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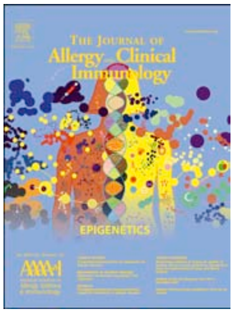


Epigenome-wide Meta-analysis of DNA Methylation and Childhood Asthma

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# Epigenome-wide Meta-analysis of DNA Methylation and Childhood Asthma

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Running Head: DNA methylation and childhood asthma

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## ABSTRACT

Background: Epigenetic mechanisms, including methylation, may contribute to childhood asthma. Identifying DNA methylation profiles in asthma may inform disease pathogenesis.

Objective: To identify differential DNA methylation in newborns and children related to childhood asthma.

Methods: Within the Pregnancy And Childhood Epigenetics (PACE) consortium, we performed epigenome-wide meta-analyses of school-age asthma in relation to CpG methylation (Illumina450K) in blood measured either in newborns, in prospective analyses, or cross-sectionally, in school-age children. We also identified differentially methylated regions (DMRs).

Results: In newborns (8 cohorts, 668 cases), 9 CpGs (and 35 regions) were differentially methylated (epigenome-wide significance, FDR<0.05) in relation to asthma development. In cross-sectional meta-analysis of asthma and methylation in children (9 cohorts, 631 cases), we identified 179 CpGs (FDR<0.05) and 36 differentially methylated regions. In replication studies of methylation in other tissues, most of the 179 CpGs discovered in blood replicated, despite smaller sample sizes, in studies of nasal respiratory epithelium or eosinophils. Pathway analyses highlighted enrichment for asthma-relevant immune processes and overlap in pathways enriched both in newborns and children. Gene expression correlated with methylation at most loci. Functional annotation supports regulatory impact on gene expression at many asthma-associated CpGs. Several implicated genes are targets for approved or experimental drugs, including *IL5RA* and *KCNH2*.

Conclusion: Novel loci differentially methylated in newborns represent potential biomarkers of risk of developing asthma by school age. Cross-sectional associations in children may reflect both risk for and effects of disease. Asthma-related differential methylation in blood in children substantially replicated in eosinophils and respiratory epithelium.

Abstract Word Count: 249

**Key Messages**: This large-scale genome-wide meta-analysis of DNA methylation and childhood asthma identified novel epigenetic variations related to asthma in newborns and children.

**Capsule Summary:**

This large-scale genome-wide meta-analysis identified variation in DNA methylation related to childhood asthma, prospectively in newborns and cross-sectionally in children; these biomarkers of asthma development and biologic effects that may shed light on disease mechanisms.

Key words: epigenetics, methylation, asthma, childhood, newborn, drug development.

Abbreviations:

CpG – C phosphate G site

OR – odds ratio

CI – confidence interval

GWAS – Genome-Wide Association Study

## INTRODUCTION

Asthma is the most common chronic disease of childhood[1], but the underlying mechanisms remain poorly understood. GWAS meta-analyses have identified many loci related to asthma[2], but these explain only a modest proportion of variation in asthma risk[3]. Increasing evidence suggests that epigenetic variation may play a role in asthma pathogenesis[4]. DNA methylation is the most studied epigenetic modification in humans. Prospective examination of methylation patterns in newborns in relation to asthma development may identify genes and mechanisms involved in the developmental origins of asthma[5].

Epigenome-wide association studies (EWAS) of DNA methylation in blood in relation to asthma (number of cases range from 16 to 149)[6-12] have identified differential methylation at some specific gene regions. The only meta-analysis of epigenome-wide methylation in childhood asthma included 392 cases but did not examine newborn methylation[13]. Larger meta-analysis, including both methylation in newborns and at later ages, would increase power for identification of novel loci.

Using the Illumina HumanMethylation450K BeadChip (Illumina450K), we performed a large-scale meta-analysis of childhood asthma in relation to whole blood DNA methylation in newborns to evaluate whether methylation patterns at birth relate to disease development. We separately examined cross-sectional associations between whole blood DNA methylation and the presence of asthma in children, at least of school age. We investigated the association of DNA methylation in blood and asthma at both individual sites and over genomic regions and evaluated the potential functional impact of findings by integrating gene expression, pathway analyses, detailed functional annotation, and searching for druggable targets of differentially methylated loci. We also followed up our findings using methylation data in eosinophils and from nasal respiratory epithelium.

# METHODS

The Online Repository provides additional details on methods.

## STUDY POPULATION

Pregnancy and Childhood Epigenetics (PACE) is an international consortium of cohorts with Illumina450K DNA methylation data at birth (newborns) or in childhood[14]. In prospective analyses, we evaluated childhood asthma at school age in relation to blood DNA methylation data from newborns (8 cohorts: ALSPAC, CHS, EDEN, Generation R, GOYA, MoBa1, MoBa2, NEST). We also conducted cross-sectional analyses of methylation measured in children in relation to asthma status at that same time point (9 cohorts: BAMSE EpiGene, BAMSE MeDALL, CHOP, GALA II, ICAC, NFBC 1986, PIAMA, Raine Study, STOPPA). To avoid problems from small numbers, we set a minimum of 15 cases for participating cohorts to perform analyses.

## HARMONIZATION OF CHILDHOOD ASTHMA VARIABLES

We developed a harmonized definition of asthma based on the questionnaire data available in each cohort. Asthma was assessed at school age, defined as age 5 years or older and varied by cohort. Asthma was defined by doctor diagnosis of asthma and the report of at least one of the following: (a) current asthma, (b) asthma in the past year, or (c) asthma medication use in the last year. Non-cases were children who had never had asthma.

## METHYLATION DATA MEASUREMENTS AND QUALITY CONTROL

DNA methylation was measured using the Illumina450K platform. Cohorts performed their own quality control, normalization, and analyzed untransformed beta values. We previously found that the use of different pre-processing or normalization methods did not influence meta-analysis results[15, 16]. Probes on the X and Y chromosomes were removed as were those where a SNP was present in the last 5 base pairs of the probe which could interfere with binding. Rather than remove probes a priori that have appeared on various published lists of potentially cross-reactive probes or probes nearby SNPs, we examined post hoc those that appear in statistically significant results[17, 18].

### Annotation of CpGs

Tables include the UCSC RefGene name from Illumina's annotation file and enhanced annotation to UCSC Known Gene. UCSC Known Gene annotations include the nearest gene within 10 Mb of each CpG and fill in many missing gene names. All annotations use the human February 2009 (GRCh37/hg19) assembly.

### Cohort Specific Statistical Analyses

The association of methylation and asthma was assessed using logistic regression. Covariates included in adjusted models were maternal age, sustained maternal smoking during pregnancy[15], maternal asthma, socioeconomic status, and child's sex. Cohorts adjusted for batch effects using ComBat[19], SVA[20], or by including a batch covariate in their models. We also adjusted for potential cell type confounding by including estimated proportions calculated using the Houseman method[21] with a cord blood reference panel[22] for newborn cohorts or an adult blood reference panel[23] for child cohorts. The primary models presented include adjustment for covariates and cell type; reduced models are presented for comparison.

### META-ANALYSES

As in other consortium genomic analyses[24, 25], we meta-analyzed the study specific results using inverse variance-weighting, also referred to as fixed effects meta-analysis, with METAL[26]. We accounted for multiple testing by controlling for the false discovery rate (FDR) at 0.05[27]. To enable readers to assess whether the results across studies are consistent, we provide forest plots of the study specific effect estimates and 95% confidence intervals. As another way to visualize meaningful heterogeneity or influential results, we also provide plots, for all significant CpGs, of regression coefficients and 95% confidence intervals where we leave out one cohort at a time. Although inverse-variance weighted meta-analysis does not require the assumption of homogeneity[25], where there is even nominal evidence for heterogeneity (P-value for heterogeneity <0.05, without correction for multiple testing) for any CpG we report as genome wide significant, we also provide meta-analysis P-values from standard random effects meta-analysis using METASOFT[28].

### ANALYSES OF DIFFERENTIALLY METHYLATED REGIONS (DMRS)

Differentially methylated regions (DMRs) were identified using two methods, comb-p[29] and DMRcate[30]. To correct for multiple comparisons, comb-p uses a one-step Šidák correction[29], while DMRcate uses an FDR correction[30]. Each method requires the input of parameters to be used in selecting the regions. DMRcate[30] has default values for the minimum number of CpGs in a region (=2) and minimum length=1000 nucleotides; we used these values in comb-p to maximize comparability. To be conservative, we set the significance threshold at 0.01, rather than 0.05, and only considered a DMR to be statistically significant if it met this threshold in both packages (Šidák corrected P-value<0.01 from comb-p and FDR<0.01 from DMRcate). DMRcate annotates DMRs to UCSC RefGene from the Illumina annotation file.

### FUNCTIONAL FOLLOW-UP OF SIGNIFICANT DNA METHYLATION FINDINGS

*Correlation of differentially methylated sites with expression of nearby genes*

To examine whether differentially methylated sites impact gene expression, we analyzed paired methylation and gene expression data, both measured in blood, from several datasets[31-37] (see Online Repository): two with methylation and gene expression in newborns[32-34] (GEO [GSE62924 and GSE48354], N=38 and IoW, N=157), one with newborn methylation and gene expression at age four years[35] (INMA, N=113), another with gene expression and methylation both measured at age four[35] (INMA, N=112), one with both measured at age 16[38] (BAMSE, N=248), and the largest with both measured in adults[36, 37] (BIOS, N=3,096). For each of our significant CpGs, we examined the association with expression of transcripts within a 500kb window (+/-250kb from the CpG). For differentially methylated regions, we used a window 250kb up- and down-stream of the end and start site of each region. A given CpG or region may have more than one gene transcript in this window. In the smaller datasets of paired gene expression and methylation in newborns or children, we report nominal evidence for significance (P<0.05); for the much larger adult dataset, we report associations based on FDR<0.05.

*Functional annotation*

To identify tissue or cell type specific signals in significant EWAS results, we used eFORGE[39]. Pathway and network analyses were conducted using Ingenuity Pathway Analysis (IPA) (QIAGEN Inc., Venlo, the Netherlands) (https://www.qiagenbioinformatics.com/products/ingenuity-pathway-analysis)[40]. Due to possible uncertainty regarding genome annotation of probes flagged in the literature as potentially cross-reactive[41], we excluded those from pathway analyses. We also compared our methylation findings to published studies of methylation in relation to asthma and evaluated whether the implicated genes overlap with loci identified in GWAS[42, 43]. Additionally, we matched the genes to which our asthma-associated CpGs and DMRs annotated against the ChEMBL database (v22.1) to identify whether any are targets of approved drugs or drugs in development[44].

