Supplemental material for:

Integrating Genetic, Transcriptional, and Functional Analyses to Identify Five Novel Genes for Atrial Fibrillation

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Supplemental methods

Study samples: Europeans

Cohorts contributing to the discovery sample included the **Age, Gene / Environment Susceptibility** (**AGES**) study from Reykjavik, Iceland, the **German Competence Network on Atrial Fibrillation** (**AFNET**) with controls from the **Cooperative Health Research in the Region of Augsburg** (**KORA**) **S4** study, the **Atherosclerosis Risk in Communities** (**ARIC**) study, the **Cleveland Clinics Lone Atrial Fibrillation GeneBank Study** (**CC**), the **Cardiovascular Health Study** (**CHS**), the **Framingham Heart Study** (**FHS**), the **Heart and Vascular Health** (**HVH**) Study, the **Massachusetts General Hospital** (**MGH**) and controls from the **MIGEN** study, the **Rotterdam Study I** (**RS-I**), the **Study of Health in Pomerania** (**SHIP**), the **Vanderbilt Lone Atrial Fibrillation Registry**, and the **Women's Genome Health Study** (**WGHS**). Details describing the cohorts in the discovery sample can be found elsewhere.[1]

For the replication stage, we included cohorts providing *in-silico* data derived from prior genome-wide genotyping, and cohorts providing data from direct genotyping. The following cohorts contributed *in-silico* results:

The **Health Aging and Body Composition** (**Health ABC**) Study is an ongoing cohort study of factors contributing to incident disability and the decline in function of healthier older persons. A particular emphasis is on changes in body composition in senescence. The study is sponsored by the National Institute of Aging. Between April 1997 and June 1998, Health ABC enrolled well-functioning, community-dwelling black (n=1,281) and white (n=1,794) men and women age 70-79 years. Recruited from a random sample, participants were white and all black Medicare eligible residents in the Pittsburgh, PA, and Memphis, TN, metropolitan areas. All participants received a baseline exam, annual follow-up clinical exams, and phone contacts every 6 months to identify major health events and document functional status between clinic visits.

The **PROspective Study of Pravastatin in the Elderly at Risk** (**PROSPER**) study has been described elsewhere.[2] In brief, PROSPER is a prospective, multicenter, randomized, placebo-controlled trial to determine if treatment with pravastatin reduces the risk of major vascular events in elderly.[3] From December 1997 to May 1999, individuals were screened and enrolled in Glasgow (Scotland), Cork (Ireland), and Leiden (Netherlands). To be recruited, men and women had to be 70-82 years of age, had to have pre-existing vascular disease or had to be at increased risk of such disease because of smoking, hypertension, or diabetes. Overall, 5,804 participants were randomized to receive pravastatin or placebo. At enrollment, bio-samples were stored and measurement of cognitive function was performed. Upon completion of the clinical trial, stored DNA samples of 5,763 participants were genotyped using the Illumina 660K beadchip (PHASE substudy).[4]

The **Rotterdam Study II** (**RS-II**), a community-based study of elderly individuals from a suburb of Rotterdam, focused on identifying determinants of health and cardiovascular, neurogeriatric, bone, and eye diseases.[5] The study started in 2000-2001. Participants ≥55 years of age were examined triennially and up to 3 times. Atrial fibrillation (AF) was diagnosed based on electrocardiograms at study visit, and upon review of hospital discharge information and general practitioner diagnoses. AF was verified by two physicians and disagreements settled by review of a cardiologist.

The following cohorts provided direct genotyping results:

We recruited AF cases from the **German Competence Network for Atrial Fibrillation** (**AFNET**) national registry.[6] Additional AF cases were recruited from the Department of Medicine I of the University Hospital Munich, Campus Großhadern of the Ludwig-Maximilians University Munich. We enriched for patients with AF onset before 60 years of age. The diagnosis of AF was made based on electrocardiograms analyzed by trained physicians. We excluded with moderate to severe heart failure, moderate to severe valve disease, or hyperthyroidism. Control individuals were enrolled in the **Cooperative Health Research in the Region of Augsburg** (**KORA**) **S4** study, which was conducted

between 1999 and 2001. All participants were 25-74 years old. Those with a history of AF, signs or symptoms of AF on physical examination, or AF on electrocardiograms, which all participants received, were excluded. Initially, 4261 participants were included, and 4073 had full data available for analysis.

From the **Danish Study of Genetic Causes of Atrial Fibrillation (DANFIB)**,[7-9] 396 consecutive patients with AF were included between 2003 and 2011. All enrolled individuals originate from the region of Copenhagen in Denmark. From the same area, a control cohort (n=750) free of AF was recruited. Additional cardiologic evaluation was performed to adjudicate concomitant cardiovascular conditions including, diabetes mellitus, myocardial infarction and heart failure. All enrolled participants provided written informed consent.

The Heart and Vascular Health Study (**HVH**) is a study of incident AF in the setting of Group Health Cooperative, a large integrated healthcare system in Washington State, USA. All plan members assigned a new ICD-9 code of 427.31 or 427.32 in the inpatient or outpatient setting between October 1st, 2001 and December 31st, 2004 were identified. Incident AF was verified by review of medical records with the requirement that the AF be documented by 12-lead electrocardiogram and clinically recognized by a physician, with no previous evidence of AF in the medical record. Control subjects were identified from the Group Health membership, and had no history of AF. Included in the HVH replication sample for this analysis were atrial fibrillation cases of ≥66 years of age or below age 66 but with clinically recognized structural heart disease at atrial fibrillation diagnosis, and referent subjects without atrial fibrillation, who were frequency matched to atrial fibrillation cases on the basis of age, sex, hypertension and year of identification.[10]

The Malmö AF cohort (**MAC**) consists of cases with prevalent or incident AF recruited from two large population-based cohorts in Malmö, Sweden (Malmö Diet and Cancer Study;[11] reexamination of the Malmö Preventive Project[12]). All AF cases were identified from national registers as previously described,[11] and then matched in a 1:1 fashion to controls from the same

cohort by sex, age (±1 year), and date of baseline exam (±1 year). Also, controls required a follow-up exceeding that of the corresponding AF case.

From the **Massachusetts General Hospital Atrial Fibrillation Study** (**MGH**) in Boston, MA, we enrolled additional AF cases that were not available for genome-wide genotyping. Enrollment took place at the hospital's arrhythmia service from 2001 to 2008, and individuals had to be ≤65 years of age at the AF diagnosis, and present without structural heart disease, hyperthyroidism, myocardial infarction, or heart failure. Control patients were also recruited from the **MIGEN** study, which was composed of healthy patients recruited at MGH, particularly free of AF and myocardial infarction.

The **Ottawa Heart AF study** (**Ottawa**) consists of patients with lone AF, or AF and hypertension, recruited from the Arrhythmia Clinic at the University of Ottawa Heart Institute (UOHI), Ottawa, Ontario, Canada. Enrollment required at least one episode of electrocardiographically documented AF characterized by erratic atrial activity without distinct P waves and irregular QRS intervals. Exclusion criteria consisted of a history of coronary artery disease, left ventricular ejection fraction <50%, or significant valvular disease on echocardiography. Control subjects were drawn from the control arm of the Ottawa Heart Genomics Study (OHGS), an ongoing case control study for coronary artery disease at the UOHI. Male control participants were ≥ 65 years, while female controls were ≥ 70 years of age. Controls with a documented history of AF were excluded from this study. All cases and controls were of Western European ancestry and provided written informed consent under a protocol approved by the Human Research Ethics Board at UOHI.

Study samples: Japanese

Japanese samples examined in this study had been investigated earlier.[1] In brief, all AF cases and AF-free controls in the first stage, as well as almost all cases and controls of the second stages were obtained from BioBank Japan. BioBank Japan is a hospital-based disease cohort of 47 common diseases including AF, in which 66 clinical hospitals in Japan participated. Cases in this study are participants of BioBank Japan enrolled between 2003 and 2006. We also enrolled AF samples from

Tokyo Medical and Dental University as part of the second stage. Control individuals for GWAS included participants free of AF who presented with at least one of the following 11 diseases registered in BioBank Japan: hepatic cirrhosis, osteoporosis, colorectal cancer, breast cancer, prostate cancer, lung cancer, uterine myoma, amyotrophic lateral sclerosis, drug eruption, gallbladder and bile duct cancer, and pancreatic cancer. Additional 906 healthy volunteers were recruited from Osaka-Midosuji Rotary Club. The controls in the replication study comprised 17,190 different participants enrolled from Biobank Japan as individuals suffering from one of the following diseases: liver cancer, uterine cervical cancer, chronic type B hepatitis, esophageal cancer, hematological malignancy, uterine endometrial cancer, ovarian cancer, pulmonary tuberculosis, keloid, febrile seizure, rheumatoid arthritis, gastric cancer, and adverse reaction to chemotherapy. Description of cohorts used at the discovery stage can be found in detail elsewhere.[1]

Analysis of eQTLs

We accessed the publicly available Genotype-Tissue Expression Portal (GTEx) of the Broad Institute of Harvard and MIT (available at: http://www.broadinstitute.org/gtex/#; accessed September 1st, 2013) for significant findings in various tissues including subcutaneous adipose tissue, tibial artery, whole blood, cardiac left ventricle, lung, skeletal muscle, tibial nerve, sun-exposed skin, and thyroid. We first searched GTEx for all 49 SNPs considered for replication analysis in Europeans as well as the 2 SNPs identified in Japanese. Second, for those SNPs exceeding or approaching genome-wide significance after replication (**Table 1**), we additionally searched for all proxy SNPs defined as those with at least moderate linkage disequilibrium ($r2 \geq 0.5$) with the sentinel SNPs.

For the analysis of human atrial tissue we obtained samples from the Cleveland Clinic Atrial Tissue Bank (ATB), which consists of atrial tissue samples from consented surgical and transplant donor patients of self-identified European descent obtained between 2001-2011 at the Cleveland Clinic. Samples were processed on the Illumina Human Hap550v3 or Hap610v1 chips and Illumina

HumanHT-12v3 or -v4 chips to obtain genotype and RNA expression data, respectively. Genotypes were called with the GenCall algorithm using the Illumina BeadStudio software; bead-level expression data were extracted using the R package beadarray.

SNP genotype data were filtered for Hardy-Weinberg equilibrium and call rate. Samples were filtered for excess heterozygosity, genetic relatedness, sex mismatch, call rate and genetic population outliers. Genotypes were subsequently passed to SHAPEIT v2 and IMPUTE v2 to generate imputed variant dosage data based on the 1000 Genomes cosmopolitan phase 1 integrated v3 reference panel. Imputed variants with a imputation information score <0.5 were dropped, as were variants with a MAF <0.01.

Natural logarithm (ln)-transformed bead-level expression data were averaged to obtain probe-level measurements for each sample. Probes common to the Illumina Human HT-12v3/v4 chips were subset; missing data were imputed using a KNN method from the R package impute. Probe data were unlogged, background adjusted using a normal-gamma deconvolution method from the R package NormalGamma, ln-transformed with an offset of 10, and then quantile normalized using the R package beadarray. MDS plots were used to filter samples with aberrant expression profiles. Filtered and normalized data were then batch corrected at the chip level using the ComBat empirical-Bayes approach. Validity of the correction was assessed by examining duplicate samples run on multiple chips across batches. We dropped probes not uniquely mapping to the human Ensembl71 transcriptome and the IlluminaHumanv4 R annotation package, not mapping to automosomes, containing imputed variants with MAF ≥0.01, and those that had <5 samples with a detection p-value ≤0.05 or an interquartile range <ln(1.2).

We conducted a genome-wide cis eQTL analysis using the R package MatrixEQTL. For each probe and corresponding variant within 250kb of the probe's mapped gene boundaries (cis probe-variant pair), we linearly regressed the probe's expression values against the variant's imputed dosages along with sex, tissue location (LAA vs. PVT), the top 4 principal coordinates from a MDS

analysis of the genetic-relatedness matrix calculated from a subsample of the filtered genotyped SNPs, and 35 expression surrogate variables. The expression surrogate variables were included to reduce expression heterogeneity and improve power to detect eQTLs; they were calculated using the R package sva on the filtered expression data with a model including sex, principal coordinates and tissue location. For each cis probe-variant pair, we obtained the variant's linear regression coefficient and corresponding p-value under the null of no dosage effect. False discovery rate (FDR) values were calculated from the p-values using the Benjamini and Hochberg method. Cis probe-variant pairs with an FDR value <0.05 were considered genome-wide significant.

Knockdown of candidate genes in zebrafish

Zebrafish of the Tübingen/AB strain were maintained according to standard methods. Morpholino oligonucleotides (MOs) designed to disrupt the proper splicing or translation of zebrafish genes *neurla* (Exon1/Intron1 (1), Exon2/Intron2 (2), 5'UTR (3)), *cand2* (Exon1/Intron1), *cand1* (Exon3/Intron3 (1), Exon10/Intron10 (2), and *cux2b* (Exon12/Intron12)) were obtained from Genetools LLC (Corvallis, OR, USA). A non-targeting MO of equal length was utilized as a control for non-specific toxicity. MOs were diluted in injection buffer (0.4 mM $MgSO_4$, 0.6 mM $CaCl_2$, 0.7 mMKCl, 58 mMNaCl, 25 mM HEPES pH 7.1) and microinjected into the yolks of single cell stage embryos at a final concentration of 0.2 mM in a standardized volume. Consistent injection volumes were confirmed by measurement of 100 µm droplet diameters after injection into mineral oil. Post injection, all embryos were maintained at 28°C in E3 embryo media supplemented with 0.0005% methylene blue and 0.003% phenylthiourea. Effective knockdown was confirmed by RT-PCR analysis of n*eurla*(1) and *cand2*, and by semi-quantitative PCR of *cand1*(1,2), *neurla*(2), and *cux2b*. In brief, mRNA was extracted from 72 hours post fertilization (hpf) embryos using Trizol according to manufacturer's instructions, followed by cDNA production by iScript (BioRad). RT-PCR analysis was conducted using SYBR green supermix (BioRad) on a BioRad CFX384 Real-Time System. *ef-1α* and *β-*

actin were utilized as reference genes for ΔΔct analysis of relative gene expression. All MOs and primers sequences are listed in **Supplemental Table 8**.

Color brightfield images of morpholino-injected embryos were obtained on an Olympus SZX16 microscope at 72 hpf. Heart rate measurement was accomplished at 72 hpf by phase contrast imaging on a Nikon Eclipse Ti base equipped with a Hamamatsu Orca-Flashcam 2.8. Effective frame rate of acquisition was 45 fps. Heart rate was determined manually using ImageJ version 1.47. Measurements of cardiac contractility were conducted according to methods published previously,[13] although with slight modifications. In brief, 72 hpf embryos were anesthetized in 0.016% MS222 (Sigma Aldrich) and positioned for viewing of the ventral surface in 1% agarose dissolved in E3 medium. Ventricular contractility was assayed by measuring the change in inner wall diameter through 3 cardiac cycles when measured perpendicular to the blood flow. Optical mapping was performed to assay action potential durations at 72hpf as previously described.[14]

Supplemental Table 1. Characteristics of the study cohorts

Europeans									
Cohorts used for replication by direct genotyping									
		n	**Age, years**	**Men, %**	**HTN, %**	**BMI, kg/m^2**	**Diabetes, %**	**MI, %**	**CHF, %**
AFNET / KORA	**Cases**	1,780	61.6 ± 12.5	71	60	27.5 ± 4.3	9	4	6
	Controls	3,604	48.3 ± 14.3	49	18	27.1 ± 4.7	4	2	3
DANFIB	**Cases**	396	43.4 ± 2.1	77	22	26.9 ± 4.8	4	4	6
	Controls	750	61.5 ± 17.4	52	58	26.7 ± 4.4	4	2	0
HVH	**Cases**	647	74.0 ± 9.1	39	76	30.3 ± 7.1	16	9	7
	Controls	1,076	72.5 ± 8.2	36	77	29.0 ± 5.8	13	6	3
MAC	**Cases**	2,316	64.8 ± 7.4	63	83	27.3 ± 4.4	8	7	4
	Controls	2,322	64.8 ± 7.4	63	72	26.3 ± 3.9	5	-	-
MGH	**Cases**	181	59.7 ± 11.3	75	55	28.7 ± 5.8	8	4	8
	Controls	362	68.9 ± 11.6	53	61	27.0 ± 5.0	-	-	-
Ottawa	**Cases**	301	47.2 ± 11.4	80	22	-	-	-	-
	Controls	1,517	75.1 ± 5.4	48	43	26.4 ± 4.1	-	-	-
Cohorts used for *in-silico* replication									
		n	**Age, years**	**Men, %**	**HTN, %**	**BMI, kg/m^2**	**Diabetes, %**	**MI, %**	**CHF, %**
HealthABC	**Cases**	434	74.1 ± 2.9	61	66	27.2 ± 4.3	20	26	3
	Controls	1,100	73.6 ± 2.8	49	60	26.4 ± 4.1	16	16	1
PROSPER	**Cases**	505	76.0 ± 3.5	58	64	27.1 ± 4.3	11	19	0
	Controls	4,739	75.3 ± 3.3	47	62	26.8 ± 4.2	10	13	0
RS-II	**Cases**	131	71.9 ± 9.6	55	76	27.3 ± 3.6	18	8	5
	Controls	1,674	64.6 ± 7.8	55	60	27.3 ± 4.3	10	3	1
Japanese									
GWAS	**Cases**	843	67.3 ± 10.4	69	78	23.9 ± 3.6	45	20	-
	Controls	3,350	52.4 ± 15.2	54	33	22.5 ± 3.7	8	2	-
Second stage	**Cases**	1,618	67.8± 10.2	72	71	23.3 ± 3.6	20	12.9	-
	Controls	17,190	61.1± 12.8	44	42	22.2 ± 3.7	0	0	-
Third stage	**Cases**	5,912	68.2± 10.4	70	74	23.5 ± 3.4	14	18	-

HTN – hypertension, defined as systolic blood pressure >140 mmHg, or diastolic blood pressure >90 mmHg, or antihypertensive treatment. BMI – body mass index; Diabetes – diabetes mellitus; MI – myocardial infarction; CHF – heart failure. "-" – data not available.

