Supplementary material

Nurses' Health Study (NHS) and Health Professional Follow-up Study (HPFS)

The NHS is a prospective cohort study of 121,700 female registered nurses who were 30–55 year old at study inception in 1976 when all of them completed a mailed questionnaire on their medical history and lifestyle. Between 1989 and1990, a blood sample was obtained from 32,826 of the study participants. The HPFS is a prospective cohort study of 51,529 U.S. male health professionals who were 40 to 75 year old at study inception in 1986. A blood sample was obtained from 18,159 of these men between 1993 and 1999. In both cohorts, information about health and disease has been collected biennially by self-administered questionnaires since inception.

Supplementary Table 1. Genetic variants for CHD considered in this study.

SNPs	Genes (chr)	Alleles	Reported OR (95% CI)	References
rs4977574	*CDKN2A/CDKN2B* (9p21)	A/G	1.29 (1.25-1.34)	Kathiresan et al.(1)
rs17465637	MIA3 (1q41)	A/C	1.14 (1.10-1.19)	Kathiresan et al.(1)
rs9818870	MRAS (3q22)	C/T	1.15 (1.11-1.19)	Erdmann et al. (2)
rs12526453	PHACTR1 (6p24)	C/G	1.12 (1.08-1.17)	Kathiresan et al.(1)
rs9982601	MRPS6-SCL5A3-KCNE2 (21q22)	C/T	1.20 (1.14-1.27)	Kathiresan et al.(1)
rs646776	CELSR2-PSRC1-SORT1 (1p21)	C/T	1.19 (1.13-1.26)	Kathiresan et al.(1)
rs6725887	WDR12 (2q33)	C/T	1.17 (1.11-1.23)	Kathiresan et al.(1)
rs2259816	HNF1A (12q24)	G/T	1.08 (1.05-1.11)	Erdmann et al. (2)
rs1746048	CXCL12 (10q11)	C/T	1.17 (1.11-1.24)	Kathiresan et al.(1)
rs1122608	LDLR (19p13)	G/T	1.15 (1.10-1.20)	Kathiresan et al.(1)
rs11206510	PCSK9 (1p32)	C/T	1.15 (1.10-1.21)	Kathiresan et al.(1)
rs2048327	SLC22A3-LPAL2-LPA (6q26-q27)	T/C	Haplotypes	Tregouet et al. (3)
rs3127599	SLC22A3-LPAL2-LPA (6q26-q27)	C/T	CCTC: 1.82 (1.57-2.12)	Tregouet et al. (3)
rs7767084	SLC22A3-LPAL2-LPA (6q26-q27)	T/C	CTTG: 1.20 (1.13-1.27)	Tregouet et al. (3)
rs10755578	SLC22A3-LPAL2-LPA (6q26-q27)	C/G		Tregouet et al. (3)

Supplementary Table 2. Allele frequency of CHD SNPs

SNPs	Alleles	Allele frequency†			
		Ref	NHS	HPFS	JHS
rs4977574	G	0.5	0.49	0.5	0.52
rs17465637	C	0.75	0.73	0.73	0.71
rs9818870	T	0.15	0.16	0.16	0.17
rs12526453	C	0.66	0.65	0.65	0.62
rs9982601	T	0.21	0.26	0.24	0.18
rs646776	T	0.71	0.79	0.77	0.77
rs6725887	C	0.14	0.16*	0.16*	0.12
rs2259816	T	0.38	0.32	0.34	0.37
rs1746048	C	0.83	0.85	0.83	0.84
rs1122608	G	0.73	0.75	0.75	0.77
rs11206510	T	0.85	0.82	0.81	0.80
rs2048327	C	0.35	0.36	0.33	0.31
rs3127599	T	0.33	0.29	0.3	0.29
rs7767084	C	0.16	0.17	0.16	0.16
rs10755578	G	0.43	0.47	0.49	0.44

*: showing significant deviation from HWE.

†: frequency of risk alleles, except for SNPs at SLC22A3-LPAL2-LPA locus for which minor minor allele freqencies are presented; Ref, reference allele frequencies in the CEU panel of HapMap.

Supplementary Table 3. Haplotype associations of SLC22A3-LPAL2-LPA locus with CHD in NHS, HPFS, and JHS

SLC22A3-LPAL2-LPA haplotypes				Odds Ratios, 95% CI		
rs2048327	rs3127599	rs7767084	rs10755578	NHS	HPFS	JHS
T	C	T	C	1.0	1.0	1.0
T	T	T	G	1.35 (1.01-1.81)	1.13 (0.81-1.58)	1.32 (0.99-1.76)
C	C	C	G	1.14 (0.86-1.53)	1.19 (0.88-1.62)	1.05 (0.79-1.40)
C	T	T	G	1.21 (0.91-1.62)	0.97 (0.69-1.37)	1.13 (0.85-1.50)
C	C	T	G	2.11 (0.90-4.94)	0.97 (0.53-1.78)	1.91 (0.87-4.17)
C	C	T	C	1.02 (0.40-2.56)	0.93 (0.34-2.56)	0.98 (0.41-2.32)
T	T	T	C	1.95 (0.99-3.81)	1.60 (0.85-3.01)	1.79 (0.92-3.51)
Test of haplotype associations				χ^2=10.8, with 6 d.f	χ^2=3.8, with 6 d.f	χ^2=9.0, with 6 d.f
				P=0.09	P=0.7	P=0.17

Supplementary Figure 1. Genetic Risk Score (GRS) Distribution: Normal distributions of the GRS in the NHS, HPFS, and JHS controls.

Supplementary Reference:

1. Kathiresan S, Voight BF, Purcell S, et al. Genome-wide association of early-onset myocardial infarction with single nucleotide polymorphisms and copy number variants. Nat Genet 2009;41:334-41.
2. Erdmann J, Grosshennig A, Braund PS, et al. New susceptibility locus for coronary artery disease on chromosome 3q22.3. Nat Genet 2009;41:280-2.
3. Tregouet DA, Konig IR, Erdmann J, et al. Genome-wide haplotype association study identifies the SLC22A3-LPAL2-LPA gene cluster as a risk locus for coronary artery disease. Nat Genet 2009;41:283-5.

Supplementary Figure 1