SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods.

In order to assess possible residual confounding in the association between the APOE/C1/C2/C4 variant and CEC when controlling for HDL-C and triglycerides that would be due to non-linear relationships between HDL-C and CEC and between triglycerides and CEC, we used non-parametric smoothing techniques which support a linear relationship for both parameters. In order to assess remaining non-linearity, we tested models with restricted cubic spline transformation for HDL-C and triglycerides. Results show that the spline transformation did not impact the significance of the APOE/C1/C2/C4 association. In order to assess whether there may be residual confounding due to effect modifiers, we tested models including interaction terms between HDL-C and other covariates, and between triglycerides and other covariates. Again, results show that the addition of the interaction terms did not impact the significance of the APOE/C1/C2/C4 association

1. **METHODS**
   Residual confounding is a bias that remains after controlling for a confounding factor in a model. For a continuous confounder, residual bias may occur if the controlled factor is measured with error, or entered in the statistical model with inappropriate coding, or when it is coded by a linear term while its real effect corresponds to a non-linear shape.

1.1. **Methodology**
   In this manuscript, the CEC (J774 stimulated) was transformed to normality using inverse normal transformation. The association between CEC and APOE/C1/C2/C4 variant was tested in phase1 and phase2 separately and then combined using an inverse variance meta-analysis method.

   The following two models were tested:

   Model 1
   CEC ~ SNP + Age-squared + Sex + CAD status + Statins + PC1-10 + batches
   Model 2
   CEC ~ SNP + Age-squared + Sex + CAD status + Statins + PC1-10 + batches + HDL-C + Log (TG)
   where log (TG) is the natural log-transformed TG

   To assess if there is any residual confounding in **Model 2**, we tested 4 other models. Three models including interaction between HDL and log (TG) and other covariates and one model including HDL and log (TG) splines:
   Model 3
   CEC ~ SNP + Age-squared + Sex + CAD status + Statins + PC1-10 + batches + HDL-C + Log (TG) +HDL * log (TG)
   Model 4
   CEC ~ SNP + Age-squared + Sex + CAD status + Statins + PC1-10 + batches + HDL-C + Log (TG) +HDL * log (TG) + age2*HDL +age2 * log (TG) + sex *HDL +sex *log (TG) +CAD status *HDL +CAD status *log (TG) +statin *HDL +statin *log (TG)
   Model 5
   Model 5 keeps only the significant interactions in Model 4, separately for phase 1 and phase 2.
   Phase1:
   CEC ~ SNP + Age-squared + Sex + CAD status + Statins + PC1-10 + batches + HDL-C + Log (TG) +HDL * log (TG) + age2*HDL + CAD status *HDL
   Phase2:

CEC ~ SNP + Age-squared + Sex + CAD status + Statins + PC1-10 + batches + HDL-C + Log (TG) +HDL * log (TG) + sex *HDL +statin *log (TG)

Model 6

CEC ~ SNP + Age-squared + Sex + CAD status + Statins + PC1-10 + batches + HDL-C + Log (TG) +spline (HDL) +spline (log (TG))

2. RESULTS

Table 2-1: Association between non-normalized CEC and ApoE_rs445925 variant in phase1

Model	Beta	Std Err	P-value
Model1	0.0241	0.0061	7.56E-05
Model2	0.0114	0.0047	0.0162
Model3	0.0112	0.0047	0.0184
Model4	0.0110	0.0047	0.0196
Model5	0.0104	0.0047	0.0268
Model6	0.0109	0.0047	0.0204

Table 2-2: Association between non-normalized CEC and ApoE_rs445925 in phase2

Model	Beta	Std Err	P-value
Model1	0.0265	0.0054	8.37E-07
Model2	0.0178	0.0041	1.84E-05
Model3	0.0177	0.0041	1.94E-05
Model4	0.0177	0.0041	1.89E-05
Model5	0.0176	0.0041	2.04E-05
Model6	0.0177	0.0041	1.64E-05

Table 2-3: Association between normalized CEC and ApoE_rs445925 variant in phase1

Model	Beta	Std Err	P-value
Model1	0.1776	0.0444	6.59E-05
Model2	0.0848	0.0346	0.0145
Model3	0.0829	0.0346	0.0166
Model4	0.0821	0.0345	0.0173
Model5	0.0772	0.0343	0.0246
Model6	0.0809	0.0341	0.0180

