Table S1. Colocalization of mQTLs of CpG sites and SNPs of cardiometabolic traits in the replication study

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Trait  (Source) | CpG site | Lead SNP  (A1 allele) | Association\* | | Colocalization results | | |
| B | P | B | PSMR | PHEIDI |
| Body fat percentage  (UKBB) | cg23627948 | rs798549(C) | 0.01 | 1.30E-08 | 0.06 | 1.61E-08 | 0.3 |
| 0.15 | <2e-200 |
| DBP  (UKBB) | cg21153102 | rs11070317(C) | 0.18 | 1.70E-24 | 2.06 | 6.07E-23 | 0.3 |
| 0.09 | 5.20E-294 |
| Kidney function  (PMID: 31152163) | cg05280698 | rs73025481(A) | 0.004 | 2.30E-23 | 0.04 | 2.48E-16 | 0.02 |
| 0.08 | 3.20E-47 |
| SBP  (UKBB) | cg03186999 | rs222851(A) | -0.27 | 8.60E-19 | -11.22 | 4.30E-14 | 0.03 |
| 0.02 | 1.70E-47 |
| \* It indicates the association of the lead SNP with the trait (first row of the cell) and the CpG site (second row of the cell). | | | | | | | |

Table S2. Association of CpG sites identified in this study with environmental chemicals according to the EWAS Atlas data

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Probe ID | Trait | Correlation | Sample size |  | P-value | PMID |
| cg23627948 | Prenatal lead exposure | - | 268 |  | 7.8e-05 | 28858830 |
| cg23627948 | Organophosphate exposure | + | 580 |  | 2.2e-07 | 30248838 |
| cg21153102 | Prenatal perfluorooctane  sulfonate (PFOS) exposure | + | 266 |  | 0.00001 | 35266797 |
| cg05280698 | Vitamin B12 supplement | + | 12 |  | 5.0e-07 | 29135286 |
| cg03186999 | Air pollution (Pb) | - | 695 |  | 2.0e-10 | 34717175 |
| cg03186999 | Air pollution (Na) | - | 695 |  | 2.8e-13 | 34717175 |

Table S3. The outcome of Mendelian randomization; nature of association between the identified CpG sites, genes and cardiometabolic traits

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Predictor | Outcome | B | SE | P | NSNPs |
| cg23627948-GNA12-Obesity | | | | | |
| cg23627948 | Body fat percentage | 0.01 | 1.e-03 | 1.0e-08 | 17 |
| cg23627948 | GNA12 | -0.10 | 7.e-03 | 4.4e-47 | 7 |
| GNA12 | Body fat percentage | -0.03 | 4.e-03 | 4.5e-12 | 20 |
|  |  |  |  |  |  |
| cg21153102-GCHFR/CHP1-DBP | | | | | |
| cg21153102 | DBP | 0.18 | 2.e-02 | 1.8e-23 | 12 |
| cg21153102 | CHP1 | -0.15 | 9.e-03 | 1.7e-53 | 12 |
| cg21153102 | GCHFR | 0.05 | 8.e-03 | 1.9e-11 | 7 |
| CHP1 | DBP | -0.57 | 8.e-02 | 9.8e-13 | 6 |
| GCHFR | DBP | 0.39 | 6.e-02 | 4.1e-10 | 9 |
|  |  |  |  |  |  |
| cg05280698-HKR1-Kidney function | | | | | |
| cg05280698 | Kidney Function | 0.01 | 1.e-03 | 2.3e-09 | 3 |
| cg05280698 | HKR1 | -0.42 | 2.e-02 | 5.4e-87 | 3 |
| HKR1 | Kidney Function | -0.01 | 1.e-03 | 5.1e-11 | 17 |
|  |  |  |  |  |  |
| cg03186999-CTDNEP1-SBP | | | | | |
| cg03186999 | SBP | -0.44 | 5.e-02 | 7.2e-16 | 3 |
| cg03186999 | CTDNEP1 | 0.26 | 2.e-02 | 2.4e-46 | 3 |
| CTDNEP1 | SBP | -1.05 | 1.e-01 | 1.0e-19 | 5 |
|  |  |  |  |  |  |