Supplementary Table 1. Clinical and laboratory characteristics of subjects by study and type 2 diabetes status.

	Copenhagen City Heart Study		Copenhagen General Population Study	
	No event	**Type 2 Diabetes**	**No event**	**Type 2 diabetes**
No. of subjects	9,396	789	29,179	1,236
Age (years)	58 (43-69)	64 (57-71)*	60 (50-69)	66 (59-73)*
Sex (F/M)	5,318/4,078	357/432	15,508/14,091	523/741
HbA1c (%)	5.8 (5.5-6.1)	6.9 (6.3-7.9)*	NA	NA
Total cholesterol (mmol/L)	5.9 (5.1-6.8)	6.3 (5.5-7.1)*	5.7 (5.0-6.4)	5.1 (4.3-5.9)*
LDL cholesterol (mmol/L)	3.6 (2.9-4.4)	3.8 (3.0-4.6)*	3.2 (2.6-3.9)	2.6 (1.9-3.3)*
Apolipoprotein B (mg/dL)	84 (70-100)	94 (78-109)*	110 (91-134)	110 (87-140)
HDL cholesterol (mmol/L)	1.5 (1.2-1.9)	1.2 (1.0-1.5)*	1.6 (1.3-2.0)	1.3 (1.0-1.7)*
Apolipoprotein A-I (mg/dL)	141 (123-162)	129 (114-147)*	156 (139-176)	147 (130-166)*
Triglycerides (mmol/L)	1.5 (1.0-2.1)	2.3 (1.6-3.3)*	1.5 (1.0-2.2)	2.0 (1.4-3.0)*
Body mass index (kg/m^2)	24.6 (22.3-27.5)	28.9 (26.1-32.2)*	25.7 (23.3-28.5)	29.1 (26.3-32.8)*
Lipid-lowering therapy (%)	1.1	1.7	8	43*
Hypertension (%)	50	77*	62	86*
Smoking (%)	47	45	24	24
Physical inactivity (%)	63	72*	53	66*

Values are median (interquartile range) or number (percent). Mann-Whitney U test or Pearson χ^2 test was used for continuous and categorical traits, respectively. Body mass index was measured weight (kg) divided by measured height squared (m^2). Use of lipid-lowering therapy was self-reported. The risk factors, hypertension, smoking, and physical activity were dichotomized and defined as hypertension (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg and/or use of antihypertensive therapy); smoking as current smoking; physical inactivity was the fraction of individuals with less than 2-4 hours per week of light physical activity at leisure time. No.=number; HbA1c=Hemoglobin A1c; NA=not available; LDL=low-density lipoprotein; HDL=high-density lipoprotein. Measurements of HbA1c were available on 5,661 individuals in the Copenhagen City Heart Study. *P<0.0001

Supplementary Table 2. Promoter and nonsynonymous variants in the *ABCA1* and *ABCG1* genes identified in the Copenhagen City Heart Study (CCHS) and in the CEU 1000 Genomes Project.

Gene region	Nucleotide substitution*	MAF (%) in CCHS (no. of alleles=20,370)	MAF (%) in CEU 1000 Genomes Project (no. of alleles=116-226)	Amino acid residue	Reference SNP (rs) number
ABCA1					
Promoter	g.-413C>G	31.3	43.3	-	rs2740483
Promoter	g.-354A>C	Not identified	No frequency data	-	rs184242372
Promoter	g.-328C>T	34.1	32.7	-	rs1800977
5'UTR	g.-279G>C	4.1	3.3	-	rs111292742
Exon 3	c.103A>G	Not identified	0.03†	I35V	rs138992952
Exon 4	c.254C>T	Not identified	0.07†	P85L	rs145183203
Exon 7	c.551T>G	Not identified	0.01†	L184W	rs141420090
Exon 7	c.634T>A	Not identified	0.01†	S212T	rs115216814
Exon 7	c.656G>A	26.0	20.8	R219K	rs2230806
Exon 11	c.1196T>C	0.2	0.9	V399A	rs9282543
Exon 12	c.1441G>T	Not identified	No frequency data	V481L	rs183293176
Exon 15	c.2020A>C	Not identified	No frequency data	M674L	rs145105484
Exon 15	c.2089G>A	Not identified	0.01†	A697T	rs114620717
Exon 16	c.2170G>A	Not identified	No frequency data	V724M	rs138271089
Exon 16	c.2311G>A	3.0	1.3	V771M	rs2066718
Exon 16	c.2320A>C	0.2	0.3†	T774P	rs35819696
Exon 16	c.2328G>C	0.2	0.3†	K776N	rs138880920
Exon 17	c.2473G>A	6.0	8.5	V825I	rs2066715
Exon 18	c.2602G>A	Not identified	0.01†	E868K	rs35207495
Exon 18	c.2649A>G	12.0	13.3	I883M	rs2066714
Exon 19	c.2660G>T	Not identified	0.01†	C887F	rs187652566
Exon 22	c.3121C>G	Not identified	No frequency data	L1041V	rs192935024
Exon 24	c.3515A>G	Not identified	0.01†	E1172G	rs142877738