## LOOK-UP REPLICATION OF SIGNIFICANT DNA METHYLATION FINDINGS IN NASAL RESPIRATORY EPITHELIUM AND EOSINOPHILS

We examined the cell-type specificity of significant findings in whole blood in childhood by doing a look-up in two datasets with methylation measured with the Illumina450K in respiratory epithelium collected by nasal brushing [455 16-year-old Dutch children (37 with asthma) from the PIAMA study[13] and 72 African-American children (36 asthmatics, 38 non-asthmatics)[45]] and in a study with methylation measured with the Illumina450K in eosinophils isolated from blood[46] [16 asthmatics and 8 non-asthmatics aged 2-56 years from the Saguenay-Lac-Saint-Jean (SLSJ) region in Canada[13, 47]].

## RESULTS

The prospective analysis of newborn methylation in relation to asthma development included eight cohorts; the cross-sectional analysis of methylation in children in relation to asthma included 9 cohorts with mean ages at assessment of both asthma status and methylation ranging from 7 to 17 years (Table 1 contains counts by cohort; Table E1 in the Online Repository contains descriptive statistics). As newborn DNA methylation is measured at birth, the age at asthma assessment is the time between assessment of methylation and asthma status in the prospective analyses. All models included covariates and cell type unless otherwise noted. Some studies oversampled asthma cases within their population-based cohorts using a nested case-control or case-cohort design for methylation measurement, hence the case-control ratio varies across studies.

### ASTHMA IN RELATION TO NEWBORN DNA METHYLATION

Meta-analysis of asthma and newborn methylation (668 cases, 2,904 non-cases, 8 cohorts, ALSPAC, CHS, EDEN, Generation R, GOYA, MoBA1, MoBa2, and NEST), identified 9 statistically significant (FDR<0.05) individual CpGs (Manhattan and volcano plots in Figure 1). The 9 CpGs include two that have appeared on a list of poorly hybridizing probes[41] and thus must be regarded with caution (ch.11.109687686R and ch.6.1218502R). The other seven CpGs annotated to the following genes: *CLNS1A*, *MAML2/Mir_548*, *GPATCH2/STATA17*, *SCOC/LOC100129858*, *AK091866*, *SUB1*, and *WDR20* (Table 2). We identified 35 significant DMRs (Table 3; Table E2 for individual CpGs within DMRs); DMRs did not overlap the significant CpGs. Seven of the 9 significant CpGs showed higher methylation in children who developed asthma than in non-cases. All 9 CpGs had P≤3.55x10$^{-3}$ in a crude model and P≤4.16x10$^{-4}$ in the covariate-adjusted models that did not include cell-type (Table E3 in the Online Repository). None of the 9 CpGs had been previously reported in the literature (Table E4 in the Online Repository).

Forest plots, showing the cohort specific odds ratios and 95% confidence intervals for the 9 CpGs, are shown in Figure E1 in the Online Repository. Two cohorts in the newborn analysis include individuals of non-European ancestry (NEST and CHS), therefore we evaluated whether these were influential. The forest plots (Figure E1) suggest that for just 1 of the 9 CpGs (cg07156990), the size of the effect estimate was larger in NEST than in other studies, but the P-value for heterogeneity was not close to statistically significant ($P_{heterogeneity}$=0.26) and after removing NEST, the meta-analysis p-value was attenuated only slightly to 2.8x10$^{-6}$ from 9.5x10$^{-7}$. When we repeated the meta-analysis removing both NEST and CHS, results were very consistent with those from all cohorts (correlation of the regression coefficients = 0.996). With respect to tests of heterogeneity, only one of the 9 CpGs, cg13289553, gave a p-value for heterogeneity that was even nominally significant ($P_{heterogeneity}$=0.04, Table E3 in the Online Repository includes $P_{heterogeneity}$ for all 9 CpGs and the random effects meta-analysis results for this CpG); GOYA had the largest magnitude of association but effect estimates were in the same positive direction across studies (Figure E1). Analyses leaving out one cohort at a time does not suggest that any of the results are driven by a single cohort (plots of untransformed effect estimates and 95% CI are in Figure E2 in the Online Repository).

### ASTHMA IN RELATION TO CHILDHOOD DNA METHYLATION

In meta-analysis of asthma in relation to DNA methylation measured in childhood (631 cases, 2,231 non-cases, 9 cohorts, BAMSE EpiGene, BAMSE MeDALL, CHOP, GALA II, ICAC, NFBC, PIAMA, Raine Study, and STOPPA), we identified 179 CpGs at genome-wide significance (FDR<0.05) (Manhattan and volcano plots in Figure 2; results for all 179 CpGs in Table E5 in the Online Repository). Nearly all (173 of 179) showed decreased methylation in asthma versus non-cases; similar predominant directionality was seen in a recent study[13].

As in the newborn analysis, results were consistent across studies for the 179 significant CpGs (forest plots in Figure E3, plots of regression coefficients and 95% confidence intervals from analyses leaving one cohort out at a time in Figure E4 in the Online Repository). Two of the cohorts were adolescents (NFBC: mean age=16.0, SD=0.4; Raine: mean age=17.0, SD=0.2); repeating the meta-analysis without these two cohorts gave high correlations with the values for our FDR significant findings from all cohorts (correlation of coefficients = 0.96). Because two studies included individuals who were not of European ancestry – ICAC and GALA – we compared significant results with and without including these two studies and found them to be very similar (correlation of coefficients = 0.99). Table E5 in the Online Repository provides P-values for heterogeneity and, where those are even nominally significant ($P_{heterogeneity}$ <0.05), random effects meta-analysis results.

Of the 179 FDR significant CpGs, 34 CpGs were not singletons (i.e., more than one significant CpG annotated to a given gene). These 34 non-singleton CpGs correspond to 13 genes: *ACOT7*, *LOC100189589*, *IL5RA*, *SLC25A26*/*LRIG1*, *RPS6KA2*, *KCNH2*, *ZNF862*/*BC045757*, *AK096249*, *PRG2*, *EVL*/*AX747103*, *KIAA0182*, *ZFPM1*, and *EPX* (Table 4). We identified 36 significant DMRs by both calling methods (Table 5). Of the 179 FDR significant CpGs, 31 fell within one of these 36 DMRs, and 21 of the 36 DMRs contained at least one FDR significant CpG.

Three studies in our meta-analysis of asthma in relation to childhood methylation (PIAMA, BAMSE-MeDALL, and BAMSE-Epigene) also contributed to a recent meta-analysis of both preschool and school-aged asthma outcomes[13]; these studies contributed only a quarter (n=155) of the 636 cases in our meta-analysis. That EWAS meta-analysis of asthma at preschool and school-age[13] identified 14 CpGs at genome-wide significance; seven were among our 179 genome-wide significant findings for childhood methylation (cg13835688, cg14011077, cg03131767, cg13628444, cg10142874, cg01901579, cg01445399) and six others represented in our dataset (cg15344640, cg11456013, cg01770400, cg19764973, cg08085199, cg16592897), were nominally statistically significant ($P<0.05$) and direction matched for all 13. When repeating the meta-analysis excluding those three studies, 13 out of the 14 CpGs had $P<0.05$ and directions of association matched; only cg06483820 gave no evidence for association ($P=0.74$). In additional comparison to the literature, differential methylation in *ACOT7* and *ZFPM1* was previously identified in EWAS of blood in relation to immunoglobulin E[48] and in two of our contributing studies, ICAC and ALSPAC, to asthma[10, 12] as well as in an EWAS of nasal epithelium to asthma[45].

Comparing newborn and childhood methylation models, none of the 9 FDR-significant CpGs for newborn methylation were nominally significant ($p<0.05$) in the childhood methylation analysis. Only 6 of the 179 CpGs significant for asthma in relation to childhood methylation were at least nominally significant for newborn methylation; two of these had consistent directions of effect [cg16409452 (*EVL*) and cg09423651 (*NCK1*)].

**REPLICATION OF FINDINGS FOR ASTHMA IN RELATION TO CHILDHOOD METHYLATION IN NASAL EPITHELIUM**

We assessed whether the 179 CpGs differentially methylated in blood in relation to asthma in childhood were also differentially methylated in relation to current asthma in nasal epithelium from two studies (Table E6 in the Online Repository). Among 455 Dutch children (37 with asthma) studied at age 16[13], we found evidence for replication for 20 CpGs: matching direction of effect estimates and nominal significance (P<0.05). Among African-American children aged 10-12 with persistent asthma plus atopy (36 cases) compared with 36 non-asthmatic, non-atopic children, 128 of the 179 CpGs gave effect estimates for asthma in the same direction and also had P<0.05 for association.

**REPLICATION OF FINDINGS FOR ASTHMA IN RELATION TO CHILDHOOD METHYLATION IN EOSINOPHILS**

We looked up the 179 CpGs differentially methylated in childhood in relation to asthma in EWAS of 16 asthma cases and 8 non-cases in whom methylation had been measured in purified eosinophils. Of the 177 CpGs included in this dataset, all directions of association with asthma were the same as in PACE and 148 gave P<0.05 (Table E7 in the Online Repository).

**FUNCTIONAL ANNOTATION**

For the newborn analysis, among the 7 significant CpGs (after removing the 2 “ch”-probes), all 7 were near a transcription factor binding site and 6 were in a DNase hypersensitivity site, identified in at least one ENCODE cell line, supporting a potential functional relevance to transcriptional activity (Figure E5 in the Online Repository).

Among the 179 CpGs significantly differentially methylated in childhood in relation to asthma, there was significant depletion of localization to CpG islands (17 CpGs, 9.5%, P=$1.09\times10^{-11}$) and promoters (34 CpGs, 19.0%, P=$1.10\times10^{-4}$). Functional annotation plots are shown in Figure E6 in the Online Repository for the 13 gene regions to which the 34 nonsingleton CpGs annotate. Among the 179 CpGs, 113 were in DNAse hypersensitivity sites. Using eFORGE[39] to examine enrichment of all 179 significant CpGs for histone marks (H3K27me3, H3K36me3, H3K4me3, H3K9me3, and H3K4me1), we found significant enrichment for H3K4me1 in blood and lung and H3K36me3 in blood (Figure E7 in the Online Repository).

### Association of Methylation and Gene Expression

For the CpGs and regions we identified as differentially methylated in either newborns or children in relation to asthma, we assessed association between paired levels of blood DNA methylation and whole blood gene expression for nearby transcripts, defined as within a 500kb window of the significant CpG or DMR, in newborns (GEO n=38, INMA n=113, IoW n=157), children (4-year-olds in INMA n=112, 16-year-olds in BAMSE n=248) and adults (BIOS n=3,096).

