

DESCRIPTION OF ADDITIONAL SUPPLEMENTARY FILES

File Name: Supplementary Data 1.

Description: Contingency table of significant CpGs from the INMA permuted *cis*-mQTL database, and Relation to Island and UCSC RefGene annotation from the IlluminaHumanMethylationEPICanno.ilm10b4.hg19 R package. Promoter is defined as 5' UTR, TSS1500 and TSS200.

File Name: Supplementary Data 2.

Description: List of the top 10,000 CpGs with their corresponding top p-value used for the eFORGE analysis. eFORGE results from the top 10,000 mQTL-CpGs, from the permuted database. Enrichments and depletions of overlaps with tissue-specific DHS/all H3/H3k4me1 marks from the consolidated ROADMAP Epigenomics Mapping Consortium. Zscore = Z score of the test data enrichment count versus the background; Pvalue = P value of the test data enrichment count versus the background; Cell = cell for which the enrichment is calculated; Tissue = tissue of the Cell according to ENCODE or BioSamples; Datatype = Regulatory feature assessed; File = ROADMAP Epigenomics Mapping Consortium file; Probe = probes that overlap features in that file; Accession = GEO accession number of the data set; Qvalue = Q value of the test data enrichment versus the background.

File Name: Supplementary Data 3.

Description: Over-representation analysis (ORA) of the permuted database genes performed with MissMethyl R package and Gene Ontology (GO) sets. ID = gene set ID from the GO database; Ontology = ontology to which the GO term belongs, "BP" - biological process, "CC" - cellular component, "MF" - molecular function; Term = GO term; N = number of genes in the GO set; DE = number of genes that are differentially methylated; P.DE = P value of the over-representation analysis for the GO term; FDR = P value adjusted by False Discovery Rate.

Over-representation analysis (ORA) of the permuted database genes performed with MissMethyl R package and Kyoto Encyclopaedia of Genes and Genomes (KEGG) sets. ID = gene set ID from the KEGG database; N = number of genes in the KEGG set; DE = number of genes that are differentially methylated; P.DE = P value of the over-representation analysis for the KEGG term; FDR = P value adjusted by False Discovery Rate.

Gene set enrichment analysis (GSEA) of the permuted database genes performed with DOSE R package and Disease Ontology (DO) sets. ID = gene set ID from the DO database; setSize = gene set size; enrichmentScore = Enrichment score; NES = Normalized enriched score; pvalue = P value of the gene set enrichment analysis; p.adjust = P value adjusted by Benjamini-Hochberg; qvalue = Q value of the gene set enrichment analysis; rank = Rank position of the gene set in the ranked gene set list; leading_edge = Leading edge reporting tags, which indicate the percentage of genes contributing to the enrichment score; list, which indicate where in the list of the enrichment score is attained, and signal, for enrichment signal strength; core_enrichment = core enriched genes that contribute to the enrichment of GSEA analysis.

File Name: Supplementary Data 4.

Description: Syncytiotrophoblast-interacting mQTLs (STB-imQTLs) / Trophoblast-interacting mQTLs (TB-imQTLs) mapped with TensorQTL. The top SNP is highlighted in blue. SNP = corresponds to the chromosome:position ID according to hg19; Tss_distance = Distance

between the CpG and the SNP in bp; af = allele frequency of the tested allele; ma_samples = number of samples with at least one copy of the minor allele; ma_count = number of minor alleles across samples; pval_g = p-value of the linear regression between the CpG methylation levels and the genotype of the SNP; b_g = effect size of the linear regression between the CpG methylation levels and the genotype of the SNP; b_g_se = standard error of the linear regression between the CpG methylation levels and the genotype of the SNP; pval_i = p-value of the linear regression between the CpG methylation levels and the interaction term, syncytiotrophoblast / trophoblast enrichment; b_i = effect size of the linear regression between the CpG methylation levels and the interaction term (syncytiotrophoblast / trophoblast enrichment); b_i_se = standard error of the linear regression between the CpG methylation levels and the interaction term; pval_gi = p-value of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; b_gi = effect size of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; b_gi_se = standard error of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; test_emt = effective number of independent variants in the *cis*-window estimated with eigenMT; pval_gi_x_n_test = p-value of the linear regression between the CpG methylation levels and the interaction term and the genotype of the SNP, multiplied with the effective number of independent variants in the *cis*-window estimated with eigenMT.

