

Supporting Information

Levy et al. 10.1073/pnas.0911494107

SI Text

Framingham Heart Study. The Framingham Heart Study began in 1948 when an original cohort of 5,209 men and women who were 28–62 years of age were enrolled. In 1971, recruitment of an offspring cohort occurred; this cohort consisted of 5,124 children and spouses of children of the original cohort (mean age = 37 years; 52% women). Leukocyte telomere length (LTL) measurements and genotyping results were available for 1,150 (558 men and 592 women) offspring participants who attended the sixth examination cycle (1995–1998). The final number of subjects with complete information on telomere length and imputed genotyping data was 1,146 (557 men and 589 women).

Family Heart Study. The National Heart, Lung, and Blood Institute (NHLBI) Family Heart Study was begun in 1992 with the ascertainment of 1,200 families, of which one-half were randomly sampled and one-half were selected because of an excess of coronary heart disease or risk factor abnormalities compared with age- and sex-specific population rates. The families, consisting of ~6,000 individuals, were sampled on the basis of information on probands from three population-based parent studies: the Framingham Heart Study, the Utah Family Tree Study, and two centers of the Atherosclerosis Risk in Communities (ARIC) study (Minneapolis, MN and Forsyth County, NC). Approximately 8 years later, study participants belonging to the largest pedigrees were invited for a second clinical examination. A total of 2,757 subjects of European descent in 510 extended families were examined; this sample is the focus of the LTL genome-wide association (GWA) study. A two-stage design was adopted for the GWA. In the first stage, 1,007 individuals of European descent were chosen, equally distributed between the upper and lower quartile of age- and sex-adjusted values for coronary artery calcification, and assessed by computerized tomography scan. These subjects were chosen to be largely unrelated; 34% of the subjects were from unique families, whereas 200 other subjects had one or more siblings selected into the sample, yielding a total sample of 465 unrelated subjects and 542 relatives. LTL measurements were available for 907 of these subjects. Thirty subjects overlapped with the Framingham Heart Study and were removed, leaving a final sample size of 877. The remaining family members were genotyped in the second stage for replication of the top hits from the first stage. Table S7 shows the demographics for the replication sample.

Cardiovascular Health Study. The Cardiovascular Health Study (CHS) is a multisite observational cohort study designed to evaluate risk factors for heart disease and stroke in adults aged 65 and older. The study was initiated in 1989 with the recruitment of 5,201 older adults, primarily whites, from four clinical field centers: Forsyth County, NC, Sacramento County, CA, Washington County, MD, and Pittsburgh, PA. Beginning in 1992, 687 African Americans were recruited. To reduce the possibility of confounding by population stratification, African-American participants were not included in the CHS GWA. The samples for LTL measurements were collected between 1989 and 1990. The sample size of whites of European descent with GWA and LTL data was 1,061 men and women.

Bogalusa Heart Study. The Bogalusa Heart Study (BHS) is a biracial (African Americans and individuals of European descent) community-based longitudinal study of the early natural history of cardiovascular disease beginning in childhood. GWA was per-

formed on white BHS participants with LTL measurements (obtained from samples collected between 2001 and 2002) and genotype data after filtering for relatedness.

TwinsU.K. TwinsU.K. I and II cohort (www.twinsuk.ac.uk) is an adult twin British registry shown to be representative of singleton populations and the United Kingdom population. LTL and genotypic data were available for 1,194 (TwinsU.K. I) and 1,682 (TwinsU.K. II) women.