Supplemental Table 2. *In-silico* replication genotyping information.			
Study	**HealthABC**	**PROSPER**	**RS-II**
Reference	-	[4]	[5]
Genotyping platform	Illumina Human1M-Duo	Illumina Human660K	Illumina550K Duo, 610KQuad
Calling Software	BeadChip	Beadstudio	GenomeStudio
Callrate / SNP	<97%	<97.5%	<98%
HWE p-value	$<10^{-6}$	NA	$<10^{-6}$
Mendelian Errors	NA	NA	NA
Excess heterozygosity	NA	NA	Excluded F-values < mean-4SD (F<-0.055)
MAF	<1%	NA	<5%
SNP for imputation	914,263	557,192	537,405
Total SNPs	2,543,887	2,543,887	2,541,494
Imputation software	MACH v1.0.16	MACH	Mach v1.0.16
Imputation backbone	Build 36	Build 36	Build 36
Inflation factor λ	1.004	-	1.006
Analysis software	R	ProbABEL	ProbABEL, R

Supplemental Table 3. SNP replication results in Europeans, by cohort

	AF	Direct genotyping												*In-silico* Replication					
	Risk	AFNET		DANFIB		HVH		MAC		MGH		Ottawa		HealthABC		PROSPER		RS-II	
SNP	Allele	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*
rs10137710	T	1.02 (0.89 - 1.16)	$7.8x10^{-01}$	1.18 (0.90 - 1.54)	$2.4x10^{-01}$	0.97 (0.80 - 1.17)	$7.2x10^{-01}$	1.08 (0.97 - 1.21)	$1.7x10^{-01}$	1.16 (0.91 - 1.47)	$2.4x10^{-01}$	-	-	1.01 (0.83 - 1.23)	$9.3x10^{-01}$	0.88 (0.73 - 1.05)	$1.6x10^{-01}$	0.91 (0.64 - 1.30)	$5.9x10^{-01}$
rs10212121	A	0.90 (0.82 – 1.00)	$4.7x10^{-02}$	1.21 (0.95 - 1.53)	$1.2x10^{-01}$	1.03 (0.89 - 1.19)	$7.2x10^{-01}$	0.97 (0.89 - 1.06)	$5.2x10^{-01}$	1.01 (0.83 - 1.23)	$9.1x10^{-01}$	-	-	1.03 (0.88 - 1.21)	$6.9x10^{-01}$	0.91 (0.79 - 1.05)	$2.2x10^{-01}$	1.09 (0.84 - 1.42)	$525x10^{-01}$
rs10267684	T	0.99 (0.89 - 1.10)	$8.6x10^{-01}$	1.16 (0.92 - 1.45)	$2.1x10^{-01}$	0.95 (0.82 - 1.10)	$5.1x10^{-01}$	1.03 (0.94 - 1.13)	$5.3x10^{-01}$	1.31 (1.08 - 1.59)	$6.6x10^{-03}$	-	-	1.05 (0.89 - 1.23)	$5.7x10^{-01}$	0.97 (0.84 - 1.12)	$6.8x10^{-01}$	1.04 (0.79 - 1.38)	$7.3x10^{-01}$
rs10507248	T	1.23 (1.10 - 1.37)	$1.5x10^{-04}$	1.06 (0.83 - 1.35)	$6.2x10^{-01}$	1.02 (0.88 - 1.19)	$7.9x10^{-01}$	1.14 (1.03 - 1.25)	$9.0x10^{-03}$	1.10 (0.89 - 1.35)	$3.8x10^{-01}$	-	-	1.00 (0.85 - 1.18)	$9.9x10^{-01}$	1.05 (0.91 - 1.22)	$5.1x10^{-01}$	1.04 (0.78 - 1.37)	$8.0x10^{-01}$
rs10762941	A	1.03 (0.93 - 1.14)	$5.3x10^{-01}$	0.91 (0.73 - 1.12)	$3.7x10^{-01}$	1.15 (1.00 - 1.32)	$5.3x10^{-02}$	0.97 (0.89 - 1.05)	$4.2x10^{-01}$	0.89 (0.74 - 1.07)	$2.0x10^{-01}$	-	-	1.04 (0.89 - 1.20)	$6.4x10^{-01}$	1.01 (0.88 - 1.15)	$9.3x10^{-01}$	0.80 (0.61 - 1.06)	$1.1x10^{-01}$
rs10800507	C	1.14 (1.03 - 1.27)	$1.0x10^{-02}$	1.12 (0.91 - 1.39)	$2.9x10^{-01}$	1.01 (0.88 - 1.16)	$9.2x10^{-01}$	1.08 (0.99 - 1.18)	$8.5x10^{-02}$	1.15 (0.96 - 1.37)	$1.4x10^{-01}$	-	-	1.00 (0.86 - 1.16)	$9.7x10^{-01}$	0.95 (0.83 - 1.09)	$4.9x10^{-01}$	1.08 (0.83 - 1.39)	$6.1x10^{-01}$
rs10849152	T	0.93 (0.83 - 1.02)	$1.01x10^{-01}$	1.08 (0.86 - 1.33)	$5.1x10^{-01}$	1.08 (0.93 - 1.23)	$3.1x10^{-01}$	0.99 (0.91 - 1.08)	$8.3x10^{-01}$	1.05 (0.88 - 1.27)	$5.4x10^{-01}$	-	-	0.85 (0.73 - 0.98)	$3.0x10^{-02}$	1.20 (1.05 - 1.37)	$7.3x10^{-03}$	1.19 (0.92 - 1.54)	$2.0x10^{-01}$
rs10919369	T	1.13 (1.00 - 1.27)	$4.3x10^{-02}$	1.03 (0.82 - 1.31)	$7.8x10^{-01}$	0.87 (0.74 - 1.03)	$1.2x10^{-01}$	1.08 (0.98 - 1.19)	$1.0x10^{-01}$	1.25 (1.00 - 1.55)	$4.5x10^{-02}$	-	-	1.06 (0.89 - 1.25)	$5.4x10^{-01}$	1.04 (0.88 - 1.22)	$6.7x10^{-01}$	0.84 (0.61 - 1.17)	$3.1x10^{-01}$
rs10947261	G	1.2 (1.01 - 1.43)	$3.7x10^{-02}$	1.45 (0.93 - 2.22)	$1.0x10^{-01}$	1.15 (0.88 - 1.49)	$3.1x10^{-01}$	1.01 (0.87 - 1.16)	$9.4x10^{-01}$	1.14 (0.82 - 1.59)	$4.4x10^{-01}$	-	-	0.93 (0.71 - 1.20)	$5.7x10^{-01}$	0.93 (0.70 - 1.20)	$5.5x10^{-01}$	0.93 (0.58 - 1.47)	$7.5x10^{-01}$
rs11466656	C	-	-	-	-	-	-	-	-	-	-	-	-	10.00 (0.01 -)	$5.3x10^{-01}$	0.23 (0.00 - 50.00)	$6.0x10^{-01}$	0.29 (0.00 -)	$8.1x10^{-01}$
rs12370365	G	1.11 (0.99 - 1.25)	$7.3x10^{-02}$	0.99 (0.76 - 1.30)	$9.4x10^{-01}$	1.28 (1.09 - 1.54)	$4.0x10^{-03}$	1.06 (0.96 - 1.18)	$2.3x10^{-01}$	1.12 (0.91 - 1.39)	$3.0x10^{-01}$	-	-	1.05 (0.88 - 1.25)	$5.8x10^{-01}$	1.02 (0.87 - 1.20)	$7.8x10^{-01}$	1.16 (0.83 - 1.61)	$3.7x10^{-01}$
rs12406668	T	1.00 (0.84 - 1.19)	$9.9x10^{-01}$	1.17 (0.78 - 1.75)	$4.6x10^{-01}$	0.86 (0.66 - 1.13)	$2.8x10^{-01}$	1.07 (0.91 - 1.26)	$4.2x10^{-01}$	1.16 (0.83 - 1.62)	$3.9x10^{-01}$	-	-	0.97 (0.75 - 1.26)	$8.2x10^{-01}$	0.9 (0.69 - 1.17)	$4.3x10^{-01}$	0.86 (0.5 - 1.50)	$6.1x10^{-01}$
rs12415501	T	1.31 (1.16 - 1.49)	$2.0x10^{-05}$	-	-	1.05 (0.88 - 1.26)	$5.7x10^{-01}$	1.27 (1.14 - 1.41)	$2.0x10^{-05}$	-	-	1.11 (0.87 – 1.41)	$4.0x10^{-1}$	1.03 (0.85 - 1.24)	$7.6x10^{-01}$	1.31 (1.07 - 1.60)	$9.0x10^{-03}$	1.30 (0.93 - 1.82)	$1.3x10^{-01}$
rs12733930	C	0.90 (0.80 - 1.02)	$1.1x10^{-01}$	0.95 (0.74 - 1.23)	$7.3x10^{-01}$	1.09 (0.91 - 1.30)	$3.6x10^{-01}$	1.05 (0.94 - 1.16)	$3.5x10^{-01}$	1.12 (0.89 - 1.41)	$3.1x10^{-01}$	-	-	0.94 (0.79 - 1.12)	$5.2x10^{-01}$	1.04 (0.89 - 1.23)	$5.8x10^{-01}$	1.00 (0.72 - 1.39)	$1.0x10^{-00}$
rs12991989	C	1.09 (0.99 - 1.20)	$9.3x10^{-02}$	1.02 (0.83 - 1.27)	$8.5x10^{-01}$	0.90 (0.78 - 1.04)	$1.5x10^{-01}$	0.97 (0.89 - 1.05)	$4.3x10^{-01}$	1.12 (0.94 - 1.35)	$1.9x10^{-01}$	-	-	1.11 (0.95 - 1.28)	$1.8x10^{-01}$	0.99 (0.86 - 1.12)	$8.3x10^{-01}$	0.90 (0.69 - 1.18)	$4.5x10^{-01}$
rs13169864	G	1.02 (0.91 - 1.15)	$7.4x10^{-01}$	1.10 (0.85 - 1.45)	$4.6x10^{-01}$	1.01 (0.85 - 1.19)	$9.0x10^{-01}$	0.95 (0.85 - 1.05)	$3.4x10^{-01}$	1.19 (0.96 - 1.47)	$1.2x10^{-01}$	-	-	1.23 (1.00 - 1.52)	$5.4x10^{-02}$	1.11 (0.93 - 1.33)	$2.6x10^{-01}$	1.43 (0.93 - 2.22)	$1.0x10^{-01}$
rs13216675	T	1.19 (1.08 - 1.33)	$1.0x10^{-03}$	1.11 (0.88 - 1.41)	$3.5x10^{-01}$	0.97 (0.83 - 1.13)	$6.7x10^{-01}$	1.06 (0.98 - 1.16)	$1.4x10^{-01}$	1.02 (0.83 - 1.25)	$8.5x10^{-01}$	-	-	1.03 (0.88 - 1.20)	$6.9x10^{-01}$	1.2 (1.04 - 1.39)	$1.4x10^{-02}$	1.16 (0.87 - 1.54)	$3.1x10^{-01}$
rs1324739	G	1.29 (0.87 - 1.90)	$2.0x10^{-01}$	1.02 (0.53 - 1.94)	$9.6x10^{-01}$	1.63 (1.08 - 2.47)	$2.1x10^{-02}$	0.98 (0.77 - 1.23)	$8.3x10^{-01}$	1.27 (0.70 - 2.30)	$4.3x10^{-01}$	-	-	0.71 (0.43 - 1.17)	$1.8x10^{-01}$	0.74 (0.47 - 1.17)	$2.0x10^{-01}$	0.61 (0.21 - 1.78)	$3.7x10^{-01}$
rs13396611	T	1.29 (0.99 - 1.67)	$5.5x10^{-02}$	0.86 (0.47 - 1.58)	$6.2x10^{-01}$	0.74 (0.50 - 1.11)	$1.5x10^{-01}$	0.81 (0.64 - 1.03)	$7.9x10^{-02}$	1.01 (0.65 - 1.58)	$9.7x10^{-01}$	-	-	1.31 (0.91 - 1.88)	$1.4x10^{-01}$	0.79 (0.51 - 1.23)	$3.0x10^{-01}$	0.71 (0.32 - 1.59)	$4.1x10^{-01}$
rs2118254	C	1.00 (0.91 - 1.09)	$9.5x10^{-01}$	1.04 (0.85 - 1.28)	$7.0x10^{-01}$	1.25 (1.10 - 1.42)	$1.0x10^{-03}$	0.98 (0.91 - 1.06)	$6.4x10^{-01}$	1.01 (0.85 - 1.19)	$9.5x10^{-01}$	-	-	1.01 (0.87 - 1.17)	$9.1x10^{-01}$	1.00 (0.87 - 1.14)	$9.5x10^{-01}$	1.16 (0.89 - 1.50)	$2.7x10^{-01}$
rs2204224	T	-	-	-	-	-	-	-	-	-	-	-	-	1.00 (0.79 - 1.27)	$9.8x10^{-01}$	0.91 (0.73 - 1.13)	$3.9x10^{-01}$	1.1 (0.72 - 1.69)	$6.6x10^{-01}$
rs2249965	A	0.92 (0.82 - 1.02)	$1.0x10^{-01}$	1.00 (0.80 - 1.24)	$9.7x10^{-01}$	0.99 (0.86 - 1.15)	$9.1x10^{-01}$	1.03 (0.94 - 1.12)	$5.1x10^{-01}$	1.04 (0.87 - 1.26)	$6.4x10^{-01}$	-	-	1.15 (0.99 - 1.35)	$7.5x10^{-02}$	0.99 (0.86 - 1.14)	$8.7x10^{-01}$	0.92 (0.69 - 1.22)	$5.6x10^{-01}$
rs2305398	G	1.12 (1.02 - 1.25)	$2.3x10^{-02}$	1.08 (0.86 - 1.33)	$5.2x10^{-01}$	1.06 (0.93 - 1.23)	$3.7x10^{-01}$	1.09 (1.00 - 1.19)	$4.7x10^{-02}$	0.93 (0.76 - 1.11)	$4.0x10^{-01}$	-	-	0.97 (0.83 - 1.12)	$6.6x10^{-01}$	1.04 (0.91 - 1.19)	$5.5x10^{-01}$	0.99 (0.75 - 1.30)	$9.2x10^{-01}$
rs2358891	G	-	-	-	-	-	-	-	-	-	-	-	-	1.19 (1.00 - 1.41)	$5.3x10^{-02}$	1.03 (0.88 - 1.20)	$6.8x10^{-01}$	1.23 (0.89 - 1.69)	$2.1x10^{-01}$
rs2532144	T	1.10 (1.00 - 1.22)	$5.1x10^{-02}$	0.78 (0.62 - 0.99)	$3.8x10^{-02}$	1.09 (0.94 - 1.25)	$2.5x10^{-01}$	1.12 (0.98 - 1.28)	$1.0x10^{-01}$	1.03 (0.86 - 1.22)	$7.4x10^{-01}$	-	-	0.99 (0.85 - 1.15)	$9.0x10^{-01}$	0.92 (0.79 - 1.05)	$2.2x10^{-01}$	1.18 (0.88 - 1.56)	$2.5x10^{-01}$
rs2685217	T	1.02 (0.91 - 1.14)	$7.4x10^{-01}$	0.87 (0.67 - 1.12)	$2.8x10^{-01}$	1.04 (0.88 - 1.22)	$6.8x10^{-01}$	0.98 (0.89 - 1.08)	$7.0x10^{-01}$	1.01 (0.82 - 1.24)	$9.3x10^{-01}$	-	-	1.05 (0.88 - 1.26)	$5.6x10^{-01}$	1.06 (0.90 - 1.24)	$5.1x10^{-01}$	1.03 (0.75 - 1.41)	$8.8x10^{-01}$
rs2723065	A	1.05	$3.0x10^{-01}$	0.90	$3.4x10^{-01}$	1.12	$1.2x10^{-01}$	1.01	$8.1x10^{-01}$	1.22	$4.7x10^{-02}$	-	-	1.14	$1.1x10^{-01}$	1.15	$4.6x10^{-02}$	0.91	$4.8x10^{-01}$

