Supplemental Data

Mendelian Randomization Analysis Identifies

CpG Sites as Putative Mediators for Genetic

Influences on Cardiovascular Disease Risk

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SNP	Gene	Chr	BP	MAF	Other	Effect
rs266772	*ADIPOQ*	*3*	186546540	0.027	T	C
rs687621	*ABO*	*9*	136137065	0.328	G	A
rs13375019	*LEPR*	*1*	66123136	0.367	C	G
rs7549250	*IL6R*	*1*	154404336	0.416	C	T
rs169109	*ADIPOQ*	*3*	186525798	0.496	G	C
rs541041	*APOB*	*2*	21294975	0.181	G	A
rs7528419	*SORT1*	*1*	109817192	0.212	G	A
rs625145	*APOA1*	*11*	116727936	0.198	T	A
rs174544	*FADS1*	*11*	61567753	0.298	A	C
rs6749422	*ADCY3*	*2*	25150011	0.487	G	C

Table S1: Summary of methylation quantitative trait loci used as instruments in Mendelian randomization analysis SNP – Single Nucleotide Polymorphism, Chr – Chromosome, BP – Base position, MAF – minor allele frequency, Effect – effect allele coded additively for each SNP in all analyses, Other – other allele for this SNP

SNP	Gene	CpG	Trait	Sample Size	Beta	SE	P-value
rs266772	*ADIPOQ*	cg05578595	Adiponectin	4248	-0.990	0.070	5.97×10^{-44}
rs687621	*ABO*	cg21160290	Interleukin-6	4241	-0.260	0.023	9.74×10^{-30}
rs13375019	*LEPR*	cg04111102	C-reactive protein	4251	-0.220	0.022	1.14×10^{-22}
rs7549250	*IL6R*	cg02856953	Interleukin-6	4241	-0.169	0.022	1.87×10^{-14}
rs169109	*ADIPOQ*	cg05578595	Adiponectin	4248	-0.138	0.023	2.98×10^{-10}
rs541041	*APOB*	cg25035485	Apo B	4251	-0.211	0.028	4.98×10^{-14}
rs7528419	*SORT1*	cg00908766	Apo B	4251	-0.199	0.026	5.31×10^{-14}
rs625145	*APOA1*	cg04087571	Apo A1	4251	0.204	0.027	8.00×10^{-14}
rs174544	*FADS1*	cg19610905	Cholesterol	4250	-0.141	0.023	1.96×10^{-09}
rs6749422	*ADCY3*	cg01884057	Body mass index	6076	0.107	0.018	3.36×10^{-09}

Table S2: Results of linear regression analysis between genetic variants and traits adjusting for the top 10 principal components

Tables S3

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs7531118_T	cg01884057	BMI	-3.350	4.758	0.482
rs7550711_T	cg01884057	BMI	2.203	2.142	0.304
rs543874_G	cg01884057	BMI	0.668	1.394	0.632
rs13021737_A	cg01884057	BMI	0.077	0.749	0.918
rs10182181_G	cg01884057	BMI	0.106	0.048	0.028
rs13078960_G	cg01884057	BMI	-0.664	1.020	0.516
rs1516725_T	cg01884057	BMI	-1.972	2.343	0.400
rs13130484_T	cg01884057	BMI	1.152	2.586	0.656
rs2112347_G	cg01884057	BMI	0.665	1.117	0.552
rs943005_T	cg01884057	BMI	-1.696	2.152	0.431
rs2183825_C	cg01884057	BMI	-10.916	235.015	0.963
rs11030104_G	cg01884057	BMI	0.353	1.745	0.840
rs3817334_T	cg01884057	BMI	0.988	1.377	0.473
rs7138803_A	cg01884057	BMI	-3.670	5.625	0.514
rs7144011_T	cg01884057	BMI	-0.089	2.330	0.969
rs13329567_T	cg01884057	BMI	-1.057	1.076	0.326
rs3888190_A	cg01884057	BMI	1.067	2.579	0.679
rs6567160_C	cg01884057	BMI	-0.486	0.781	0.534
rs11672660_T	cg01884057	BMI	5.258	21.226	0.804