ACKNOWLEDGMENTS. We thank the staffs from the Genotyping Facilities at the Wellcome Trust Sanger Institute for sample preparation (quality control and genotyping led by Leena Peltonen and Panos Deloukas), the Le Centre National de Génotypage, France, (led by Mark Lathrop) for genotyping, Duke University (led by David Goldstein) for genotyping, and the Finnish Institute of Molecular Medicine, Finnish Genome Center, University of Helsinki (led by Aarno Palotie). The research reported in this article was supported by National Heart, Lung, and Blood Institute's Grants R01AG21593 and R01AG20132. The National Heart, Lung, and Blood Institute's Framingham Heart Study is a joint project of the National Institutes of Health and Boston University School of Medicine, and it was supported by the National Heart, Lung, and Blood Institute's Framingham Heart Study (Contract No. N01-HC-25195) and its contract with Affymetrix, Inc. for genotyping services (Contract N02-HL-6-4278). Analyses reflect the efforts and resource development from the Framingham Heart Study investigators participating in the SNP Health Association Resource (SHARe) project. A portion of this research was conducted using the Linux Cluster for Genetic Analysis (LinGA-II) funded by the Robert Dawson Evans Endowment of the Department of Medicine at Boston University School of Medicine and Boston Medical Center. The Family Heart Study was supported by cooperative agreements U01 HL67893, U01 HL67894, U01 HL67895, U01 HL67896, U01 HL67897, U01 HL67898, U01 HL67899, U01 HL67900, U01 HL67901, U01 HL67902, U01 HL56563, U01 HL56564, U01 HL56565, U01 HL56566, U01 HL56567, U01 HL56568, and U01 HL56569. A full list of Family Heart Study investigators and institutions can be found at <https://dsgweb.wustl.edu/scan/directory.html>. The CHS research reported in this article was supported by Contracts N01-HC-85079 through N01-HC-85086, N01-HC-35129, N01-HC-15103, N01-HC-55222, N01-HC-75150, and N01-HC-45133 and Grants U01 HL080295 and R01 HL087652 from the National Heart, Lung, and Blood Institute with additional contribution from the National Institute of Neurological Disorders and Stroke. A full list of principal CHS investigators and institutions can be found at <http://www.chs-nhlbi.org/pi.htm>. DNA handling and genotyping was supported in part by the National Center for Research Resources Grant M01RR00425 (to the Cedars-Sinai General Clinical Research Center Genotyping Core) and the National Institute of Diabetes and Digestive and Kidney Diseases Grant DK063491 (to the Southern California Diabetes Endocrinology Research Center). The Bogalusa Heart Study was supported by Grant R01AG16592 from the National Institute on Aging and Grant 0855082E from the American Heart Association. TwinsU.K. research was funded by the Wellcome Trust, the European Community's Seventh Framework Programme (FP7/2007-2013)/ Grant Agreement HEALTH-F2-2008-201865-GEFOS (FP7/2007-2013), the European Network for Genetic and Genomic Epidemiology Project Grant Agreement HEALTH-F4-2007-

201413, and the FP-5 GenomEUtwin Project (QLG2-CT-2002-01254). The study received support from the Department of Health through the National Institute for Health Research (NIHR) comprehensive Biomedical Research Centre award to Guy's and St. Thomas' National Health Service Foundation Trust in partnership with King's College, London. The project

also received support from the Biotechnology and Biological Sciences Research Council Grant G20234. The authors acknowledge the funding and support of the National Eye Institute through a National Institutes of Health/Center for Inherited Disease Research genotyping project (Principal Investigator was Terri Young). T.D.S. is an NIHR senior investigator.

Table S1. GWA results within each cohort for SNPs with meta-analysis $P < 5 \times 10^{-7}$