Table 2-4: Association between normalized CEC and ApoE_rs445925 variant in phase2

Model	Beta	Std Err	P-value
Model1	0.1659	0.0332	6.04E-07
Model2	0.1114	0.0255	1.28E-05
Model3	0.1108	0.0254	1.35E-05
Model4	0.1107	0.0254	1.3E-05
Model5	0.1103	0.0254	1.42E-05
Model6	0.1105	0.0252	1.18E-05

Table 2-5: Meta-analysis for the association between non-normalized CEC and ApoE_rs445925 variant

Model	Fixed effect p-value	Fixed effect BETA	Fixed effect STD	Random effect p-value	Random effect BETA	Random effect STD
Model 1	2.52E-10	0.0255	0.0040	2.52E-10	0.0255	0.0040
Model 2	1.49E-06	0.0150	0.0031	2.15E-06	0.0150	0.0032
Model 3	1.82E-06	0.0149	0.0031	4.97E-06	0.0148	0.0032
Model 4	1.92E-06	0.0148	0.0031	8.48E-06	0.0147	0.0033
Model 5	3.05E-06	0.0145	0.0031	6.08E-05	0.0144	0.0036
Model 6	1.8E-06	0.0147	0.0031	1.69E-05	0.0146	0.0034

Table 2-6: Meta-analysis testing the association between normalized CEC and ApoE_rs445925 variant

Model	Fixed effect p-value	Fixed effect BETA	Fixed effect STD	Random effect p-value	Random effect BETA	Random effect STD
Model1	1.56E-10	0.1701	0.0266	1.56E-10	0.1701	0.0266
Model2	6.66E-07	0.1020	0.0205	6.66E-07	0.1020	0.0205
Model3	8.19E-07	0.1010	0.0205	8.19E-07	0.1010	0.0205
Model4	8.28E-07	0.1007	0.0204	8.28E-07	0.1007	0.0204
Model5	1.34E-06	0.0986	0.0204	1.34E-06	0.0986	0.0204
Model6	7.92E-07	0.1000	0.0203	7.92E-07	0.1000	0.0203

Table S1. Demographics and clinical information for the participants involved in the study.

	MHI Biobank (phase 1)		MHI Biobank (phase 2)	
	Controls	Cases	Controls	Cases
N	996	1000	883	2589
Mean age, years (SD)	66.0 (10.1)	66.8 (8.9)	60.7 (10.8)	66.6 (8.4)
Male sex, % (n)	72.0 (717)	72.6 (726)	37.7 (333)	81.7 (2115)
Coronary artery disease, % (n)	0 (0)	100 (1000)	0 (0)	100 (2589)
Hypertension, % (n)	62.2 (620)	74.0 (740)	36.4 (321)	73.7 (1900)
Diabetes mellitus, % (n)	19.8 (197)	29.2 (292)	8.2 (72)	27.8 (717)
Dyslipidemia, % (n)	73.2 (729)	92.1 (921)	39.0 (343)	91.7 (2361)

All participants were recruited in the Montreal Heart Institute (MHI) Biobank and had four French-Canadian grandparents. For age, we provide means and standard deviations at recruitment. Coronary artery disease (CAD) is defined as previous diagnosis of myocardial infarction or revascularization procedures (percutaneous coronary intervention). Hypertension is defined as a previous diagnosis of hypertension, on antihypertensive therapy or with systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg. Diabetes mellitus is defined as a previous diagnosis of diabetes or treatment with antidiabetic drugs. Dyslipidemia is defined as a previous diagnosis of hypercholesterolemia or treatment with lipid-lowering drugs. This table includes all participants for whom we had cholesterol efflux capacity (CEC) measures. For the genome-wide association studies (GWAS), we analyzed participants with CEC and genetic data available: 943 controls and 953 CAD cases in phase 1; 863 controls and 2,534 CAD cases in phase 2.

Table S2. Technical variability of cholesterol efflux capacity assays assessed with QC sample (pooled normal human serum, apoB-depleted) in each assay batch (N=106).

