

Phenotyping

At the age 7 ALSPAC clinic (mean age: 7.5, range: 7.1 – 8.8), height was measured to the nearest 0.1cm using a Harpenden stadiometer (Holtain Crosswell, Dyfed, UK) and weight was measured to the nearest 0.1kg using Tanita electronic scales. Body Mass Index (**BMI**) was calculated as (weight (kg))/(height (m))². Blood Pressure was measured with a Dinamap 9301 vital monitor completed by trained staff using the appropriate cuff size. Two readings of both systolic and diastolic blood pressure (**SBP** & **DBP** respectively) were taken when the study participants were at rest and the mean of each were used as a measurement in our analysis.

Non-fasting blood samples were taken from participants who attended the age 10 clinic (mean age: 9.9, range: 8.9–11.5). Plasma lipid concentrations (total cholesterol (**TC**), triglycerides (**TG**) and high density lipoprotein cholesterol (**HDL**)) were measured by modification of the standard Lipid Research Clinics Protocol with enzymatic reagents for lipid determination (Myers et al., 2000). Low density lipoprotein cholesterol (**LDL**) concentration was subsequently calculated using the Friedwald equation (Warnick, 1990):

$$LDLc = TC - (HDLc + TG \times 0.45)$$

Very low density lipoprotein cholesterol (**VLDL**) concentration was calculated as:

$$VLDLc = TC - (HDLc + LDLc)$$

apolipoprotein A (**Apo A1**) and apolipoprotein b (**Apo B**) were measured by immunoturbidimetric assays (Roche UK, Welwyn Garden City, UK). Interleukin 6 (**IL-6**) and **adiponectin** were measured by enzyme-linked immunosorbent assay (R&D Systems, Abingdon, UK). High-sensitivity C-reactive protein (**CRP**) was measured by an automated particle-enhanced immunoturbidimetric assay (Roche UK, Welwyn Garden City, UK). **Leptin** was measured in-house by a linked immunosorbent assay which had been validated against commercial methods (Wallace et al., 2001). All assay coefficients of variation were < 5%.

Supplementary Tables 1: Mendelian Randomization analysis using SNPs with evidence of association with traits from GWAS as instrumental variables

ADCY3

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

ADIPOQ (low freq)

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

APOB

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

CELSR2

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

LEPR

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

FADS1

SNP	CpG site	Trait	Beta	Standard Error	P-value
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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

APOA1

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

ABO

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

IL6R

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

Supplementary Table 2: Results of Mendelian randomization analysis between DNA methylation (from cord blood) and traits

SNP	Gene	CpG	Trait	Sample Size	Beta	SE	P-value
rs266772	<i>ADIPOQ</i>	cg05578595	Adiponectin	605	-0.901	0.210	2.01E-05
rs687621	<i>ABO</i>	cg21160290	Interleukin-6	605	-2.823	1.940	0.146
rs13375019	<i>LEPR</i>	cg04111102	C-reactive protein	605	-0.406	0.142	0.005
rs7549250	<i>IL6R</i>	cg02856953	Interleukin-6	605	3.123	3.854	0.418
rs169109	<i>ADIPOQ</i>	cg05578595	Adiponectin	605	-0.435	0.169	0.009
rs541041	<i>APOB</i>	cg25035485	Apo B	605	0.427	0.165	0.010
rs7528419	<i>CELSR2</i>	cg00908766	Apo B	605	0.264	0.071	2.04E-04
rs625145	<i>APOA1</i>	cg04087571	Apo A1	605	-0.316	0.112	0.005
rs174544	<i>FADS1</i>	cg19610905	Cholesterol	605	-0.245	0.109	0.024
rs6749422	<i>ADCY3</i>	cg01884057	Body mass index	792	0.144	0.054	0.008

Supplementary Table 3: Results of Mendelian randomization analysis between DNA methylation (from blood at age 15.5) and traits

SNP	Gene	CpG	Trait	Sample Size	Beta	SE	P-value
rs266772	<i>ADIPOQ</i>	cg05578595	Adiponectin	647	-0.900	0.190	2.75E-06
rs687621	<i>ABO</i>	cg21160290	Interleukin-6	647	-0.278	0.059	2.55E-06
rs13375019	<i>LEPR</i>	cg04111102	C-reactive protein	647	-0.394	0.108	2.89E-04
rs7549250	<i>IL6R</i>	cg02856953	Interleukin-6	647	0.708	0.319	0.027
rs169109	<i>ADIPOQ</i>	cg05578595	Adiponectin	647	-0.445	0.172	0.010
rs541041	<i>APOB</i>	cg25035485	Apo B	647	0.245	0.100	0.015
rs7528419	<i>CELSR2</i>	cg00908766	Apo B	647	0.235	0.058	5.99E-05
rs625145	<i>APOA1</i>	cg04087571	Apo A1	647	-0.255	0.076	8.95E-04
rs174544	<i>FADS1</i>	cg19610905	Cholesterol	647	-0.248	0.089	0.005
rs6749422	<i>ADCY3</i>	cg01884057	Body mass index	846	0.099	0.05	0.043

Supplementary Tables 4: Bivariate fine mapping results

ABO

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

ADCY3

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

ADIPOQ (low freq)

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

ADIPOQ (common)

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

APOA1-AS

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

APOB

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

CELSR2

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

FADS1

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

IL6R

CpG effect	IL6 effect
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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