SNP	Chr	Position	Nearest gene	Bogalusa Heart Study			Cardiovascular Health Study			Family Heart Study			Framingham Heart Study			
				<i>P</i>	β	SE	<i>P</i>	β	SE	<i>P</i>	β	SE	<i>P</i>	β	SE	<i>P</i>
rs4387287	10	105667887	OBFC1	3.87E-09	0.06	0.08	4.84E-01	0.14	0.04	5.69E-04	0.12	0.04	5.02E-03	0.11	0.03	9.03E-05
rs9420907	10	105666455	OBFC1	2.01E-08	-0.04	0.15	7.76E-01	-0.13	0.04	5.24E-04	-0.10	0.04	2.28E-02	-0.12	0.03	8.27E-05
rs9419958	10	105665936	OBFC1	2.08E-08	0.04	0.15	7.76E-01	0.13	0.04	5.26E-04	0.10	0.04	2.28E-02	0.12	0.03	8.58E-05
rs2487999	10	105649816	OBFC1	2.69E-08	0.07	0.18	6.94E-01	0.12	0.04	3.81E-03	0.15	0.05	2.72E-03	0.14	0.04	1.19E-04
rs4452212	2	136732461	CXCR4	2.94E-08	-0.15	0.05	5.25E-03	-0.10	0.03	4.03E-05	-0.00	0.03	9.35E-01	-0.10	0.03	5.68E-05
rs4072435	2	136730371	CXCR4	2.96E-08	-0.15	0.05	5.27E-03	-0.10	0.03	3.99E-05	-0.00	0.03	9.35E-01	-0.10	0.03	5.83E-05
rs13024450	2	136731081	CXCR4	2.96E-08	-0.15	0.05	5.26E-03	-0.10	0.03	3.99E-05	-0.00	0.03	9.35E-01	-0.10	0.03	5.81E-05
rs13018756	2	136724705	CXCR4	2.99E-08	-0.15	0.05	5.29E-03	-0.10	0.03	3.68E-05	-0.00	0.03	9.35E-01	-0.10	0.03	6.19E-05
rs13004902	2	136744150	CXCR4	3.71E-08	0.15	0.05	5.04E-03	0.10	0.03	4.94E-05	0.00	0.03	9.43E-01	0.10	0.03	5.58E-05
rs12691881	2	136746138	CXCR4	3.76E-08	0.15	0.05	4.94E-03	0.10	0.03	5.17E-05	0.00	0.03	9.43E-01	0.10	0.03	5.41E-05
rs10883943	10	105641406	OBFC1	6.09E-08	-0.12	0.06	3.12E-02	-0.08	0.03	2.77E-03	-0.07	0.03	9.07E-03	-0.07	0.02	1.88E-03
rs10786775	10	105647306	OBFC1	6.13E-08	-0.03	0.09	7.13E-01	-0.12	0.04	3.30E-03	-0.15	0.05	2.72E-03	-0.14	0.04	1.19E-04
rs10786774	10	105634313	OBFC1	6.29E-08	-0.03	0.09	7.13E-01	-0.12	0.04	2.85E-03	-0.15	0.05	2.72E-03	-0.14	0.04	1.40E-04
rs4918068	10	105634726	OBFC1	6.33E-08	0.03	0.09	7.14E-01	0.12	0.04	2.85E-03	0.15	0.05	2.72E-03	0.14	0.04	1.41E-04
rs11598840	10	105635171	OBFC1	6.43E-08	0.03	0.09	7.14E-01	0.12	0.04	2.85E-03	0.15	0.05	2.72E-03	0.14	0.04	1.43E-04
rs10883942	10	105641376	OBFC1	6.49E-08	0.12	0.06	3.12E-02	0.08	0.03	2.97E-03	0.07	0.03	9.07E-03	0.07	0.02	1.89E-03
rs11191849	10	105640870	OBFC1	6.50E-08	-0.12	0.06	3.11E-02	-0.08	0.03	2.97E-03	-0.07	0.03	9.07E-03	-0.07	0.02	1.89E-03
rs11191848	10	105640827	OBFC1	6.52E-08	0.12	0.06	3.11E-02	0.08	0.03	2.97E-03	0.07	0.03	9.07E-03	0.07	0.02	1.90E-03
rs10883941	10	105640772	OBFC1	6.54E-08	-0.12	0.06	3.11E-02	-0.08	0.03	2.97E-03	-0.07	0.03	9.07E-03	-0.07	0.02	1.90E-03
rs2488000	10	105661099	OBFC1	6.81E-08	0.04	0.09	6.94E-01	0.12	0.04	3.55E-03	0.15	0.05	2.72E-03	0.14	0.04	1.19E-04
rs2488001	10	105661122	OBFC1	6.96E-08	0.04	0.09	6.86E-01	0.12	0.04	3.57E-03	0.15	0.05	2.72E-03	0.14	0.04	1.19E-04