Among 9 CpGs differentially methylated in newborns in relation to asthma, three CpGs were associated with expression of a nearby transcript in three datasets (cg17333211 in newborns, 4-year-olds, and adults, and cg02331902 and cg07156990 in two newborn datasets and 4-year-olds) and an additional three CpGs were associated with expression in two datasets (cg13427149 in 16-year-olds and adults, and cg13289553 and cg21486411 in newborns and 4-year-olds) (Table E8-A in the Online Repository). All regions differentially methylated in newborns in relation to asthma were related to expression in at least one dataset (Table E8-B in the Online Repository).

For methylation in childhood, nearly all (176/179) CpGs related to asthma also associated with expression in at least one dataset (Table E8-C in the Online Repository). CpGs annotated to *IL5RA* were significantly associated with expression in four cohorts (BIOS, INMA, IoW, and BAMSE). All 36 regions differentially methylated in childhood were associated with expression of a nearby transcript in at least one dataset (Table E8-D in the Online Repository).

### Pathway Analysis

Using IPA, we identified pathways, as well as disease processes and biological functions, significantly enriched (P<0.05) for the genes to which the significant individual CpGs or DMRs annotated in the meta-analysis of asthma in relation to newborn or childhood methylation (Tables E9 and E10 in the Online Repository). The genes to which the 7 significant CpGs (after removing "ch"-probes) and 35 significant DMRs in the newborn methylation analysis were annotated were significantly enriched (P<0.05) for canonical pathways relevant to immune function in asthma including eNOS signaling, the inflammasome, and NF-κB signaling (Table E9). Enriched disease processes and biologic functions included several involving immune function and others involving immune and organ development (Table E9). Given the larger number of implicated genes for childhood methylation, many more pathways, disease processes, and biological functions were enriched (Table E10 in the Online Repository). There was substantial overlap in newborns and children in the significantly enriched pathways and diseases and biological function relevant to immune function, immunologic disease and development (Figure E8). As an example, Figure 3 illustrates the network of four overlapping disease and biological processes between newborns and children – tissue morphology, immunological disease, inflammatory disease, and cell-mediated immune response.

### DRUGGABLE TARGETS

Among regions differentially methylated in newborns in relation to later asthma, *RUNX1* is the target of the agent CHEMBL2093862 and *CASP8* is the target of CHEMBL2105721 (Nivocasan), an inhibitor of this caspase and two others (1 and 9). Among genes with individual CpGs significantly differentially methylated in childhood in relation to asthma, *KCNH2* (3 significant CpGs) is a target of several approved drugs with mechanism of action of blocking *HERG* (human *Ether-à-go-go*-Related Gene), including the anti-arthymic agents amiodarone hydrochloride, dofetilide, and sotalol. Notably, sotalol is also a beta-adrenergic receptor antagonist. *IL5RA* (2 significant CpGs) is the target for a drug approved for use in severe asthma, benralizumab, whose mechanism of action is antagonism of this gene[49]. Several other genes implicated by either individual CpG (16 genes) or DMR analysis (5 genes, including *IGF1R*) are targets for approved or potential drugs (Tables E11 and E12 in the Online Repository).

## Discussion

This epigenome-wide meta-analysis of the association between childhood asthma and DNA methylation measured at birth or childhood identified numerous novel CpGs and regions differentially methylated in relation to this common health outcome. The 9 CpGs and 35 regions significantly differentially methylated in relation to asthma in newborn blood DNA are potential markers of risk for disease development. There were many more statistically significant associations of asthma in relation to childhood DNA methylation, with 179 CpGs and 36 regions; these may reflect both risk for and effects of this disease[50].

Among the significant CpGs in newborns, 6 were in DNAse hyper-sensitivity sites supporting potential regulatory impact on gene function. Additionally, genes to which cg13427149 (*GPATCH2*/*SPATA17*) and cg16792002 (*MAML2*) annotate have previously been associated with obesity phenotypes[51, 52]; conditions that are related to childhood asthma. This supports the potential functional importance and asthma relevance of our newborn findings.

Some CpGs on the 450K array have been reported as potentially polymorphic by virtue of location near SNPs[41]. Given that many of the nearby SNPs are low frequency and most will not interfere with probe binding, which would generate a truly spurious result, rather than filter these in advance, in PACE we examined statistically significant CpGs post-hoc for occurrence on lists of potentially problematic CpGs in the literature as recently recommended by others[17, 18]. Lists of potentially problematic probes change over time as do underlying gene annotations[53]. We note that two of the 9 significant CpGs in newborn methylation (ch.11.109687686R and ch.6.1218502R) were flagged as potentially non-specific ("ch") probes by Chen, et al. [41]. We provide association results for these as they may be useful to others but, acknowledging this caveat, do not include them in downstream analyses that assume certainty regarding gene localization. With respect to the issue of CpGs previously reported as near SNPs, we visually assessed plots of all significant CpGs in 3 of our largest cohorts [MoBa1 and Generation R for newborn methylation (Figure E9) and STOPPA for childhood methylation (Figure E10)] to verify unimodal distributions.

We identified many more CpGs and DMRs associated with later asthma, likely because these also capture disease effects. Our findings may also reflect different pathophysiological mechanisms related to newborn vs childhood methylation and asthma. A comprehensive search for methylation signals at birth that predict later development of asthma likely requires much larger sample sizes given the intervening effects of exposures and developmental processes that may outweigh effects of small methylation differences present at birth[54]. However, while overlap at the level of specific CpGs or DMRs was low, there was substantial overlap at the pathway and network level (Figure 3 and Figure E8).

To follow-up our differentially methylated signals for potential functional impact, we examined correlations with gene expression. Because of the relatively small sizes of the paired gene expression datasets in newborns or children, we also examined a much larger dataset of adults to increase power. Although the number of subjects in datasets of newborns or children with both gene expression and methylation data were modest (range 38 to 248), limiting power to find correlations, we found that a high proportion of CpGs and DMRs related to asthma were also correlated with gene expression in at least one dataset in this age range. This further supports the functional impact of our methylation findings.

Our search for druggable targets identified two genes from the newborn DMR analysis that are targets for either approved or potential drugs. The childhood analysis identified more drug targets. One of these genes, *IL5RA*, already has an approved asthma drug that inhibits its product. This analysis further supports the relevance to asthma pathogenesis and potential clinical usefulness of these findings. Investigating the potential to repurpose approved drugs for new indications has been recently highlighted as cost-effective way to develop new therapeutic modalities[55].

We meta-analyzed results across studies using fixed effects meta-analysis with inverse variance weighting. Rice, et al. [25] have recently summarized issues regarding the choice of meta-analytic models for combining study specific results in genomic analyses and show that inverse-variance weighted average estimates a reasonable and interpretable parameter, even under the assumption that effect sizes differ[25]. Further, they point out that fixed effects meta-analysis does not require the assumption of homogeneity. Rice, et al. [25] also emphasize the importance of evaluating meta-analyses effect estimates and significance tests along with visualization of study specific estimates rather than relying on a single statistical estimate of heterogeneity. Accordingly, we provide forest plots, to show the consistency of study specific findings for all significant meta-analysis results (Online Repository Figure E1 for newborn methylation and Figure E3 for childhood methylation). Further, we performed a systematic leave-one-out meta-analysis for all significant CpGs, where we leave each cohort, out one by one (Figure E2 for newborn and E4 for childhood methylation in the Online Repository). In addition, where there is even nominal evidence for heterogeneity ($P_{heterogeneity}<0.05$), we provide random effects results in Tables E3 (newborn methylation) and E5 (childhood) in the Online Repository.

We recognize various limitations. As in most EWAS[13], as well as GWAS meta-analyses[56], asthma was defined by questionnaires. As in Xu, et al. [13], we used reported doctor diagnosis combined with symptoms and medication use. While the use of self-reported outcomes can lead to misclassification, this should be non-differential with respect to methylation and thus should lead to bias toward the null rather than create false positive findings. We did not stratify the analyses by allergic status because most cohorts do not have objective measures of atopy and, in many cohorts, sample size would have been inadequate for stratification. We also note that the diverse cohorts included in the analysis could have introduced heterogeneity based on ancestry or, in the analysis of methylation in older children, two studies in older adolescents. However, in the studies of older children, non-European ancestry of older children did not appear to be influential in sensitivity analyses. While magnitudes of the associations are modest, this is consistent with other genome wide analyses of methylation in newborns and children in relation to various exposures[15, 57, 58]. These effect sizes are not surprising given that highly reproducible genetic signals discovered in asthma GWAS, such as *ORMDL3*[59], are also modest.

We used logistic regression in the prospective analyses of newborn methylation in relation to asthma rather than Cox regression, which is not commonly used in high dimensional genomic studies. If time to asthma were available or could be estimated reliably, a Cox model would be more efficient. However, for asthma, the exact time to disease development is poorly estimated. Thus, epidemiologic studies generally use age at diagnosis, but there can be a very long lag between disease onset and diagnosis. In our scenario, where the exact time to asthma is unknown, using error-prone outcomes can actually result in larger bias. Thus, considering the tradeoff between bias and efficiency, logistic regression is the better option. We also note that where the condition under study has lower than 10% prevalence, as is the case for our outcome, asthma diagnosed at school age, the odds ratio is a good approximation of the hazard ratio[60]. To address the important aspect of age at diagnosis of asthma, we used the diagnosis age for the harmonized definition of asthma. With the exception of a couple of studies, where sensitivity analyses removing them did not suggest undue influence, the range of mean ages is not large.

Unmeasured confounding is a concern in all analyses of observational data. With high dimensional genomic data, variability due to batch effects is an additional potential source of unmeasured confounding[61]. In this meta-analysis, each cohort corrected for batch effects using methods most suitable for their own data. In most studies, methylation analyses were completed over a short period of time which greatly reduces batch effects[61]. When using methods such as adjustment for batch variables or ComBat, one must specify the putative batch variables. To the extent that there are unknown factors contributing to laboratory variability, there may be residual confounding. Various methods have been proposed to attempt to address unmeasured confounding in high dimensional data. However, in meta-analysis, findings, tend to be significant because they are consistent across studies. Thus, the chance that in studies done in different countries, with methylation measured in different laboratories and at different times, that unmeasured confounding is operating in the same manner across studies, resulting in false positive significant associations in the meta-analysis, is greatly reduced. Further in the childhood methylation analysis, we have substantial replication of findings from a recently published meta-analysis[13], even after overlapping individuals are removed. In addition, the consistency of our findings from blood DNA with results for DNA isolated from two tissues highly relevant for asthma, eosinophils and nasal respiratory epithelium, provides compelling evidence that our findings are not driven by unmeasured confounding.