Efflux model - Component	Intra-assay CV, median (%)	Intra-assay CV, mean (%)	Inter-assay CV, (%)
J774 - Basal	6.6	7.1	18.1
J774 - cAMP-stimulated	6.2	6.5	18.4
J774 - ABCA1-dependent	4.9	6.2	22.0
BHK-ABCA1 - Mifepristone-stimulated	6.0	6.3	22.2

Intra-assay coefficient of variation (CV) is calculated from 4 QC efflux values per batch and the median or mean %CV of all batches is presented. Percent inter-assay CV is calculated from QC efflux values from all batches.

Table S3. Proteins, and corresponding genes, found in HDL particles by proteomic analyses.[2]

Protein	Gene	Protein	Gene
IPI00021841	*APOA1*	IPI00020091	*ORM2*
IPI00021854	*APOA2*	IPI00022431	*AHSG*
IPI00304273	*APOA4*	IPI00305457	*SERPINA1*
IPI00021842	*APOE*	IPI00022895	*A1BG*
IPI00021855	*APOC1*	IPI00021885	*FGA*
IPI00021856	*APOC2*	IPI00022463	*TF*
IPI00021857	*APOC3*	IPI00296170	*HPR*
IPI00022731	*APOC4*	IPI00022432	*TTR*
IPI00177869	*APOL1*	IPI00298853	*GC*
IPI00030739	*APOM*	IPI00022229	*APOB*
IPI00299435	*APOF*	IPI00022434	*ALB*
IPI00006662	*APOD*	IPI00418163	*C4B*
IPI00298828	*APOH*	IPI00032258	*C4A*
IPI00291262	*CLU*	IPI00022395	*C9*
IPI00022331	*LCAT*	IPI00298971	*VTN*
IPI00006173	*CETP*	IPI00029863	*SERPINF2*
IPI00022733	*PLTP*	IPI00022426	*AMBP*
IPI00022368	-	IPI00218192	*ITIH4*
IPI00452748	*SAA1*	IPI00032220	*AGT*
IPI00006146	*SAA2*	IPI00006114	*SERPINF1*
IPI00019399	*SAA4*	IPI00032328	*KNG1*
IPI00218732	*PON1*	IPI00022420	*RBP4*
IPI00299778	*PON3*	IPI00337558	*PCYOX1*
IPI00164623	*C3*	IPI00022488	*HPX*

Table S4. Cholesterol efflux capacity association results stratified on coronary artery disease case-control status.

Chr:Pos_A1/A2_rsID	J774 basal CONTROLS MODEL 1			J774 basal CASES MODEL 1		
	Freq1	BETA (SE)	P-value	Freq1	BETA (SE)	P-value
2:28965430_G/C_rs75657792	0.0231	0.3453 (0.1127)	0.002191	0.0179	0.18 (0.0918)	0.04989
8:19819724_C/G_rs328	0.0962	0.1376 (0.0564)	0.01471	0.0933	0.2148 (0.0414)	2.06E-07
8:19821782_T/G_rs77069344	0.0998	0.151 (0.0557)	0.006686	0.0972	0.209 (0.0406)	2.73E-07
8:19844222_A/G_rs12678919	0.093	0.1243 (0.0572)	0.02984	0.09	0.2163 (0.042)	2.57E-07
15:58683366_A/G_rs1532085	0.3872	-0.1218 (0.0347)	0.0004426	0.384	-0.1157 (0.0247)	2.75E-06
15:58692148_G/T_rs35128881	0.2062	0.1285 (0.0421)	2.30E-03	0.2132	0.1194 (0.0293)	4.71E-05
15:58723939_G/A_rs2070895	0.2335	0.0647 (0.0393)	0.0997	0.2275	0.1616 (0.0285)	1.36E-08
16:56989590_C/T_rs247616	0.3254	0.1775 (0.0359)	7.54E-07	0.3097	0.1273 (0.0259)	8.77E-07
16:56993324_C/A_rs3764261	0.3265	0.1746 (0.0359)	1.13E-06	0.3105	0.1268 (0.0259)	9.38E-07
18:47109955_A/G_rs77960347	0.0132	0.3438 (0.1493)	0.02127	0.0145	0.3519 (0.1013)	0.0005125