rs911547	10	105629411	OBFC1	6.98E-08	0.01	0.08	9.32E-01	0.13	0.04	5.42E-04	0.11	0.04	1.09E-02	-0.11	0.03	3.88E-04
rs1265165	10	105661517	OBFC1	7.01E-08	0.04	0.09	6.84E-01	0.12	0.04	3.59E-03	0.15	0.05	2.72E-03	0.14	0.04	1.19E-04
rs2756116	10	105661794	OBFC1	7.05E-08	0.04	0.09	6.82E-01	0.12	0.04	3.60E-03	0.15	0.05	2.72E-03	0.14	0.04	1.19E-04
rs11591710	10	105677622	OBFC1	7.87E-08	0.01	0.08	8.50E-01	0.14	0.04	8.94E-04	0.10	0.04	2.28E-02	-0.12	0.03	7.32E-05
rs2736428	6	31951903	SLC44A4	8.59E-08	-0.04	0.12	7.21E-01	0.09	0.03	4.50E-04	0.08	0.03	8.43E-03	0.07	0.02	1.81E-03
rs10221893	2	136730076	CXCR4	1.12E-07	-0.3	0.11	5.49E-03	-0.10	0.03	4.00E-05	0.00	0.03	9.35E-01	-0.10	0.03	5.86E-05
rs6430612	2	136722668	CXCR4	1.15E-07	-0.3	0.11	5.49E-03	-0.10	0.03	3.71E-05	0.00	0.03	9.35E-01	-0.10	0.03	6.31E-05
rs1975174	19	22307091	ZNF676	1.20E-07	0.12	0.05	2.07E-02	0.05	0.03	6.08E-02	-0.06	0.03	2.75E-02	0.09	0.02	4.25E-05
rs9325507	10	105635612	OBFC1	1.39E-07	-0.12	0.06	3.04E-02	-0.08	0.03	3.18E-03	-0.07	0.03	8.04E-03	-0.06	0.02	4.09E-03
rs7259376	19	22299545	LOC148198	1.44E-07	-0.12	0.05	2.83E-02	-0.05	0.03	5.88E-02	-0.06	0.03	2.75E-02	-0.09	0.02	4.56E-05
rs11598018	10	105651305	OBFC1	1.44E-07	-0.12	0.06	3.26E-02	-0.08	0.03	3.67E-03	-0.07	0.03	8.04E-03	-0.06	0.02	3.62E-03
rs12765878	10	105659612	OBFC1	1.45E-07	0.12	0.06	3.26E-02	0.08	0.03	3.71E-03	0.07	0.03	8.04E-03	0.06	0.02	3.62E-03
rs4954585	2	136714864	CXCR4	1.45E-07	-0.14	0.06	1.71E-02	-0.11	0.03	5.53E-05	-0.02	0.03	5.98E-01	-0.09	0.03	6.06E-04
rs2273698	10	105639148	OBFC1	1.54E-07	-0.12	0.06	3.05E-02	-0.08	0.03	3.95E-03	-0.07	0.03	8.04E-03	-0.06	0.02	3.75E-03
rs3814220	10	105637290	OBFC1	1.55E-07	0.12	0.06	3.05E-02	0.08	0.03	3.97E-03	0.07	0.03	8.04E-03	0.06	0.02	3.76E-03
rs8081000	17	39070759	MEOX1	1.59E-07	0.03	0.12	8.23E-01	-0.04	0.03	1.45E-01	0.14	0.03	1.39E-06	0.07	0.02	2.64E-03
rs351089	4	132636028	PCDH10	2.16E-07	-0.06	0.21	7.75E-01	NA	NA	NA	-0.50	0.14	2.33E-04	-0.49	0.11	1.14E-05
rs11668269	19	22305800	LOC148198	2.33E-07	-0.23	0.11	2.87E-02	-0.05	0.03	4.48E-02	-0.06	0.03	2.75E-02	0.09	0.02	4.47E-05
rs808373	19	22261073	ZNF676	2.37E-07	-0.12	0.05	2.92E-02	0.05	0.03	1.09E-01	-0.06	0.03	4.60E-02	-0.09	0.02	2.10E-05
rs8111537	19	22327385	LOC148198	3.06E-07	-0.14	0.05	9.18E-03	-0.04	0.03	1.16E-01	-0.06	0.03	1.95E-02	-0.09	0.02	1.10E-04
rs1980653	10	105644154	OBFC1	3.09E-07	0.24	0.11	3.08E-02	-0.08	0.03	3.60E-03	0.07	0.03	8.04E-03	0.06	0.02	3.65E-03
rs11191841	10	105629601	OBFC1	3.11E-07	0.13	0.06	2.40E-02	0.08	0.03	4.81E-03	0.08	0.03	7.33E-03	0.06	0.02	7.42E-03
rs7100920	10	105630968	OBFC1	3.25E-07	-0.12	0.06	3.03E-02	-0.07	0.03	4.64E-03	-0.07	0.03	8.04E-03	-0.06	0.02	6.51E-03