Table S3a: Mendelian randomization analysis using SNPs with evidence of association with BMI from GWAS as instrumental variables to investigate reverse causation at *ADCY3*

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs1108842_C	cg05578595	Adiponectin	-0.195	0.534	0.715
rs1597466_T	cg05578595	Adiponectin	3.774	9.589	0.694
rs2062632_C	cg05578595	Adiponectin	-1.319	1.352	0.330
rs6810075_C	cg05578595	Adiponectin	-1.234	0.876	0.159
rs7615090_G	cg05578595	Adiponectin	0.231	0.533	0.665
rs2980879_A	cg05578595	Adiponectin	-5.060	19.255	0.793
rs7955516_C	cg05578595	Adiponectin	1.255	2.705	0.643
rs601339_G	cg05578595	Adiponectin	0.943	1.059	0.373
rs7964945_A	cg05578595	Adiponectin	-0.600	1.779	0.736
rs8042532_G	cg05578595	Adiponectin	4.044	9.280	0.663
rs2927324_C	cg05578595	Adiponectin	5.878	31.560	0.852
rs12051272_T	cg05578595	Adiponectin	-1.967	2.146	0.360
rs731839_G	cg05578595	Adiponectin	-0.609	0.770	0.429

Table S3b: Mendelian randomization analysis using SNPs with evidence of association with adiponectin from GWAS as instrumental variables to investigate reverse causation at *ADIPOQ*

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs190934192_A	cg25035485	Apo B	4.202	23.047	0.855
rs629301_G	cg25035485	Apo B	14.004	42.476	0.742
rs1260326_T	cg25035485	Apo B	2.269	2.880	0.431
rs6756629_A	cg25035485	Apo B	1.178	0.676	0.082
rs144064722_G	cg25035485	Apo B	10.567	88.540	0.905
rs182695896_C	cg25035485	Apo B	-3.517	12.705	0.782
rs10056811_A	cg25035485	Apo B	-0.525	4.150	0.899
rs4722043_C	cg25035485	Apo B	0.078	1.094	0.943
rs115849089_A	cg25035485	Apo B	-9.912	64.961	0.879
rs2980875_G	cg25035485	Apo B	-0.420	0.816	0.607
rs635634_T	cg25035485	Apo B	-44.950	890.435	0.960
rs964184_G	cg25035485	Apo B	-1.430	0.936	0.127
rs142130958_A	cg25035485	Apo B	-5.004	19.134	0.794
rs150617279_A	cg25035485	Apo B	0.962	1.203	0.424
rs1081105_C	cg25035485	Apo B	-2.328	4.902	0.635
rs1883711_C	cg25035485	Apo B	0.099	0.674	0.883

Table S3c: Mendelian randomization analysis using SNPs with evidence of association with apolipoprotein B from GWAS as instrumental variables to investigate reverse causation at *APOB*

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs190934192_A	cg00908766	Apo B	-0.343	0.515	0.506
rs1260326_T	cg00908766	Apo B	5.730	16.260	0.725
rs6756629_A	cg00908766	Apo B	3.700	4.976	0.457
rs144064722_G	cg00908766	Apo B	-21.624	355.829	0.952
rs182695896_C	cg00908766	Apo B	-0.658	0.824	0.425
rs10056811_A	cg00908766	Apo B	0.111	0.737	0.881
rs4722043_C	cg00908766	Apo B	-0.057	0.802	0.944
rs115849089_A	cg00908766	Apo B	1.003	0.835	0.230
rs2980875_G	cg00908766	Apo B	0.473	0.831	0.569
rs635634_T	cg00908766	Apo B	22.436	206.885	0.914
rs964184_G	cg00908766	Apo B	-15.376	78.864	0.845
rs142130958_A	cg00908766	Apo B	2.558	4.578	0.577
rs150617279_A	cg00908766	Apo B	4.708	19.372	0.808
rs1081105_C	cg00908766	Apo B	-28.185	594.353	0.962
rs1883711_C	cg00908766	Apo B	0.157	1.056	0.882