Chr:Pos_A1/A2_rsID	J774 basal CONTROLS MODEL 2			J774 basal CASES MODEL 2		
	Freq1	BETA (SE)	P-value	Freq1	BETA (SE)	P-value
2:28965430_G/C_rs75657792	0.0231	0.369 (0.1127)	0.001059	0.0179	0.3595 (0.0916)	8.68E-05
8:19819724_C/G_rs328	0.0962	0.014 (0.0565)	0.8038	0.0933	0.1077 (0.0415)	0.009432
8:19821782_T/G_rs77069344	0.0998	0.0164 (0.0558)	0.7691	0.0972	0.0908 (0.0408)	0.02592
8:19844222_A/G_rs12678919	0.093	-0.0049 (0.0573)	0.9318	0.09	0.1104 (0.0421)	0.00871
15:58683366_A/G_rs1532085	0.3872	-0.0698 (0.0347)	0.04438	0.384	-0.0379 (0.0247)	0.1257
15:58692148_G/T_rs35128881	0.2062	0.1712 (0.0421)	4.66E-05	0.2132	0.0841 (0.0294)	0.004175
15:58723939_G/A_rs2070895	0.2335	-0.027 (0.0394)	0.4923	0.2275	0.0857 (0.0285)	0.002695
16:56989590_C/T_rs247616	0.3254	-0.0028 (0.0361)	0.939	0.3097	-0.0484 (0.026)	0.06266
16:56993324_C/A_rs3764261	0.3265	-0.006 (0.0361)	0.868	0.3104	-0.0476 (0.0259)	0.06636
18:47109955_A/G_rs77960347	0.0133	0.2955 (0.1493)	0.04782	0.0145	0.3188 (0.1013)	0.001649

Chr:Pos_A1/A2_rsID	J774 stim. CONTROLS MODEL 1			J774 stim. CASES MODEL 1		
	Freq1	BETA (SE)	P-value	Freq1	BETA (SE)	P-value
2:27730940_T/C_rs1260326	0.4016	-0.0624 (0.0347)	0.07174	0.3926	-0.0716 (0.0251)	0.004405
11:116648917_G/C_rs964184	0.1271	-0.1135 (0.0506)	0.02502	0.1396	-0.1152 (0.0343)	0.0007764
11:116692334_C/T_rs5104	0.1375	-0.1667 (0.0495)	0.000765	0.1373	-0.1003 (0.0349)	0.004021
16:56989590_C/T_rs247616	0.3254	0.1726 (0.0359)	1.54E-06	0.3098	0.1085 (0.0259)	2.83E-05