Table S2. Meta-analysis of GWA results for men and women for all SNPs with $P < 5 \times 10^{-7}$ in the combined analysis

SNP	Chr	Position	Closest gene	Women			Men		
				β	SE	P	β	SE	P
rs4387287	10	105667887	OBFC1	0.12	0.03	1.32E-05	0.11	0.03	5.94E-05
rs9420907	10	105666455	OBFC1	-0.11	0.03	8.20E-05	-0.12	0.03	5.30E-05
rs9419958	10	105665936	OBFC1	0.11	0.03	8.47E-05	0.12	0.03	5.32E-05
rs2487999	10	105649816	OBFC1	0.12	0.03	1.79E-04	0.14	0.03	2.85E-05
rs4452212	2	136732461	CXCR4	-0.10	0.02	4.27E-07	-0.05	0.02	9.84E-03
rs4072435	2	136730371	CXCR4	-0.10	0.02	4.33E-07	-0.05	0.02	9.89E-03
rs13024450	2	136731081	CXCR4	-0.10	0.02	4.30E-07	-0.05	0.02	9.88E-03
rs13018756	2	136724705	CXCR4	-0.10	0.02	4.55E-07	-0.06	0.02	9.66E-03
rs13004902	2	136744150	CXCR4	0.10	0.02	4.97E-07	0.05	0.02	1.06E-02
rs12691881	2	136746138	CXCR4	0.10	0.02	5.05E-07	0.05	0.02	1.05E-02
rs10883943	10	105641406	OBFC1	-0.08	0.02	2.41E-05	-0.07	0.02	5.42E-04
rs10786775	10	105647306	OBFC1	-0.12	0.03	1.93E-04	-0.13	0.03	7.14E-05
rs10786774	10	105634313	OBFC1	-0.12	0.03	1.64E-04	-0.13	0.03	8.84E-05
rs4918068	10	105634726	OBFC1	0.12	0.03	1.65E-04	0.13	0.03	8.83E-05
rs11598840	10	105635171	OBFC1	0.12	0.03	1.64E-04	0.13	0.03	9.00E-05
rs10883942	10	105641376	OBFC1	0.08	0.02	2.55E-05	0.07	0.02	5.45E-04
rs11191849	10	105640870	OBFC1	-0.08	0.02	2.55E-05	-0.07	0.02	5.48E-04
rs11191848	10	105640827	OBFC1	0.08	0.02	2.56E-05	0.07	0.02	5.48E-04
rs10883941	10	105640772	OBFC1	-0.08	0.02	2.57E-05	-0.07	0.02	5.47E-04
rs2488000	10	105661099	OBFC1	0.12	0.03	2.09E-04	0.13	0.03	7.36E-05
rs2488001	10	105661122	OBFC1	0.12	0.03	2.12E-04	0.13	0.03	7.38E-05
rs911547	10	105629411	OBFC1	-0.11	0.03	1.34E-04	-0.11	0.03	1.16E-04
rs1265165	10	105661517	OBFC1	0.12	0.03	2.14E-04	0.13	0.03	7.40E-05
rs2756116	10	105661794	OBFC1	0.12	0.03	2.15E-04	0.13	0.03	7.40E-05
rs11591710	10	105677622	OBFC1	-0.12	0.03	8.41E-05	-0.11	0.03	2.53E-04
rs2736428	6	31951903	SLC44A4	0.10	0.02	2.62E-06	0.06	0.02	4.34E-03
rs10221893	2	136730076	CXCR4	-0.10	0.02	8.17E-07	-0.05	0.02	1.61E-02
rs6430612	2	136722668	CXCR4	-0.10	0.02	8.56E-07	-0.05	0.02	1.60E-02
rs1975174	19	22307091	ZNF676	0.09	0.02	8.53E-06	0.06	0.02	2.92E-03
rs9325507	10	105635612	OBFC1	-0.08	0.02	4.54E-05	-0.07	0.02	6.57E-04
rs7259376	19	22299545	LOC148198	-0.09	0.02	9.13E-06	-0.06	0.02	3.34E-03
rs11598018	10	105651305	OBFC1	-0.08	0.02	4.14E-05	-0.07	0.02	6.72E-04
rs12765878	10	105659612	OBFC1	0.08	0.02	4.15E-05	0.07	0.02	6.75E-04
rs4954585	2	136714864	CXCR4	-0.10	0.02	1.14E-05	-0.07	0.02	3.19E-03
rs2273698	10	105639148	OBFC1	-0.08	0.02	4.32E-05	-0.07	0.02	7.64E-04
rs3814220	10	105637290	OBFC1	0.08	0.02	4.34E-05	0.07	0.02	7.65E-04
rs8081000	17	39070759	MEOX1	0.07	0.02	7.99E-04	0.09	0.02	2.05E-05
rs351089	4	132636028	PCDH10	-0.34	0.14	1.28E-02	-0.45	0.11	2.34E-05
rs11668269	19	22305800	LOC148198	0.09	0.02	1.18E-05	0.06	0.02	4.16E-03
rs808373	19	22261073	ZNF676	-0.09	0.02	8.43E-06	-0.06	0.02	6.08E-03
rs8111537	19	22327385	LOC148198	-0.08	0.02	2.17E-05	-0.06	0.02	2.47E-03
rs1980653	10	105644154	OBFC1	0.07	0.02	1.51E-04	0.07	0.02	3.94E-04
rs11191841	10	105629601	OBFC1	0.08	0.02	1.15E-04	0.07	0.02	5.66E-04
rs7100920	10	105630968	OBFC1	-0.07	0.02	9.22E-05	-0.07	0.02	7.61E-04