Identification of differentially methylated regions provides a way to reduce the dimensionality of the epigenome-wide methylation data and can identify associations at the regional level where there are not individually significant CpGs. The two methods that we used for DMR identification, DMRcate and comb-p, are the only two published methods available for use with meta-analysis results[29, 30]. A recent review noted that the various methods published for identifying DMRs employ different assumptions and statistical approaches and thus rarely identify exactly the same regions[62]. Accordingly, to reduce false positives, we reported only DMRs identified as statistically significant by both methods.

We measured DNA methylation in whole blood, a mix of cell types. Cell counts were not measured, but we adjusted our models for estimated cell counts using established reference-based methods to address confounding by cell type differences[21]. For childhood, as opposed to newborn, methylation, we used an adult reference panel, because a suitable one is not available for children. Notably, the considerable overlap between our findings in whole blood and smaller studies of two highly asthma-relevant tissues, nasal epithelium, an excellent proxy for airway epithelium in studies of asthma[63] and purified eosinophils, greatly reduces the concern that our findings are false positives due to failure to fully account for the influence of asthma on white blood cell proportions.

In addition to confirmation of findings in studies of eosinophils and nasal respiratory epithelium, and the high power resulting from meta-analysis, other strengths of the study include our efforts to standardize the definition of asthma across studies, the large sample size provided by meta-analysis, and evaluation of potential biological implications of our findings by detailed examination of functional annotation, pathway analysis, correlating differentially methylated sites with gene expression and consideration of potential druggable targets.

In summary, we identified numerous novel CpGs and regions associated with childhood asthma in relation to DNA methylation measured either at birth, in prospective analyses, or in childhood, in cross-sectional analyses. Many of the genes annotated to these CpGs and regions are significantly enriched for pathways related to immune responses crucial in asthma; several genes are targets for either approved or investigational drugs. Most differentially methylated CpGs or regions correlated with expression at a nearby gene. Many more individual CpGs were differentially methylated in childhood in relation to their current asthma status. There was appreciable overlap with findings in nasal respiratory epithelium and purified eosinophils. The CpGs and regions identified in newborns might be potential biomarkers of later asthma risk; those identified in childhood likely reflect both processes that impact disease risk and effects of having the disease. The novel genes implicated by this study may shed new light on asthma pathogenesis.

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## FIGURE LEGENDS

Figure 1: Meta-analysis of asthma in relation to newborn methylation: (A) Manhattan plot and (B) volcano plot. Model adjusted for covariates and cell-types.

Figure 2: Meta-analysis of asthma in relation to childhood methylation: (A) Manhattan plot and (B) volcano plot. Model adjusted for covariates and cell-types. CpGs corresponding to genes with more than one FDR<0.05 significant CpG are highlighted in red.

Figure 3: A network is shown for four categories of disease and biological functions overlapping between analyses of asthma in relation to either newborn or childhood methylation - immunological disease, cell-mediated immune response, inflammatory disease and tissue morphology. A gene is connected to a disease or function if it has been previously shown to be involved in it. All the genes marked in red are implicated from newborn methylation analyses and those in orange are implicated from childhood methylation analyses.

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*Table 1: Samples sizes by cohort for epigenome wide association analyses of asthma in relation to DNA methylation in newborns or children. Cohort specific information on covariates is in Supplementary Table E1.*

| Age Group | Cohort | N | N cases |
|---|---|---|---|
| Newborns | ALSPAC | 688 | 88 |
| | CHS | 229 | 39 |
| | EDEN | 150 | 34 |
| | Generation R | 661 | 37 |
| | GOYA | 507 | 37 |
| | MoBa1 | 666 | 149 |
| | MoBa2 | 458 | 239 |
| | NEST | 213 | 45 |
| | Meta-analysis | 3572 | 668 |
| Children | BAMSE EpiGene | 307 | 93 |
| | BAMSE MeDALL | 214 | 47 |
| | CHOP | 382 | 19 |
| | GALA II | 193 | 106 |
| | ICAC | 194 | 97 |
| | NFBC 1986 | 413 | 17 |
| | PIAMA | 197 | 15 |
| | Raine Study | 509 | 105 |
| | STOPPA | 460 | 137 |
| | Meta-analysis | 2869 | 636 |

*Table 2* *Nine FDR<0.05 significant CpGs from the meta-analysis of asthma in relation to newborn methylation.*

| CpG* | chr:pos | UCSC RefGene Name | UCSC Known Gene** | Average Methylation | OR*** (CI) | P-value | Direction**** |
|---|---|---|---|---|---|---|---|
| cg21486411 | chr11:77348243 | *CLNS1A* | *CLNS1A* | 0.089 | 1.13 (1.08,1.18) | 3.43E-07 | +?++++++ |
| cg16792002 | chr11:95788886 | *MAML2* | *Mir_548* | 0.840 | 0.95 (0.93,0.97) | 5.59E-07 | -------+ |
| ch.11.109687686R | chr11:110182476 | | | 0.085 | 1.08 (1.05,1.11) | 7.06E-07 | +??+++++ |
| cg13427149 | chr1:217804379 | *GPATCH2;SPATA17* | *GPATCH2* | 0.063 | 1.19 (1.11,1.27) | 8.04E-07 | ++++++++ |
| cg17333211 | chr4:141294016 | *SCOC* | *LOC100129858* | 0.074 | 1.13 (1.08,1.19) | 8.25E-07 | -+-+++++ |
| cg02331902 | chr5:90610303 | | *AK091866* | 0.089 | 1.12 (1.07,1.18) | 8.37E-07 | --++++++ |
| cg13289553 | chr5:32585524 | *SUB1* | *SUB1* | 0.085 | 1.14 (1.08,1.20) | 8.68E-07 | +++++++- |
| ch.6.1218502R | chr6:51250028 | | | 0.054 | 1.27 (1.15,1.39) | 9.32E-07 | +??+++++ |
| cg07156990 | chr14:102685678 | *WDR20* | *WDR20* | 0.930 | 0.87 (0.83,0.92) | 9.54E-07 | -++----- |

* ch probes (ch.11.109687686R and ch.6.1218502R) have been reported to be cross hybridizing and thus UCSC Known Gene is intentionally left blank.

** Annotation based on UCSC Known Gene also fills in nearest gene within 10 MB.

*** Odds ratio of developing asthma for a 1% absolute increase in methylation. Adjusted for covariates and cell type.

**** For each cohort participating in the analysis: + indicates a positive direction of effect, - indicates a negative direction of effect, and ? indicates missing information for that CpG in a given cohort. Cohort Order: ALSPAC, CHS, EDEN, Generation R, GOYA, MoBa1, MoBa2, NEST.

*Table 3 Differentially methylated regions (DMRs; N=35) for asthma in relation to newborn methylation identified by both comb-p (P-value<0.01) and DMRcate (FDR<0.01) methods*

| chr:pos | Gene Name* | N CpGs in region | P-value from comb-p** | FDR from DMRCate*** |
|---|---|---|---|---|
| chr1:59280290-59280842 | *LINC01135* | 5 | 1.23E-03 | 1.01E-03 |
| chr1:220263017-220263699 | *BPNT1; RNU5F-1* | 11 | 4.49E-04 | 7.74E-05 |
| chr1:1296093-1296489 | *MXRA8* | 2 | 9.83E-03 | 3.86E-04 |
| chr2:202097062-202097608 | *CASP8* | 5 | 1.14E-03 | 1.64E-05 |
| chr2:235004843-235005012 | *SPP2* | 2 | 6.22E-03 | 1.15E-03 |
| chr3:194188646-194189444 | *ATP13A3* | 3 | 1.06E-03 | 7.14E-04 |
| chr4:113218385-113218525 | *ALPK1* | 3 | 2.00E-03 | 3.69E-04 |
| chr5:158526108-158526694 | *EBF1* | 6 | 9.56E-04 | 2.16E-05 |
| chr5:81573780-81574461 | *RPS23* | 11 | 3.75E-03 | 1.47E-04 |
| chr5:64777678-64778186 | *ADAMTS6* | 10 | 7.09E-03 | 9.97E-05 |
| chr6:291687-292824 | *DUSP22* | 9 | 6.69E-06 | 1.18E-05 |
| chr6:32799997-32801050 | *TAP2* | 13 | 1.27E-03 | 6.66E-05 |
| chr6:26234819-26235610 | *HIST1H1D* | 9 | 6.12E-03 | 7.67E-05 |
| chr6:29648161-29649085 | *ZFP57* | 22 | 1.82E-08 | 3.13E-11 |
| chr6:31055396-31055503 | *C6orf15* | 5 | 3.61E-04 | 7.05E-05 |
| chr7:106694832-106695007 | *PRKAR2B* | 2 | 6.86E-03 | 7.92E-04 |
| chr7:87974722-87975316 | *STEAP4* | 4 | 2.32E-03 | 7.44E-05 |
| chr7:158045980-158046359 | *PTPRN2* | 6 | 1.98E-03 | 5.94E-04 |
| chr8:127889010-127889296 | *PCAT1* | 4 | 2.68E-05 | 1.44E-05 |
| chr8:33370172-33371226 | *TTI2* | 9 | 1.08E-04 | 6.40E-06 |
| chr10:71871364-71871634 | *H2AFY2* | 4 | 8.06E-03 | 6.19E-04 |
| chr10:65028929-65029169 | *JMJD1C* | 5 | 8.56E-03 | 6.12E-04 |
| chr11:268923-269469 | *NLRP6* | 5 | 3.71E-03 | 1.42E-03 |
| chr11:107328442-107328915 | *CWF19L2* | 10 | 5.10E-03 | 2.13E-05 |
| chr12:74931289-74932008 | *ATXN7L3B* | 10 | 1.03E-03 | 2.81E-06 |
| chr12:58329764-58330116 | *LOC100506844* | 5 | 1.58E-03 | 5.22E-04 |
| chr13:108953659-108954055 | *TNFSF13B* | 2 | 5.19E-03 | 2.37E-03 |
| chr13:31618695-31618744 | *TEX26* | 2 | 4.63E-03 | 2.09E-04 |
| chr14:69341139-69341739 | *ACTN1* | 4 | 1.36E-03 | 9.96E-04 |
| chr16:20774873-20775353 | *ACSM3* | 5 | 3.47E-03 | 1.58E-03 |
| chr17:74667833-74668253 | *LOC105274304* | 6 | 2.13E-03 | 8.34E-07 |
| chr17:21029189-21029296 | *DHRS7B* | 2 | 7.18E-03 | 5.11E-05 |
| chr18:47813745-47815431 | *CXXC1* | 10 | 2.58E-05 | 1.68E-03 |
| chr21:36421467-36421956 | *RUNX1* | 6 | 2.23E-03 | 1.67E-04 |
| chr22:24372913-24374013 | *LOC391322* | 12 | 3.21E-04 | 1.35E-07 |

* DMRcate annotates to UCSC RefGene from Illumina annotation file.

