SUPPLEMENTAL MATERIAL

Supplemental Methods

There were concerns raised[1] and subsequently addressed by the authors[2] about the correlations of the lipoprotein concentrations measured by ion mobility with levels of the apolipoproteins that characterize these particles. Briefly, because concentrations of particles are determined by direct measurement of the particles, accounting for all particle losses during the preparation and routing of samples through the ion mobility system permits calculation of accurate particle concentrations. In the original publication,[3] one aspect of particle loss was not fully accounted for, a diffusional loss that primarily affects the smallest particles (HDL). Correcting for this diffusional loss improved the correlations between the immunologically measured apolipoproteins and the particle concentrations measured by ion mobility.[2] This diffusional loss has been accounted for in all the lipoprotein fractionation data used in this study.

In addition, since the original publication we have carefully re-calibrated the lipoprotein size intervals, based on additional analyses of samples run in the ion mobility system compared to samples run using gradient gel electrophoresis (data not shown). The refined lipoprotein intervals differ somewhat from the original publication and were used in this study (Supplemental Table 1). The inter-assay variation of control material run during these analyses was similar to that originally reported.[3] The coefficient of variation for controls A and B (N=66) run during the course of the ion mobility analysis were: total HDL, 15.0% and 20.7%; peak LDL diameter, 1.1% and 0.8%; total LDL, 17.2% and 17.3%; total non-HDL, 17.3% and 15.7%, respectively.

Supplemental References

1. Otvos JD, Rudel LL, McConenell JP. Concerns regarding lipoprotein particle measurements by ion mobility analysis. *Clin Chem*. 2008:54;2086-2087.

2. Caulfield MP, Li S, Lee G, Blanche PJ, Salameh WA, Benner WH, Reitz RE, Krauss RM. Concerns regarding lipoprotein particle measurement by ion mobility analysis. In reply. *Clin Chem*. 2008;54:2088-2089.

3. Caulfield MP, Li S, Lee G, Blanche PJ, Salameh WA, Benner WH, Reitz RE, Krauss RM. Direct determination of lipoprotein particle sizes and concentrations by ion mobility analysis. *Clin Chem*. 2008;54:1307-1316.

Supplemental Table I. Distribution of lipid and lipoprotein measures among 4,594 initially healthy individuals

Trait	5th	10th	25th	50th	75th	90th	95th	Mean	Standard deviation
HDL-C	0.87	0.96	1.1	1.3	1.6	1.9	2.1	1.4	0.37
LDL-C	2.7	3.0	3.5	4.1	4.8	5.5	5.9	4.2	1.0
TG	0.61	0.68	0.86	1.2	1.6	2.2	2.7	1.3	0.64
HDL-S (7.7-10.5 nm)	1207	1490	2003	2658	3497	4533	5454	2957	1721
HDL-L 10.5-14.5 nm)	491	596	861	1380	2108	3037	3602	1634	1074
LDL-VS (18.0-20.8 nm)	52.7	59.7	74.6	96.0	125	165	205	108	55.2
LDL-S (20.8-21.4 nm)	29.3	34.1	43.7	58.7	85.1	151	223	79.7	65.8
LDL-M (21.4-22.0 nm)	43.5	52.2	68.8	95.1	153	240	293	123	80.6
LDL-L (22.0-23.3 nm)	205	246	316	414	531	651	744	435	170
IDL-S (23.3-25.0 nm)	83	104	139	194	266	357	420	216	108
IDL-L (25.0-29.6 nm)	63.9	72.2	89.4	112	141	174	198	119	44.0
VLDL-S (29.6-33.5 nm)	27.4	31.7	39.9	50.6	64.1	79.2	90.4	53.8	20.3
VLDL-M (33.5-42.4 nm)	16.2	19.5	25.5	34.3	44.4	55.5	63.0	36.3	14.9
VLDL-L (42.4-52.0 nm)	3.07	3.89	5.75	8.50	11.8	15.7	18.3	9.32	5.01

HDL-C, LDL-C, and TG are in units of mmol/L. The lipoprotein particle concentrations are in units of nmol/L.

Supplemental Table II. Multivariable-adjusted associations of SNPs to PCs.

Chr	SNP	Locus	Alleles maj/min/ MAF	*P* value		
				PCA1	PCA2	PCA3
2p24	rs693	*APOB*	A/G/0.48	$2.7x10^{-8}$	0.75	0.17
19q13	rs4420638	*APOE*	A/G/0.20	$8.7x10^{-7}$	0.03	0.94
19p13	rs6511720	*LDLR*	G/T/0.10	0.003	0.03	0.10
5q13	rs12654264	*HMGCR*	A/T/0.39	0.30	0.18	0.36
1p32	rs11206510	*PCSK9*	T/C/0.18	0.12	0.31	0.76
2p21	rs6544713	*ABCG8*	C/T/0.30	0.72	0.005	0.10
1p13	rs646776	*CELSR2/PSRC1/SORT1*	A/G/0.24	$5.7x10^{-5}$	0.65	0.28
19p13	rs10401969	*CSPG3*	T/C/0.10	0.43	0.01	0.72
20q12	rs6102059	*MAFB*	C/T/0.28	0.94	0.01	0.53
12q24	rs2650000	*TCF1*	C/A/0.38	0.29	0.33	0.70
16q13	rs1800775	*CETP*	C/A/0.49	0.02	$4.2x10^{-5}$	0.0005
15q22	rs1800588	*LIPC*	C/T/0.21	0.93	$1.0x10^{-9}$	0.69
18q21	rs2156552	*LIPG*	A/T/0.18	0.20	0.15	0.89
9q31	rs3890182	*ABCA1*	G/A/0.13	0.36	0.60	0.84
16q22	rs3785100	*LCAT*	T/C/0.14	0.57	0.53	0.10
12q24	rs2338104	*MVK*	G/C/0.47	0.53	0.86	0.60
1q42	rs4846914	*GALNT2*	A/G/0.40	0.37	$1.9x10^{-5}$	0.42
9p22	rs471364	*TTC39B*	T/C/0.11	0.83	0.18	0.22
20q13	rs1800961	*HNF4A*	C/T/0.04	0.43	0.15	0.04
19p13	rs2967605	*ANGPTL4*	C/T/0.17	0.54	0.73	0.05
1p31	rs12130333	*ANGPTL3*	C/T/0.22	0.60	0.90	0.74
2p23	rs1260326	*GCKR*	C/T/0.36	0.16	0.005	0.24
8q24	rs17321515	*TRIB1*	A/G/0.49	0.01	0.02	0.29
7q11	rs17145738	*MLXIPL*	C/T/0.13	0.04	$8.6x10^{-7}$	0.85
8p23	rs7819412	*XKR6*	A/G/0.49	0.79	0.50	0.05
11q23	rs3133506	*APOA1/A5*	T/G/0.07	0.004	$6.9x10^{-5}$	0.40
8p21	rs328	*LPL*	C/G/0.09	0.002	$7.2x10^{-6}$	0.04
20q13	rs7679	*PLTP*	T/C/0.19	0.10	0.14	0.50
11q12	rs174548	*FADS1*	C/G/0.31	0.08	0.01	0.82

P values shown are adjusted for age, gender, and diabetes status. The major allele, minor allele, and minor allele frequency (MAF) for each SNP is indicated; all modeling was performed with the major allele as the reference allele.