Table S3. Mean LTL by genotype of top SNPs in *OBFC1* and *CXCR4* from the four-study meta-analysis

	Genotype*		
	1	2	3
<i>OBFC1</i> rs4387287 (C/A)			
Men <i>N</i>	6.72 (6.02–7.41) 1,087	6.76 (6.20–7.32) 399	7.12 (6.15–8.10) 40
Women <i>N</i>	6.81 (6.23–7.39) 1,364	6.94 (6.34–7.53) 486	6.97 (6.68–7.25) 39
<i>CXCR4</i> rs4452212 (A/G)			
Men <i>N</i>	6.65 (6.10–7.21) 361	6.78 (6.01–7.55) 509	6.77 (6.12–7.42) 230
Women <i>N</i>	6.77 (6.20–7.34) 620	6.85 (6.25–7.46) 904	6.96 (6.35–7.57) 365

*Genotype 1 indicates zero copies, genotype 2 indicates one copy, and genotype 3 indicates two copies of the minor allele. The minor allele is listed second next to the rs number for each SNP. All subjects are of European descent [mean LTL (95% confidence interval) and *N*].

Table S4. SNPs in the region of *TERC*

SNP	Chr	Position	Nearest gene	Coded allele	Coded allele frequency	β	SE	<i>P</i>
rs11718804	3	170941266	TERC	T	0.33	-0.04	0.02	7.93E-03
rs16854335	3	170944265	TERC	T	0.32	-0.05	0.02	2.04E-03
rs12638862	3	170960200	TERC	A	0.78	0.06	0.02	7.31E-05
rs12630450	3	170962898	TERC	A	0.77	0.06	0.02	1.58E-04
rs12696304	3	170963965	TERC	C	0.77	0.06	0.02	1.57E-04
TERC gene	3	170965092– 170965542						
rs9822885	3	170968838	ARPM1	A	0.77	0.07	0.02	5.33E-05
rs9860874	3	170968965	ARPM1	A	0.22	-0.06	0.02	1.54E-04
rs3821383	3	170972640	MYNN	A	0.78	0.06	0.02	1.68E-04
rs10936599	3	170974795	MYNN	T	0.22	-0.07	0.02	4.26E-05
rs3950296	3	170975977	MYNN	C	0.78	0.07	0.02	1.22E-05
rs1317082	3	170980279	MYNN	A	0.78	0.07	0.02	1.23E-05
rs3772190	3	170983181	MYNN	A	0.21	-0.07	0.02	1.13E-05
rs1920120	3	170984874	MYNN	T	0.76	0.06	0.02	2.47E-04
rs2141595	3	170986126	MYNN	T	0.23	-0.06	0.02	2.42E-04
rs1920122	3	170988835	MYNN	T	0.23	-0.06	0.02	2.86E-04
rs13069553	3	170990966	MYNN	A	0.80	0.07	0.02	1.44E-05
rs7625734	3	170991609	LRRC34	T	0.77	0.06	0.02	2.74E-04
rs7633750	3	170991938	LRRC34	A	0.23	-0.06	0.02	2.70E-04
rs1997392	3	170992346	LRRC34	T	0.23	-0.06	0.02	6.27E-04