Table S3d: Mendelian randomization analysis using SNPs with evidence of association with apolipoprotein B from GWAS as instrumental variables to investigate reverse causation at *SORT1*

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs7553007_A	cg04111102	C-reactive protein	-6.406	7.637	0.402
rs6734238_G	cg04111102	C-reactive protein	-0.473	0.935	0.613
rs7748513_G	cg04111102	C-reactive protein	2.352	3.575	0.511
rs7979473_A	cg04111102	C-reactive protein	-1.538	1.883	0.414
rs1183910_A	cg04111102	C-reactive protein	-11.801	70.720	0.868
rs2259816_T	cg04111102	C-reactive protein	-0.507	1.846	0.784
rs4420638_G	cg04111102	C-reactive protein	-14.441	88.345	0.870

Table S3e: Mendelian randomization analysis using SNPs with evidence of association with C-reactive protein from GWAS as instrumental variables to investigate reverse causation at *LEPR*

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs646776_C	cg19610905	Cholesterol	-8.414	13.767	0.541
rs558971_A	cg19610905	Cholesterol	0.260	0.700	0.710
rs9306897_T	cg19610905	Cholesterol	1.047	1.266	0.409
rs515135_T	cg19610905	Cholesterol	-2.715	2.897	0.349
rs780093_T	cg19610905	Cholesterol	2.606	8.452	0.758
rs6544713_T	cg19610905	Cholesterol	-1.870	2.846	0.511
rs6882076_T	cg19610905	Cholesterol	0.497	1.436	0.730
rs9987289_A	cg19610905	Cholesterol	0.294	5.115	0.954
rs1883025_T	cg19610905	Cholesterol	9.927	41.901	0.813
rs579459_C	cg19610905	Cholesterol	-3.494	4.691	0.457
rs1535_G	cg19610905	Cholesterol	0.197	0.077	0.011
rs10468017_T	cg19610905	Cholesterol	-1.610	2.099	0.443
rs2000999_A	cg19610905	Cholesterol	-2.258	2.097	0.282
rs2156552_A	cg19610905	Cholesterol	1.762	1.360	0.196
rs6511720_T	cg19610905	Cholesterol	-1.389	1.847	0.452
rs2228603_T	cg19610905	Cholesterol	-2.052	2.096	0.328

Table S3f: Mendelian randomization analysis using SNPs with evidence of association with cholesterol from GWAS as instrumental variables to investigate reverse causation at *FADS1*

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs144064722_G	cg04087571	Apo AI	-0.028	2.809	0.992
rs1461729_A	cg04087571	Apo AI	8.999	78.078	0.908
rs75835816_C	cg04087571	Apo AI	-2.291	3.653	0.531
rs1883025_T	cg04087571	Apo AI	15.825	54.031	0.770
rs174594_C	cg04087571	Apo AI	-2.513	2.835	0.376
rs261291_C	cg04087571	Apo AI	1.106	0.840	0.188
rs73424577_G	cg04087571	Apo AI	0.491	0.934	0.599
rs6507939_A	cg04087571	Apo AI	6.219	8.531	0.466

Table S3g: Mendelian randomization analysis using SNPs with evidence of association with apolipoprotein A1 from GWAS as instrumental variables to investigate reverse causation at *APOA1*

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs2228145_C	cg21160290	Interleukin-6	0.013	0.183	0.942

Table S3h: Mendelian randomization analysis using SNPs with evidence of association with interleukin-6 from GWAS as instrumental variables to investigate reverse causation at *ABO*

SNP	CpG site	Trait	Beta	Standard Error	P-value
rs643434_A	cg02856953	Interleukin-6	0.173	0.194	0.372

