**Description of Supplementary Files**

**File Name:** **Supplementary Data 1.**

**Description:** Identified VMRs in PREDO I all CpGs located in VMRs are depicted MAD: median absolute deviation bp\_CpG: genomic position of CpG in base-pairs (hg19) Relation to Island is given according to Illumina 450k annotation: Island, N\_Shore (north shore), N\_Shelf (north shelf), S\_Shore (south shore), S\_Shelf (south shelf), OpenSea genes are given according to Illumina 450K annotation.

**File Name: Supplementary Data 2.**

**Description:** Nominal significant results for model G in pruned PREDO I dataset only the SNP with the lowest AIC for the respective tagCpG is displayed bp\_CpG: genomic position of CpG in base-pairs (hg19) bp\_SNP: genomic position of SNP in base-pairs (hg19) AIC\_SNP: AIC of specific G model num\_snps in cis window: number of SNPs in the respective cis window which were tested for in the pruned data set p\_SNP: nominal p-value of G effect p\_SNP\_corrected\_cis\_window: p-value of G effect corrected for the number of tested SNPs in the specific cis window (based on Bonferroni-correction) p\_SNP-corrected\_overall: FDR corrected p-value of G effect (corrected for the number of tested SNPs in the specific cis window and corrected for all tested tagCpGs).

**File Name:** **Supplementary Data 3.**

**Description:** Nominal significant results for model E in pruned PREDO I dataset only the E with the lowest AIC for the respective tagCpG is displayed bp\_CpG: genomic position of CpG in base-pairs (hg19) best\_E: environment giving the lowest AIC AIC\_E: AIC of specific E model p\_E: nominal p-value of E effect p\_E\_corrected\_env: p-value of E effect corrected for all tested environmental phenotypes (based on Bonferroni-correction) p\_E\_corrected\_overall: FDR-corrected p-value of E effect (corrected for all tested environmental phenotypes and corrected for all tested tagCpGs).

**File Name:** **Supplementary Data 4.**

**Description:** Nominal significant association results for model G+E in pruned PREDO I dataset only the SNP-environment combinations with the lowest AIC for the respective tagCpG are displayed bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP\_add: SNP included in G+E model bp\_SNP: genomic position of SNP in base-pairs (hg19) E\_add: environment included in G+E model AIC\_add: AIC of specific G+E model num\_snps in cis window: number of SNPs in the respective cis window which were tested for in the pruned data set p\_add: nominal p-value of G+E model (based on ANOVA of model G and model G+E) p\_add\_corrected\_combinations: p-value of G+E model corrected for all tested SNP-environment combinations in cis-window (based on Bonferroni-correction) p\_add\_corrected\_overall: FDR-corrected p-value of G+E model (corrected for all tested SNP-environment combinations in cis-window and corrected for all tested tagCpGs).

**File Name:** **Supplementary Data 5.**

**Description:** Nominal significant association results for model GxE in pruned PREDO I dataset only the SNP-environment combinations with the lowest AIC for the respective tagCpG are displayed bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP\_int: SNP included in GxE model bp\_SNP: genomic position of SNP in base-pairs (hg19) E\_int: environment included in GxE model AIC\_int: AIC of specific GxE model num\_snps in cis window: number of SNPs in the respective cis window which were tested for in the pruned data set p\_int: nominal p-value for GxE effect p\_int\_corrected\_combinations: p-value of GxE model corrected for all tested SNP-environment combinations in cis-window (based on Bonferroni-correction) p\_int\_corrected\_overall: FDR-corrected p-value of GxE model (corrected for all tested SNP-environment combinations in cis-window and corrected for all tested tagCpGs).

**File Name:** **Supplementary Data 6.**

**Description:** tagCpGs with best model G in pruned PREDO I dataset bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP: SNP included in G model bp\_SNP: genomic position of SNP in base-pairs (hg19) AIC\_SNP: AIC of specific G model p\_SNP: nominal p-value of G effect.