** Comb-p uses a one-step Sidak multiple-testing correction on the regional P-value assigned using Stouffer-Liptak method.

*** DMRcate takes the minimum Benjamini-Hochberg False Discovery Rate (FDR) corrected P-value in the region as representative after recalculating P-values using Gaussian kernel smoothing.

*Table 4* *34 CpGs annotated to 13 genes with more than one FDR<0.05 significant CpG from the meta-analysis of asthma in relation to childhood methylation*

| CpG | chr:pos | UCSC RefGene Name | UCSC Known Gene* | P-value | Average Methylation | OR** (CI) | Direction*** |
|---|---|---|---|---|---|---|---|
| cg13066938 | chr1:6341140 | *ACOT7* | *ACOT7* | 1.67E-05 | 0.682 | 0.91 (0.88,0.95) | --+?--+-- |
| cg21220721 | chr1:6341230 | *ACOT7* | *ACOT7* | 1.02E-08 | 0.763 | 0.94 (0.92,0.96) | --+------ |
| cg09249800 | chr1:6341287 | *ACOT7* | *ACOT7* | 1.19E-08 | 0.916 | 0.88 (0.84,0.92) | ???---?-- |
| cg11699125 | chr1:6341327 | *ACOT7* | *ACOT8* | 7.54E-10 | 0.799 | 0.90 (0.87,0.93) | --+------ |
| cg00043800 | chr2:74612144 | *LOC100189589* | *LOC100189589* | 1.32E-05 | 0.585 | 0.91 (0.87,0.95) | -----++-- |
| cg17988187 | chr2:74612222 | *LOC100189589* | *LOC100189590* | 1.21E-06 | 0.699 | 0.90 (0.86,0.94) | --+?--+-- |
| cg01310029 | chr3:3152374 | *IL5RA* | *IL5RA* | 4.18E-06 | 0.744 | 0.89 (0.85,0.94) | ---?--+-- |
| cg10159529 | chr3:3152530 | *IL5RA* | *IL5RA* | 4.48E-06 | 0.736 | 0.90 (0.86,0.94) | ---?----- |
| cg07410597 | chr3:66404129 | *SLC25A26* | *LRIG1* | 2.70E-07 | 0.773 | 0.88 (0.84,0.93) | --+---+-- |
| cg04217850 | chr3:66428294 | *SLC25A26* | *LRIG2* | 2.35E-06 | 0.747 | 0.88 (0.83,0.93) | --+------ |
| cg15304012 | chr6:166876490 | *RPS6KA2* | *RPS6KA2* | 1.86E-05 | 0.697 | 1.08 (1.04,1.13) | +++++++++ |
| cg19851574 | chr6:167178233 | *RPS6KA2* | *RPS6KA2* | 3.42E-06 | 0.671 | 0.95 (0.94,0.97) | --+------ |
| cg03329755 | chr6:167189272 | *RPS6KA2* | *RPS6KA2* | 6.14E-06 | 0.818 | 0.91 (0.88,0.95) | -++------ |
| cg05184016 | chr7:149543136 | *ZNF862* | *BC045757* | 2.74E-08 | 0.817 | 0.85 (0.80,0.90) | --+------ |
| cg07970948 | chr7:149543165 | *ZNF862* | *BC045757* | 6.39E-08 | 0.771 | 0.91 (0.88,0.94) | ---+--+-- |
| cg06558622 | chr7:149543177 | *ZNF862* | *BC045757* | 3.39E-09 | 0.818 | 0.88 (0.85,0.92) | --------- |
| cg24576940 | chr7:150648283 | *KCNH2* | *KCNH2* | 1.83E-05 | 0.848 | 0.87 (0.81,0.93) | --------- |
| cg23147443 | chr7:150649655 | *KCNH2* | *KCNH2* | 1.83E-06 | 0.842 | 0.89 (0.85,0.93) | ???---?-- |
| cg18666454 | chr7:150651937 | *KCNH2* | *KCNH2* | 1.46E-07 | 0.761 | 0.89 (0.86,0.93) | --------- |
| cg13850063 | chr9:138362321 | | *AK096249* | 5.49E-08 | 0.819 | 0.78 (0.71,0.85) | --+?----- |
| cg14011077 | chr9:138362327 | | *AK096249* | 7.02E-09 | 0.797 | 0.86 (0.82,0.90) | ---?----- |
| cg15700636 | chr11:57156050 | *PRG2* | *PRG2* | 2.35E-07 | 0.746 | 0.89 (0.85,0.93) | --+------ |
| cg08773180 | chr11:57157607 | *PRG2* | *PRG2* | 1.77E-07 | 0.741 | 0.89 (0.85,0.93) | --+---+-- |
| cg12819873 | chr11:57157632 | *PRG2* | *PRG2* | 9.55E-06 | 0.760 | 0.90 (0.86,0.94) | ------+-- |
| cg16409452 | chr14:100610186 | *EVL* | *AX747103* | 4.89E-07 | 0.770 | 0.91 (0.87,0.94) | --+------ |
| cg14084609 | chr14:100610407 | *EVL* | *AX747103* | 2.96E-09 | 0.780 | 0.89 (0.85,0.92) | --------- |
| cg18550847 | chr14:100610570 | *EVL* | *AX747103* | 7.10E-07 | 0.730 | 0.91 (0.88,0.94) | --+?----- |
| cg08640475 | chr16:85551478 | | *KIAA0182* | 2.36E-06 | 0.815 | 0.92 (0.89,0.95) | --+------ |
| cg10099827 | chr16:85551514 | | *KIAA0182* | 1.32E-06 | 0.808 | 0.92 (0.89,0.95) | --------- |
| cg08940169 | chr16:88540241 | *ZFPM1* | *ZFPM1* | 2.93E-07 | 0.778 | 0.91 (0.87,0.94) | ------+-- |
| cg04983687 | chr16:88558223 | *ZFPM1* | *ZFPM1* | 1.33E-10 | 0.744 | 0.93 (0.90,0.95) | --------- |
| cg25173129 | chr17:56269410 | *EPX* | *EPX* | 8.09E-07 | 0.753 | 0.88 (0.84,0.93) | --+---+-- |
| cg02970679 | chr17:56269818 | *EPX* | *EPX* | 9.99E-07 | 0.776 | 0.88 (0.83,0.92) | ------+-- |
| cg17374802 | chr17:56270828 | *EPX* | *EPX* | 2.06E-06 | 0.713 | 0.90 (0.86,0.94) | ---?--+-- |

* Annotation based on UCSC Known Gene also fills in nearest gene within 10 MB.
** Odds ratio of developing asthma for a 1% absolute increase in methylation. Adjusted for covariates and cell type.
*** For each cohort: + indicates a positive direction of effect, - indicates a negative direction of effect, and ? indicates missing information for that CpG. Cohort Order: BAMSE EpiGene, BAMSE MeDALL, CHOP, GALAII, ICAC, NFBC1986, PIAMA, RAINE, STOPPA

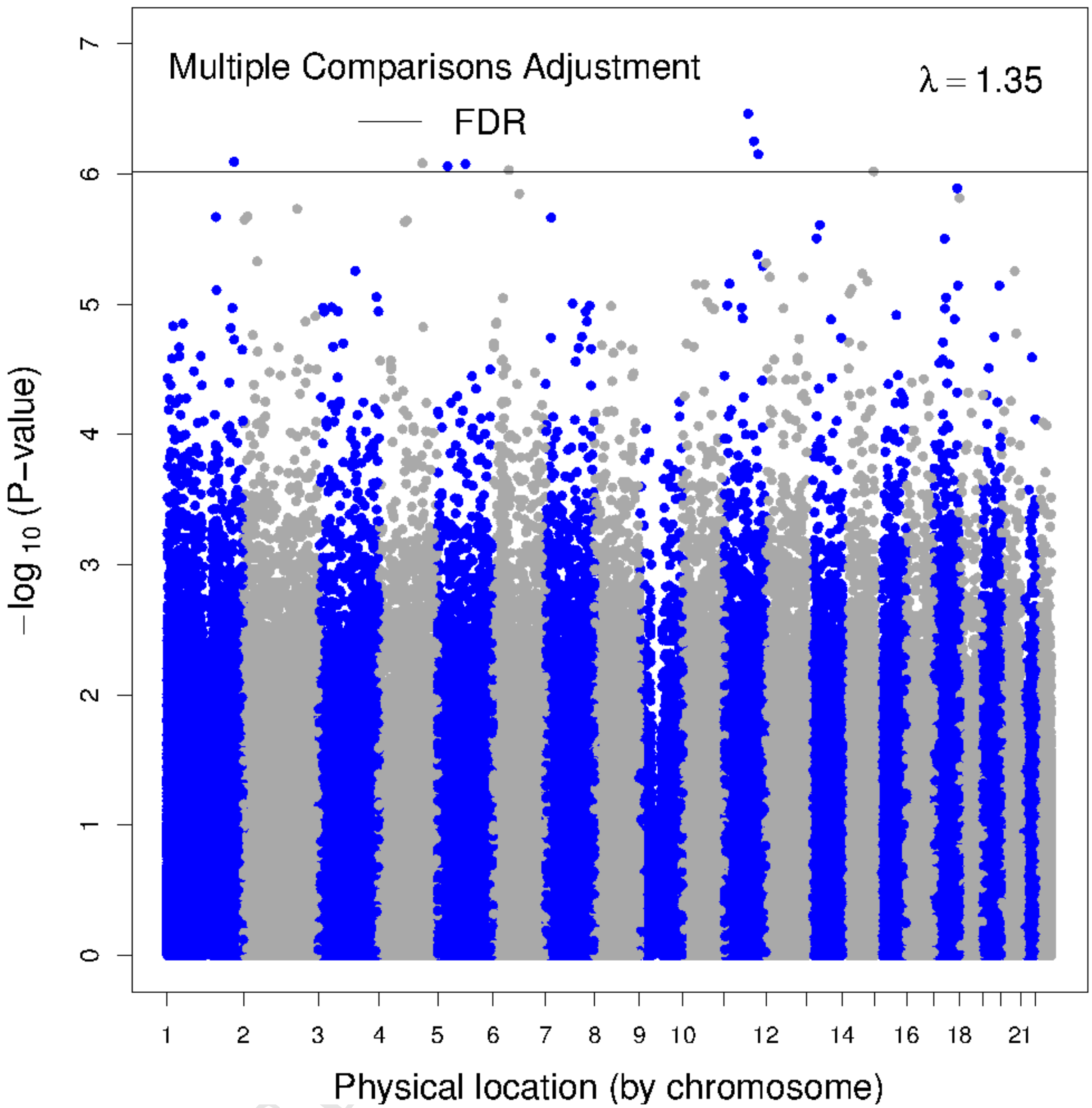
*Table 5 Differentially methylated regions for asthma in relation to childhood methylation with adjustment for covariates and cell type identified by both comb-p (P-value<0.01) and DMRcate (FDR<0.01) methods*