Supplemental Table 3. SNP replication results in Europeans, by cohort

	AF	Direct genotyping												*In-silico* Replication					
	Risk	AFNET		DANFIB		HVH		MAC		MGH		Ottawa		HealthABC		PROSPER		RS-II	
		(0.95 - 1.16)		(0.72 - 1.12)		(0.97 - 1.30)		(0.93 - 1.10)		(1.00 - 1.47)				(0.97 - 1.32)		(1.00 - 1.32)		(0.70 - 1.19)	
rs276857	G	1.15 (0.99 - 1.34)	$6.6x10^{-02}$	0.93 (0.67 - 1.28)	$6.4x10^{-01}$	0.95 (0.78 - 1.17)	$6.4x10^{-01}$	1.08 (0.96 - 1.21)	$2.0x10^{-01}$	1.14 (0.86 - 1.51)	$3.5x10^{-01}$	-	-	1.06 (0.85 - 1.33)	$6.0x10^{-01}$	1.08 (0.86 - 1.35)	$5.2x10^{-01}$	0.81 (0.50 - 1.33)	$4.2x10^{-01}$
rs3780190	G	1.18 (1.06 - 1.30)	$1.0x10^{-03}$	0.85 (0.68 - 1.05)	$1.3x10^{-01}$	1.00 (0.88 - 1.15)	$9.7x10^{-01}$	1.03 (0.94 - 1.12)	$4.9x10^{-01}$	1.01 (0.85 - 1.20)	$8.7x10^{-01}$	-	-	1.05 (0.91 - 1.22)	$5.0x10^{-01}$	1.05 (0.93 - 1.20)	$4.4x10^{-01}$	1.16 (0.89 - 1.54)	$2.6x10^{-01}$
rs3922843	A	1.02 (0.92 - 1.15)	$6.7x10^{-01}$	1.02 (0.79 - 1.31)	$9.0x10^{-01}$	0.96 (0.82 - 1.12)	$6.1x10^{-01}$	1.10 (1.00 - 1.21)	$4.3x10^{-02}$	1.17 (0.96 - 1.42)	$1.2x10^{-01}$	-	-	1.13 (0.96 - 1.33)	$1.5x10^{-01}$	1.06 (0.92 - 1.24)	$4.2x10^{-01}$	0.89 (0.65 - 1.21)	$4.6x10^{-01}$
rs4238314	A	1.04 (0.94 - 1.14)	$4.8x10^{-01}$	1.21 (0.97 - 1.52)	$8.9x10^{-02}$	1.00 (0.87 - 1.16)	$9.5x10^{-01}$	1.01 (0.93 - 1.09)	$8.6x10^{-01}$	1.08 (0.91 - 1.28)	$3.9x10^{-01}$	-	-	0.96 (0.83 - 1.12)	$6.3x10^{-01}$	0.98 (0.85 - 1.12)	$7.4x10^{-01}$	1.00 (0.76 - 1.31)	$9.9x10^{-01}$
rs4642101	G	1.16 (1.05 - 1.30)	$4.2x10^{-03}$	-	-	1.15 (0.99 - 1.33)	$6.4x10^{-02}$	1.11 (1.01 - 1.20)	$2.4x10^{-02}$	-	-	1.19 (0.83 - 1.45)	$8.5x10^{-2}$	0.96 (0.83 - 1.18)	$6.3x10^{-01}$	1.03 (0.89 - 1.18)	$7.1x10^{-01}$	0.85 (0.65 - 1.10)	$2.2x10^{-01}$
rs4824051	C	1.09 (0.97 - 1.20)	$1.6x10^{-01}$	1.12 (0.87 - 1.47)	$3.6x10^{-01}$	1.22 (1.03 - 1.45)	$2.3x10^{-02}$	1.00 (0.90 - 1.10)	$9.3x10^{-01}$	0.93 (0.75 - 1.16)	$5.4x10^{-01}$	-	-	1.05 (0.88 - 1.27)	$5.8x10^{-01}$	1.05 (0.89 - 1.23)	$5.3x10^{-01}$	1.10 (0.81 - 1.52)	$5.4x10^{-01}$
rs56235003		0.56 (0.41 - 0.76)	$9.2x10^{-05}$	0.96 (0.31 - 2.94)	$9.5x10^{-01}$	0.89 (0.40 - 1.95)	$7.7x10^{-01}$	-	-	0.94 (0.44 - 2.01)	$8.7x10^{-01}$	-	-	-	-	-	-	-	-
rs6062468	C	1.03 (0.94 - 1.14)	$5.3x10^{-01}$	1.04 (0.84 - 1.28)	$7.5x10^{-01}$	0.99 (0.86 - 1.14)	$8.8x10^{-01}$	0.97 (0.89 - 1.05)	$4.3x10^{-01}$	1.03 (0.85 - 1.24)	$7.9x10^{-01}$	-	-	0.98 (0.85 - 1.13)	$8.1x10^{-01}$	1.16 (1.01 - 1.34)	$4.2x10^{-02}$	1.31 (0.98 - 1.74)	$6.7x10^{-02}$
rs6540690	C	1.11 (0.98 - 1.25)	$1.1x10^{-01}$	0.95 (0.74 - 1.22)	$7.1x10^{-01}$	0.89 (0.75 - 1.05)	$1.9x10^{-01}$	0.98 (0.88 - 1.09)	$7.2x10^{-01}$	1.12 (0.91 - 1.41)	$2.8x10^{-01}$	-	-	0.99 (0.83 - 1.18)	$9.2x10^{-01}$	0.85 (0.72 - 1.01)	$6.8x10^{-02}$	0.92 (0.65 - 1.28)	$560x10^{-01}$
rs6749773	A	0.93 (0.85 - 1.03)	$1.8x10^{-01}$	0.91 (0.73 - 1.13)	$3.9x10^{-01}$	1.06 (0.92 - 1.22)	$4.1x10^{-01}$	1.01 (0.93 - 1.09)	$2.0x10^{-01}$	0.95 (0.79 - 1.14)	$6.1x10^{-01}$	-	-	1.13 (0.98 - 1.31)	$9.9x10^{-02}$	1.00 (0.88 - 1.14)	$9.9x10^{-01}$	1.13 (0.87 - 1.48)	$3.61x10^{-01}$
rs6882776	A	0.95 (0.85 - 1.06)	$3.9x10^{-01}$	1.02 (0.81 - 1.29)	$8.7x10^{-01}$	0.83 (0.71 - 0.97)	$1.8x10^{-02}$	0.91 (0.83 – 1.00)	$3.9x10^{-02}$	0.83 (0.68 - 1.01)	$6.4x10^{-02}$	-	-	0.99 (0.84 - 1.16)	$8.8x10^{-01}$	1.02 (0.89 - 1.18)	$7.5x10^{-01}$	0.97 (0.72 - 1.30)	$8.4x10^{-01}$
rs6884185	C	1.08 (0.97 - 1.18)	$1.8x10^{-01}$	1.11 (0.88 - 1.39)	$3.7x10^{-01}$	0.98 (0.85 - 1.14)	$8.1x10^{-01}$	1.01 (0.93 - 1.10)	$7.8x10^{-01}$	1.08 (0.90 - 1.28)	$4.3x10^{-01}$	-	-	0.97 (0.82 - 1.15)	$7.3x10^{-01}$	1.11 (0.95 - 1.28)	$2.0x10^{-01}$	0.91 (0.68 - 1.22)	$5.2x10^{-01}$
rs6968408	C	0.98 (0.83 - 1.15)	$7.8x10^{-01}$	1.35 (0.93 - 1.96)	$1.2x10^{-01}$	0.79 (0.63 - 1.00)	$4.7x10^{-02}$	1.02 (0.89 - 1.18)	$7.3x10^{-01}$	1.11 (0.83 - 1.49)	$4.7x10^{-01}$	-	-	0.88 (0.69 - 1.14)	$3.2x10^{-01}$	0.76 (0.62 - 0.94)	$1.3x10^{-02}$	0.88 (0.57 - 1.35)	$5.6x10^{-01}$
rs7160770	T	0.94 (0.85 - 1.04)	$2.8x10^{-01}$	0.88 (0.71 - 1.11)	$2.9x10^{-01}$	1.02 (0.88 - 1.18)	$7.8x10^{-01}$	0.96 (0.88 - 1.04)	$3.4x10^{-01}$	0.98 (0.82 - 1.18)	$8.4x10^{-01}$	-	-	1.08 (0.93 - 1.25)	$3.6x10^{-01}$	1.05 (0.93 - 1.20)	$4.4x10^{-01}$	1.28 (0.98 - 1.67)	$7.0x10^{-02}$
rs7295704	T	1.01 (0.90 - 1.14)	$8.8x10^{-01}$	1.40 (1.07 - 1.83)	$1.4x10^{-02}$	1.20 (1.01 - 1.42)	$4.2x10^{-02}$	0.99 (0.89 - 1.10)	$8.2x10^{-01}$	0.92 (0.75 - 1.12)	$4.0x10^{-01}$	-	-	1.03 (0.87 - 1.23)	$7.2x10^{-01}$	1.06 (0.90 - 1.25)	$4.6x10^{-01}$	1.01 (0.73 - 1.38)	$9.6x10^{-01}$
rs752282	T	1.01 (0.85 - 1.19)	$9.3x10^{-01}$	1.00 (0.69 - 1.44)	$1.0x10^{-00}$	0.87 (0.69 - 1.11)	$2.6x10^{-01}$	1.02 (0.89 - 1.16)	$8.2x10^{-01}$	1.19 (0.87 - 1.62)	$2.8x10^{-01}$	-	-	-	-	1.49 (0.17 - 13.18)	$7.2x10^{-01}$	-	-
rs7682872	G	0.97 (0.88 - 1.08)	$6.1x10^{-01}$	0.94 (0.76 - 1.19)	$6.4x10^{-01}$	0.96 (0.83 1.12)	$6.3x10^{-01}$	1.14 (1.04 - 1.23)	$4.0x10^{-03}$	1.11 (0.93 - 1.33)	$2.6x10^{-01}$	-	-	0.93 (0.80 - 1.09)	$4.0x10^{-01}$	0.92 (0.80 - 1.04)	$1.9x10^{-01}$	0.79 (0.60 - 1.03)	$8.6x10^{-02}$
rs768347	T	1.03 (0.90 - 1.17)	$6.8x10^{-01}$	0.91 (0.68 - 1.22)	$5.2x10^{-01}$	1.01 (0.84 - 1.21)	$9.2x10^{-01}$	1.00 (0.89 - 1.12)	$9.8x10^{-01}$	0.94 (0.76 - 1.18)	$6.1x10^{-01}$	-	-	1.01 (0.83 - 1.22)	$9.3x10^{-01}$	1.01 (0.86 - 1.19)	$8.9x10^{-01}$	1.09 (0.78 - 1.51)	$6.2x10^{-01}$
rs7835679	C	1.12 (0.92 - 1.39)	$2.6x10^{-01}$	0.93 (0.58 - 1.47)	$7.4x10^{-01}$	1.54 (1.11 - 2.08)	$9.0x10^{-03}$	1.00 (0.82 - 1.22)	$9.9x10^{-01}$	0.88 (0.63 - 1.25)	$4.9x10^{-01}$	-	-	1.23 (0.91 - 1.67)	$1.7x10^{-01}$	1.04 (0.79 - 1.37)	$7.6x10^{-01}$	0.76 (0.48 - 1.22)	$2.6x10^{-01}$
rs7987944	C	1.01 (0.92 - 1.12)	$8.0x10^{-01}$	1.19 (0.94 - 1.50)	$1.4x10^{-01}$	0.98 (0.84 - 1.13)	$7.6x10^{-01}$	1.03 (0.95 - 1.13)	$4.7x10^{-01}$	1.21 (1.01 - 1.45)	$4.2x10^{-02}$	-	-	0.99 (0.85 - 1.16)	$9.3x10^{-01}$	1.01 (0.88 - 1.16)	$8.5x10^{-01}$	0.89 (0.67 - 1.17)	$4.0x10^{-01}$
rs9267992	G	1.16 (1.01 - 1.33)	$3.7x10^{-02}$	0.91 (0.68 - 1.22)	$5.3x10^{-01}$	1.26 (1.04 - 1.53)	$1.8x10^{-02}$	0.99 (0.88 - 1.11)	$8.3x10^{-01}$	1.17 (0.91 - 1.51)	$2.3x10^{-01}$	-	-	0.92 (0.74 - 1.14)	$4.3x10^{-01}$	1.03 (0.87 - 1.22)	$7.4x10^{-01}$	1.03 (0.71 - 1.47)	$8.9x10^{-01}$
rs9284844	G	1.03 (0.90 - 1.18)	$6.6x10^{-01}$	1.08 (0.79 - 1.47)	$6.3x10^{-01}$	1.19 (0.98 - 1.45)	$7.3x10^{-02}$	1.08 (0.94 - 1.22)	$2.7x10^{-01}$	0.86 (0.68 - 1.11)	$2.5x10^{-01}$	-	-	0.83 (0.69 - 1.01)	$6.6x10^{-02}$	0.98 (0.83 - 1.18)	$8.7x10^{-01}$	1.08 (0.74 - 1.56)	$7.0x10^{-01}$

In Ottawa, we used rs3825214 as a proxy SNP for rs12415501 (r2=0.76). SNP – single nucleotide polymorphism; RR – relative risk; CI – confidence interval.

Supplemental Table 4. Meta-analysis association results in Europeans.