rs9868000	3	170993483	LRRC34	A	0.23	-0.06	0.02	2.79E-04
rs7621631	3	170994839	LRRC34	A	0.78	-0.07	0.02	1.49E-05
rs10936600	3	170997279	LRRC34	A	0.22	0.07	0.02	1.49E-05
rs6793295	3	171001149	LRRC34	T	0.77	0.06	0.02	6.00E-04
rs9827710	3	171005081	LRRC34	C	0.23	-0.06	0.02	2.35E-04
rs3796145	3	171007556	LRRC34	A	0.79	0.07	0.02	1.20E-05
rs10936601	3	171011143	LRRC34	T	0.23	-0.06	0.02	2.29E-04
rs9831661	3	171011217	LRRC34	T	0.23	-0.06	0.02	2.28E-04
rs9841443	3	171012770	LRRC34	A	0.46	-0.04	0.02	5.74E-03
rs6793160	3	171017960	LRRIQ4	T	0.41	-0.04	0.01	8.47E-03
rs10936602	3	171019331	LRRIQ4	T	0.72	0.05	0.02	4.06E-03
rs7632991	3	171021306	LRRIQ4	A	0.28	-0.05	0.02	4.04E-03
rs1920119	3	171023091	LRRIQ4	T	0.59	0.04	0.01	7.96E-03
rs10936603	3	171028346	LRRIQ4	T	0.28	-0.05	0.02	8.60E-03
rs12486767	3	171033453	LRRIQ4	A	0.38	-0.05	0.02	1.85E-03
rs7647824	3	171035075	LRRIQ4	A	0.73	0.05	0.02	3.20E-03
rs9833035	3	171036192	LRRIQ4	T	0.28	-0.05	0.02	3.23E-03
rs4352416	3	171036778	LRRIQ4	A	0.28	-0.05	0.02	3.29E-03
rs2421830	3	171036823	LRRIQ4	A	0.28	-0.05	0.02	3.33E-03
rs2421829	3	171036958	LRRIQ4	T	0.73	0.05	0.02	3.35E-03
rs3732451	3	171040719	LRRC31	T	0.38	-0.04	0.02	5.18E-03
rs9831336	3	171041067	LRRC31	C	0.28	-0.05	0.02	3.43E-03
rs12492588	3	171041405	LRRC31	A	0.28	-0.05	0.02	3.55E-03
rs12489230	3	171041515	LRRC31	A	0.28	-0.05	0.02	3.58E-03
rs16854453	3	171041928	LRRC31	A	0.28	-0.05	0.02	7.08E-03
rs6785618	3	171045491	LRRC31	A	0.27	-0.05	0.02	3.70E-03
rs11928433	3	171046144	LRRC31	T	0.73	0.05	0.02	3.81E-03
rs10049456	3	171046217	LRRC31	T	0.61	0.04	0.01	3.16E-03
rs13074500	3	171048265	LRRC31	T	0.72	0.05	0.02	3.87E-03
rs9290375	3	171048784	LRRC31	A	0.62	0.04	0.02	6.05E-03
rs11717389	3	171048941	LRRC31	T	0.72	0.05	0.02	3.94E-03
rs12485940	3	171049935	LRRC31	A	0.73	0.05	0.02	3.97E-03
rs16847897	3	171050810	LRRC31	A	0.70	-0.04	0.02	1.21E-02
rs4955676	3	171051186	LRRC31	C	0.30	0.04	0.02	1.21E-02
rs4955677	3	171051204	LRRC31	T	0.70	0.04	0.02	1.20E-02
rs6764267	3	171051364	LRRC31	C	0.59	0.04	0.01	5.82E-03

