

Supplementary Data 1. 32 Genome-wide significant loci associated with cfDNA motif frequencies in GWAS analysis

Note: The p-values reported in the “P” column are unadjusted p-values from GWAS, specifically a linear regression analysis, based on two-sided Wald tests.

Supplementary Data 2. 15 Study-wide significant loci associated with cfDNA motif frequencies in GWAS analysis

Note: The p-values reported in the “Wuhan pvalue”, “Natural pvalue”, and “Dutch pvalue” columns are unadjusted p-values from GWAS (linear regression), based on two-sided Wald tests.

Supplementary Data 3. 345 study-wide significant motif-locus association pairs and detailed replication performance

Note: The p-values reported in the “P” columns for “Discovery study”, “Wuhan replication study”, “Natural population replication study”, and “Dutch replication study” groups are unadjusted p-values from GWAS (linear regression), based on two-sided Wald tests. If a p-value is missing in a row, it indicates that no SNP at that locus met the replication inclusion threshold (p-values < 1e-5) in the corresponding replication study.

Supplementary Data 4. Heritability and number of significant loci for each cfDNA motif

Supplementary Data 5. P-values of heritability partition analysis

Note: All values reported in this table are unadjusted p-values from the heritability partition LD score regression (LDSC), based on two-sided Wald tests.

Supplementary Data 6. P-values for pathway-based analysis

Note: All values reported in this table are unadjusted empirical p-value from the pathway score algorithm (PASCAL).

Supplementary Data 7. Results for genetic correlation analysis

Note: The p-values reported in the “p” column are unadjusted p-values from the genetic correlation LD score regression (LDSC), based on two-sided Wald tests.

Supplementary Data 8. Results for P->M Mendelian Randomization analysis

Note: The p-values reported in the “p” column are unadjusted p-values from the Mendelian Randomization (MR) analysis, using the method specified in the “method” column and based on two-sided Wald tests.

Supplementary Data 9. Results of sensitivity tests and MRlap test for 168 causal associations in Mendelian randomization

Note: The p-values reported in the “pval_i” column are unadjusted p-values from the sensitivity test of the MR-Egger method, which tests the intercept using a two-sided Wald test to assess directional pleiotropy. The p-values reported in the “Q_pval” column are unadjusted p-values for the heterogeneity test, derived from right-tailed chi-square tests. The p-value reported in the “pval” column is the unadjusted p-value for the MRlap method.

Supplementary Data 10. Colocalization results between cfDNA motifs and pregnancy phenotypes

Supplementary Data 11. Pleiotropy analysis results of traits from GWAS catalog database