**File Name:** **Supplementary Data 7.**

**Description:** tagCpGs with best model G+E in pruned PREDO I dataset bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP\_add: SNP included in G+E model bp\_SNP: genomic position of SNP in base-pairs (hg19) E\_add: E included in G+E model AIC\_add: AIC of specific G+E model p\_add: nominal p-value of G+E model (based on ANOVA of model G and model G+E).

**File Name:** **Supplementary Data 8**

**Description:** tagCpGs with best model GxE in pruned PREDO I dataset bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP\_int: SNP included in GxE model bp\_SNP: genomic position of SNP in base-pairs (hg19) E\_int: E included in GxE model AIC\_int: AIC of specific GxE model p\_int: nominal p-value of GxE effect.

**File Name:** **Supplementary Data 9**

**Description:** nominal significant results for CpGs for model G using DeepSEA variants in PREDO I only the SNP with the lowest AIC for the respective tagCpG is displayed bp\_CpG: genomic position of CpG in base-pairs (hg19) bp\_SNP: genomic position of SNP in base-pairs (hg19) AIC\_SNP: AIC of specific G model num\_snps in cis window: number of deepSEA SNPs in the respective cis window which were tested for p\_SNP: nominal p-value of G effect p\_SNP\_corrected\_cis\_window: p-value of G effect corrected for the number of tested SNPs in the specific cis window (based on Bonferroni-correction) p\_SNP-corrected\_overall: FDR corrected p-value of G effect (corrected for the number of tested SNPs in the specific cis window and corrected for all tested tagCpGs).

**File Name:** **Supplementary Data 10.**

**Description:** nominal significant results for model E using DeepSEA variants in PREDO I only the E with the lowest AIC for the respective tagCpG is displayed bp\_CpG: genomic position of CpG in base-pairs (hg19) best\_E: environment giving the lowest AIC AIC\_E: AIC of specific E model p\_E: nominal p-value of E effect p\_E\_corrected\_env: p-value of E effect corrected for all tested environmental phenotypes (based on Bonferroni-correction) p\_E\_corrected\_overall: FDR-corrected p-value of E effect (corrected for all tested environmental phenotypes and corrected for all tested tagCpGs).

**File Name:** **Supplementary Data 11.**

**Description:** nominal significant results for model G+E using DeepSEA variants in PREDO I only the SNP-environment combinations with the lowest AIC for the respective tagCpG are displayed bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP\_add: SNP included in G+E model bp\_SNP: genomic position of SNP in base-pairs (hg19) E\_add: environment included in G+E model AIC\_add: AIC of specific G+E model num\_snps in cis window: number of deepSEA SNPs in the respective cis window which were tested for p\_add: nominal p-value of G+E model (based on ANOVA of model G and model G+E) p\_add\_corrected\_combinations: p-value of G+E model corrected for all tested SNP-environment combinations in cis-window (based on Bonferroni-correction) \_add\_corrected\_overall: FDR-corrected p-value of G+E model (corrected for all tested SNP-environment combinations in cis-window and corrected for all tested tagCpGs).

**File Name:** **Supplementary Data 12.**

**Description:** nominal significant results for model GxE using DeepSEA variants in PREDO I only the SNP-environment combinations with the lowest AIC for the respective tagCpG are displayed bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP\_int: SNP included in GxE model bp\_SNP: genomic position of SNP in base-pairs E\_int: environment included in GxE model (hg19) AIC\_int: AIC of specific GxE model num\_funct\_snps in cis window: number of DeepSEA SNPs in the respective cis window which were tested for p\_int: nominal p-value for GxE effect p\_int\_corrected\_combinations: p-value of GxE model corrected for all tested SNP-environment combinations in cis-window (based on Bonferroni-correction) p\_int\_corrected\_overall: FDR-corrected p-value of GxE model (corrected for all tested SNP-environment combinations in cis-window and corrected for all tested tagCpGs).