| chr:pos | Gene Name* | N CpGs in region | P-value from comb-p** | FDR from DMRCate*** |
|---|---|---|---|---|
| chr1:161575716-161576323 | *HSPA7* | 4 | 8.61E-03 | 1.24E-03 |
| chr1:209979111-209979780 | *IRF6* | 13 | 4.62E-04 | 1.90E-04 |
| chr1:2036283-2036644 | *PRKCZ* | 4 | 2.00E-04 | 3.14E-05 |
| chr1:87596820-87596935 | *LINC01140* | 3 | 1.58E-03 | 2.79E-05 |
| chr2:149639612-149640260 | *KIF5C* | 4 | 3.50E-03 | 1.14E-05 |
| chr2:11917490-11917788 | *LPIN1* | 3 | 4.81E-03 | 6.25E-04 |
| chr3:195974258-195974330 | *PCYT1A* | 3 | 5.07E-05 | 2.00E-05 |
| chr3:3151795-3152917 | *IL5RA* | 6 | 1.35E-08 | 2.12E-09 |
| chr5:38445220-38446193 | *EGFLAM* | 9 | 5.11E-06 | 1.28E-05 |
| chr5:132008525-132009631 | *IL4* | 4 | 5.36E-07 | 3.11E-05 |
| chr6:112688010-112688931 | *RFPL4B* | 4 | 4.89E-05 | 5.19E-04 |
| chr6:166876490-166877039 | *RPS6KA2;RPS6KA2-IT1* | 8 | 3.08E-05 | 1.74E-06 |
| chr7:156735383-156735657 | *NOM1* | 3 | 7.11E-03 | 2.82E-03 |
| chr7:149543136-149543178 | *ZNF862* | 3 | 3.85E-16 | 1.43E-16 |
| chr7:65419185-65419289 | *VKORC1L1* | 7 | 2.82E-03 | 1.04E-03 |
| chr8:832917-833049 | *ERICH1-AS1;DLGAP2* | 3 | 6.15E-03 | 6.44E-03 |
| chr8:141046436-141046853 | *TRAPPC9* | 5 | 8.93E-07 | 3.45E-09 |
| chr9:138362321-138362505 | *PPP1R26-AS1* | 3 | 2.72E-05 | 1.44E-09 |
| chr9:130859454-130859607 | *SLC25A25* | 2 | 2.69E-08 | 5.84E-08 |
| chr11:65545808-65547173 | *AP5B1* | 8 | 1.31E-10 | 9.73E-12 |
| chr11:69291998-69292065 | *LINC01488* | 3 | 4.55E-04 | 1.65E-04 |
| chr11:59856225-59856359 | *MS4A2* | 2 | 1.50E-03 | 3.25E-04 |
| chr12:15125458-15126021 | *PDE6H* | 4 | 6.93E-03 | 7.65E-06 |
| chr14:100610071-100610668 | *EVL* | 6 | 7.79E-16 | 1.24E-19 |
| chr15:64275810-64275854 | *DAPK2* | 2 | 4.91E-04 | 2.04E-04 |
| chr15:99443213-99443667 | *IGF1R* | 4 | 6.57E-05 | 2.41E-04 |
| chr16:875257-875627 | *PRR25* | 4 | 3.34E-03 | 3.21E-03 |
| chr16:88539861-88540397 | *ZFPM1* | 5 | 1.09E-04 | 1.13E-05 |
| chr16:615709-616221 | *PRR35* | 5 | 1.62E-04 | 2.70E-07 |
| chr16:85551478-85551749 | *GSE1* | 3 | 5.27E-07 | 2.37E-07 |
| chr17:56269410-56270829 | *EPX* | 5 | 6.20E-11 | 1.41E-08 |
| chr17:78682785-78683458 | *RPTOR* | 5 | 1.18E-04 | 4.03E-04 |
| chr19:51961666-51961938 | *SIGLEC8* | 3 | 2.37E-04 | 5.07E-04 |
| chr19:50553682-50554511 | *LOC400710* | 10 | 1.78E-07 | 3.81E-06 |
| chr20:35503832-35504554 | *TLDC2* | 8 | 1.23E-03 | 5.90E-08 |
| chr21:42520365-42520903 | *LINC00323* | 3 | 1.41E-04 | 2.64E-05 |

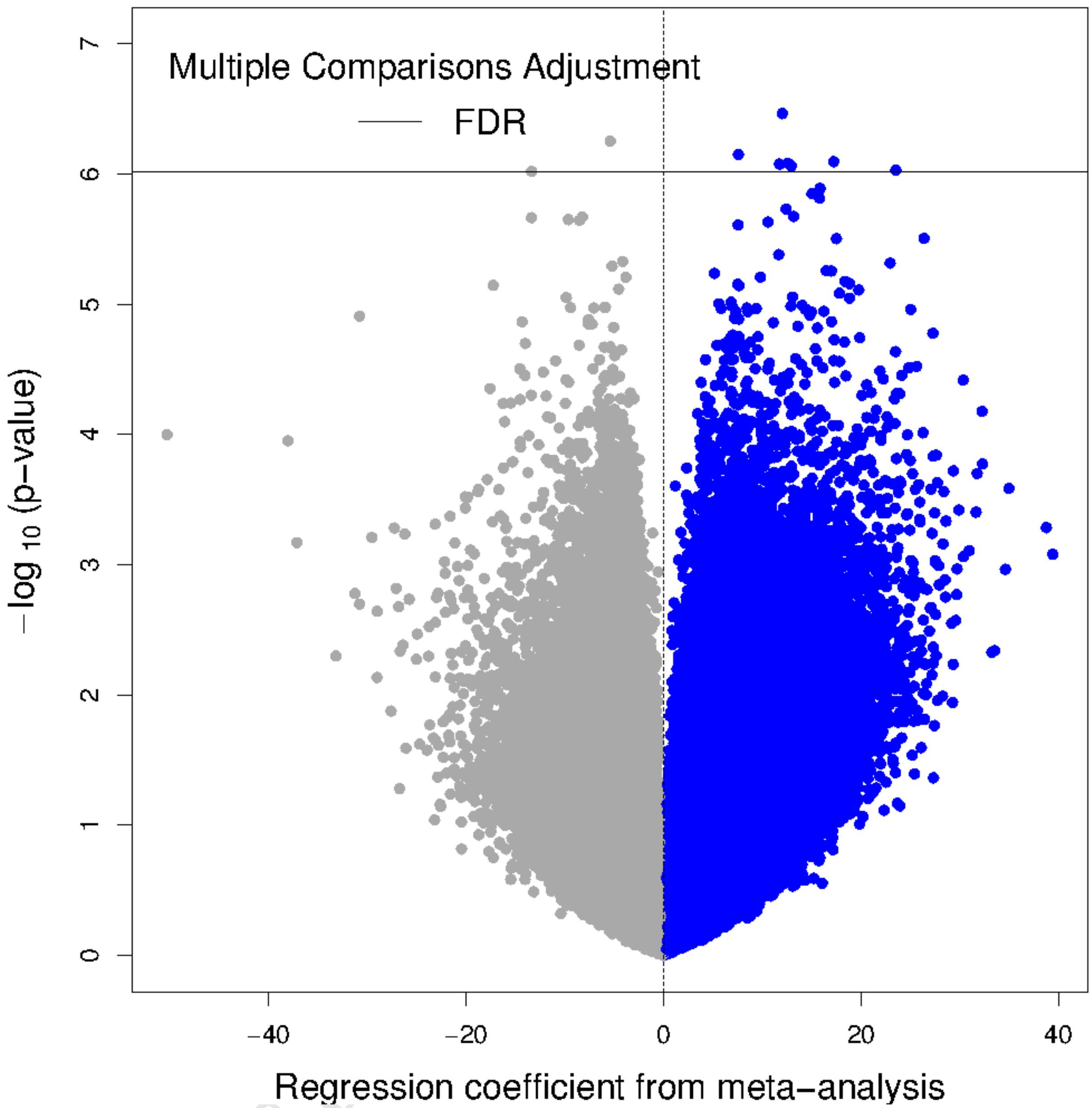
* DMRcate annotates to UCSC RefGene from Illumina annotation file. First listed gene shown.

** Comb-p uses a one-step Sidak multiple-testing correction on the regional P-value assigned using Stouffer-Liptak method.

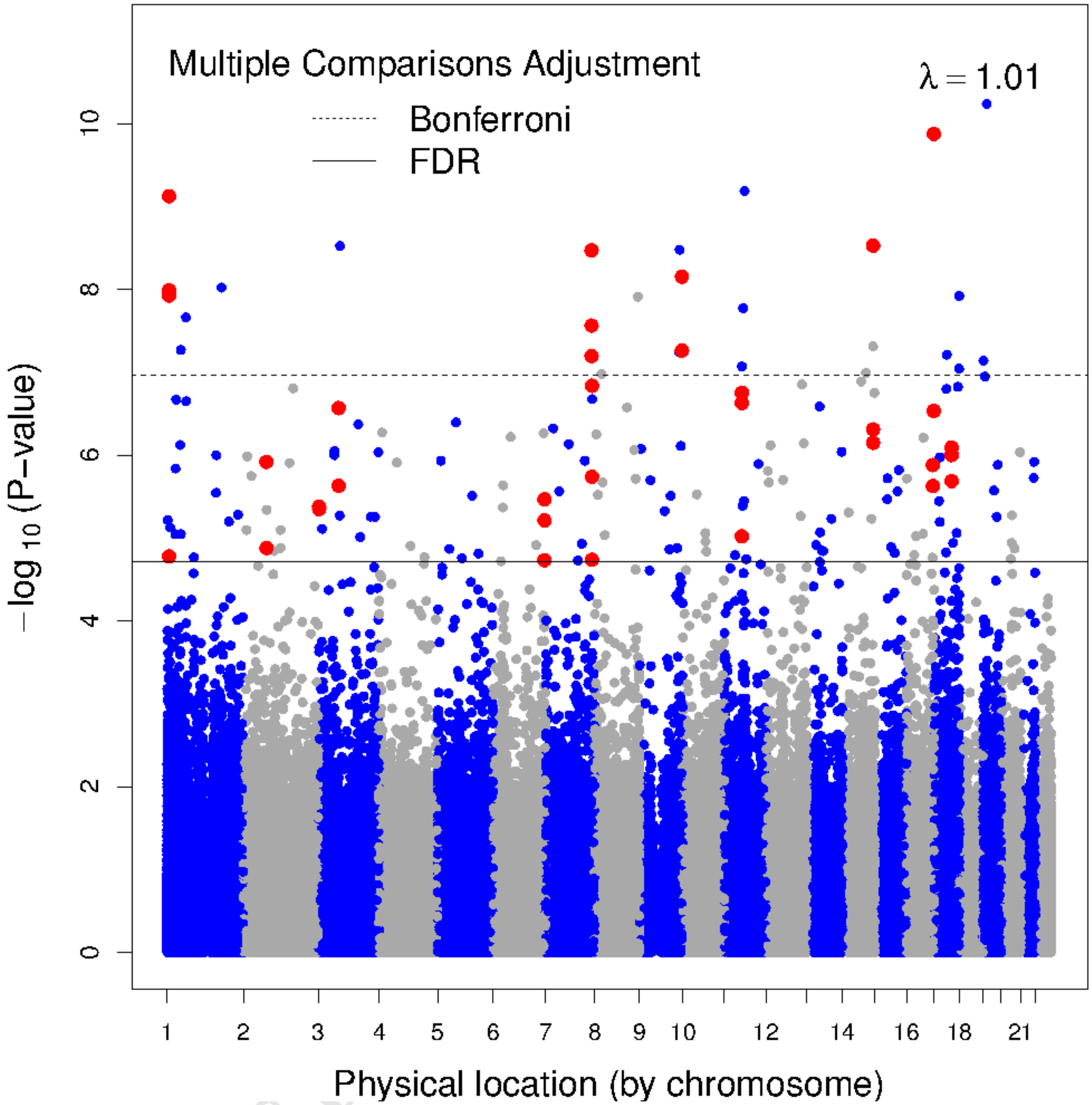
*** DMRcate takes the minimum Benjamini-Hochberg False Discovery Rate (FDR) corrected P-value in the region as representative after recalculating P-values using Gaussian kernel smoothing.