Table S3i: Mendelian randomization analysis using SNPs with evidence of association with interleukin-6 from GWAS as instrumental variables to investigate reverse causation at *IL6R*

SNP	Gene	CpG	Trait	Sample Size	Beta	SE	P-value
rs266772	*ADIPOQ*	cg05578595	Adiponectin	605	-0.901	0.210	2.01E-05
rs687621	*ABO*	cg21160290	Interleukin-6	605	-2.823	1.940	0.146
rs13375019	*LEPR*	cg04111102	C-reactive protein	605	-0.406	0.142	0.005
rs7549250	*IL6R*	cg02856953	Interleukin-6	605	3.123	3.854	0.418
rs169109	*ADIPOQ*	cg05578595	Adiponectin	605	-0.435	0.169	0.009
rs541041	*APOB*	cg25035485	Apo B	605	0.427	0.165	0.010
rs7528419	*SORT1*	cg00908766	Apo B	605	0.264	0.071	2.04E-04
rs625145	*APOA1*	cg04087571	Apo A1	605	-0.316	0.112	0.005
rs174544	*FADS1*	cg19610905	Cholesterol	605	-0.245	0.109	0.024
rs6749422	*ADCY3*	cg01884057	Body mass index	792	0.144	0.054	0.008

Table S4: Results of Mendelian randomization analysis between DNA methylation (from cord blood) and traits

SNP	Gene	CpG	Trait	Sample Size	Beta	SE	P-value
rs266772	*ADIPOQ*	cg05578595	Adiponectin	647	-0.900	0.190	2.75E-06
rs687621	*ABO*	cg21160290	Interleukin-6	647	-0.278	0.059	2.55E-06
rs13375019	*LEPR*	cg04111102	C-reactive protein	647	-0.394	0.108	2.89E-04
rs7549250	*IL6R*	cg02856953	Interleukin-6	647	0.708	0.319	0.027
rs169109	*ADIPOQ*	cg05578595	Adiponectin	647	-0.445	0.172	0.010
rs541041	*APOB*	cg25035485	Apo B	647	0.245	0.100	0.015
rs7528419	*SORT1*	cg00908766	Apo B	647	0.235	0.058	5.99E-05
rs625145	*APOA1*	cg04087571	Apo A1	647	-0.255	0.076	8.95E-04
rs174544	*FADS1*	cg19610905	Cholesterol	647	-0.248	0.089	0.005
rs6749422	*ADCY3*	cg01884057	Body mass index	846	0.099	0.05	0.043

Table S5: Results of Mendelian randomization analysis between DNA methylation (from blood at age 15.5) and traits

Tables S6

CpG effect			IL6 effect		
SNP	**snp_prob**	**snp_log10bf**	**SNP**	**snp_prob**	**snp_log10bf**
rs200533593_A	0.994	3.628	rs200533593_A	0.232	0.892
rs116552240_A	0.569	1.533	rs687621_G	0.154	0.670
rs543040_T	0.312	1.069	rs116552240_A	0.123	0.558
rs644234_G	0.298	1.039	rs687289_A	0.109	0.499
rs493246_A	0.199	0.807	rs657152_A	0.106	0.487
rs8176646_C	0.084	0.376	rs8176646_C	0.058	0.200
rs200700167_A	0.071	0.293	rs544873_A	0.057	0.191
rs676457_T	0.067	0.266	rs582094_T	0.055	0.177
rs612169_G	0.067	0.266	rs582118_G	0.054	0.167
rs491626_T	0.062	0.233	rs494242_T	0.053	0.159