Exon 24	c.3516G>C	3.0	3.3	E1172D	rs33918808
Exon 25	c.3542C>T	Not identified	0.2†	F1181A	rs76881554
Exon 25	c.3544G>A	Not identified	0.1†	A1182T	rs143180998
Exon 28	c.4030C>T	Not identified	No frequency data	R1344W	rs193087674
Exon 30	c.4219G>A	Not identified	No frequency data	A1407T	rs189206655
Exon 35	c.4760G>A	24.0	19.9	R1587K	rs2230808
Exon 37	c.5020G>A	Not identified	0.04†	V1674I	rs138422574
Exon 40	c.5398A>C	0.1	0.1†	N1800H	rs146292819
Exon 43	c.5774G>A	Not identified	0.3†	R1925Q	rs142688906
Exon 50	c.6729C>A	Not identified	0.01†	D2243E	rs34879708
ABCG1					
Promoter	g.-1091G>A	0.2	No frequency data	-	rs146451474
Promoter	g.-1082C>T	0.6	No frequency data	-	rs140837853
Promoter	g.-1054G>T	Not identified	No frequency data	-	rs188048293
Promoter	g.-841T>C	27.7	22.5	-	rs564010
Promoter	g.-785G>T	Not identified	No frequency data	-	rs144594264
Promoter	g.-768G>A	25.8	23.3	-	rs2234714
Promoter	g.-686G>A	0.1	Not identified	-	New
Promoter	g.-638G>T	Not identified	No frequency data	-	rs192673417
Promoter	g.-576C>T	Not identified	No frequency data	-	rs185003565
Promoter	g.-530A>G	6.7	3.1	-	rs2234715
Promoter	g.-491G>T	Not identified	No frequency data		rs188964954
Promoter	g.-438T>G	0.03	No frequency data	-	rs181652186

Promoter	g.-376C>T	0.2	0.2‡	-	rs72542412
Promoter	g.-367G>A	14.3	9.2	-	rs57137919
Promoter	g.-335G>T	Not identified	No frequency data	-	rs184756729
Promoter	g.-311T>A	0.4	No frequency data	-	rs138515663
Promoter	g.-269G>A	0.07	Not identified	-	New
Promoter	g.-224C>T	0.06	0.2‡	-	rs72542414
Promoter	g.-217C>A	4.5	2.6‡	-	rs72542415
Exon 2	c.38G>A	Not identified	0.1†	S13N	rs148797794
Exon 6	c.640T>G	Not identified	No frequency data	S214A	rs139214949
Exon 7	c.775G>A	Not identified	No frequency data	A259T	rs143199611
Exon 9	c.1003G>A	Not identified	No frequency data	R335Q	rs148226451
Exon 10	c.1208C>T	Not identified	No frequency data	T299M	rs139448062
Exon 15	c.1889C>T	0.02	Not identified	S630L	New

*Nucleotide 1 denotes A in the startcodon ATG in exon 2 of *ABCA1*, corresponding to base position 24,568 in reference sequence NG_007981.1, and in exon 1 of *ABCG1*, corresponding to base position 53,133 in reference sequence AP001746. When minor allele frequencies were not available in the CEU 1000 Genomes Project (n=116-226 chromosomes), data were derived from †population cohorts participating in the National Heart, Lung and Blood Institute Exome Sequencing Project (NHLBI-ESP, https://esp.gs.washington.edu/drupal, n=4,548-4,552 chromosomes), or from ‡Pharmacogenetics of Membrane Transporters (PHARMGKB_PMT, http://www.pharmgkb.org, n=502 chromosomes). CCHS= the Copenhagen City Heart Study; CEU=Utah residents with ancestry from northern and western Europe; MAF=minor allele frequency; no.=number; rs=reference SNP; UTR=untranslated region.