Trophoblasts / Gestational Age-interacting mQTLs (TB-imQTLs) mapped with TensorQTL used to compute Storey pi1. SNP = corresponds to the chromosome:position ID according to hg19; Tss_distance = Distance between the CpG and the SNP in bp; af = allele frequency of the tested allele; ma_samples = number of samples with at least one copy of the minor allele; ma_count = number of minor alleles across samples; pval_g = p-value of the linear regression between the CpG methylation levels and the genotype of the SNP; b_g = effect size of the linear regression between the CpG methylation levels and the genotype of the SNP; b_g_se = standard error of the linear regression between the CpG methylation levels and the genotype of the SNP; pval_i = p-value of the linear regression between the CpG methylation levels and the interaction term (trophoblast enrichment / gestational age); b_i = effect size of the linear regression between the CpG methylation levels and the interaction term; b_i_se = standard error of the linear regression between the CpG methylation levels and the interaction term; pval_gi = p-value of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; b_gi = effect size of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; b_gi_se = standard error of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; test_emt = effective number of independent variants in the *cis*-window estimated with eigenMT; pval_gi_x_n_test = p-value of the linear regression between the CpG methylation levels and the interaction term and the genotype of the SNP, multiplied with the effective number of independent variants in the *cis*-window estimated with eigenMT.

File Name: Supplementary Data 5.

Description: SMR results from attention deficit and hyperactivity disorder (ADHD), autism spectrum disorder (ASD), bipolar disorder (BIP), major depressive disorder (MDD) and schizophrenia (SCZ), and INMA nominal *cis*-mQTLs. ProbeChr = CpG chromosome; Gene = gene annotated in the IlluminaHumanMethylationEPICanno.ilm10b4.hg19 R package; Probe_bp = CpG bp location; topSNP = CpG top SNP, most significant; topSNP_chr = top SNP chromosome;

topSNP_bp = top SNP bp location; A1 = top SNP tested allele; A2 = top SNP other allele; Freq = top SNP tested allele frequency; b_GWAS = effect size of the effect allele top SNP in original GWAS; se_GWAS = standard error of the effect allele top SNP in original GWAS; p_GWAS = p-value of the effect allele top SNP in original GWAS; b_eQTL = effect size of the mQTL in INMA nominal *cis*-mQTL database; se_eQTL = standard error of the mQTL in INMA nominal *cis*-mQTL database; p_eQTL = p-value of the mQTL in INMA nominal *cis*-mQTL database; b_SMR = effect size from SMR test; se_SMR = standard error from SMR test; p_SMR = p-value from SMR test; p_SMR_multi = p-value from multi-SNP-based SMR test; p_HEIDI = p-value from HEIDI test; nsnp HEIDI = number of SNPs used in the HEIDI test; bonf = p-value from multi-SNP-based SMR test adjusted by Bonferroni.

File Name: Supplementary Data 6.

Description: Colocalization results from bipolar disorder (BIP), major depressive disorder (MDD) and schizophrenia (SCZ), and INMA nominal *cis*-mQTLs. In green common hits (CpGs) between SMR test and colocalization, and in yellow, common hits (CpGs) between SMR test, colocalization and eQTLs. Region = original genomic region from GWAS; Lead SNP = original lead SNP from GWAS; nsnp = number of SNPs analysed; Position = base pair position of the CpG; PP.H0.abf = posterior probability of H0 being true; PP.H1.abf = posterior probability of H1 being true; PP.H2.abf = posterior probability of H2 being true; PP.H3.abf = posterior probability of H3 being true; PP.H4.abf = posterior probability of H4 being true.