Table S6a: Bivariate fine mapping results at the *ABO* locus

CpG effect			BMI effect		
SNP	**snp_prob**	**snp_log10bf**	**SNP**	**snp_prob**	**snp_log10bf**
rs6737082_C	0.886	2.595	rs6737082_C	0.067	0.561
rs59086897_A	0.815	2.346	rs6746013_G	0.062	0.526
rs10865321_C	0.521	1.740	rs10182181_G	0.062	0.520
rs10865322_G	0.479	1.667	rs10182458_G	0.060	0.512
rs6746013_G	0.175	1.030	rs6752378_A	0.058	0.493
rs58048722_C	0.099	0.742	rs6749422_G	0.053	0.452
rs2118826_A	0.092	0.709	rs59086897_A	0.050	0.422
rs1470039_G	0.090	0.701	rs10203482_C	0.035	0.268
rs4665736_C	0.088	0.690	rs10185143_C	0.033	0.239
rs1172294_G	0.081	0.650	rs58048722_C	0.031	0.213

Table S6b: Bivariate fine mapping results at the *ADCY3* locus

CpG effect			Adiponectin effect		
SNP	**snp_prob**	**snp_log10bf**	**SNP**	**snp_prob**	**snp_log10bf**
rs266772_T	0.367	0.732	rs115527175_T	0.821	1.631
rs150411458_C	0.192	0.346	rs74577862_A	0.126	0.129
rs78800820_C	0.156	0.234	rs266772_T	0.124	0.12
rs146920076_A	0.156	0.234	rs201071850_G	0.081	-0.088
rs201071850_G	0.140	0.182	rs150411458_C	0.072	-0.142
rs74577862_A	0.126	0.128	rs78800820_C	0.054	-0.275
rs76786086_T	0.123	0.115	rs146920076_A	0.054	-0.275
rs141134215_A	0.120	0.106	rs76786086_T	0.029	-0.559
rs189214085_G	0.120	0.106	rs202214354_G	0.027	-0.580
rs143257534_T	0.120	0.106	rs1011551_T	0.026	-0.608

Table S6c: Bivariate fine mapping results at the *ADIPOQ* (low freq) locus

CpG effect			Adiponectin effect		
SNP	**snp_prob**	**snp_log10bf**	**SNP**	**snp_prob**	**snp_log10bf**
rs169109_G	0.472	1.001	rs169109_G	0.421	0.911
rs67654560_A	0.374	0.826	rs34587333_A	0.306	0.695
rs34587333_A	0.294	0.669	rs266728_G	0.282	0.645
rs266728_G	0.279	0.638	rs58575091_T	0.161	0.333
rs58575091_T	0.266	0.609	rs864264_C	0.043	-0.297
rs266720_A	0.183	0.400	rs67654560_A	0.034	-0.399
rs864264_C	0.167	0.353	rs266750_C	0.027	-0.502
rs843991_T	0.161	0.333	rs266759_T	0.026	-0.528
rs16861153_A	0.111	0.145	rs201648331_T	0.026	-0.531
rs266754_T	0.085	0.018	rs843991_T	0.025	-0.541

Table S6d: Bivariate fine mapping results at the *ADIPOQ* (common) locus

CpG effect			APOAI effect		
SNP	snp_prob	snp_log10bf	SNP	snp_prob	snp_log10bf
rs688456_T	0.957	2.519	rs625145_T	0.225	0.639
rs12225230_C	0.494	1.166	rs688456_T	0.167	0.478
rs11216162_A	0.335	0.879	rs11216162_A	0.059	-0.028
rs61903423_A	0.153	0.435	rs12225230_C	0.053	-0.078
rs61905689_T	0.105	0.244	rs7932655_A	0.052	-0.082
rs7928320_T	0.077	0.095	rs34999185_A	0.051	-0.098
rs59511712_T	0.070	0.054	rs61905717_A	0.050	-0.103
rs17120244_T	0.069	0.049	rs7928320_T	0.049	-0.110
rs7946729_T	0.063	0.049	rs17120244_T	0.047	-0.127
rs7932655_A	0.059	-0.027	rs7930783_A	0.044	-0.166