SUPPLEMENTARY DATA

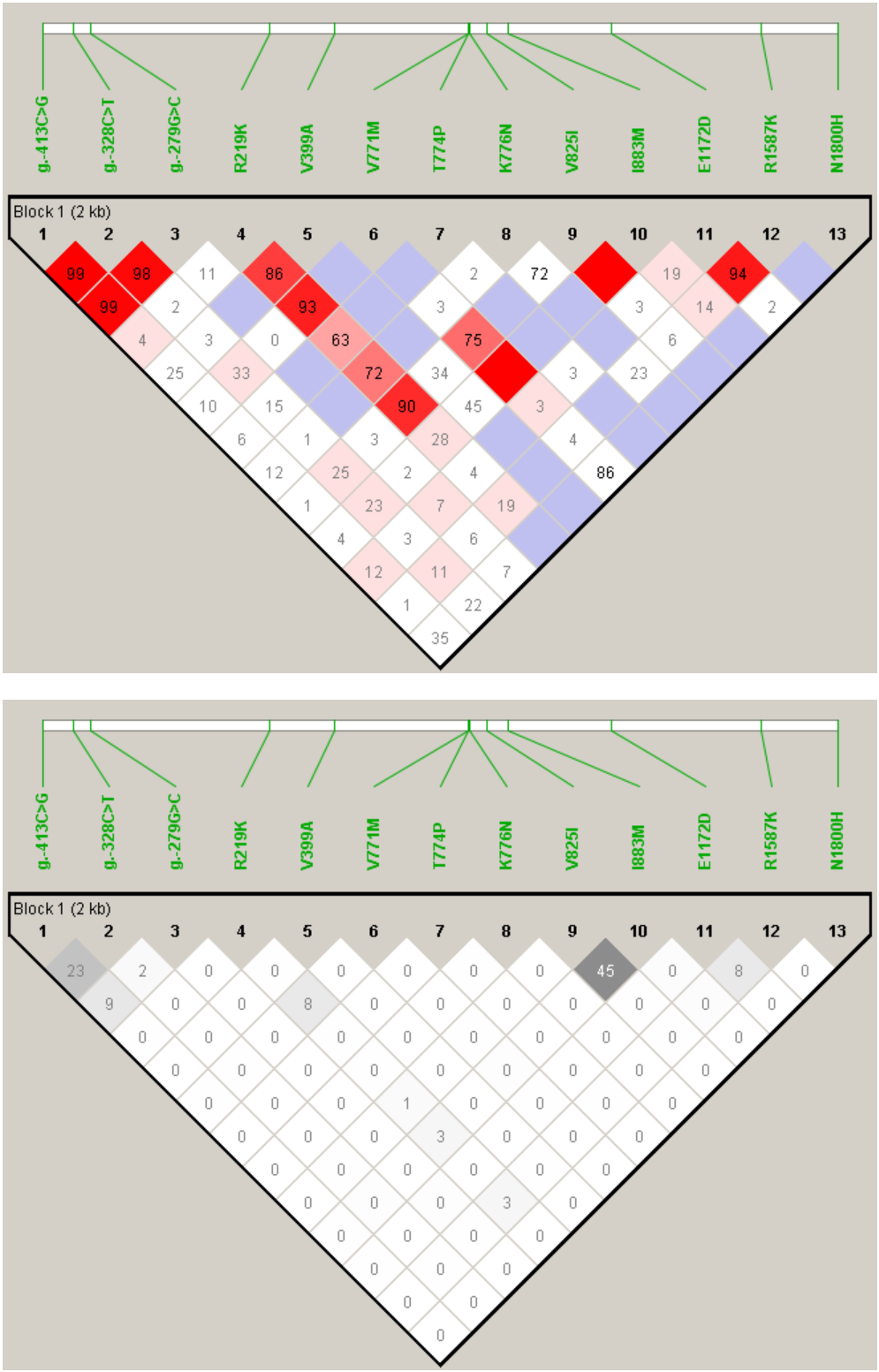
Supplementary Table 3. *ABCA1* and *ABCG1* haplotype frequencies and association with risk of type 2 diabetes in the general population.

