those seen for PR-related variants. Red diamonds indicate scores for enrichment of PR variants in the selected regions, significant after Bonferroni correction ($P_{adj} < 0.05$). Black diamonds indicate non-significant enrichment scores. The PR-related variants were enriched in evolutionarily conserved regions and cardiac-specific regulatory regions, but not in general regulatory regions.



Conserved_primate: phastCons 46-way primate conserved elements;
Conserved_mammal: phastCons 46-way mammalian conserved elements;
Encode_Dnase_all: ENCODE DNaseHS master sites (125 cell types);
Encode_Dnase_heart: ENCODE DNaseHS cardiac sites (cardiac fibroblasts, atrial fibroblasts, cardiac myocytes)
Roadmap_H3K27ac_all: Any Roadmap Epigenome H3K27ac gapped peak (98 cell types);
Roadmap_H3K27ac_heart: Any Roadmap Epigenome H3K27ac gapped peak (aorta, right atrium, left ventricle, right ventricle)

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