Table S6e: Bivariate fine mapping results at the *APOA1* locus

CpG effect			APOB effect		
SNP	snp_prob	snp_log10bf	SNP	snp_prob	snp_log10bf
rs541041_G	0.148	1.285	rs580889_C	0.108	1.128
rs581411_G	0.127	1.211	rs201027918_C	0.100	1.091
rs562338_A	0.122	1.188	rs10692845_T	0.095	1.068
rs515135_T	0.111	1.144	rs548145_T	0.080	0.984
rs563290_G	0.104	1.111	rs541041_G	0.073	0.942
rs10692845_T	0.100	1.093	rs515135_T	0.072	0.939
rs668948_G	0.100	1.091	rs562338_A	0.067	0.901
rs580889_C	0.098	1.080	rs563290_G	0.062	0.865
rs548145_T	0.075	0.958	rs668948_G	0.060	0.855
rs1652416_A	0.016	0.250	rs581411_G	0.060	0.848

Table S6f: Bivariate fine mapping results at the *APOB* locus

CpG effect			APOB effect		
SNP	snp_prob	snp_log10bf	SNP	snp_prob	snp_log10bf
rs646776_C	0.771	1.316	rs4970836_G	0.164	0.080
rs7528419_G	0.207	0.206	rs629301_G	0.159	0.066
rs629301_G	0.020	-0.897	rs599839_G	0.123	-0.064
rs12740374_T	0.002	-1.924	rs646776_C	0.116	-0.092
rs4970836_G	0	-6.704	rs7528419_G	0.108	-0.130
rs583104_G	0	-7.790	rs583104_G	0.107	-0.132
rs1277930_G	0	-9.292	rs1277930_G	0.080	-0.272
rs599839_G	0	-9.556	rs12740374_T	0.055	-0.446
rs660240_T	0	-9.783	rs602633_T	0.033	-0.676
rs57677983_C	0	-9.783	rs57677983_C	0.029	-0.743

Table S6g: Bivariate fine mapping results at the *SORT1* locus

CpG effect			Cholesterol effect		
SNP	snp_prob	snp_log10bf	SNP	snp_prob	snp_log10bf
rs174559_A	0.986	3.274	rs174548_G	0.134	0.612
rs1535_G	0.527	1.469	rs174560_C	0.116	0.540
rs5792235_C	0.226	0.887	rs174555_C	0.106	0.494
rs174561_C	0.221	0.875	rs199977718_C	0.102	0.479
rs174555_C	0.206	0.836	rs174549_A	0.102	0.477
rs174556_T	0.197	0.812	rs174561_C	0.079	0.356
rs174544_A	0.179	0.760	rs174556_T	0.076	0.338
rs174549_A	0.154	0.682	rs28456_G	0.043	0.076
rs174568_T	0.039	0.031	rs174544_A	0.042	0.059
rs174537_T	0.038	0.014	rs174574_A	0.035	-0.020

Table S6h: Bivariate fine mapping results at the *FADS1* locus

CpG effect			IL6 effect		
SNP	**snp_prob**	**snp_log10bf**	**SNP**	**snp_prob**	**snp_log10bf**
rs10908837_G	0.187	0.607	rs12118721_T	0.130	0.420
rs4845618_G	0.164	0.538	rs10908837_G	0.124	0.397
rs6687726_A	0.163	0.535	rs6687726_A	0.113	0.349
rs12117832_A	0.150	0.490	rs12117832_A	0.079	0.179
rs7536152_A	0.141	0.459	rs4845618_G	0.076	0.161
rs12118721_T	0.136	0.440	rs10908836_C	0.056	0.020
rs12129500_T	0.126	0.403	rs4553185_C	0.047	-0.059
rs6686750_A	0.125	0.400	rs6694817_T	0.043	-0.102
rs6689393_A	0.124	0.394	rs10908838_T	0.042	-0.111
rs7526131_G	0.123	0.393	rs34926346_A	0.039	-0.143