Chr:Pos_A1/A2_rsID	Freq1	BETA (SE)	P-value	Freq1	BETA (SE)	P-value
16:56993324_C/A_rs3764261	0.3265	0.169 (0.0359)	2.52E-06	0.3105	0.1094 (0.0259)	2.35E-05
19:45412079_C/T_rs7412	0.0845	0.1772 (0.0601)	0.003179	0.081	0.2321 (0.0436)	1.03E-07
19:45415640_G/A_rs445925	0.1151	0.1795 (0.0522)	0.0005918	0.112	0.1983 (0.0379)	1.65E-07
22:46627603_C/T_rs4253772	0.1153	0.101 (0.052)	0.05219	0.1141	0.127 (0.0387)	0.001018
		J774 stim. CONTROLS MODEL 2			**J774 stim. CASES MODEL 2**	
Chr:Pos_A1/A2_rsID	**Freq1**	**BETA (SE)**	**P-value**	**Freq1**	**BETA (SE)**	**P-value**
2:27730940_T/C_rs1260326	0.4016	-0.0699 (0.0347)	0.04373	0.3926	-0.0235 (0.0252)	0.3509
11:116648917_G/C_rs964184	0.1271	-0.0927 (0.0507)	0.06725	0.1395	-0.0386 (0.0344)	0.2611
11:116692334_C/T_rs5104	0.1375	-0.1229 (0.0496)	0.01326	0.1373	-0.0104 (0.0349)	0.7649
16:56989590_C/T_rs247616	0.3254	0.0214 (0.0361)	0.554	0.3098	-0.0454 (0.026)	0.08065
16:56993324_C/A_rs3764261	0.3265	0.0173 (0.0361)	0.6321	0.3105	-0.0436 (0.0259)	0.09299
19:45412079_C/T_rs7412	0.0845	0.1044 (0.0602)	0.0826	0.081	0.1918 (0.0437)	1.13E-05
19:45415640_G/A_rs445925	0.1151	0.1001 (0.0524)	0.05605	0.112	0.1675 (0.0379)	1.01E-05
22:46627603_C/T_rs4253772	0.1153	0.0897 (0.052)	0.0848	0.1141	0.0946 (0.0387)	0.01454
		J774 ABCA1-dep. CONTROLS MODEL 1			**J774 ABCA1-dep. CASES MODEL 1**	
Chr:Pos_A1/A2_rsID	**Freq1**	**BETA (SE)**	**P-value**	**Freq1**	**BETA (SE)**	**P-value**
2:27730940_T/C_rs1260326	0.4013	-0.1286 (0.0345)	0.0001978	0.3928	-0.056 (0.0251)	0.02585
8:126490972_A/T_rs2954029	0.4656	-0.1019 (0.0336)	0.002441	0.4477	-0.0835 (0.024)	0.0005021
11:116648917_G/C_rs964184	0.1271	-0.1988 (0.0505)	8.25E-05	0.1396	-0.2069 (0.0342)	1.41E-09
11:116692334_C/T_rs5104	0.1376	-0.1598 (0.0495)	0.001255	0.1373	-0.1305 (0.0348)	0.0001797
17:77657521_C/T_rs4889908	0.2898	-0.1469 (0.0365)	5.86E-05	0.2815	-0.0848 (0.0271)	0.001733
19:45412079_C/T_rs7412	0.0845	0.1729 (0.0601)	0.00401	0.0811	0.2414 (0.0436)	3.07E-08
19:45415640_G/A_rs445925	0.1151	0.1761 (0.0523)	0.0007521	0.112	0.2165 (0.0378)	1.04E-08
		J774 ABCA1-dep. CONTROLS MODEL 2			**J774 ABCA1-dep. CASES MODEL 2**	
Chr:Pos_A1/A2_rsID	**Freq1**	**BETA (SE)**	**P-value**	**Freq1**	**BETA (SE)**	**P-value**
2:27730940_T/C_rs1260326	0.4015	-0.0865 (0.0346)	0.01248	0.3927	-0.0092 (0.0252)	0.7159
8:126490972_A/T_rs2954029	0.4656	-0.0842 (0.0336)	0.01236	0.4477	-0.0468 (0.024)	0.0515
11:116648917_G/C_rs964184	0.1271	-0.0993 (0.0506)	0.04998	0.1396	-0.0668 (0.0343)	0.05196
11:116692334_C/T_rs5104	0.1376	-0.0899 (0.0496)	0.07013	0.1373	-0.0307 (0.0349)	0.3789
17:77657521_C/T_rs4889908	0.2897	-0.1857 (0.0364)	3.39E-07	0.2815	-0.1051 (0.027)	0.0001019
19:45412079_C/T_rs7412	0.0845	0.0976 (0.0602)	0.1049	0.081	0.1776 (0.0437)	4.80E-05
19:45415640_G/A_rs445925	0.1151	0.0866 (0.0524)	0.0982	0.112	0.1809 (0.0379)	1.82E-06
		BHK stim. CONTROLS MODEL 1			**BHK stim. CASES MODEL 1**	
Chr:Pos_A1/A2_rsID	**Freq1**	**BETA (SE)**	**P-value**	**Freq1**	**BETA (SE)**	**P-value**