**File Name:** **Supplementary Data 13.**

**Description:** tagCpGs with best model G using DeepSEA variants in PREDO I bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP: SNP included in G model bp\_SNP: genomic position of SNP in base-pairs (hg19) AIC\_SNP: AIC of specific G model p\_SNP: nominal p-value of G effect.

**File Name:** **Supplementary Data 14.**

**Description:** tagCpGs with best model E using DeepSEA variants in PREDO I bp\_CpG: genomic position of CpG in base-pairs (hg19) E: environment included in E model AIC\_E: AIC of E model p\_E: nominal p-value of E effect.

**File Name:** **Supplementary Data 15.**

**Description:** tagCpGs with best model G+E using DeepSEA variants in PREDO I bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP\_add: SNP included in G+E model bp\_SNP: genomic position of SNP in base-pairs (hg19) E\_add: E included in G+E model AIC\_add: AIC of specific G+E model p\_add: nominal p-value of G+E model (based on ANOVA of model G and model G+E)

**File Name:** **Supplementary Data 16.**

**Description:** tagCpGs with best model GxE using DeepSEA variants in PREDO I bp\_CpG: genomic position of CpG in base-pairs (hg19) SNP\_int: SNP included in GxE model bp\_SNP: genomic position of SNP in base-pairs (hg19) E\_int: E included in GxE model AIC\_int: AIC of specific GxE model p\_int: nominal p-value of GxE effect.

**File Name:** **Supplementary Data 17.**

**Description:** top-results of meta-analysis of PREDO and MoBa for G+E model bp\_CpG: genomic position of CpG in base-pairs SNP\_add: SNP included in G+E model bp\_SNP: genomic position of SNP in base-pairs E\_add: E included in G+E model MAF\_PREDO: minor allele frequency in PREDO beta\_add\_SNP\_PREDO: effect size estimator for main G effect in PREDO p\_add\_SNP\_PREDO: nominal p-value of G effect in G+E model in PREDO beta\_add\_E\_PREDO: effect size estimator for main E effect in PREDO p\_add\_E\_PREDO: nominal p-value of E effect in G+E model in PREDO MAF\_MoBa: minor allele frequency in MoBa beta\_add\_SNP\_MoBa: effect size estimator for main G effect in MoBa p\_add\_SNP\_MoBa: nominal p-value of G effect in G+E model in MoBa beta\_add\_E\_MoBa: effect size estimator for main E effect in MoBa p\_add\_E\_MoBa: nominal p-value of E effect in G+E model in MoBa beta\_add\_SNP\_meta: effect size estimator for main G effect in meta-analysis p\_add\_SNP\_meta: nominal p-value for G effect in meta-analysis p\_add\_SNP\_meta\_FDR: FDR corrected p-value for G effect in meta-analysis across all tested SNP-E combinations beta\_add\_E\_meta: effect size estimator for main E effect in meta-analysis p\_add\_E\_meta: nominal p-value for E effect in meta-analysis p\_add\_E\_meta\_FDR: FDR corrected p-value for E effect in meta-analysis across all tested SNP-E combination.

**File Name:** **Supplementary Data 18.**

**Description:** top-results of meta-analysis of PREDO and MoBa for GxE model bp\_CpG: genomic position of CpG in base-pairs SNP\_int: SNP included in G+E model bp\_SNP: genomic position of SNP in base-pairs E\_int: E included in G+E model MAF\_PREDO: minor allele frequency in PREDO beta\_int\_PREDO: effect size estimator for GxE effect in PREDO p\_int\_PREDO: nominal p-value for GxE in PREDO MAF\_MoBa: minor allele frequency in MoBa beta\_int\_MoBa: effect size estimator for GxE effect in MoBa p\_int\_MoBa: nominal p-value for GxE in MoBa beta\_int\_meta: effect size estimator for GxEt in meta-analysis p\_int\_meta: p-value for GxE in meta-analysis p\_int\_meta\_FDR: FDR-corrected p-value for GxE in meta-analysis across all tested SNP-E combinations.