Haplotype*	Without type 2 diabetes	With type 2 diabetes	P-value†	P-value after permutation‡
ABCA1	N=18,792§	N=1,578§		
GCGGTGAGGAGGA	0.204	0.212	0.42	0.37
CCGGTGAGAGGGA	0.182	0.191	0.36	0.89
CCGGTGAGGAGGA	0.149	0.133	0.08	0.99
GCGGTGAGGAGAA	0.047	0.049	0.70	0.99
CTGATGAGGAGGA	0.041	0.036	0.38	0.99
CTGGTGAGGAGGA	0.034	0.035	0.81	1.00
CCGGTGAGGAGAA	0.032	0.034	0.56	1.00
CCGATGAGGAGGA	0.031	0.034	0.57	1.00
CTGGTGAGGAGAA	0.024	0.027	0.37	1.00
GCGATGAGGAGGA	0.023	0.021	0.56	1.00
CTGATGAGGAGAA	0.023	0.020	0.47	1.00
GCCGTGAGGAGGA	0.020	0.016	0.24	1.00
CCGATGAGGAGAA	0.019	0.019	1.00	1.00
GCGATGAGGAGAA	0.018	0.019	0.62	1.00
GCGGTGAGAGGGA	0.011	0.012	0.68	1.00
CCGATGAGGGGGA	0.010	0.010	0.80	1.00
ABCG1	N=18,792§	N=1,578§		
GCTGGACGTC	0.722	0.737	0.19	0.27
GCCAGACATC	0.140	0.146	0.47	0.65
GCCAGGCGTC	0.067	0.055	0.06	0.76
GCCAGACGTA	0.039	0.033	0.25	0.96
GCCGGACGTC	0.014	0.013	0.94	1.00

*Haplotypes of the 13 common *ABCA1* and 10 common *ABCG1* variants in the following order (from left to right): *ABCA1* g.-413C>G, g.-328C>T, g.-279G>C, R219K (G>A), V399A (T>C), V771M (G>A), T774P (A>C), K776N (G>C), V825I (G>A), I883M (A>G), E1172D (G>C), R1587K (G>A), N1800H (A>C); *ABCG1* g.-1091G>A, G.-1082C>T, g.-841T>C, g.-768G>A, g.-686G>A, g.-530A>G, g.-376C>T, g.-367G>A, g.-311T>A, g.-217C>A. Only estimated haplotypes with frequencies above 1% were included. †P-values for haplotype frequencies in cases versus controls by Pearson χ^2 test. ‡P-values obtained after 1000 permutations using the permutation testing option of Haploview. §Number of haplotypes, i.e. twice the number of participants without type 2 diabetes and with type 2 diabetes in the study.