File Name: Supplementary Data 7.

Description: eQTL results ($FDR < 0.05$) from SMR significant CpGs in major depressive disorder (MDD) and schizophrenia (SCZ). In yellow, common hits (CpGs) between SMR test, colocalization and eQTLs. Gene = Ensembl gene id; hgnc_symbol = HUGO Gene Nomenclature Committee (HGNC) gene symbol; chr = CpG and gene chromosome; band = CpG and gene cytogenetic band; beta = effect size of the linear regression between CpG methylation values and gene expression in placenta; t-stat = t-test statistic of the linear regression between CpG methylation values and gene expression in placenta; p-value = p-value of the linear regression between CpG methylation values and gene expression in placenta; FDR = p-value adjusted by False Discovery Rate; slope = slope value of the linear regression between CpG methylation values and gene expression in placenta; SCZ = CpG SMR significant in SCZ; MDD = CpG SMR significant in MDD.

File Name: Supplementary Data 8.

Description: Reactome results from the significant eQTL-genes from schizophrenia analysis. Entities found = number of analysed genes involved in the pathway; entities total = number of total genes involved in the pathway; entities ratio = the proportion of Reactome pathway genes represented by this pathway; entities pValue = the result of the statistical test for over-representation; entities FDR = p-value adjusted by false discovery rate; reactions found = the number of reactions in the pathway that are represented by at least one gene in the submitted data set; reactions total = the number of reactions in the pathway that contain genes; reaction ratio = the proportion of Reactome reactions represented by this pathway.

File Name: Supplementary Data 9.

Description: List of CpGs considered for the conditional analysis failing HEIDI test and with $PP3+PP4 > 0.9$.

Top SNPs conditioned INMA nominal *cis*-mQTLs. Tss-distance = distance between CpG and SNP in bp; nominal pvalue = p-value of the conditioned mQTL; beta = effect size of the conditioned mQTL.

Top SNP conditioned schizophrenia (SCZ) GWAS. A1 = tested allele; A2 = other allele; freq = frequency of the tested allele; b = effect size of the tested allele; p = p-value of the tested allele; n = sample size.

SMR results from top SNP conditioned schizophrenia (SCZ) GWAS and INMA nominal *cis*-mQTLs. ProbeChr = CpG chromosome; Gene = CpG gene annotated in IlluminaHumanMethylationEPICanno.ilm10b4.hg19 R package; Probe_bp = CpG bp location; topSNP = CpG top SNP, most significant; topSNP_chr = top SNP chromosome; topSNP_bp = top SNP bp location; A1 = top SNP tested allele; A2 = top SNP other allele; Freq = top SNP tested allele frequency; b_GWAS = effect size of the effect allele top SNP in conditional SCZ GWAS; se_GWAS = standard error of the effect allele top SNP in conditional SCZ GWAS; p_GWAS = p-value of the effect allele top SNP in conditional SCZ GWAS; b_eQTL = effect size of the mQTL in SCZ conditional INMA nominal *cis*-mQTL database; se_eQTL = standard error of the mQTL in SCZ conditional INMA nominal *cis*-mQTL database; p_eQTL = p-value of the mQTL in SCZ conditional INMA nominal *cis*-mQTL database; b_SMR = effect size from SMR test; se_SMR = standard error from SMR test; p_SMR = p-value from SMR test; p_SMR_multi = p-value from multi-SNP-based SMR test; p_HEIDI = p-value from HEIDI test; nsnp_HEIDI = number of SNPs used in the HEIDI test; bonf = p-value from multi-SNP-based SMR test adjusted by Bonferroni.

File Name: Supplementary Data 10.