	AF Risk Allele	Risk Allele Frequency	Original GWAS dataset[1]		Direct genotyping		*In-silico* replication		Combined replication		Overall Meta-analysis	
SNP			RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*
rs10137710	T	0.16	1.13 (1.08 - 1.19)	$1.8x10^{-06}$	1.06 (0.99 - 1.14)	$1.2x10^{-01}$	0.93 (0.82 - 1.06)	$2.6x10^{-01}$	1.03 (0.96 - 1.09)	$4.2x10^{-01}$	1.09 (1.05 - 1.13)	$2.9x10^{-05}$
rs10212121	A	0.67	1.10 (1.05 - 1.14)	$1.8x10^{-05}$	1.03 (0.97 - 1.09)	$3.3x10^{-01}$	1.02 (0.93 - 1.12)	$7.1x10^{-01}$	1.03 (0.98 - 1.08)	$3.0x10^{-01}$	1.06 (1.03 - 1.10)	$9.9x10^{-05}$
rs10267684	T	0.31	1.10 (1.06 - 1.15)	$4.1x10^{-06}$	1.04 (0.98 - 1.10)	$2.4x10^{-01}$	1.01 (0.91 - 1.11)	$8.7x10^{-01}$	1.03 (0.98 - 1.08)	$2.7x10^{-01}$	1.07 (1.04 - 1.11)	$2.2x10^{-05}$
rs10507248	T	0.73	1.13 (1.08 - 1.18)	$8.5x10^{-08}$	1.14 (1.06 - 1.20)	$4.0x10^{-05}$	1.03 (0.93 - 1.14)	$5.9x10^{-01}$	1.11 (1.05 - 1.17)	$1.3x10^{-04}$	1.12 (1-08 - 1.16)	$5.7x10^{-11}$
rs10762941	A	0.40	1.09 (1.04 - 1.13)	$3.9x10^{-05}$	1.00 (0.95 - 1.05)	$9.8x10^{-01}$	0.99 (0.90 - 1.09)	$8.5x10^{-01}$	1.00 (0.95 - 1.05)	$9.1x10^{-01}$	1.05 (1.02 - 1.08)	$2.2x10^{-03}$
rs10800507	C	0.50	1.11 (1.06 - 1.15)	$8.8x10^{-07}$	1.10 (1.03 - 1.15)	$1.2x10^{-03}$	0.98 (0.90 - 1.08)	$7.4x10^{-01}$	1.06 (1.02 - 1.12)	$8.7x10^{-03}$	1.09 (1.05 - 1.12)	$5.7x10^{-08}$
rs10849152	T	0.55	1.09 (1.04 - 1.13)	$4.9x10^{-05}$	0.99 (0.94 - 1.05)	$7.9x10^{-01}$	1.05 (0.95 - 1.15)	$3.3x10^{-01}$	1.01 (0.96 - 1.05)	$8.0x10^{-01}$	1.05 (1.02 - 1.09)	$1.2x10^{-03}$
rs10919369	T	0.22	1.12 (1.07 - 1.17)	$2.6x10^{-06}$	1.07 (1.01 - 1.14)	$2.8x10^{-02}$	1.02 (0.91 - 1.14)	$7.2x10^{-01}$	1.06 (1.00 - 1.12)	$3.6x10^{-02}$	1.09 (1.06 - 1.13)	$8.9x10^{-07}$
rs10947261	G	0.92	1.18 (1.09 - 1.27)	$2.7x10^{-05}$	1.11 (1.01 - 1.22)	$3.0x10^{-02}$	0.93 (0.78 - 1.10)	$3.8x10^{-01}$	1.06 (0.98 - 1.16)	$1.4x10^{-01}$	1.12 (1.06 - 1.19)	$3.8x10^{-05}$
rs11466656	C	0.01	7.25 (3.14 - 16.78)	$3.6x10^{-06}$	-	-	1.29 (0.02 - 72.45)	$9.0x10^{-01}$	1.29 (0.02 - 72.45)	$9.0x10^{-01}$	6.75 (2.97 - 15.34)	$5.1x10^{-06}$
rs12370365	G	0.77	1.10 (1.05 - 1.15)	$4.4x10^{-05}$	1.11 (1.04 - 1.18)	$1.9x10^{-03}$	1.05 (0.93 - 1.18)	$4.0x10^{-01}$	1.09 (1.03 - 1.15)	$1.8x10^{-03}$	1.10 (1.06 - 1.14)	$2.8x10^{-07}$
rs12406668	T	0.08	1.16 (1.08 - 1.24)	$4.9x10^{-05}$	1.03 (0.93 - 1.14)	$6.0x10^{-01}$	0.93 (0.78 - 1.11)	$4.0x10^{-01}$	1.00 (0.92 - 1.09)	$9.7x10^{-01}$	1.09 (1.04 - 1.15)	$1.3x10^{-03}$
rs12415501	T	0.16	1.15 (1.10 - 1.22)	$9.0x10^{-08}$	1.27 (1.18 - 1.37)	$6.5x10^{-10}$	1.17 (1.03 - 1.33)	$1.4x10^{-02}$	1.22 (1.14 - 1.29)	$6.0x10^{-10}$	1.18 (1.14 - 1.23)	$6.5x10^{-16}$
rs12733930	C	0.78	1.11 (1.06 - 1.16)	$3.2x10^{-05}$	1.01 (0.94 - 1.08)	$7.6x10^{-01}$	1.00 (0.89 - 1.11)	$9.8x10^{-01}$	1.01 (0.95 - 1.06)	$8.1x10^{-01}$	1.06 (1.03 - 1.10)	$8.2x10^{-04}$
rs12991989	C	0.51	1.10 (1.06 - 1.15)	$1.5x10^{-06}$	1.01 (0.94 - 1.06)	$7.5x10^{-01}$	1.02 (0.93 - 1.12)	$6.8x10^{-01}$	1.01 (0.96 - 1.06)	$6.3x10^{-01}$	1.06 (1.03 - 1.10)	$7.7x10^{-05}$
rs13169864	G	0.82	1.13 (1.06 - 1.19)	$4.5x10^{-05}$	1.01 (0.94 - 1.08)	$7.8x10^{-01}$	1.19 (1.04 - 1.35)	$1.2x10^{-02}$	1.04 (0.98 - 1.10)	$1.7x10^{-01}$	1.09 (1.04 - 1.12)	$1.1x10^{-04}$
rs13216675	T	0.69	1.10 (1.05 - 1.15)	$5.0x10^{-05}$	1.10 (1.03 - 1.16)	$1.7x10^{-03}$	1.12 (1.02 - 1.25)	$2.2x10^{-02}$	1.10 (1.05 - 1.16)	$1.1x10^{-04}$	1.10 (1.06 - 1.14)	$2.2x10^{-08}$
rs1324739	G	0.04	1.40 (1.22 - 1.61)	$1.6x10^{-06}$	1.14 (0.97 - 1.35)	$1.2x10^{-01}$	0.72 (0.52 - 0.99)	$4.2x10^{-02}$	1.03 (0.89 - 1.20)	$6.5x10^{-01}$	1.22 (1.10 - 1.35)	$1.4x10^{-04}$
rs13396611	T	0.04	1.27 (1.14 - 1.42)	$1.2x10^{-05}$	0.95 (0.82 - 1.10)	$5.3x10^{-01}$	1.03 (0.79 - 1.34)	$8.5x10^{-01}$	0.97 (0.85 - 1.10)	$6.4x10^{-01}$	1.14 (1.05 - 1.23)	$2.3x10^{-03}$
rs2118254	C	0.42	1.09 (1.04 - 1.13)	$3.5x10^{-05}$	1.03 (0.98 - 1.08)	$2.9x10^{-01}$	1.02 (0.93 - 1.12)	$6.8x10^{-01}$	1.03 (0.98 - 1.07)	$2.6x10^{-01}$	1.06 (1.03 - 1.09)	$1.2x10^{-04}$
rs2204224	T	0.71	1.19 (1.09 - 1.29)	$3.6x10^{-05}$	-	-	1.03 (0.88 - 1.20)	$6.8x10^{-01}$	1.03 (0.88 - 1.20)	$6.8x10^{-01}$	1.15 (1.08 - 1.23)	$1.3x10^{-04}$
rs2249965	A	0.36	1.11 (1.07 - 1.16)	$5.7x10^{-07}$	0.99 (0.94 - 1.05)	$7.2x10^{-01}$	1.04 (0.94 - 1.15)	$4.2x10^{-01}$	1.00 (0.95 - 1.05)	$9.3x10^{-01}$	1.06 (1.03 - 1.10)	$1.2x10^{-04}$
rs2305398	G	0.60	1.10 (1.05 - 1.16)	$4.2x10^{-06}$	1.08 (10.2 - 1.14)	$5.7x10^{-03}$	1.01 (0.92 - 1.10)	$9.1x10^{-01}$	1.06 (1.01 - 1.11)	$1.5x10^{-02}$	1.09 (1.05 - 1.12)	$3.9x10^{-07}$
rs2358891	G	0.74	1.11 (1.06 - 1.16)	$1.5x10^{-05}$	-	-	1.11 (1.00 - 1.23)	$5.3x10^{-02}$	1.11 (1.00 - 1.23)	$5.3x10^{-02}$	1.11 (1.06 - 1.16)	$2.0x10^{-06}$
rs2532144	T	0.51	1.10 (1.05 - 1.14)	$3.0x10^{-05}$	1.06 (1.00 - 1.14)	$3.9x10^{-02}$	0.97 (0.89 - 1.08)	$5.9x10^{-01}$	1.04 (0.99 - 1.10)	$1.4x10^{-01}$	1.08 (1.04 - 1.11)	$3.4x10^{-05}$
rs2685217	T	0.24	1.11 (1.06 - 1.17)	$2.6x10^{-05}$	1.00 (0.94 - 1.06)	$8.8x10^{-01}$	1.05 (0.94 - 1.17)	$3.8x10^{-01}$	1.01 (0.96 - 1.06)	$7.7x10^{-01}$	1.06 (1.03 - 1.10)	$9.3x10^{-04}$
rs2723065	A	0.60	1.10 (1.06 - 1.15)	$9.7x10^{-07}$	1.05 (0.99 - 1.11)	$9.7x10^{-02}$	1.11 (1.01 - 1.22)	$3.3x10^{-02}$	1.06 (1.01 - 1.11)	$1.2x10^{-02}$	1.09 (1.05 - 1.12)	$7.6x10^{-08}$
rs276857	G	0.13	1.16 (1.08 - 1.23)	$1.0x10^{-05}$	1.07 (0.99 - 1.16)	$7.5x10^{-02}$	1.04 (0.90 - 1.21)	$5.9x10^{-01}$	1.07 (1.00 - 1.14)	$6.7x10^{-02}$	1.11 (1.06 - 1.17)	$7.5x10^{-06}$
rs3780190	G	0.54	1.11 (1.06 - 1.15)	$6.3x10^{-06}$	1.05 (1.00 - 1.11)	$6.0x10^{-02}$	1.06 (0.97 - 1.16)	$1.8x10^{-01}$	1.05 (1.01 - 1.11)	$2.1x10^{-02}$	1.09 (1.05 - 1.11)	$1.1x10^{-06}$
rs3922843	A	0.26	1.10 (1.06 - 1.15)	$9.7x10^{-06}$	1.06 (1.00 - 1.12)	$6.5x10^{-02}$	1.07 (0.96 - 1.18)	$2.2x10^{-01}$	1.06 (1.01 - 1.12)	$2.7x10^{-02}$	1.09 (1.05 - 1.12)	$1.5x10^{-06}$
rs4238314	A	0.50	1.09 (1.05 - 1.13)	$2.7x10^{-05}$	1.03 (0.98 - 1.09)	$2.3x10^{-01}$	0.97 (0.89 - 1.07)	$5.9x10^{-01}$	1.02 (0.97 - 1.07)	$4.3x10^{-01}$	1.06 (1.03 - 1.09)	$2.2x10^{-04}$
rs4642101	G	0.65	1.11 (1.06 - 1.15)	$4.2x10^{-06}$	1.12 (1.05 - 1.19)	$3.9x10^{-04}$	0.98 (0.88 - 1.08)	$6.2x10^{-01}$	1.09 (1.04 - 1.15)	$5.6x10^{-04}$	1.10 (1.06 - 1.14)	$9.8x10^{-09}$
rs4824051	C	0.75	1.11 (1.06 - 1.16)	$4.6x10^{-05}$	1.05 (0.99 - 1.12)	$1.1x10^{-01}$	1.06 (0.94 - 1.19)	$3.2x10^{-01}$	1.05 (1.00 - 1.11)	$6.0x10^{-02}$	1.09 (1.04 - 1.12)	$1.8x10^{-05}$

Supplemental Table 4. Meta-analysis association results in Europeans.

SNP	AF Risk Allele	Risk Allele Frequency	Original GWAS dataset[1]		Direct genotyping		*In-silico* replication		Combined replication		Overall Meta-analysis	
			RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*	RR (95% CI)	*P value*
rs6062468	C	0.51	1.10 (1.05 - 1.15)	$4.7x10^{-05}$	1.00 (0.95 - 1.05)	$9.3x10^{-01}$	1.09 (0.99 - 1.20)	$7.1x10^{-02}$	1.02 (0.97 - 1.07)	$4.2x10^{-01}$	1.06 (1.03 - 1.09)	$4.9x10^{-04}$
rs6540690	C	0.76	1.12 (1.06 - 1.18)	$3.6x10^{-05}$	1.01 (0.95 - 1.08)	$7.2x10^{-01}$	0.92 (0.82 - 1.03)	$1.3x10^{-01}$	0.99 (0.93 - 1.04)	$6.7x10^{-01}$	1.05 (1.01 - 1.10)	$6.9x10^{-03}$
rs6749773	A	0.47	1.08 (1.04 - 1.13)	$4.9x10^{-05}$	0.98 (0.93 - 1.03)	$4.8x10^{-01}$	1.06 (0.97 - 1.17)	$1.8x10^{-01}$	1.00 (0.96 - 1.05)	$9.5x10^{-01}$	1.05 (1.02 - 1.08)	$1.7x10^{-03}$
rs6882776	A	0.71	1.10 (1.05 - 1.16)	$3.7x10^{-05}$	1.10 (1.04 - 1.16)	$1.4x10^{-03}$	1.00 (0.90 - 1.10)	$9.6x10^{-01}$	1.08 (1.02 - 1.12)	$6.2x10^{-03}$	1.09 (1.05 - 1.12)	$1.0x10^{-06}$
rs6884185	C	0.54	1.10 (1.05 - 1.15)	$4.5x10^{-05}$	1.03 (0.98 - 1.10)	$2.0x10^{-01}$	1.02 (0.92 - 1.14)	$6.6x10^{-01}$	1.03 (0.97 - 1.09)	$1.8x10^{-01}$	1.06 (1.03 - 1.10)	$8.9x10^{-05}$
rs6968408	C	0.91	1.16 (1.09 - 1.25)	$1.8x10^{-05}$	1.00 (0.91 - 1.09)	$9.3x10^{-01}$	0.82 (0.70 - 0.95)	$9.9x10^{-03}$	0.95 (0.88 - 1.02)	$1.7x10^{-01}$	1.06 (1.01 - 1.11)	$2.5x10^{-02}$
rs7160770	T	0.50	1.09 (1.04 - 1.13)	$5.0x10^{-05}$	0.96 (0.91 - 1.01)	$1.6x10^{-01}$	1.09 (0.99 - 1.19)	$7.9x10^{-02}$	0.99 (0.94 - 1.04)	$7.3x10^{-01}$	1.04 (1.01 - 1.08)	$4.4x10^{-03}$
rs7295704	T	0.21	1.10 (1.05 - 1.16)	$4.9x10^{-05}$	1.04 (0.97 - 1.11)	$2.9x10^{-01}$	1.04 (0.93 - 1.17)	$4.5x10^{-01}$	1.04 (0.98 - 1.10)	$2.0x10^{-01}$	1.08 (1.04 - 1.12)	$7.7x10^{-05}$
rs752282	T	0.02	2.91 (1.82 - 4.63)	$7.5x10^{-06}$	1.00 (0.92 - 1.10)	$9.3x10^{-01}$	1.77 (0.22 - 14.2)	$5.9x10^{-01}$	1.01 (0.92 - 1.10)	$9.1x10^{-01}$	1.04 (0.96 - 1.14)	$3.4x10^{-01}$
rs7682872	G	0.61	1.09 (1.05 - 1.14)	$2.8x10^{-05}$	1.04 (0.99 - 1.10)	$1.0x10^{-01}$	0.91 (0.82 - 1.00)	$4.0x10^{-02}$	1.01 (0.96 - 1.06)	$7.0x10^{-01}$	1.05 (1.02 - 1.09)	$6.1x10^{-04}$
rs768347	T	0.19	1.11 (1.06 - 1.17)	$1.4x10^{-05}$	1.00 (0.93 - 1.07)	$9.5x10^{-01}$	1.02 (0.91 - 1.15)	$7.5x10^{-01}$	1.00 (0.94 - 1.07)	$9.1x10^{-01}$	1.07 (1.03 - 1.11)	$5.3x10^{-04}$
rs7835679	C	0.93	1.20 (1.10 - 1.30)	$2.2x10^{-05}$	1.08 (0.96 - 1.01)	$2.1x10^{-01}$	1.06 (0.88 - 1.28)	$5.4x10^{-01}$	1.08 (0.97 - 1.19)	$1.7x10^{-01}$	1.15 (1.08 - 1.22)	$3.4x10^{-05}$
rs7987944	C	0.34	1.09 (1.05 - 1.14)	$4.9x10^{-05}$	1.04 (0.99 - 1.10)	$1.4x10^{-01}$	0.99 (0.90 - 1.09)	$8.3x10^{-01}$	1.03 (0.98 - 1.08)	$2.5x10^{-01}$	1.06 (1.03 - 1.10)	$1.2x10^{-04}$
rs9267992	G	0.15	1.12 (1.06 - 1.18)	$4.0x10^{-05}$	1.08 (1.00 - 1.17)	$3.7x10^{-02}$	0.99 (0.87 - 1.12)	$8.7x10^{-01}$	1.06 (0.99 - 1.13)	$8.7x10^{-02}$	1.09 (1.05 - 1.14)	$2.1x10^{-05}$
rs9284844	G	0.84	1.12 (1.06 - 1.18)	$2.7x10^{-05}$	1.05 (0.98 - 1.14)	$1.7x10^{-01}$	0.93 (0.82 - 1.05)	$2.4x10^{-01}$	1.02 (0.95 - 1.09)	$5.9x10^{-01}$	1.08 (1.03 - 1.12)	$3.2x10^{-04}$
rs9857326	A	0.23	1.09 (1.05 - 1.14)	$3.9x10^{-05}$	0.99 (0.94 - 1.05)	$7.9x10^{-01}$	1.01 (0.91 - 1.11)	$9.0x10^{-01}$	1.00 (0.95 - 1.05)	$8.7x10^{-01}$	1.05 (1.02 - 1.08)	$2.3x10^{-03}$

In Ottawa, we used rs3825214 as a proxy SNP for rs12415501 (r2=0.76). SNP – single nucleotide polymorphism; RR – relative risk; CI – confidence interval.

Supplemental Table 5. Six genome-wide significant AF loci in Japanese.