Chr:Pos_A1/A2_rsID	Freq1	BETA (SE)	P-value	Freq1	BETA (SE)	P-value
11:116648917_G/C_rs964184	0.1295	-0.0948 (0.05)	0.05768	0.1396	-0.132 (0.0342)	0.0001117
11:116692334_C/T_rs5104	0.1383	-0.1801 (0.0495)	0.0002708	0.1374	-0.1493 (0.0347)	1.73E-05
16:56993324_C/A_rs3764261	0.3289	0.1538 (0.0359)	1.81E-05	0.3119	0.0941 (0.0258)	0.0002663
18:47109955_A/G_rs77960347	0.0136	0.5513 (0.1473)	0.0001817	0.0146	0.2218 (0.1004)	0.02714
19:45412079_C/T_rs7412	0.0844	0.1739 (0.0599)	0.003716	0.0827	0.269 (0.0431)	4.55E-10
19:45426792_G/A_rs141622900	0.0587	0.2387 (0.0722)	0.0009406	0.0584	0.3058 (0.0509)	1.85E-09
20:44554015_T/C_rs6065906	0.221	-0.0581 (0.0408)	0.1541	0.2128	-0.0744 (0.0295)	0.01173
20:44570192_C/T_rs6073966	0.1986	-0.0567 (0.0419)	0.1762	0.1951	-0.0788 (0.0304)	0.009457
	BHK stim. CONTROLS MODEL 2			BHK stim. CASES MODEL 2		
Chr:Pos_A1/A2_rsID	Freq1	BETA (SE)	P-value	Freq1	BETA (SE)	P-value
11:116648917_G/C_rs964184	0.1295	-0.0403 (0.05)	0.4198	0.1396	-0.0503 (0.0342)	0.1422
11:116692334_C/T_rs5104	0.1383	-0.141 (0.0495)	0.004423	0.1374	-0.0749 (0.0348)	0.03141
16:56993324_C/A_rs3764261	0.3288	0.0023 (0.0361)	0.9487	0.3119	-0.0399 (0.0258)	0.1222
18:47109955_A/G_rs77960347	0.0136	0.5381 (0.1472)	0.0002578	0.0146	0.0991 (0.1005)	0.3241
19:45412079_C/T_rs7412	0.0844	0.0941 (0.06)	0.1169	0.0827	0.2155 (0.0432)	6.26E-07
19:45426792_G/A_rs141622900	0.0587	0.1435 (0.0723)	0.04729	0.0584	0.2768 (0.0509)	5.49E-08
20:44554015_T/C_rs6065906	0.221	-0.012 (0.0408)	0.7686	0.2128	-0.1284 (0.0295)	1.33E-05
20:44570192_C/T_rs6073966	0.1986	-0.0268 (0.042)	0.5232	0.1951	-0.1291 (0.0303)	2.07E-05

Chromosome and position are on build hg19 of the human genome. Allele frequency (Freq1) and the direction of the effect (BETA) are for allele A2. Statistical models 1 and 2 are defined in the **Methods** section. For these analyses, there were maxima of 1,752 controls and 3,433 cases.

Table S5. Association results between variants associated with cholesterol efflux capacity and HDL-cholesterol levels in 5,168 French Canadians from the MHI Biobank.

Chr:Pos_A1/A2_rsID	Freq1	Effect	StdErr	P-value
2:27730940_T/C_rs1260326	0.3957	0.0014	0.0204	0.9441
2:28965430_G/C_rs75657792	0.0195	0.0497	0.0712	0.4851
8:19819724_C/G_rs328	0.0942	0.2378	0.0333	9.08E-13
8:19821782_T/G_rs77069344	0.098	0.245	0.0328	7.36E-14
8:19844222_A/G_rs12678919	0.091	0.2339	0.0338	4.45E-12
8:126490972_A/T_rs2954029	0.4539	0.064	0.0195	0.001059
11:116648917_G/C_rs964184	0.1352	0.0947	0.0284	0.0008485
11:116692334_C/T_rs5104	0.1372	-0.0077	0.0286	0.7886
15:58683366_A/G_rs1532085	0.3853	-0.1222	0.0201	1.19E-09
15:58692148_G/T_rs35128881	0.2108	0.0589	0.0241	0.01457
15:58723939_G/A_rs2070895	0.2296	0.1309	0.023	1.35E-08
16:56989590_C/T_rs247616	0.315	0.2145	0.0209	8.97E-25
16:56993324_C/A_rs3764261	0.3159	0.2128	0.0209	1.90E-24
17:77657521_C/T_rs4889908	0.2843	-0.0034	0.0218	0.8767
18:47109955_A/G_rs77960347	0.014	0.2042	0.0839	0.01493
19:45412079_C/T_rs7412	0.0821	0.0082	0.0354	0.8167
19:45415640_G/A_rs445925	0.113	0.0186	0.0308	0.5447
19:45426792_G/A_rs141622900	0.0578	-0.0222	0.042	0.5977
20:44554015_T/C_rs6065906	0.2149	-0.0278	0.024	0.2466
20:44570192_C/T_rs6073966	0.1955	-0.0276	0.0247	0.2645
22:46627603_C/T_rs4253772	0.1144	0.0313	0.0311	0.3136