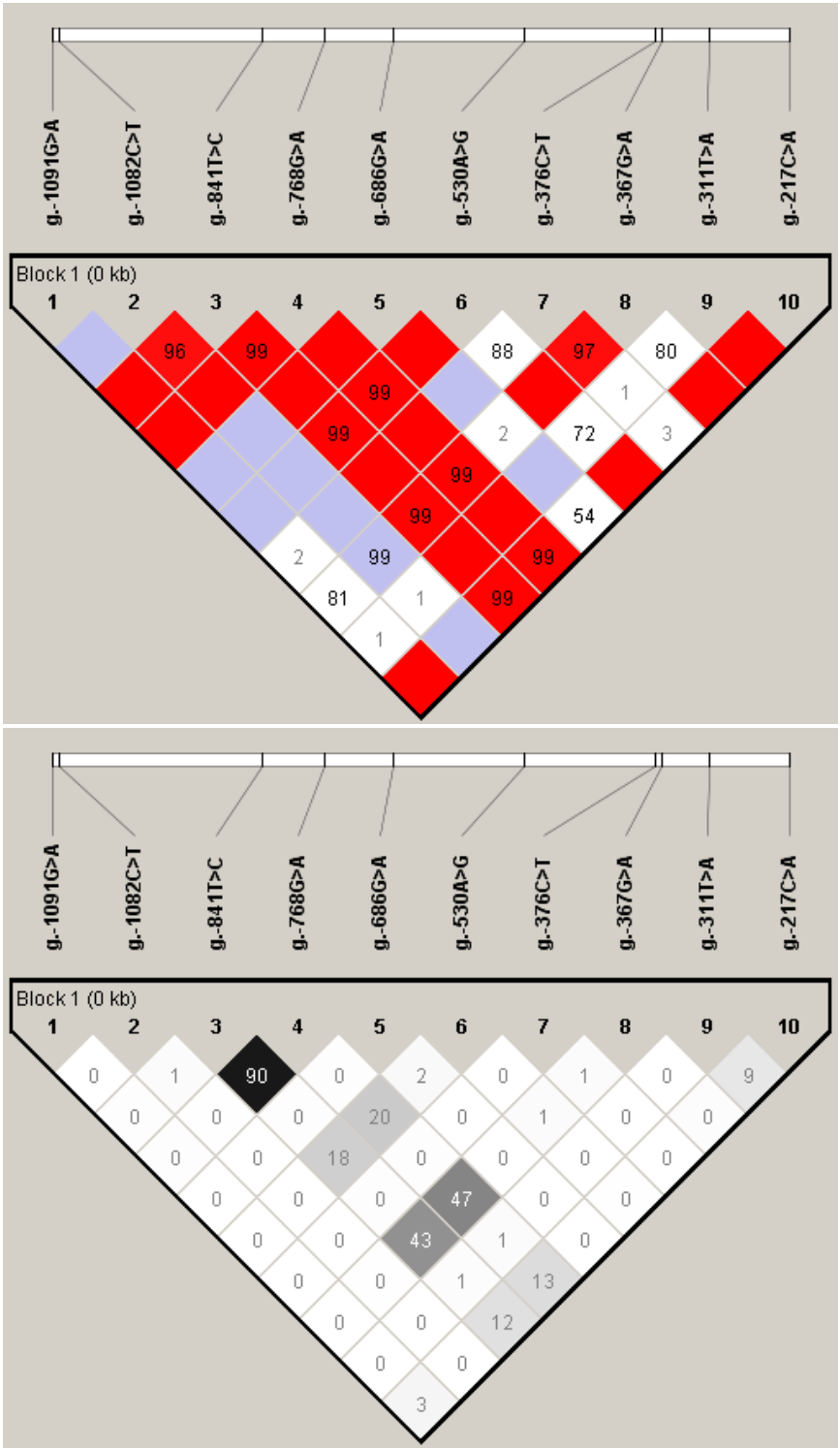
SUPPLEMENTARY DATA

Supplementary Figure 1. Pairwise linkage disequilibria between 13 variants identified after screening the *ABCA1* gene in individuals with the lowest 1% and highest 1% HDL cholesterol levels in the Copenhagen City Heart Study and subsequently genotyped in the entire study. *D'* values in upper panel and r^2 values in lower panel. Pairwise linkage disequilibrium was estimated using the software Haploview 4.2 (www.broad.mit.edu/mpg/haploview/download.php)



SUPPLEMENTARY DATA

Supplementary Figure 2. Pairwise linkage disequilibria between 10 variants identified after screening the *ABCG1* gene in individuals with the lowest 2% and highest 2% HDL cholesterol levels in the Copenhagen City Heart Study and subsequently genotyped in the entire study. *D'* values in upper panel and r^2 values in lower panel. Pairwise linkage disequilibrium was estimated using the software Haploview 4.2 (www.broad.mit.edu/mpg/haploview/download.php).



SUPPLEMENTARY DATA

Supplementary Figure 3: Risk of prediabetes as a function of *ABCA1* and *ABCG1* genotype in the Copenhagen City Heart Study. Prediabetes was defined as body mass index ≥25 kg/m^2, HbA1c ≥5.7%, physical inactivity, and hypertension. Odds ratios were adjusted for age and sex. P-values from logistic regression or logistic regression trend test. CI=confidence interval.