					Original GWAS[1] Stage 1		Replication Stage 2		Meta-analysis Stages 1-3	
SNP	**Chr**	**AF Risk Allele**	**Closest gene**	**Relative location**	**RR 95% CI**	***P value***	**RR 95% CI**	***P value***	**RR 95% CI**	***P value***
rs639652	1q24	G	*PRRX1*	Intronic	1.21 1.08-1.35	$6.6x10^{-4}$	1.21 1.13-1.30	$3.2x10^{-7}$	1.18 1.12-1.21	$2.7x10^{-15}$
rs1906599	4q25	T	*PITX2*	Intergenic	1.75 1.54-1.98	$9.0 x10^{-18}$	2.05 1.87-2.25	$1.9x10^{-54}$	1.78 1.71-1.86	$6.9 x10^{-151}$
rs6466579	7q31	C	*CAV1/2*	Intronic	1.24 1.09-1.40	$7.6 x10^{-4}$	1.23 1.13-1.34	$2.5x10^{-6}$	1.16 1.11-1.21	$7.8 x10^{-12}$
rs6584555	10q25	C	*NEURL*	Intronic	1.33 1.14-1.55	$2.8x10^{-4}$	1.36 1.23-1.50	$3.3x10^{-9}$	1.32 1.26-1.39	$2.0x10^{-25}$
rs6490029	12q24	A	*CUX2*	Intronic	1.22 1.09-1.37	$6.3x10^{-4}$	1.11 1.12-1.30	$2.6x10^{-6}$	1.12 1.08-1.16	$3.9x10^{-9}$
rs12932445	16q22	C	*ZFHX3*	Intronic	1.26 1.13-1.40	$3.1 x10^{-5}$	1.38 1.28-1.49	$1.8x10^{-17}$	1.26 1.22-1.31	$4.4 x10^{-34}$

SNP – single nucleotide polymorphism; AF – atrial fibrillation; Chr – chromosome; RR – relative risk; CI – confidence interval.

Supplemental Table 6. Fine mapping of the *NEURL* locus in Japanese							
				First stage		**Confirmation**	
SNP	**AF Risk Allele**	**r^2 with rs6584555**	**D Prime with rs6584555**	**OR 95% CI**	***P value***	**OR 95% CI**	***P value***
rs6584555	C	–	–	1.27 1.07-1.52	$7.2x10^{-3}$	1.34 1.24-1.45	$3.1x10^{-14}$
rs117577689	T	0.01	0.99	1.00 0.75-1.35	$9.9x10^{-1}$		
rs141902653	C	<0.01	1.00	1.18 0.73-1.91	$5.0x10^{-1}$		
rs180924020	G	<0.01	0.14	1.04 0.56-1.93	$9.1x10^{-1}$		
rs75733446	A	<0.01	0.79	1.46 0.95-2.25	$8.9x10^{-2}$		
rs80065416	T	0.49	1.00	1.55 1.23-1.97	$1.8x10^{-4}$	1.65 1.48-1.84	$3.1x10^{-19}$
rs2208322	G	0.39	1.00	1.09 0.95-1.24	$2.3x10^{-1}$		
rs72848976	A	0.01	1.00	1.01 0.85-1.20	$9.0x10^{-1}$		
rs6584558	A	0.18	0.62	1.17 1.02-1.34	$3.2x10^{-2}$		
rs74154533	A	0.65	1.00	1.46 1.20-1.78	$1.3x10^{-4}$	1.51 1.39-1.65	$1.6x10^{-20}$
Linkage disequilibrium reported as r2 and DPrime relative to the Sentinel SNP rs658455, determined based on the HapMap CHB+JPT panel.							

Supplemental Table 7. Comparison of AF association results between individuals of European and Japanese ancestry

				European ancestry			Japanese ancestry		
SNP	**Chr**	**AF risk allele**	**Closest gene**	**RAF**	**RR (95% CI)**	**p**	**RAF**	**RR (95% CI)**	**p**
rs10507248	12q24	T	*TBX5*	0.73	1.12 (1.08 - 1.16)	$5.7x10^{-11}$	0.44	1.16 (1.10-1.22)	$2.7x10^{-8\dagger}$
rs4642101	3p25	G	*CAND2*	0.65	1.10 (1.06 – 1.14)	$9.8x10^{-9}$	0.31	1.08 (1.02-1.14)	$9.1x10^{-3\dagger}$
rs13216675	6q22	T	*GJA1*	0.69	1.10 (1.06 - 1.14)	$2.2x10^{-8}$	0.70	1.11 (1.05-1.17)	$3.2x10^{-4\dagger}$
rs6490029	12q24	A	*CUX2*	0.22	1.02 (0.97-1.07)	0.412*	0.64	1.12 (1.08-1.16)	$3.9x10^{-9}$

Abbreviations: SNP, single nucleotide polymorphism; RAF, risk allele frequency; RR, relative risk; CI, confidence intervals.

†The results for *TBX5*/rs10507248, *CAND2/*rs4642101, and *GJA1/*rs13216675 were obtained by directly genotyping these SNPs in the Japanese samples in a total of 8,220 AF cases and 4,657 controls.

*The results for *CUX2*/rs6490029 in Europeans was obtained from Ellinor et al.[1]

Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Europeans

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
rs10137710	T	rs10137710	0	1	1	No					
rs10212121	A	rs10212121	0	1	1	No					
rs10267684	T	rs10267684	0	1	1	No					
rs10507248	T	rs10507248	0	1	1	Yes	Heart, LA	*TBX5*	1.10 (1.05-1.15)	increase	$2.14x10^{-04}$
	G	rs7955405	213	1	1	Yes	Heart, LA	*TBX5*	1.10 (1.05-1.15)	increase	$2.14x10^{-04}$
	A	rs7312625	2881	1	1	Yes	Heart, LA	*TBX5*	1.11 (1.06-1.16)	increase	$3.93x10^{-05}$
	G	rs4767237	3720	0.96	1	Yes	Heart, LA	*TBX5*	1.12 (1.08-1.18)	increase	$1.47x10^{-05}$
	A	rs883079	3853	0.92	1	Yes	Heart, LA	*TBX5*	1.10 (1.06-1.15)	increase	$9.37x10^{-05}$
	A	rs7135659	4679	0.92	1	Yes	Heart, LA	*TBX5*	1.11 (1.06-1.16)	increase	$9.12x10^{-05}$
	T	rs1946293	5667	0.92	1	Yes	Heart, LA	*TBX5*	1.11 (1.06-1.16)	increase	$9.04x10^{-05}$
	C	rs3825215	7805	0.92	1	Yes	Heart, LA	*TBX5*	1.12 (1.08-1.18)	increase	$1.41x10^{-05}$
	C	rs1895583	9792	0.92	1	Yes	Heart, LA	*TBX5*	1.12 (1.08-1.18)	increase	$2.26x10^{-05}$
	C	rs1895585	5045	0.87	0.96	Yes	Heart, LA	*TBX5*	1.12 (1.08-1.18)	increase	$1.46x10^{-05}$
	C	rs1946295	5268	0.87	0.96	Yes	Heart, LA	*TBX5*	1.12 (1.08-1.18)	increase	$1.36x10^{-05}$
		rs10850315	30358	0.83	0.91	No					
	T	rs1895582	9942	0.8	0.91	Yes	Heart, LA	*TBX5*	1.12 (1.08-1.18)	increase	$1.74x10^{-05}$
		rs10744823	989	0.76	1	No					
		rs3825214	1650	0.76	1	No					
		rs10744824	11545	0.76	1	No					
		rs5015007	7990	0.72	1	No					
		rs1895597	6209	0.72	0.95	No					
		rs7964303	17193	0.68	0.82	No					
		rs12367410	405	0.67	0.9	No					
		rs7977083	6593	0.67	0.9	No					
		rs7308120	8047	0.67	0.9	No					
		rs4767239	19455	0.64	0.94	No					
		rs7964836	30373	0.64	0.94	No					
		rs1862909	9988	0.64	0.94	No					
		rs2891503	7283	0.64	0.85	No					
		rs1895596	5565	0.62	1	No					
		rs7309910	10839	0.62	1	No					
		rs6489955	11814	0.62	1	No					
		rs6489953	32331	0.61	0.94	No					
		rs6489956	4857	0.6	0.89	No					
		rs7316919	5638	0.6	0.89	No					
		rs2384409	7615	0.6	0.89	No					
		rs1895587	27564	0.57	0.94	No					
		rs10774752	28781	0.57	0.94	No					
		rs10744820	28966	0.57	0.94	No					
		rs10744819	35263	0.57	0.94	No					
		rs8181627	35329	0.57	0.94	No					
		rs8181683	35375	0.57	0.94	No					
		rs10744818	35408	0.57	0.94	No					
		rs8181608	35510	0.57	0.94	No					
		rs1895593	36278	0.57	0.94	No					
		rs933748	36437	0.57	0.94	No					
		rs11067054	24536	0.54	0.93	No					
		rs7966567	35613	0.53	0.88	No					
		rs7307520	32394	0.53	0.88	No					
rs10762941	A	rs10762941	0	1	1	No					
rs10800507	C	rs10800507	0	1	1	No					
		rs4656206	6577	0.7	0.96	No					
		rs10919327	14127	0.57	1	No					
		rs10753800	4406	0.55	0.95	No					
rs10849152	T	rs10849152	0	1	1	No					
rs10919369	T	rs10919369	0	1	1	No					
rs10947261	G	rs10947261	0	1	1	No					
rs11466656	C	rs11466656	0	1	1	No					
rs12370365	G	rs12370365	0	1	1	No					
		rs12828578	3073	1	1	No					
		rs73142614	14693	1	1	No					
		rs12367127	17951	0.95	1	No					
		rs11177719	22504	0.95	1	No					
		rs11177730	42852	0.95	1	No					
		rs11177731	42976	0.95	1	No					
		rs11177732	45010	0.95	1	No					
		rs11177733	46753	0.95	1	No					
		rs1043434	50687	0.95	1	No					
		rs11177738	51835	0.95	1	No					
		rs35956654	51990	0.95	1	No					
		rs11832926	55559	0.95	1	No					
		rs4761246	56347	0.95	1	No					
		rs7200	59172	0.95	1	No					
		rs3177122	59246	0.95	1	No					
		rs35232489	61181	0.95	1	No					
		rs4761247	62214	0.95	1	No					
		rs11177748	63964	0.95	1	No					

Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Europeans

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
		rs727948	64417	0.95	1	No					
		rs11177751	66387	0.95	1	No					
rs12370365 (cont.)		rs10784788	72658	0.95	1	No					
		rs11177710	1513	0.95	1	No					
		rs11177699	28499	0.95	1	No					
		rs11829505	30972	0.95	1	No					
	A	rs11177695	40356	0.95	1	No					
		rs35612761	16274	0.9	1	No					
		rs12319536	42522	0.9	1	No					
		rs73140582	30361	0.9	1	No					
		rs11177694	42127	0.9	1	No					
		rs12371904	55142	0.9	1	No					
		rs4761243	13299	0.89	0.95	No					
		rs3759202	41243	0.89	0.95	No					
		rs12370028	43037	0.89	0.95	No					
		rs11177752	69433	0.89	0.95	No					
		rs3858594	49351	0.85	0.95	No					
		rs73140585	29559	0.84	1	No					
		rs11177742	58938	0.84	0.94	No					
		rs11177726	32909	0.82	1	No					
		rs34929418	77222	0.67	0.88	No					
rs12406668	T	rs12406668	0	1	1	No					
rs12415501	T	rs12415501	0	1	1	No					
		rs12253987	6173	0.75	1	No					
		rs7893473	15172	0.56	0.83	No					
		rs7904046	24868	0.56	0.83	No					
		rs6584557	24888	0.56	0.83	No					
		rs6584555	25163	0.56	0.83	No					
		rs6584554	25298	0.56	0.83	No					
		rs11191727	2401	0.53	0.76	No					
rs12733930	C	rs12733930	0	1	1	Yes	Heart, LA	*LINC00467*	0.81 (0.78-0.83)	decrease	$1.59x10^{-24}$
rs12991989	C	rs12991989	0	1	1	No					
rs13169864	G	rs13169864	0	1	1	No					
rs13216675	T	rs13216675	0	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$9.84x10^{-05}$
	T	rs9482226	4700	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$9.90x10^{-05}$
	T	rs35492344	5176	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$9.93x10^{-05}$
	T	rs12664873	10862	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.24x10^{-05}$
	G	rs2315817	13289	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$1.48x10^{-04}$
	C	rs6914962	20494	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.53x10^{-05}$
	T	rs6929586	24286	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.72x10^{-05}$
	C	rs6907053	24366	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.60x10^{-05}$
	C	rs13194963	33998	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.59x10^{-05}$
	G	rs13195388	34163	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.57x10^{-05}$
	T	rs12662754	35466	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.36x10^{-05}$
	G	rs12661247	35634	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$7.10x10^{-05}$
	C	rs13216068	38739	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.11x10^{-05}$
	C	rs34247913	46175	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$3.93x10^{-05}$
	C	rs12662023	48074	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.02x10^{-05}$
	G	rs17084326	53264	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.02x10^{-05}$
	T	rs7772537	54213	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.40x10^{-05}$
	C	rs17084333	56081	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.95)	decrease	$2.65x10^{-05}$
	A	rs35735278	56368	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.95)	decrease	$2.65x10^{-05}$
	T	rs34379825	56661	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.95)	decrease	$2.69x10^{-05}$
	G	rs1456696	58558	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$7.01x10^{-05}$
	G	rs13197292	74258	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.74x10^{-05}$
	C	rs1531187	76146	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.54x10^{-05}$
	T	rs12664347	79887	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.48x10^{-05}$
	G	rs12662844	79944	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.48x10^{-05}$
	T	rs6905707	85458	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.48x10^{-05}$
	T	rs1379090	87053	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.46x10^{-05}$
	G	rs13204964	88784	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$7.41x10^{-05}$
	G	rs12664221	93989	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.36x10^{-05}$
	C	rs1350228	94808	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.34x10^{-05}$
	A	rs2316267	95710	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.33x10^{-05}$
	G	rs786101	100364	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.27x10^{-05}$
	C	rs1456694	102250	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.24x10^{-05}$
	T	rs12661882	103760	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.22x10^{-05}$
	T	rs17084362	107847	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.17x10^{-05}$
	C	rs786100	110424	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.13x10^{-05}$
	G	rs2770118	117395	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.02x10^{-05}$
	A	rs2606593	120794	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.20x10^{-05}$
	C	rs2606592	121483	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.20x10^{-05}$
	A	rs2770119	121627	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.19x10^{-05}$
	A	rs35099519	125942	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$2.97x10^{-05}$
	A	rs225089	126727	1	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.69x10^{-05}$
	G	rs6916464	13897	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$3.72x10^{-05}$
	A	rs12665325	15783	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$2.90x10^{-05}$
	A	rs2078231	30387	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$3.15x10^{-05}$
	A	rs12664154	35982	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.95)	decrease	$2.82x10^{-05}$

Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Europeans

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
	G	rs7450267	36705	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.95)	decrease	$2.78x10^{-05}$
	C	rs1456699	37617	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.95)	decrease	$2.72x10^{-05}$
rs13216675 (cont.)	C	rs2316266	44298	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.95)	decrease	$2.67x10^{-05}$
		rs71571139	68131	0.96	1	Yes	Heart, LA	*GJA1*			$4.43x10^{-05}$
	A	rs35085009	74725	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.51x10^{-05}$
	C	rs12661091	75488	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.19x10^{-05}$
	A	rs1379088	92575	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.96)	decrease	$4.29x10^{-05}$
	T	rs1456693	102299	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.20x10^{-05}$
	A	rs1456692	102354	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.20x10^{-05}$
	C	rs1585127	102914	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.19x10^{-05}$
	C	rs12660649	104268	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.18x10^{-05}$
	A	rs1870005	115810	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.32x10^{-05}$
	G	rs2085400	117016	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.05x10^{-05}$
	A	rs2770117	117281	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.07x10^{-05}$
	A	rs12661260	123757	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.46x10^{-05}$
	G	rs12662551	39193	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.14x10^{-05}$
	T	rs12665385	57279	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.74x10^{-05}$
	T	rs1947540	59846	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$7.01x10^{-05}$
	G	rs7738124	70512	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.93x10^{-05}$
	G	rs1085381	113181	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$7.27x10^{-05}$
	A	rs225090	127148	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.68x10^{-05}$
	G	rs225072	133807	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.56x10^{-05}$
	C	rs225075	137551	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	T	rs225076	138042	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	C	rs12663999	142878	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	A	rs225084	143880	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	T	rs225086	146040	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	A	rs12660540	151433	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.51x10^{-05}$
	G	rs13212529	153658	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	T	rs12663673	153812	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	A	rs34528281	154554	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	A	rs2066121	157547	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	G	rs80080630	167729	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.96)	decrease	$5.34x10^{-05}$
	G	rs1840763	169446	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	T	rs1011654	172940	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.45x10^{-05}$
	G	rs1339527	177975	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	T	rs517442	188091	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	C	rs509860	193433	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.37x10^{-05}$
	A	rs35622021	201279	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.53x10^{-05}$
	T	rs17662069	201879	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.53x10^{-05}$
	G	rs13204922	206664	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	G	rs589593	208468	0.96	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$7.40x10^{-05}$
	C	rs1456697	41438	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$3.72x10^{-05}$
	T	rs6569253	81488	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.35x10^{-05}$
	C	rs1870006	115649	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.06x10^{-05}$
	G	rs1870004	115897	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.06x10^{-05}$
	G	rs1870001	116308	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.98x10^{-05}$
	T	rs2085401	116906	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.03x10^{-05}$
	C	rs35461771	15518	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$5.58x10^{-05}$
	C	rs587465	167728	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.96)	decrease	$5.89x10^{-05}$
	T	rs13209385	168730	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	G	rs620105	209281	0.92	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.42x10^{-05}$
	G	rs6569252	67844	0.92	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.70x10^{-05}$
	T	rs7757343	105976	0.92	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$6.20x10^{-05}$
	T	rs225073	133909	0.92	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.56x10^{-05}$
	G	rs761955	149047	0.92	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	G	rs536165	167986	0.92	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.52x10^{-05}$
	G	rs537456	199007	0.92	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.96)	decrease	$3.83x10^{-05}$
	A	rs528991	211128	0.92	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$4.84x10^{-05}$
	G	rs1456698	41435	0.88	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$2.58x10^{-05}$
	T	rs35859246	58146	0.88	1	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$7.46x10^{-05}$
	T	rs225078	163096	0.88	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$3.80x10^{-05}$
	C	rs59472001	216442	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$2.38x10^{-05}$
	A	rs6929685	216461	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$2.37x10^{-05}$
	G	rs10499118	221398	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.28x10^{-05}$
	G	rs34607745	223006	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$2.52x10^{-05}$
	G	rs3968436	223803	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.21x10^{-05}$
	T	rs13192258	224748	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.16x10^{-05}$
	G	rs1610023	225035	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.14x10^{-05}$
	A	rs117131686	227756	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.36x10^{-05}$
	C	rs35347829	229401	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.47x10^{-05}$
	C	rs12661045	230466	0.87	0.96	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.44x10^{-05}$
	G	rs34531455	230872	0.83	0.91	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.38x10^{-05}$
	G	rs1416731	256357	0.83	0.91	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$2.06x10^{-05}$
	C	rs13218584	227314	0.83	0.95	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.04x10^{-05}$
	C	rs61379124	19087	0.8	0.95	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.32x10^{-05}$
	T	rs11758026	20300	0.8	0.95	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$8.08x10^{-06}$
	T	rs71571147	224205	0.79	0.95	Yes	Heart, LA	*GJA1*	0.92 (0.88-0.94)	decrease	$8.23x10^{-06}$
	C	rs7741444	231629	0.79	0.91	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.16x10^{-05}$

Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Europeans

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
	T	rs7761904	231727	0.79	0.91	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.14x10^{-05}$
	A	rs7742289	232136	0.79	0.91	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$9.93x10^{-06}$
rs13216675 (cont.)	G	rs2316672	245634	0.79	0.91	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$2.34x10^{-05}$
	C	rs7773091	57695	0.76	1	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.08x10^{-05}$
		rs75033796	226772	0.75	0.95	No					
	A	rs1379096	19917	0.72	0.87	Yes	Heart, LA	*GJA1*	0.93 (0.89-0.94)	decrease	$2.76x10^{-06}$
	C	rs34070579	7770	0.72	0.95	Yes	Heart, LA	*GJA1*	0.92 (0.89-0.95)	decrease	$2.45x10^{-05}$
	C	rs12665212	196287	0.7	0.91	No					
	A	rs9490444	260048	0.67	0.9	No					
	A	rs939601	62686	0.66	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.43x10^{-06}$
	T	rs17084191	33248	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.80x10^{-05}$
	C	rs13219206	38172	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.74x10^{-05}$
	A	rs34483874	42367	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.73x10^{-05}$
	C	rs6928224	44347	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.53x10^{-05}$
	T	rs6907870	44485	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.53x10^{-05}$
	C	rs72966339	54088	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$4.12x10^{-06}$
	C	rs6930575	56329	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$4.21x10^{-06}$
	C	rs6930219	56465	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$4.15x10^{-06}$
	C	rs6901617	56860	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$4.71x10^{-06}$
	C	rs6938223	58057	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.93x10^{-06}$
	C	rs17084158	58687	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.83x10^{-06}$
	C	rs17084154	58885	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.80x10^{-06}$
	G	rs2816099	59647	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.05x10^{-05}$
	C	rs2259327	60584	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.56x10^{-06}$
	A	rs1357050	61194	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.50x10^{-06}$
	A	rs868153	62374	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$4.90x10^{-06}$
	C	rs868154	62389	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.43x10^{-06}$
	G	rs868155	62423	0.63	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.43x10^{-06}$
	G	rs1357051	61245	0.6	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$1.02x10^{-05}$
	C	rs1402538	63478	0.6	0.86	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$9.90x10^{-06}$
	A	rs2684249	59818	0.59	0.9	Yes	Heart, LA	*GJA1*	0.93 (0.91-0.96)	decrease	$8.36x10^{-05}$
	G	rs2816098	59622	0.58	0.81	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.75x10^{-06}$
	A	rs2816097	56682	0.57	0.85	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$3.88x10^{-06}$
	T	rs17199931	278629	0.57	0.77	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.96)	decrease	$1.43x10^{-04}$
	G	rs3799545	283289	0.57	0.77	No					
	G	rs17201852	339761	0.57	0.77	No					
	G	rs13199730	431186	0.57	0.77	No					
	A	rs36084496	52438	0.55	0.85	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$4.10x10^{-06}$
	G	rs2176990	58611	0.54	0.77	Yes	Heart, LA	*GJA1*	0.93 (0.90-0.95)	decrease	$2.66x10^{-06}$
		rs3823188	291357	0.54	0.73	No			0.93 (0.91-0.96)	decrease	
rs1324739	G	rs1324739	0	1	1	No					
rs13396611	T	rs13396611	0	1	1	No					
rs2118254	C	rs2118254	0	1	1	No					
rs2204224	T	rs2204224	0	1	1	No					
rs2249965	A	rs2249965	0	1	1	No					
rs2305398	G	rs2305398	0	1	1	Yes	Skeletal Muscle	*CAND2*		decrease	$1.91x10^{-11}$
						Yes	Skeletal Muscle	*KRT18P17*		decrease	$7.07x10^{-3}$
rs2358891	G	rs2358891	0	1	1	Yes	Heart, LA	*WIPF1*	0.88 (0.85-0.91)	decrese	$8.87x10^{-10}$
rs2532144	T	rs2532144	0	1	1	No					
rs2685217	T	rs2685217	0	1	1	No					
rs2723065	A	rs2723065	0	1	1	Yes	Tibial Artery	*CEP68*		decrese	$1.66x10^{-07}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$2.45x10^{-16}$
	A	rs2540951	2678	1	1	Yes	Tibial Artery	*CEP68*			$2.22x10^{-07}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$2.39x10^{-16}$
	T	rs1009358	2962	1	1	Yes	Tibial Artery	*CEP68*			$2.31x10^{-07}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$2.38x10^{-16}$
	A	rs2540949	4817	1	1	Yes	Tibial Artery	*CEP68*			$1.64x10^{-07}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.27)	increase	$1.10x10^{-15}$
	T	rs2540948	5209	1	1	Yes	Tibial Artery	*CEP68*			$5.58x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.27)	increase	$5.52x10^{-16}$
	T	rs2723064	391	0.96	1	Yes	Tibial Artery	*CEP68*			$1.65x10^{-07}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$2.74x10^{-16}$
	T	rs74181299	4558	0.96	1	Yes	Tibial Artery	*CEP68*			$2.21x10^{-07}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$1.04x10^{-15}$
	C	rs2540950	191	0.93	1	Yes	Tibial Artery	*CEP68*			$4.88x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$9.70x10^{-17}$
	G	rs2723062	806	0.93	1	Yes	Tibial Artery	*CEP68*			$4.88x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$1.44x10^{-16}$
	A	rs2249105	8482	0.93	0.96	Yes	Tibial Artery	*CEP68*			$4.81x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$2.08x10^{-15}$
	A	rs2540945	10411	0.93	0.96	Yes	Tibial Artery	*CEP68*			$4.81x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$1.90x10^{-15}$
	T	rs2723066	93	0.89	1	Yes	Tibial Artery	*CEP68*			$4.88x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$1.11x10^{-16}$
	T	rs2252867	16866	0.86	0.96	Yes	Tibial Artery	*CEP68*			$4.81x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$2.09x10^{-15}$
	C	rs2723086	18272	0.86	0.96	Yes	Heart, LA	*CEP68*	1.23 (1.18-1.27)	increase	$6.03x10^{-16}$
	T	rs2723087	18868	0.86	0.96	Yes	Tibial Artery	*CEP68*			$9.39x10^{-05}$

Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Europeans

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$2.42x10^{-15}$
	A	rs2723063	771	0.84	1	Yes	Tibial Artery	*CEP68*			$3.86x10^{-05}$
rs2723065 (cont.)						Yes	Heart, LV	*CEP68*			$5.15x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.19 (1.14-1.24)	increase	$4.51x10^{-12}$
	T	rs1009360	3365	0.84	1	Yes	Tibial Artery	*CEP68*			$8.25x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.18 (1.13-1.23)	increase	$1.52x10^{-10}$
	C	rs2723082	10209	0.82	0.96	Yes	Tibial Artery	*CEP68*			$1.88x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$8.83x10^{-16}$
	C	rs2723085	17945	0.82	0.96	Yes	Tibial Artery	*CEP68*			$1.93x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.22 (1.18-1.27)	increase	$8.93x10^{-16}$
	A	rs1420185	36489	0.79	0.96	Yes	Tibial Artery	*CEP68*			$2.64x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.27)	increase	$3.18x10^{-13}$
	A	rs12472718	48206	0.79	0.96	Yes	Tibial Artery	*CEP68*			$5.80x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.27)	increase	$3.19x10^{-13}$
	A	rs13421845	56619	0.79	0.96	Yes	Tibial Artery	*CEP68*			$5.80x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.27)	increase	$8.93x10^{-13}$
	C	rs58342673	68170	0.79	0.96	Yes	Tibial Artery	*CEP68*			$8.30x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.21 (1.16-1.26)	increase	$1.28x10^{-12}$
	A	rs2723067	1463	0.79	0.92	Yes	Heart, LA	*CEP68*	1.16 (1.12-1.21)	increase	$6.50x10^{-09}$
	A	rs11893423	71535	0.76	0.96	Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$9.75x10^{-14}$
	C	rs2241161	11428	0.74	0.96	Yes	Heart, LA	*CEP68*	1.19 (1.14-1.24)	increase	$1.08x10^{-11}$
	A	rs2241160	12132	0.74	0.96	Yes	Heart, LA	*CEP68*	1.19 (1.14-1.24)	increase	$3.16x10^{-11}$
	T	rs6736728	26085	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.17x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$5.86x10^{-14}$
	T	rs6741255	27491	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.06x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$5.94x10^{-14}$
	C	rs1420183	30574	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.06x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$6.07x10^{-14}$
	T	rs1228	32141	0.73	0.96	Yes	Tibial Artery	*CEP68*			$9.40x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$6.08x10^{-14}$
	C	rs1420184	36466	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.06x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$6.07x10^{-14}$
	C	rs6713746	45078	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.06x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$6.01x10^{-14}$
	A	rs17040050	47628	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.06x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$6.00x10^{-14}$
	G	rs2302631	52245	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.06x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.28)	increase	$2.02x10^{-13}$
	C	rs9797989	57115	0.73	0.96	Yes	Heart, LA	*CEP68*	1.22 (1.17-1.28)	increase	$2.02x10^{-13}$
	C	rs11126028	58736	0.73	0.96	Yes	Heart, LA	*CEP68*	1.22 (1.17-1.28)	increase	$2.02x10^{-13}$
	T	rs11126029	58850	0.73	0.96	Yes	Heart, LA	*CEP68*	1.22 (1.17-1.28)	increase	$2.44x10^{-13}$
	A	rs60136636	59008	0.73	0.96	Yes	Tibial Artery	*CEP68*			$6.82x10^{-07}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.27)	increase	$8.91x10^{-13}$
	A	rs6756585	60656	0.73	0.96	Yes	Heart, LA	*CEP68*	1.22 (1.17-1.28)	increase	$2.02x10^{-13}$
	A	rs2052261	75856	0.73	0.96	Yes	Tibial Artery	*CEP68*			$9.40x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$6.01x10^{-14}$
	T	rs10185243	76330	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.56x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.27)	increase	$6.78x10^{-13}$
	C	rs12713532	77138	0.73	0.96	Yes	Tibial Artery	*CEP68*			$1.16x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.17-1.28)	increase	$7.63x10^{-14}$
	C	rs2723091	22603	0.7	0.95	Yes	Tibial Artery	*CEP68*			$1.04x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$5.63x10^{-14}$
	T	rs1050676	31417	0.69	0.91	Yes	Tibial Artery	*CEP68*			$1.06x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$6.08x10^{-14}$
	T	rs6730986	74135	0.69	0.91	Yes	Tibial Artery	*CEP68*			$9.40x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.23 (1.18-1.28)	increase	$6.02x10^{-14}$
	C	rs6546123	24168	0.65	0.81	Yes	Tibial Artery	*CEP68*			$5.92x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.22 (1.17-1.27)	increase	$6.18x10^{-13}$
	A	rs1894875	84165	0.64	0.95	Yes	Tibial Artery	*CEP68*			$9.75x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.17 (1.12-1.22)	increase	$9.97x10^{-09}$
	G	rs2422441	91352	0.64	0.95	Yes	Tibial Artery	*CEP68*			$4.44x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.16 (1.11-1.22)	increase	$3.59x10^{-08}$
	T	rs10205598	99837	0.64	0.95	Yes	Tibial Artery	*CEP68*			$2.27x10^{-06}$
						Yes	Heart, LA	*CEP68*	1.17 (1.12-1.22)	increase	$3.03x10^{-08}$
	C	rs7559813	1391	0.62	1	Yes	Heart, LA	*CEP68*	1.17 (1.12-1.23)	increase	$6.00x10^{-08}$
	G	rs71424153	1480	0.62	1	Yes	Heart, LA	*CEP68*	1.17 (1.12-1.23)	increase	$6.05x10^{-08}$
	C	rs12990465	1987	0.62	1	Yes	Heart, LA	*CEP68*	1.17 (1.12-1.23)	increase	$5.69x10^{-08}$
	G	rs6728523	3294	0.62	1	Yes	Heart, LA	*CEP68*	1.17 (1.12-1.23)	increase	$6.07x10^{-08}$
	G	rs2302647	3760	0.62	1	Yes	Heart, LA	*CEP68*	1.17 (1.12-1.23)	increase	$6.07x10^{-08}$
	T	rs2422437	78915	0.61	0.95	Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$1.07x10^{-09}$
		rs10197530	76190	0.6	0.83	No					
	G	rs6748462	79868	0.6	0.9	Yes	Tibial Artery	*CEP68*			$3.56x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.17 (1.12-1.23)	increase	$6.93x10^{-09}$
	T	rs3732096	78669	0.58	0.95	Yes	Heart, LA	*CEP68*	1.19 (1.14-1.24)	increase	$1.05x10^{-09}$
	T	rs12713533	85288	0.58	0.95	Yes	Heart, LA	*CEP68*	1.19 (1.14-1.24)	increase	$1.17x10^{-09}$
	A	rs6705891	88681	0.58	0.95	Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$1.62x10^{-09}$
	G	rs11678917	88800	0.58	0.95	Yes	Heart, LA	*CEP68*	1.18 (1.13-1.24)	increase	$2.28x10^{-09}$
		rs113605762	89254	0.58	0.95	No					
	C	rs984748	90550	0.58	0.95	Yes	Tibial Artery	*CEP68*			$6.58x10^{-05}$

Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Europeans

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
						Yes	Heart, LA	*CEP68*	1.18 (1.13-1.24)	increase	$3.11x10^{-09}$
	T	rs10173422	92137	0.58	0.95	Yes	Heart, LA	*CEP68*	1.18 (1.13-1.24)	increase	$2.24x10^{-09}$
rs2723065 (cont.)	A	rs10173678	92243	0.58	0.95	Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$2.21x10^{-09}$
	C	rs7585500	92923	0.58	0.95	Yes	Heart, LA	*CEP68*	1.18 (1.13-1.24)	increase	$2.83x10^{-09}$
	A	rs6546128	94713	0.58	0.95	Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$1.93x10^{-09}$
	T	rs6751786	95181	0.58	0.95	Yes	Tibial Artery	*CEP68*			$7.00x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$5.15x10^{-09}$
	T	rs6722972	95182	0.58	0.95	Yes	Tibial Artery	*CEP68*			$7.56x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$6.34x10^{-09}$
	C	rs7603736	96064	0.58	0.95	Yes	Tibial Artery	*CEP68*			$6.58x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$2.68x10^{-09}$
	A	rs11888531	97727	0.58	0.95	Yes	Heart, LA	*CEP68*	1.19 (1.14-1.24)	increase	$1.98x10^{-09}$
	C	rs6546131	98717	0.58	0.95	Yes	Tibial Artery	*CEP68*			$4.54x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$2.79x10^{-09}$
	C	rs7563881	106178	0.58	0.95	Yes	Heart, LA	*CEP68*	1.17 (1.12-1.23)	increase	$1.52x10^{-07}$
	G	rs4671119	82797	0.57	0.9	Yes	Heart, LA	*CEP68*	1.19 (1.14-1.24)	increase	$9.33x10^{-10}$
	G	rs11684110	88876	0.56	0.86	Yes	Tibial Artery	*CEP68*			$1.66x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.17 (1.12-1.22)	increase	$1.53x10^{-08}$
	T	rs11126031	100943	0.56	0.82	Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$2.89x10^{-09}$
	T	rs4671638	32803	0.55	0.94	Yes	Heart, LA	*CEP68*	1.18 (1.12-1.23)	increase	$1.26x10^{-08}$
	T	rs9989843	102847	0.54	0.89	Yes	Tibial Artery	*CEP68*			$3.78x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.17 (1.12-1.23)	increase	$3.52x10^{-08}$
	G	rs6750146	104794	0.54	0.89	Yes	Tibial Artery	*CEP68*			$1.02x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.18 (1.12-1.23)	increase	$4.66x10^{-08}$
	C	rs4671118	82755	0.54	0.89	Yes	Heart, LA	*CEP68*	1.19 (1.14-1.24)	increase	$9.35x10^{-10}$
	G	rs12472873	95907	0.54	0.89	Yes	Tibial Artery	*CEP68*			$6.58x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.19 (1.13-1.24)	increase	$2.67x10^{-09}$
	T	rs2540970	24315	0.54	0.89	Yes	Thyroid	*AC008074.4*			$1.15x10^{-04}$
						Yes	Heart, LA	*CEP68*	1.13 (1.08-1.18)	increase	$3.53x10^{-06}$
		rs2540971	27029	0.54	0.89	No					
	G	rs2080385	13348	0.52	0.94	Yes	Whole Blood	*CEP68*			$1.10x10^{-05}$
						Yes	Heart, LA	*CEP68*	1.18 (1.12-1.23)	increase	$2.50x10^{-08}$
	A	rs4671120	91698	0.5	0.85	Yes	Heart, LA	*CEP68*	1.18 (1.13-1.24)	increase	$2.34x10^{-09}$
	T	rs10195785	104113	0.5	0.72	Yes	Heart, LA	*CEP68*	1.15 (1.10-1.21)	increase	$4.42x10^{-07}$
rs276857	G	rs276857	0	1	1	No					
rs3780190	G	rs3780190	0	1	1	No					
rs3922843	A	rs3922843	0	1	1	Yes	Skeletal Muscle	*XIPR1*		decrease	$7.15x10^{-3}$
rs4238314	A	rs4238314	0	1	1	No					
rs4642101	G	rs4642101	0	1	1	Yes	Skeletal Muscle	*CAND2*		increase	$2.57x10^{-09}$
						Yes	Skeletal Muscle	*KRT18P17*		increase	$3.46x10^{-06}$
		rs7650482	419	1	1	Yes	Skeletal Muscle	*CAND2*			$1.74x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$5.32x10^{-06}$
		rs6810325	1289	0.88	1	Yes	Skeletal Muscle	*CAND2*			$3.25x10^{-09}$
						Yes	Skeletal Muscle	*KRT18P17*			$5.96x10^{-06}$
		rs11718898	6599	0.88	1	Yes	Skeletal Muscle	*CAND2*			$1.63x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.99x10^{-06}$
		rs9873475	3199	0.86	1	Yes	Skeletal Muscle	*CAND2*			$4.04x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.43x10^{-09}$
		rs9836128	3203	0.86	1	Yes	Skeletal Muscle	*CAND2*			$4.04x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.43x10^{-09}$
		rs9820977	709	0.82	1	Yes	Skeletal Muscle	*CAND2*			$4.09x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.24x10^{-09}$
		rs9825233	1145	0.82	1	Yes	Skeletal Muscle	*CAND2*			$4.08x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.27x10^{-09}$
		rs11717013	1639	0.82	1	Yes	Skeletal Muscle	*CAND2*			$4.07x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.31x10^{-09}$
		rs3889514	1849	0.82	1	Yes	Skeletal Muscle	*CAND2*			$4.06x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.33x10^{-09}$
		rs3889515	1889	0.82	1	Yes	Skeletal Muscle	*CAND2*			$4.06x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.34x10^{-09}$
		rs9835677	2935	0.82	1	Yes	Skeletal Muscle	*CAND2*			$4.04x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.43x10^{-09}$
		rs9852222	6268	0.82	1	Yes	Skeletal Muscle	*CAND2*			$4.12x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.21x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.42x10^{-09}$
		rs3889513	1847	0.79	1	Yes	Skeletal Muscle	*CAND2*			$4.06x10^{-14}$
						Yes	Thyroid	*CAND2*			$1.22x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.33x10^{-09}$
	T	rs56082700	8390	0.79	1	No					
		rs13086170	9619	0.79	1	Yes	Skeletal Muscle	*CAND2*			$9.14x10^{-11}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.90x10^{-05}$

Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Europeans

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
		rs12714880	10122	0.79	1	Yes	Skeletal Muscle	*CAND2*			$3.12x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.66x10^{-05}$
rs4642101 (cont.)		rs6799179	13128	0.79	1	Yes	Skeletal Muscle	*CAND2*			$3.13x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.37x10^{-05}$
		rs6763619	20076	0.79	1	Yes	Skeletal Muscle	*CAND2*			$2.82x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.14x10^{-05}$
		rs13320486	20154	0.79	1	Yes	Skeletal Muscle	*CAND2*			$2.82x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.13x10^{-05}$
		rs9870269	11227	0.77	1	Yes	Skeletal Muscle	*CAND2*			$9.19x10^{-13}$
						Yes	Skeletal Muscle	*KRT18P17*			$3.47x10^{-05}$
		rs1985428	12908	0.77	1	Yes	Skeletal Muscle	*CAND2*			$8.66x10^{-11}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.83x10^{-05}$
		rs9871991	14698	0.77	1	Yes	Skeletal Muscle	*CAND2*			$1.02x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$5.63x10^{-05}$
		rs9872103	14771	0.77	1	Yes	Skeletal Muscle	*CAND2*			$1.40x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$7.48x10^{-06}$
		rs6791647	15798	0.77	1	Yes	Skeletal Muscle	*CAND2*			$1.18x10^{-11}$
						Yes	Skeletal Muscle	*KRT18P17*			$6.18x10^{-06}$
		rs3732675	15805	0.77	1	Yes	Skeletal Muscle	*CAND2*			$4.84x10^{-13}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.69x10^{-05}$
		rs4321514	16322	0.77	1	Yes	Skeletal Muscle	*CAND2*			$2.91x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.29x10^{-05}$
		rs3901665	17613	0.77	1	Yes	Skeletal Muscle	*CAND2*			$2.91x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.29x10^{-05}$
		rs9877165	13726	0.74	1	Yes	Skeletal Muscle	*CAND2*			$8.73x10^{-11}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.87x10^{-05}$
		rs6767504	15556	0.74	1	Yes	Skeletal Muscle	*CAND2*			$2.90x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.29x10^{-05}$
		rs4299468	16664	0.74	1	Yes	Skeletal Muscle	*CAND2*			$3.01x10^{-10}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.32x10^{-05}$
		rs4447735	16710	0.74	1	Yes	Skeletal Muscle	*CAND2*			$3.44x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$7.12x10^{-05}$
		rs12631514	3930	0.69	0.95	Yes	Skeletal Muscle	*CAND2*			$2.87x10^{-16}$
						Yes	Thyroid	*CAND2*			$2.92x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.07x10^{-08}$
		rs13085726	9551	0.69	1	Yes	Skeletal Muscle	*CAND2*			$1.56x10^{-16}$
						Yes	Thyroid	*CAND2*			$1.08x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$6.82x10^{-08}$
		rs9822382	13395	0.69	1	Yes	Skeletal Muscle	*CAND2*			$8.73x10^{-11}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.87x10^{-05}$
		rs6442330	21722	0.68	0.91	Yes	Skeletal Muscle	*CAND2*			$7.29x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$3.82x10^{-05}$
		rs7626609	36143	0.68	0.91	Yes	Skeletal Muscle	*CAND2*			$2.84x10^{-07}$
						Yes	Thyroid	*CAND2*			$1.10x10^{-05}$
		rs1467026	11448	0.67	0.87	Yes	Skeletal Muscle	*CAND2*			$7.76x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$4.48x10^{-05}$
		rs4034942	5431	0.66	1	Yes	Skeletal Muscle	*CAND2*			$1.82x10^{-18}$
						Yes	Thyroid	*CAND2*			$3.92x10^{-06}$
						Yes	Skeletal Muscle	*KRT18P17*			$4.16x10^{-07}$
		rs9874893	9144	0.66	1	Yes	Skeletal Muscle	*CAND2*			$3.15x10^{-16}$
						Yes	Thyroid	*CAND2*			$3.32x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$6.35x10^{-08}$
		rs1969154	13067	0.66	1	Yes	Skeletal Muscle	*CAND2*			$3.13x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.37x10^{-05}$
		rs3901664	17563	0.66	1	Yes	Skeletal Muscle	*CAND2*			$1.76x10^{-16}$
						Yes	Thyroid	*CAND2*			$4.64x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$6.23x10^{-08}$
		rs9840766	20353	0.66	1	Yes	Skeletal Muscle	*CAND2*			$4.67x10^{-16}$
						Yes	Thyroid	*CAND2*			$3.54x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.14x10^{-07}$
		rs57411588	21839	0.66	1	Yes	Skeletal Muscle	*CAND2*			$9.96x10^{-17}$
						Yes	Thyroid	*CAND2*			$1.29x10^{-04}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.13x10^{-08}$
		rs3732678	16781	0.64	0.95	Yes	Skeletal Muscle	*CAND2*			$2.47x10^{-11}$
		rs7629354	14477	0.64	0.87	Yes	Skeletal Muscle	*CAND2*			$7.76x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$4.48x10^{-05}$
		rs2305398	14633	0.64	0.87	Yes	Skeletal Muscle	*CAND2*			$1.91x10^{-11}$
						Yes	Skeletal Muscle	*KRT18P17*			$7.07x10^{-05}$
		rs12629398	15424	0.64	1	Yes	Skeletal Muscle	*CAND2*			$1.73x10^{-16}$
						Yes	Thyroid	*CAND2*			$4.76x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$5.44x10^{-08}$
		rs731646	15600	0.64	1	Yes	Skeletal Muscle	*CAND2*			$5.68x10^{-18}$
						Yes	Thyroid	*CAND2*			$3.11x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$5.14x10^{-09}$
		rs3901666	17860	0.64	0.87	Yes	Skeletal Muscle	*CAND2*			$7.76x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$4.48x10^{-05}$
		rs9877049	20992	0.64	1	Yes	Skeletal Muscle	*CAND2*			$2.64x10^{-19}$
						Yes	Thyroid	*CAND2*			$1.00x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.19x10^{-08}$

Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Europeans

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
		rs9870433	11343	0.64	0.86	Yes	Skeletal Muscle	*CAND2*			$9.12x10^{-13}$
	T					Yes	Skeletal Muscle	*KRT18P17*			$3.48x10^{-05}$
rs4642101 (cont.)		rs1003080	30595	0.63	0.82	Yes	Skeletal Muscle	*CAND2*			$1.77x10^{-07}$
						Yes	Thyroid	*CAND2*			$2.50x10^{-06}$
		rs13086564	9370	0.62	1	Yes	Skeletal Muscle	*CAND2*			$6.36x10^{-17}$
						Yes	Thyroid	*CAND2*			$3.78x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$6.97x10^{-08}$
		rs9877079	20936	0.62	1	Yes	Skeletal Muscle	*CAND2*			$7.75x10^{-17}$
						Yes	Thyroid	*CAND2*			$5.97x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.77x10^{-08}$
		rs7612317	21665	0.62	1	Yes	Skeletal Muscle	*CAND2*			$3.67x10^{-14}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.83x10^{-07}$
		rs60270583	21883	0.62	1	Yes	Skeletal Muscle	*CAND2*			$1.55x10^{-16}$
						Yes	Thyroid	*CAND2*			$7.00x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.49x10^{-08}$
		rs11128614	23011	0.62	1	Yes	Skeletal Muscle	*CAND2*			$9.14x10^{-18}$
						Yes	Thyroid	*CAND2*			$7.36x10^{-06}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.23x10^{-07}$
		rs6442331	21587	0.61	0.86	Yes	Skeletal Muscle	*CAND2*			$1.25x10^{-11}$
						Yes	Skeletal Muscle	*KRT18P17*			$5.41x10^{-05}$
		rs2305397	15270	0.6	1	Yes	Skeletal Muscle	*CAND2*			$1.02x10^{-17}$
						Yes	Thyroid	*CAND2*			$2.74x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.38x10^{-08}$
		rs9865624	19437	0.6	1	Yes	Skeletal Muscle	*CAND2*			$9.67x10^{-07}$
		rs9839769	20818	0.6	1	Yes	Skeletal Muscle	*CAND2*			$7.75x10^{-17}$
						Yes	Thyroid	*CAND2*			$5.97x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.77x10^{-08}$
		rs9839768	20820	0.6	1	Yes	Skeletal Muscle	*CAND2*			$7.75x10^{-17}$
						Yes	Thyroid	*CAND2*			$5.97x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$2.77x10^{-08}$
		rs12638595	22942	0.6	1	Yes	Skeletal Muscle	*CAND2*			$3.60x10^{-18}$
						Yes	Thyroid	*CAND2*			$3.92x10^{-06}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.04x10^{-07}$
		rs6799544	29244	0.59	0.78	Yes	Skeletal Muscle	*CAND2*			$6.69x10^{-06}$
						Yes	Thyroid	*CAND2*			$3.04x10^{-06}$
		rs7641959	31468	0.56	0.78	Yes	Skeletal Muscle	*CAND2*			$7.15x10^{-06}$
						Yes	Thyroid	*CAND2*			$3.60x10^{-06}$
		rs4560285	33157	0.56	0.78	Yes	Skeletal Muscle	*CAND2*			$1.32x10^{-05}$
						Yes	Thyroid	*CAND2*			$9.07x10^{-05}$
		rs7638333	36081	0.56	0.78	Yes	Skeletal Muscle	*CAND2*			$5.15x10^{-06}$
						Yes	Thyroid	*CAND2*			$6.55x10^{-06}$
		rs9831765	36289	0.56	0.78	Yes	Skeletal Muscle	*CAND2*			$5.15x10^{-06}$
						Yes	Thyroid	*CAND2*			$6.55x10^{-06}$
		rs9812144	36313	0.56	0.78	Yes	Skeletal Muscle	*CAND2*			$5.15x10^{-06}$
						Yes	Thyroid	*CAND2*			$6.55x10^{-06}$
		rs6766744	40380	0.56	0.78	Yes	Skeletal Muscle	*CAND2*			$5.16x10^{-06}$
						Yes	Thyroid	*CAND2*			$1.56x10^{-06}$
		rs4535210	2606	0.56	0.86	Yes	Skeletal Muscle	*CAND2*			$2.57x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$3.86x10^{-05}$
		rs11719501	18020	0.54	1	Yes	Skeletal Muscle	*CAND2*			$7.98x10^{-16}$
						Yes	Skeletal Muscle	*KRT18P17*			$6.14x10^{-05}$
		rs34871776	26854	0.54	1	Yes	Skeletal Muscle	*CAND2*			$6.11x10^{-12}$
						Yes	Skeletal Muscle	*KRT18P17*			$5.19x10^{-05}$
		rs4997708	2620	0.54	0.85	No					
		rs55692304	2166	0.54	0.85	Yes	Skeletal Muscle	*CAND2*			$6.25x10^{-18}$
						Yes	Thyroid	*CAND2*			$2.47x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.47x10^{-08}$
		rs13316229	34852	0.53	0.78	Yes	Skeletal Muscle	*CAND2*			$5.15x10^{-06}$
						Yes	Thyroid	*CAND2*			$6.55x10^{-06}$
		rs12629892	23303	0.51	0.85	Yes	Skeletal Muscle	*CAND2*			$3.74x10^{-16}$
						Yes	Thyroid	*CAND2*			$1.36x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$7.90x10^{-07}$
		rs9813960	24018	0.51	0.85	Yes	Skeletal Muscle	*CAND2*			$3.74x10^{-16}$
						Yes	Thyroid	*CAND2*			$1.36x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$7.90x10^{-07}$
		rs9809596	1710	0.51	0.85	Yes	Skeletal Muscle	*CAND2*			$5.42x10^{-18}$
						Yes	Thyroid	*CAND2*			$2.71x10^{-05}$
						Yes	Skeletal Muscle	*KRT18P17*			$1.72x10^{-08}$
rs4824051	C	rs4824051	0	1	1	No					
rs6062468	C	rs6062468	0	1	1	No					
rs6540690	C	rs6540690	0	1	1	No					
rs6749773	A	rs6749773	0	1	1	Yes	Thyroid	*PPP1R21*		increase	$3.80x10^{-06}$
rs6882776	A	rs6882776	0	1	1	Yes	Heart, LA	*NKX2-5*	0.93 (0.90-0.95)	decrease	$8.78x10^{-06}$
rs6884185	C	rs6884185	0	1	1	No					
rs6968408	C	rs6968408	0	1	1	No					
rs7160770	T	rs7160770	0	1	1	No					
rs7295704	T	rs7295704	0	1	1	No					
rs752282	T	rs752282	0	1	1	No					
rs7682872	G	rs7682872	0	1	1	No					