Only variants highlighted in **Tables 1-3** of the main article are presented. HDL-C levels were inverse normal-transformed after correction for sex, age-squared, coronary artery disease status, technical batches, statin treatment, and the first ten principal components. We applied an additive genetic model. Chromosome and position are on build hg19 of the human genome. Allele frequency (Freq1) and the direction of the effect are for allele A2.

Table S6. Association results between variants associated with cholesterol efflux capacity and triglyceride (TG) levels in 5,168 French Canadians from the MHI Biobank.

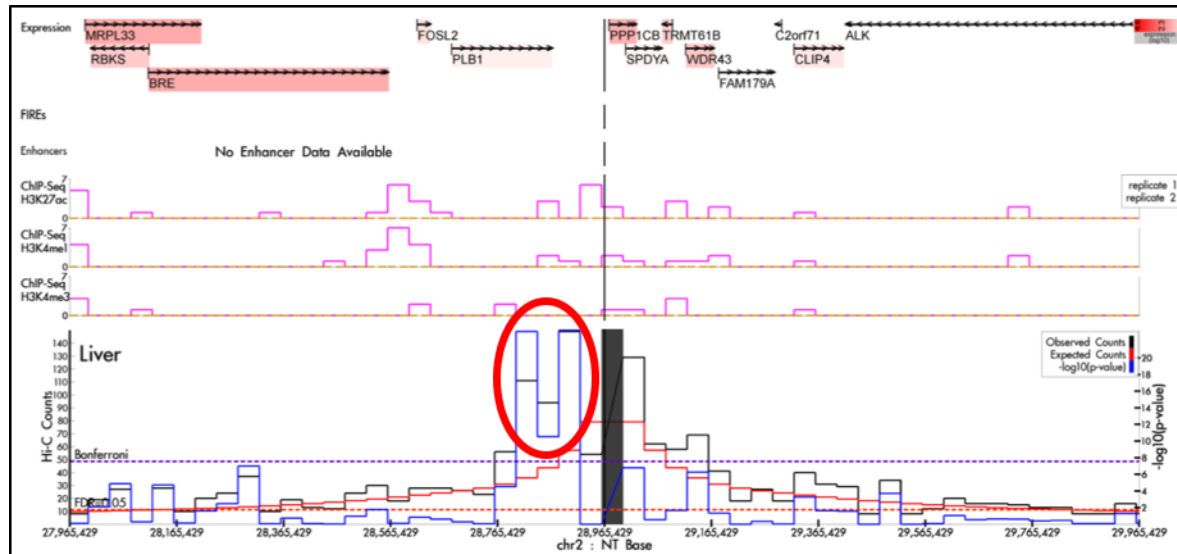| Chr:Pos_A1/A2_rsID	Freq1	Effect	StdErr	P-value
2:27730940_T/C_rs1260326	0.3958	-0.0822	0.0203	5.21E-05
2:28965430_G/C_rs75657792	0.0195	-0.1005	0.0712	0.1581
8:19819724_C/G_rs328	0.0942	-0.1824	0.0334	4.52E-08
8:19821782_T/G_rs77069344	0.098	-0.17	0.0328	2.27E-07
8:19844222_A/G_rs12678919	0.091	-0.1736	0.0339	2.96E-07
8:126490972_A/T_rs2954029	0.4539	-0.0804	0.0195	3.85E-05
11:116648917_G/C_rs964184	0.1352	-0.2795	0.0282	3.34E-23
11:116692334_C/T_rs5104	0.1372	-0.162	0.0285	1.24E-08
15:58683366_A/G_rs1532085	0.3853	0.036	0.0201	0.07377
15:58692148_G/T_rs35128881	0.2108	0.0137	0.0241	0.571
15:58723939_G/A_rs2070895	0.2296	0.0008	0.0231	0.9718
16:56989590_C/T_rs247616	0.315	0.0044	0.0211	0.8339
16:56993324_C/A_rs3764261	0.3159	0.0056	0.0211	0.7898
17:77657521_C/T_rs4889908	0.2843	0.0206	0.0218	0.344
18:47109955_A/G_rs77960347	0.014	0.0618	0.0839	0.4618
19:45412079_C/T_rs7412	0.0821	0.1721	0.0353	1.10E-06
19:45415640_G/A_rs445925	0.113	0.1401	0.0307	5.06E-06
19:45426792_G/A_rs141622900	0.0578	0.21	0.0419	5.31E-07
20:44554015_T/C_rs6065906	0.2149	0.0226	0.024	0.3469
20:44570192_C/T_rs6073966	0.1955	0.029	0.0247	0.2408
22:46627603_C/T_rs4253772	0.1144	0.0546	0.0311	0.07867