Table S5. SNPs in regions previously reported

SNP	Chr	Position	Closest gene	Coded allele	Coded allele frequency	β	SE	<i>P</i>
rs7514514	1	31180643	PUM1	T	0.28	0.00	0.02	0.86
rs12406355	1	31190045	PUM1	T	0.61	0.01	0.01	0.73
rs238102	1	227549771	C1orf96	A	0.34	0.01	0.02	0.37
rs238099	1	227575528	C1orf96	T	0.42	-0.01	0.01	0.71
rs7549589	1	227586550	C1orf96	A	0.60	-0.02	0.02	0.17
rs3102458	1	242606491	C1orf100	A	0.77	0.00	0.02	0.92
rs3123710	1	242611441	C1orf100	A	0.68	0.00	0.02	0.91
rs3003211	1	242679607	ADSS	T	0.72	0.01	0.02	0.71
rs1376749	2	143683862	ARHGAP15	A	0.13	-0.03	0.02	0.10
rs12993643	2	143749432	ARHGAP15	A	0.32	-0.04	0.02	0.02
rs4662198	2	143764197	ARHGAP15	T	0.23	-0.01	0.02	0.43
rs1036533	2	201105969	SGOL2	A	0.08	0.02	0.03	0.58
rs10497853	2	201183402	AOX1	A	0.92	-0.01	0.03	0.66
rs3774601	3	53797933	CACNA1D	A	0.38	0.01	0.02	0.57
rs3774605	3	53805807	CACNA1D	A	0.37	0.01	0.02	0.49
rs3774609	3	53807943	CACNA1D	T	0.59	-0.01	0.02	0.54
rs1858740	3	38413376	XYLB	T	0.33	-0.02	0.01	0.24
rs4407366	3	38496429	ACVR2B	T	0.72	-0.01	0.01	0.56
rs7374458	3	38506215	ACVR2B	T	0.28	0.01	0.01	0.66
rs1907107	4	143449084	INPP4B	A	0.55	0.00	0.01	0.81
rs2635429	4	143463006	INPP4B	T	0.39	-0.01	0.01	0.69
rs1497393	4	143493161	INPP4B	A	0.34	0.03	0.02	0.04
rs4841067	8	8784655	MFHAS1	A	0.83	-0.01	0.02	0.80
rs11778913	8	8852300	THEX1	A	0.78	0.02	0.02	0.32
rs11249943	8	9645273	TNKS	A	0.83	0.02	0.02	0.33
rs6989782	8	9647948	TNKS	T	0.25	0.00	0.02	0.83
rs1570504	9	110094630	ACTL7B	A	0.17	0.00	0.02	0.87
rs1535619	9	110094886	ACTL7B	A	0.81	0.00	0.02	0.82
rs7028041	9	110096538	ACTL7B	A	0.17	0.00	0.02	0.82
rs9301921	13	93432990	GPC6	A	0.88	0.01	0.02	0.70
rs1415736	13	93444937	GPC6	T	0.12	-0.01	0.02	0.47
rs4898848	14	54266336	SAMD4A	T	0.69	-0.01	0.02	0.47
rs6572971	14	54280838	SAMD4A	T	0.14	-0.04	0.02	0.07
rs1957356	14	54288744	SAMD4A	T	0.18	-0.01	0.02	0.45
rs17214677	16	82008463	CDH13	A	0.91	0.02	0.02	0.48
rs11861722	16	82125547	CDH13	A	0.91	0.01	0.02	0.77
rs9934005	16	82137699	CDH13	A	0.23	0.00	0.02	0.80
rs12598842	16	82145455	CDH13	A	0.63	-0.02	0.02	0.14
rs2162440	18	33468004	BRUNOL4	A	0.23	0.02	0.02	0.24
rs7235755	18	33470259	BRUNOL4	A	0.23	0.02	0.02	0.35
rs2217127	18	33475628	BRUNOL4	T	0.32	0.03	0.02	0.04

Table S6. Demographics of the Family Heart Study replication sample

Parameter	Whites	African Americans
Number of individuals	1,593	597
Percent women	56	65
Mean age in years (range)	54 (30–93)	53 (30–83)
Mean BMI (kg/m ²)	28.8 ± 5.8	32.6 ± 7.4

Table S7. Technical details of genotyping, SNP exclusion, and SNP imputation methods

Study	FraminghamHeart Study	Family Heart Study	Cardiovascular Health Study	Bogalusa Heart Study
Array type	Affymetrix 500K and MIPS 50K combined	Illumina HumMap 550	Illumina 370CNV	Illumina Human610 and Illumina HumanCVD
Genotype calling algorithm	BRLMM	BeadStudio	BeadStudio	BeadStudio
Exclusion of SNPs used for imputation	Call rate < 97% Hardy-Weinberg Equilibrium (HWE) $P < 10^{-6}$ Mishap $P < 10^{-9}$ Mendelian errors > 100	Call rate < 98% HWE $P < 10^{-6}$	Call rate $\leq 95\%$ HWE $P < 10^{-5}$ More than two replicate errors or Mendelian inconsistencies heterozygote frequency = 0	Call rate $\leq 90\%$ visual inspection of cluster plots when call rate < 95% or cluster separation score < 0.30
Imputation method	MACH 1.0.15	MACH 1.0.15	BIMBAM10 v0.99	MACH 1.0.16
Imputation backbone (NCLBI build)	HapMap CEU release 22; build 36	HapMap CEU release 22; build 36	HapMap CEU release 22, build 36	HapMap CEU release 22; build 36
Filtering of imputed genotypes	None	HWE $P < 5 \times 10^{-5}$ minor allele frequency (MAF) < 0.01	Variance of allele dosage < 0.005	HWE p HWE $P < 5 \times 10^{-5}$ MAF < 0.01
Data handling and statistical tests	LMEKIN package in R—linear mixed-effects model incorporating familial covariance based on degree of relatedness	PLINK	R	NLME package in R—linear mixed-effects model incorporating multiple measures over time