Table S6i: Bivariate fine mapping results at the *IL6R* locus

CpG effect			IL6 effect		
SNP	**snp_prob**	**snp_log10bf**	**SNP**	**snp_prob**	**snp_log10bf**
rs6693842_C	0.754	2.232	rs6700896_T	0.122	0.887
rs4655764_T	0.583	1.890	rs200641814_TA	0.078	0.670
rs59508186_A	0.353	1.481	rs7535218_A	0.067	0.602
rs4655582_G	0.173	1.066	rs7524581_T	0.051	0.476
rs10889574_A	0.141	0.959	rs10443261_C	0.039	0.349
rs11208715_T	0.139	0.951	rs7518710_G	0.037	0.328
rs79653480_A	0.139	0.951	rs7541434_A	0.034	0.289
rs12021623_C	0.139	0.951	rs12067936_A	0.032	0.267
rs78052673_C	0.139	0.951	rs7515766_G	0.030	0.241
rs6664374_T	0.129	0.916	rs12753193_G	0.029	0.218

Table S6j: Bivariate fine mapping results at the *LEPR* locus

SNP	Gene	CpG	Pr(single var | trait)	Concordance rate	P_{JLIM}
rs266772	*ADIPOQ*	cg05578595	0.746	0.188	$<10^{-6}$
rs200533593	*ABO*	cg21160290	0.699	0.024	NA
rs6693842	*LEPR*	cg04111102	0.785	0.213	0.95
rs10908837	*IL6R*	cg02856953	0.929	0.069	NA
rs541041	*APOB*	cg25035485	0.736	0.028	1
rs169109	*ADIPOQ*	cg05578595	0.725	0.048	$<10^{-6}$
rs646776	*SORT1*	cg00908766	0.984	0.360	1
rs688456	*APOA1*	cg04087571	0.841	0.077	1
rs174559	*FADS1*	cg19610905	0.809	0.488	0.99
rs6737082	*ADCY3*	cg01884057	0.761	0.012	$<10^{-6}$

Table S7: Results of bivariate fine mapping concordance and joint likelihood mapping (JLIM) SNP – Single Nucleotide Polymorphism, Gene – likely implicated gene, CpG – 450K probe ID, Pr(single var \| trait) – the posterior probability that a single causal variant is responsible for the observed effect on complex traits (based on a maximum of 5 causal variants), Concordance rate – concordance rate generated from bivariate fine mapping results, P_{JLIM} – P value reported by the JLIM method

mQTL	Gene	CpG	CpG effect	hQTL	Histone Mark	hQTL effect	hQTL P	2SMR	P-value
rs625145	*APOA1*	cg04087571	-0.884 (0.044)	rs688456	H3K4ME3	0.913 (0.166)	5.58×10^{-7}	-1.033 (0.195)	1.13×10^{-7}
rs625145	*APOA1*	cg04087571	-0.884 (0.044)	rs688456	H3K27AC	0.758 (0.176)	4.95×10^{-5}	-0.857 (0.204)	2.54×10^{-5}
rs625145	*APOA1*	cg04087571	-0.884 (0.044)	rs688456	H3K4ME1	0.930 (0.165)	3.04×10^{-7}	-1.052 (0.194)	5.74×10^{-8}
rs10908837	*IL6R*	cg02856953	-0.303 (0.039)	rs59632925	H3K4ME1	0.620 (0.138)	2.53×10^{-5}	-2.045 (0.526)	1.01×10^{-4}
rs10908837	*IL6R*	cg02856953	-0.303 (0.039)	rs59632925	H3K27AC	0.658 (0.124)	1.14×10^{-6}	-2.172 (0.496)	1.18×10^{-5}

Table S8: Results of analysis investigating causal relationship between methylation and histone modification using Two-Sample Mendelian randomization mQTL – methylation quantitative trait loci, Gene – likely implicated gene, CpG – 450K probe ID, CpG effect – effect estimate of SNP on methylation, hQTL – histone quantitative trait loci,, hQTL effect - effect estimate of LD SNP on histone mark from Grubert et al (2015), hQTL P – P-value for hQTL effect, 2SMR effect – effect estimates from 2-Sample MR analysis, P-value – P-value for observed 2SMR effect