Only variants highlighted in **Tables 1-3** of the main article are presented. TG levels were inverse normal-transformed after correction for sex, age-squared, coronary artery disease status, technical batches, statin treatment, and the first ten principal components. We applied an additive genetic model. Chromosome and position are on build hg19 of the human genome. Allele frequency (Freq1) and the direction of the effect are for allele A2.

Table S7. Association results between HDL-C-associated SNPs that were reported previously to be nominally associated with cholesterol efflux capacity (CEC) in 850 individuals from GRAPHIC. [3]

SNP	Chr. (position)	A1/A2	EAF	Model 1			Model 2 (adjusted for HDL-C and TG)		
				BETA	SE	*P*	BETA	SE	*P*
rs13326165	3 (52532118)	A/G	0.2123	-0.0118	0.0241	0.6238	-0.0152	0.0244	0.532
rs13107325	4 (103188709)	T/C	0.08273	0.0763	0.0383	0.04658	0.0587	0.0388	0.13
rs6450176	5 (53298025)	A/G	0.76299	-0.0117	0.023	0.611	0	0.0234	0.9985
rs605066	6 (139829666)	T/C	0.60377	0.0122	0.02	0.5416	0.022	0.0202	0.2758
rs581080	9 (15305378)	C/G	0.61722	0.0175	0.0261	0.5023	0.0119	0.0262	0.6495
rs970548	10 (46013277)	A/C	0.26224	0.0056	0.0226	0.8036	-0.0193	0.0228	0.3968
rs1532085	15 (58683366)	A/G	0.38563	-0.0651	0.0204	0.0014	-0.0127	0.0202	0.5302
rs3764261	16 (56993324)	A/C	0.68461	-0.1301	0.0209	4.93E-10	0.0201	0.0211	0.3389
rs7255436	19 (8433196)	A/C	0.51263	-0.0257	0.0194	0.1854	-0.0015	0.0196	0.9404
rs737337	19 (11347493)	T/C	0.0705	-0.0231	0.0392	0.555	0.0083	0.0394	0.8331

Association results for CEC (J774-stimulated assay) were generated using data from 5,293 French-Canadian individuals from the Montreal Heart Institute Biobank. Coordinates are for build hg19 of the human genome. Alleles are on the positive strand. The effect allele frequency (EAF) and the direction of the effect size (beta) are for allele A2. Model 1 is adjusted for sex, age-squared, coronary artery disease status, experimental batches, statin treatment, and the first 10 principal components. Model 2 includes the same covariates as Model 1, but also HDL-cholesterol and triglyceride (TG) levels. SE, standard error.

Figure S1. Chromosome conformation (Hi-C) data from human liver obtained from the HUGIn browser[1] around SNP rs75657792, which is associated with J774-basal CEC values.

The top panel represents the gene at the locus (shades of red indicate expression levels in human liver). Histone tail marks obtained by ChIP-seq are represented in the middle panel. The Hi-C data is summarized in the bottom panel. The black rectangle corresponds to the anchor point and includes rs75657792. The black and red lines indicate the number of observed and expected Hi-C contacts between the anchor point and the corresponding regions. The line in blue corresponds to the -$\log_{10}$(P-value). We can observe two strong Hi-C signals between the anchor point and the *PLB1* gene (red oval).

Supplemental References:

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