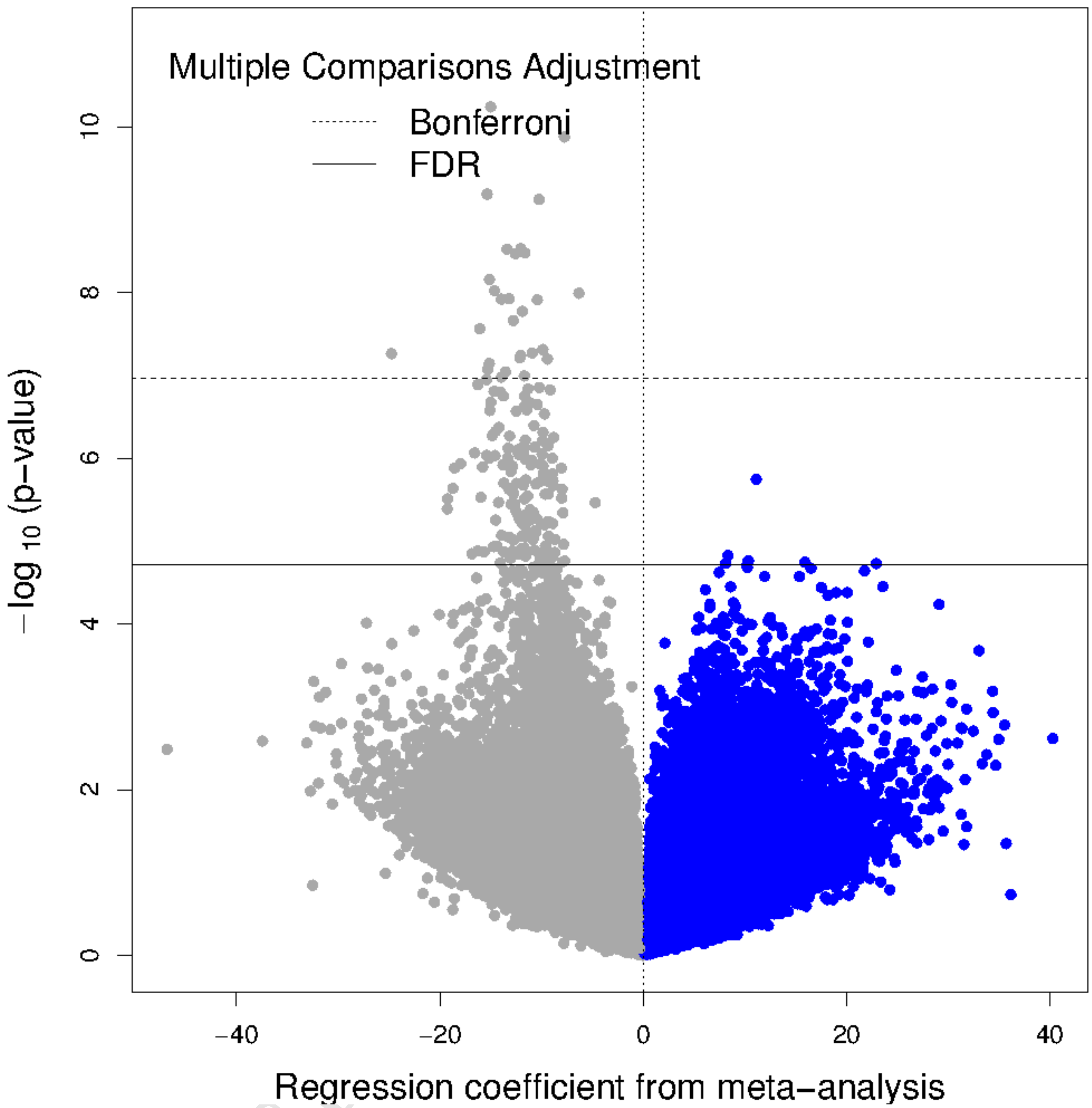


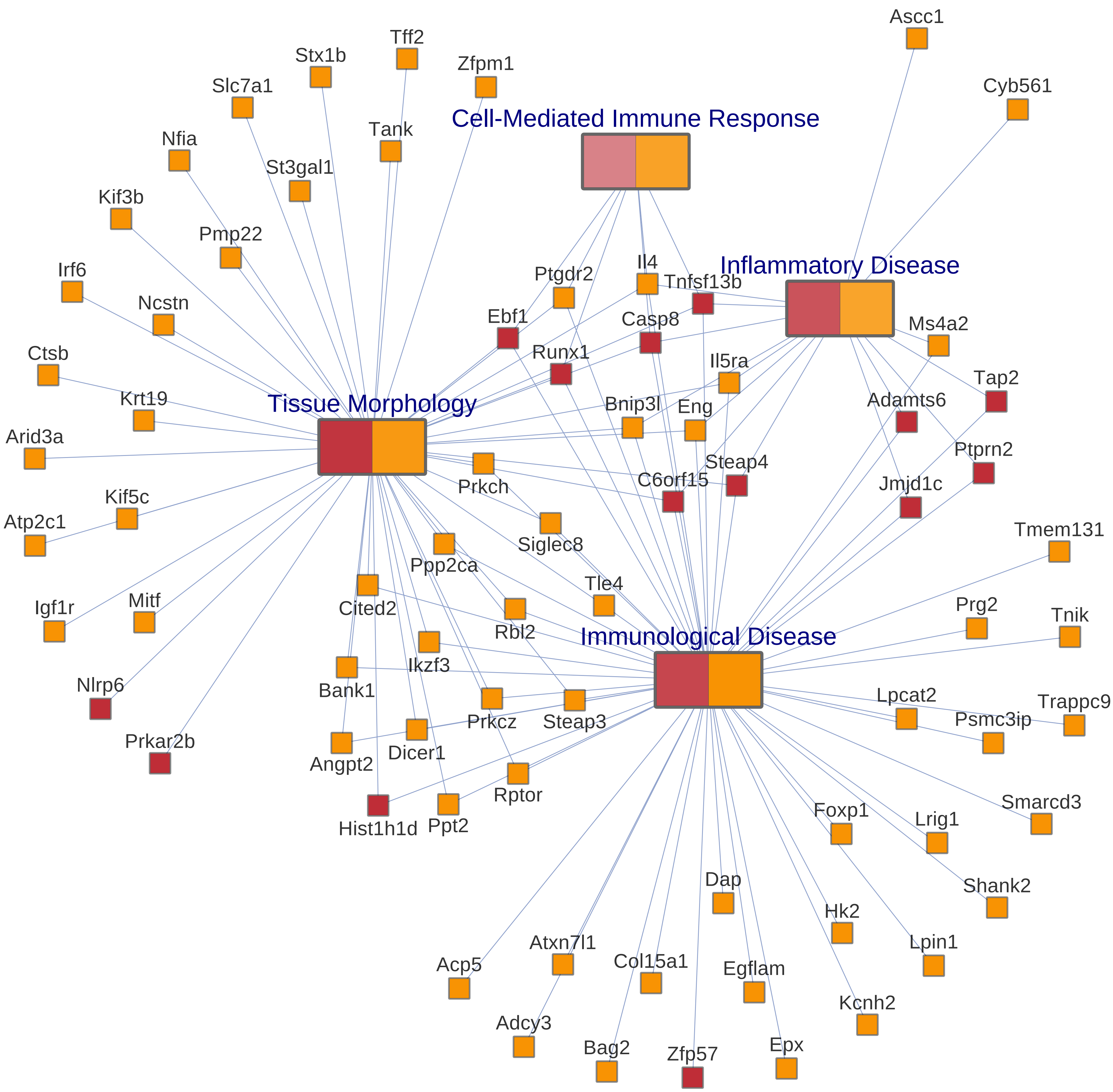
Multiple Comparisons Adjustment
FDR
λ = 1.35
−log 10 (P−value)
0
1
2
3
4
5
6
7
1
2
3
4
5
6
7
8
9
10
12
14
16
18
21
Physical location (by chromosome)



Multiple Comparisons Adjustment
FDR
−log 10 (p−value)
Regression coefficient from meta−analysis
0
1
2
3
4
5
6
7
−40
−20
0
20
40


Multiple Comparisons Adjustment
Bonferroni
FDR
λ = 1.01
−log 10 (P−value)
0
2
4
6
8
10
1
2
3
4
5
6
7
8
9
10
12
14
16
18
21
Physical location (by chromosome)


Multiple Comparisons Adjustment
Bonferroni
FDR
$-\log_{10}$ (p−value)
0
2
4
6
8
10
−40
−20
0
20
40
Regression coefficient from meta−analysis