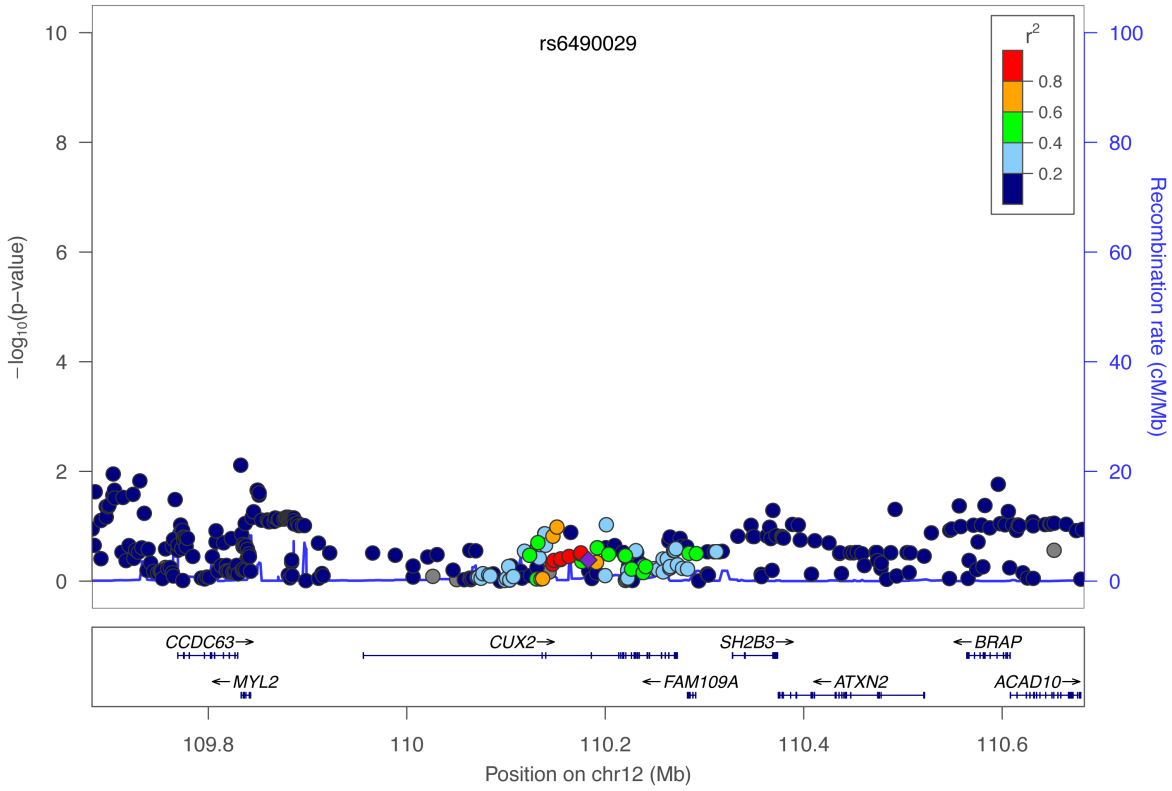
Supplemental Table 8. eQTL analyses using the Genotype-Tissue Expression Portal (GTEx) and Cleveland Clinic Atrial Tissue Bank.

Sentinel SNP	AF Risk Allele	Proxy SNP	Distance from Sentinel SNP (bp)	r2	DPrime	eQTL Yes/No	Tissue	Gene	fold change per AF risk allele	Direction of expression change	*P value*
Europeans											
rs768347	T	rs768347	0	1	1	No					
rs7835679	C	rs7835679	0	1	1	No					
rs7987944	C	rs7987944	0	1	1	No					
rs9267992	G	rs9267992	0	1	1	No					
rs9284844	G	rs9284844	0	1	1	No					
rs9857326	A	rs9857326	0	1	1	No					
Japanese											
rs6584555	C	rs6584555	0	1	1	No					
rs6490029	A	rs6490029	0	1	1	Yes	Heart, LA	*TMEM116*	1.12 (1.08-1.17)	increase	4.28×10^{-06}

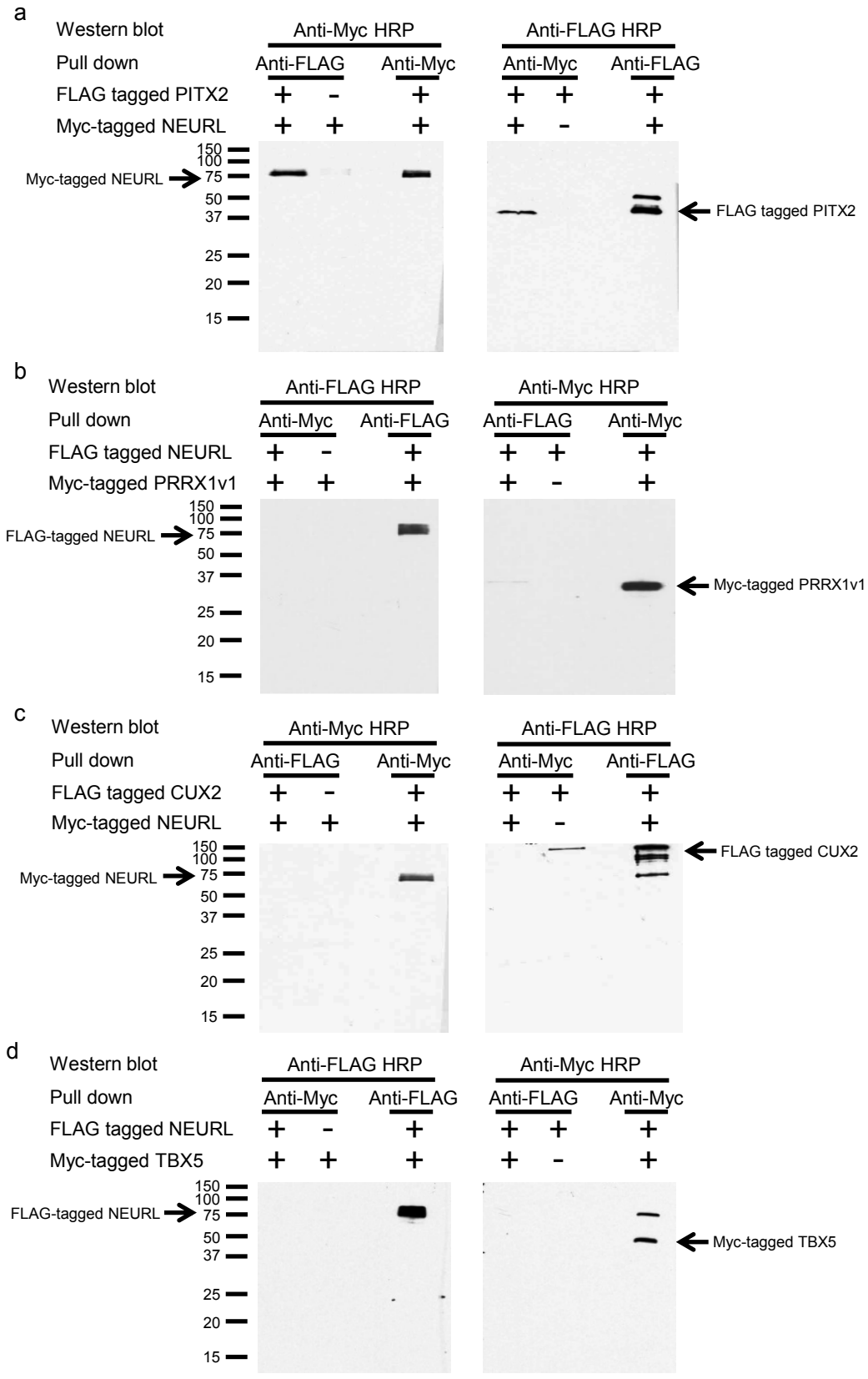
Supplemental Table 9. Nucleotide sequences used for morpholinos and PCR analyses, morpholino efficacy.		
	Sequence	**Morpholino efficacy (72 hpf)**
Control MO	5’-ATCCTCTTGAGGCGAACAAAGAGTC-3’	
Anti-*neurla* E1I1 MO	5’-ATTGGAGATCAGTTGCTCACCGTAC-3’	81.4 ± 6.9%
Anti-*neurla* E2I2 MO	5’-CCGTCTTTCCTTGTTCTTACCTTTA-3’	56.1 ± 1.1%
Anti-*neurla* 5’UTR	5’-TCCAGAGAGCGATAATTCCACACCG-3’	Not measureable
Anti-*cand1* E3I3 MO	5’-AGCAGGAAAGGATGTTTTACCACT-3’	70.7 ± 16.3%
Anti-*cand1* E10I10 MO	5’-AGCAGAAATGGACATTAACCTGATA-3’	70.2 ± 2.4%
Anti-*cand2* MO	5’-GCGTCTCTAAAATACTCTTACCTAA-3’	98.1 ± 1.2%
Anti-*cux2b* E12I12 MO	5’- AGGGTTTGTTCATCACTCACCTCTC-3’	53.1 ± 20.8%
***neurla* E1I1 qRT-PCR**	5’-CTCTGGACCTTTGAGAAATAAACG-3’ 5’-ACACTGATGCAAGGGCAAAC-3’	
***neurla* E2I2 semi-q PCR**	5’-CTCTGGACCTTTGAGAAATAAACG-3’ 5’-TCATTTGCAAACTCCTCTGGTAG-3’	
***cand1* E3I3 semi-q PCR**	5’-AAACACACACACAAGTGGTTTTC-3’ 5’-AAGAGGCGAACTACATCATTCTG-3’	
***cand1* E10I10 semi-q PCR**	5’-GGAGAAGTCGGTCATCATGTTG-3’ 5’-TTAACAGCTGTAACTACCGAGC-3’	
***cand2* qRT-PCR**	5’-AAAAATGACATCCACTGACAAAG-3’ 5’-ACATAGTCACGACTTTCCTCTCG-3’	
***cux2b* E12I12 semi-q PCR**	5’- CATCAGCCAATGGAAGTTCGTC-3’ 5’- CTGACCCAGTTTCCGGAGTTC-3’	
***ef-1α* qRT-PCR**	5’-TTGAGAAGAAAATCGGTGGTGCTG-3’ 5’-GGAACGGTGTGATTGAGGGAAATTC-3’	
***ef-1α* semi-q PCR**	5’-AAGAGAACCATCGAGAAGTTCG-3’ 5’-CTCAATCTTCCATCCCTTGAAC-3’	
***β-actin* qRT-PCR**	5’-CGAGCAGGAGATGGGAACC-3’ 5’-CAACGGAAACGCTCATTGC-3’	

Supplemental Table 10. Atrial action potential durations following morpholino microinjection				
Morpholino	**Average atrial action potential duration (ms)**	**Standard Deviation**	**n**	***p-value***
Control	110.1	8.8	18	N.A.
***neurla* E1I1**	128.9	14.5	17	5.0×10^{-5}
***neurla* E2I2**	147.0	15.8	12	6.4×10^{-9}
***neurla* 5'UTR**	130.9	12.3	15	3.5×10^{-6}
***cand1* E3I3**	159.1	21.5	9	8.3×10^{-9}
***cand1* E10I10**	143.7	11.1	6	1.4×10^{-7}
***cand2* E1I1**	113.3	10.3	6	0.48
***cux2b* E12I12**	109.1	13.0	10	0.79

Supplemental Figure 1. Regional plot for the association of *CUX2* with atrial fibrillation in Europeans. SNPs are plotted using the genomic position (NCBI Build 36) and discovery stage *P* values. The sentinel SNP from the Japanese analysis is labeled in purple. Each dot represents a SNP. The strength of the linkage disequilibrium of SNPs with the sentinel-SNP is indicated by a color gradient according to the legend. Estimated recombination rates are shown by the blue line, and spikes indicate locations of frequent recombination. Below, the chromosomal positions of the SNPs and regional candidate genes are annotated. Linkage disequilibrium and recombination rates are based on the CEU HapMap release 22. Plots prepared using LocusZoom.[15]

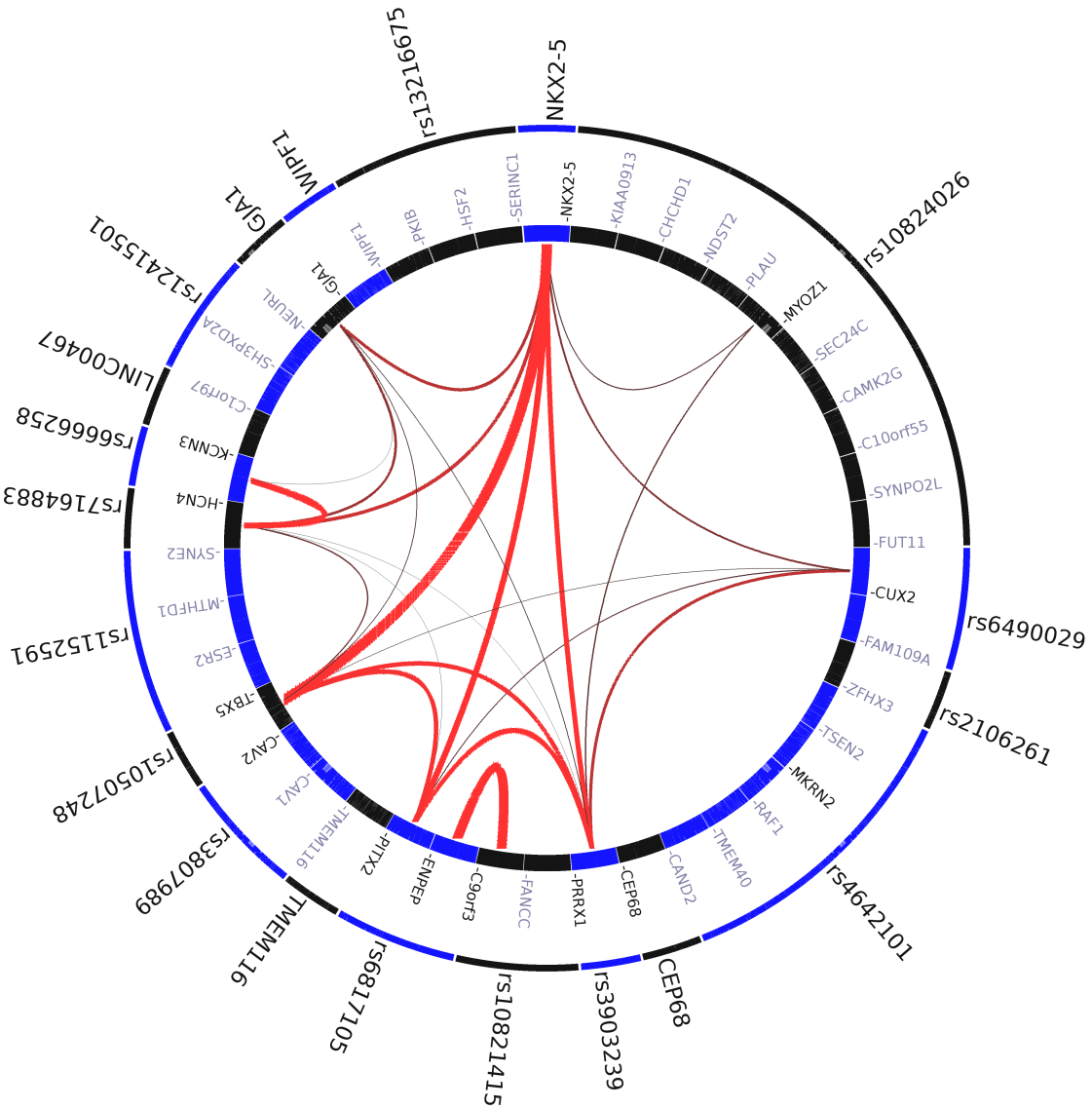


Supplemental Figure 2. Protein interaction analyses in COS7 cells. Interactions between NEURL and PITX2 (a), PRRX1 (b), CUX2 (c), or TBX5 (d) in COS7 cells.



Supplemental Figure 3. Pathway analysis for 14 atrial fibrillation loci

The outer circle marks the 5 novel and 9 previously reported susceptibility loci for AF,[1] as well as 6 genes implicated by our eQTL analysis. The inner circle shows the genes encoded at each locus. Connecting lines in the center represent relations between these genes that were reported in the literature. Red lines indicate significant relations between genes (p<0.05).



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