Description: Syncytiotrophoblast / Trophoblast-interacting mQTLs (STB / TB-imQTLs) mapped with TensorQTL with nominal p-value $< 5 \times 10^{-8}$. SNP = corresponds to the chromosome:position ID according to hg19; Tss_distance = Distance between the CpG and the SNP in bp; af = allele frequency of the tested allele; ma_samples = number of samples with at least one copy of the minor allele; ma_count = number of minor alleles across samples; pval_g = p-value of the linear regression between the CpG methylation levels and the genotype of the SNP; b_g = effect size of the linear regression between the CpG methylation levels and the genotype of the SNP; b_g_se = standard error of the linear regression between the CpG methylation levels and the genotype of the SNP; pval_i = p-value of the linear regression between the CpG methylation levels and the interaction term (syncytiotrophoblast / trophoblast enrichment); b_i = effect size of the linear regression between the CpG methylation levels and the interaction term; b_i_se = standard error of the linear regression between the CpG methylation levels and the interaction term; pval_gi = p-value of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; b_gi = effect size of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; b_gi_se = standard error of the linear regression between the CpG methylation levels and the interaction between the interaction term and the genotype of the SNP; FDR = pval_gi adjusted by False Discovery Rate; Class = classification of the interaction mQTLs according to the beta effects from the high and low percentiles as established in Kim-Hellmuth et al.2022.

SMR results from bipolar disorder (BIP) and major depressive disorder (MDD), and positive STB / TB-interaction mQTLs (STB / TB-imQTLs). ProbeChr = CpG chromosome; Gene = CpG gene annotated in IlluminaHumanMethylationEPICanno.ilm10b4.hg19 R package; Probe_bp = CpG bp location; topSNP = CpG top SNP, most significant; topSNP_chr = top SNP chromosome;

topSNP_bp = top SNP bp location; A1 = top SNP tested allele; A2 = top SNP other allele; Freq = top SNP tested allele frequency; b_GWAS = effect size of the effect allele top SNP in original GWAS; se_GWAS = standard error of the effect allele top SNP in original GWAS; p_GWAS = p-value of the effect allele top SNP in original GWAS; b_eQTL = effect size of the imQTL; se_eQTL = standard error of the imQTL; p_eQTL = p-value of the imQTL; b_SMR = effect size from SMR test; se_SMR = standard error from SMR test; p_SMR = p-value from SMR test; p_SMR_multi = p-value from multi-SNP-based SMR test; p_HEIDI = p-value from HEIDI test; nsnp_HEIDI = number of SNPs used in the HEIDI test; bonf = p-value from multi-SNP-based SMR test adjusted by Bonferroni.

File Name: Supplementary Data 11.

Description: SMR results from bipolar disorder (BIP), major depressive disorder (MDD) and schizophrenia (SCZ), and brain / fetal brain *cis*-mQTLs. ProbeChr = CpG chromosome; Gene = CpG gene annotated in IlluminaHumanMethylationEPICanno.ilm10b4.hg19 R package; Probe_bp = CpG bp location; topSNP = CpG top SNP, most significant; topSNP_chr = top SNP chromosome; topSNP_bp = top SNP bp location; A1 = top SNP tested allele; A2 = top SNP other allele; Freq = top SNP tested allele frequency; b_GWAS = effect size of the effect allele top SNP in original GWAS; se_GWAS = standard error of the effect allele top SNP in original GWAS; p_GWAS = p-value of the effect allele top SNP in original GWAS; b_eQTL = effect size of mQTL; se_eQTL = standard error of mQTL; p_eQTL = p-value of mQTL; b_SMR = effect size from SMR test; se_SMR = standard error from SMR test; p_SMR = p-value from SMR test; p_SMR_multi = p-value from multi-SNP-based SMR test; p_HEIDI = p-value from HEIDI test; nsnp_HEIDI = number of SNPs used in the HEIDI test; bonf = p-value from multi-SNP-based SMR test adjusted by Bonferroni.