LEPR

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

Supplementary Table 5: Results of joint likelihood mapping (JLIM)

SNP	Gene	CpG	P_{JLIM}
rs266772	<i>ADIPOQ</i>	cg05578595	<10 ⁻⁶
rs6693842	<i>LEPR</i>	cg04111102	0.95
rs541041	<i>APOB</i>	cg25035485	1
rs169109	<i>ADIPOQ</i>	cg05578595	<10 ⁻⁶
rs646776	<i>CELSR2</i>	cg00908766	1
rs688456	<i>APOA1</i>	cg04087571	1
rs174559	<i>FADS1</i>	cg19610905	0.99
rs6737082	<i>ADCY3</i>	cg01884057	<10 ⁻⁶

SNP – Single Nucleotide Polymorphism, Gene – likely implicated gene, CpG – 450K probe ID, P_{JLIM} – P value reported by the JLIM method

Supplementary Table 6: Results of analysis investigating causal relationship between methylation and histone modification using Two-Sample Mendelian randomization

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

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

Supplementary Table 7: Results of functional analysis for lead SNPs based on effect estimates on DNA methylation

SNP	Gene	Consequence	Enhancer	Promoter*	H3K4me1	H3K4me3	H3K9ac	H3K9me3	H3K27ac
rs200533593	<i>ABO</i>	deletion variant					✓		
rs6737082	<i>ADCY3</i>	intergenic variant							
rs169109	<i>ADIPOQ</i>	non coding transcript variant						✓	
rs266772	<i>ADIPOQ</i>	intergenic variant					✓		
rs688456	<i>APOA1</i>	non coding transcript variant		✓	✓		✓		✓
rs541041	<i>APOB</i>	intergenic variant							
rs646776	<i>CELSR2</i>	regulatory region variant		✓					
rs174559	<i>FADS1</i>	NMD transcript variant							
rs10908837	<i>IL6R</i>	regulatory region variant			✓	✓			✓
rs6693842	<i>LEPR</i>	intergenic variant			✓	✓	✓		✓

- SNP – Single Nucleotide Polymorphism, Gene – likely implicated gene, Consequence – predicted variant consequence according to Ensembl VEP, ticks in the Enhancer/Promoter columns represent whether SNPs reside in gene enhancer or promoter regions respectively according to Ensembl, ticks in the H3K4me1, H3K4me3, H3K9ac, H3K9me3 and H3K27ac columns represent whether SNPs reside in histone mark peaks in adipose tissue from the Roadmap Epigenomics project, * denotes that these ticks could refer to the Promoter or its flanking regions

Supplementary Table 8: Results of functional analysis using histone mark data from adipose tissue for CpG sites

CpG	Gene	H3K4me1	H3K4me3	H3K9ac	H3K9me3	H3K27ac
cg21160290	<i>ABO</i>	✓	✓			
cg01884057	<i>ADCY3</i>	✓	✓	✓		
cg05578595	<i>ADIPOQ</i>	✓	✓	✓		
cg04087571	<i>APOA1</i>	✓				
cg25035485	<i>APOB</i>	✓	✓			
cg00908766	<i>CELSR2</i>	✓				✓
cg19610905	<i>FADS1</i>	✓	✓	✓		✓
cg02856953	<i>IL6R</i>		✓	✓		
cg04111102	<i>LEPR</i>	✓				

- CpG – 450K probe ID, Gene – likely implicated gene, ticks in the H3K4me1, H3K4me3, H3K9ac, H3K9me3 and H3K27ac columns represent whether CpG sites reside in histone mark peaks in adipose tissue from the Roadmap Epigenomics project

Supplementary Table 9: Results of functional analysis using regulatory features for CpG sites

CpG	Gene	Location	Enhancer	DHS	Promoter*	CTCF	Chromatin	TF binding
cg21160290	<i>ABO</i>	Gene body			✓			
cg01884057	<i>ADCY3</i>		✓		✓			
cg05578595	<i>ADIPOQ</i>							
cg04087571	<i>APOA1</i>	Gene body	✓		✓			
cg25035485	<i>APOB</i>	Gene body	✓		✓			
cg00908766	<i>CELSR2</i>	3' UTR	✓		✓			
cg19610905	<i>FADS1</i>	Gene body		✓	✓			
cg02856953	<i>IL6R</i>	1 st Exon	✓	✓	✓			
cg04111102	<i>LEPR</i>		✓			✓		✓

CpG – 450K probe ID, Gene – likely implicated gene, Location – whether CpG sites resides within gene region, ticks in the Enhancer & DHS (DNase hypersensitive sites) columns represent whether CpG sites reside in these regulatory regions according to 450K annotation file from Illumina, ticks in the Promoter, CTCF (CCCTC-binding factor), Chromatin (a region of open chromatin) and TF binding (transcription-factor binding site) columns represent whether CpG sites reside in regulatory regions of the genome according to data from Ensembl, * denotes that these ticks could refer to the Promoter or it's flanking regions

Supplementary Table 10: Enrichment analysis for lead mQTL & CpG sites

Annotation feature	mQTL enrichment P	CpG enrichment P
H3K4me1	0.0105	0.0009
H3K4me3	0.0066	0.0495
H3K9ac	0.0001	0.2392
H3K9me3	0.5154	N/A
H3K27ac	0.0037	0.7781
Enhancer	N/A	0.0039
Promoter	0.0103	0.0001

- N/A refers to features which none of the corresponding SNPs or CpGs were annotated for.