Cell-Mediated Immune Response
Inflammatory Disease
Tissue Morphology
Immunological Disease
Ascc1
Cyb561
Tff2
Stx1b
Zfpm1
Slc7a1
Tank
Nfia
St3gal1
Kif3b
Pmp22
Irf6
Ncstn
Ptgdr2
Il4
Tnfsf13b
Ebf1
Casp8
Ms4a2
Runx1
Ctsb
Krt19
Il5ra
Tap2
Adamts6
Bnip3l
Eng
Arid3a
Prkch
Steap4
Ptprn2
C6orf15
Jmjd1c
Kif5c
Siglec8
Atp2c1
Ppp2ca
Tmem131
Tle4
Mitf
Cited2
Prg2
Tnik
Igf1r
Rbl2
Ikzf3
Nlrp6
Bank1
Lpcat2
Trappc9
Prkcz
Steap3
Psmc3ip
Prkar2b
Dicer1
Angpt2
Rptor
Smarcd3
Hist1h1d
Ppt2
Foxp1
Lrig1
Dap
Shank2
Hk2
Atxn7l1
Lpin1
Acp5
Col15a1
Egflam
Kcnh2
Adcy3
Bag2
Zfp57
Epx

# ONLINE REPOSITORY

# EPIGENOME-WIDE CONSORTIUM META-ANALYSIS OF DNA METHYLATION AND CHILDHOOD ASTHMA

Supplementary Methods

## 1. COHORT SPECIFIC DESCRIPTIONS OF STUDY POPULATION, PHENOTYPE DATA, DNA METHYLATION DATA AND SUPPLEMENTAL ACKNOWLEDGEMENTS

### *ALSPAC*

Study population

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a large, prospective cohort study based in the South West of England. In total, 14,541 pregnant women residents in Avon, UK with expected delivery dates between 1st April 1991 and 31st December 1992 were initially enrolled; 13,988 children were alive at 1 year[1, 2]. Please note that the study website contains details of all the data that are available through a fully searchable data dictionary (http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/). The study has been approved by the ALSPAC Ethics & Law Committee (ALEC) and written consent was obtained from participating parents of their children.

Phenotype data

Questionnaires were sent to parents when the study children were around the age of 91 months. School age children (7 ½ years) were classified as having current asthma if the mother responded “yes” to the question “has a doctor ever actually said that your study child has asthma?” and in addition, responded “yes” to either of the following questions: “has he/she had any of the following in the past 12 months? [Asthma]” or “children often have accidents or illnesses that need treatment. Please indicate which of the following has been given to your child in the past 12 months. [Asthma medication]”.

Covariates

Maternal age at delivery was derived from the mother’s report of her own and child’s dates of birth. Maternal social class was recorded and derived from self-report questionnaire data of occupation according to the Registrar General’s Social Classes based upon SOC 2000 codes. Data were collapsed to low (classifications IV & V), middle (classifications of III (non-manual) & III (manual)) and high (classifications of I & II). Maternal smoking status was derived from self-report questionnaire data completed by the mother. Smoking status was recorded at 18 weeks and 32 weeks gestation and was defined as no smoking during pregnancy, smoked during early pregnancy and smoked throughout pregnancy. Maternal asthma was reported by questionnaire completed by the mothers at 12 weeks gestation. Child’s sex was recorded as dichotomous variable.

DNA Methylation Data

Cord blood (whole blood or buffy coats) was collected according to standard procedures, spun and frozen at -80˚C. DNA-methylation data pre-processing was conducted as part of the Accessible Resource for Integrated Epigenomic Studies (ARIES) project [ariesepigenomics.org.uk] at the University of Bristol[3]. Briefly, DNA was bisulfite converted using Zymo EZ DNA MethylationTM kit (Zymo, Irvine, CA). The Illumina Infinium® HumanMethylation450k BeadChip assay was used to measure genome-wide methylation status. Assay arrays were scanned using the Illumina iScan and initial quality review was assessed using GenomeStudio (version 2011.1). Samples were distributed across slides using a semi-random approach. Samples with >20% probes with a detection p-value ≥0.01 failed quality control and were repeated. Genotype probes on the array were compared between samples of the same individuals and against genome wide SNP chip data to assess and remove any sample mismatches. The methylation data were pre-processed using the WateRmelon package in R (version 3.0.1) according to the subset quantile normalization approach as described by Touleimat and Tost[4]. After assaying, repeat assays, pre-processing QC and normalization, 485,577 probes were available. Probes with a detection p-value of >0.05 for >5% of samples (N=3,033), probes residing on the X and Y chromosome and SNPs (N=11,713) were removed. This resulted in 471,193 probes available for association analysis.

Technical batch was included in all analyses by adding several surrogate variables generated using the sva() function in the SVA R package. Surrogate variables (SVs) were generated separately for every model and for each exposure. Ten SVs were generated and only those that were not associated with the outcome measure were included as covariates within each model.

Acknowledgements

We are extremely grateful to all the families who took part in the ALSPAC study, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses. The UK Medical Research Council and the Wellcome Trust (Grant ref: 102215/2/13/2) and the University of Bristol provide core support for ALSPAC. The Accessible Resource for Integrated Epigenomics Studies (ARIES) was funded by the UK Biotechnology and Biological Sciences Research Council (BB/I025751/1 and BB/I025263/1). This work was supported by the Medical Research Council Integrative Epidemiology Unit and the University of Bristol (MC_UU_12013_2). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

*BAMSE*

Study population

The Children's Allergy Environment Stockholm Epidemiology study is a population-based birth cohort from Stockholm, Sweden. In short, 4,089 children born between 1994 and 1996 in four municipalities of Stockholm County were enrolled[5]. At baseline, when the infant was approximately 2 months of age, parents completed a questionnaire that assessed residential characteristics, as well as socioeconomic and lifestyle factors. When children were 1, 2, 4, 8, 12 and 16 years, the parents completed questionnaires focusing on children's symptoms related to wheezing and allergic diseases, as well as various exposures. The survey response rates were 96%, 94%, 91%, 84%, 82% and 78%, respectively. Furthermore, blood was obtained at ages 4, 8 and 16 years from 2,605 (63.7%), 2,470 (60.4%) and 2,547 (62.2%) children, respectively. The baseline and follow-up studies were approved by the Regional Ethical Review Board, Karolinska Institutet, Stockholm, Sweden, and the parents of all participating children provided informed consent. BAMSE-MeDALL and BAMSE-EpiGene represent two sub-studies within BAMSE.

Phenotype Data

*Asthma*

In BAMSE, asthma is defined based on parental reports of doctor's diagnosis of asthma ("Has your child been diagnosed with asthma by a doctor up to eight years?") AND positive answer to one of the following questions at eight years:

"Has your child had trouble with wheezing or raspy breathing in the last 12 months? OR "Has your child received treatment for breathing difficulties in the last 12 months with short-acting bronchodilation treatment, cortisone inhalation, so "called combination inhalers" and/or long-acting bronchodilation treatment?"

Covariates

The current analyses include the children who had DNA methylation measurements, asthma or and covariate data (N=214 from BAMSE-MeDALL; N=214 from BAMSE- EpiGene), and each dataset was analysed independently. For both datasets, information on maternal age, smoking during pregnancy, maternal asthma, maternal socioeconomic status, and child's sex was collected via questionnaires completed by the parents[5]. Maternal age was included as a continuous variable. Maternal smoking status during pregnancy was classified into three groups: non-smoker, stopped smoking in early pregnancy, and smoked throughout pregnancy. Maternal asthma was included as a dichotomous variable. Maternal socioeconomic status was categorized into two groups: blue collar worker and white-collar worker, the latter including liberal professional patrician with university graduate jobs. Child's sex was included as a dichotomous variable.

DNA Methylation Data

The DNA methylation data were generated as part of MeDALL. For BAMSE-MeDALL Illumina450K methylation data were generated in Groningen, The Netherlands and Mutation Analysis Facility and for BAMSE-EpiGene, the data were generated at the Karolinska Institutet, Stockholm, Sweden[6]. Protocols for data generation and quality control were identical at the two sites. DNA from peripheral and cord blood samples was extracted using the QIAamp blood kit (Qiagen or equivalent protocols), followed by precipitation-based concentration using GlycoBlue (Ambion). DNA concentration was determined by Nanodrop measurement and Picogreen quantification. 500 ng of DNA was bisulphite-converted using the EZ 96-DNA methylation kit (Zymo Research), following the manufacturer's standard protocol. After verification of the bisulphite conversion step using Sanger Sequencing, DNA concentration was normalized and the samples were randomized to avoid batch effects. All paired samples were hybridized on the same chip. Standard male and female DNA samples were included in this step for quality control. In the BAMSE EpiGene study, epigenome-wide DNA methylation was measured in DNA extracted from blood samples collected at the age of 8 years. An aliquot (500 ng) of DNA per sample underwent bisulfite conversion using the EZ-96 DNA Methylation kit (Zymo Research Corporation, Irvine, USA). Samples were plated onto 96-well plates in randomized order. The same standard female DNA control sample that was also used in the MeDALL study was again included for quality control.

Acknowledgements

BAMSE was supported by The Swedish Research Council, The Swedish Heart-Lung Foundation, Stockholm County Council (ALF), Swedish foundation for strategic research (SSF) (RBc08-0027; BAMSE-EpiGene), the Strategic Research Programme (SFO) in Epidemiology at Karolinska Institutet, The Swedish Research Council Formas, and the EU-funded MeDALL project (grant agreement number 261357).

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*CHOP*

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Study population

The CHOP study (European Childhood Obesity Project) is an ongoing European multicenter randomized prospective nutritional intervention study in 1678 healthy term newborns recruited between October 1, 2002 and July 31, 2004. Currently, infants are followed up until the age of 11 years. Main objective of the CHOP study is to assess the effect of early and later nutrition on children's weight development, growth, body composition and risk of obesity and the role epigenetic and metabolic programming plays in this context. A detailed description of the study design and the comprehensive prospective measurements can be found in recent publications[7-10]. The local ethics committees of each study center approved all study procedures: Belgium (Comitè d'Ethique de L'Hopital Universitaire des Enfants Reine Fabiola; no. CEH 14/02), Germany (Bayerische Landesärztekammer Ethik-Kommission; no. 02070), Italy (Azienda Ospedaliera San Paolo Comitato Etico; no. 14/2002), Poland (Instytut Pomnik–Centrum Zdrowia Dziecka Komitet Etyczny; no 243/KE/2001), and Spain (Comité ético de investigación clinica del Hospital Universitario de Tarragona Joan XXIII). Written informed parental consent was obtained for each participating infant and from children of age 8 years onwards.

Phenotype Data

*Asthma*

In the CHOP study, asthma was defined based on the following questions asked on questionnaire completed by the mother when the child was 7 to 8 years of age (mean age (sd; range) = 7.1(0.29; 1.57)) and an evaluation of named asthma related medication by an experienced paediatrician. Children were classified as having asthma if the mother responded "YES" to the following questions: "Has your child ever been diagnosed by a physician/ paediatrician of asthma (NO/YES)" and named any asthma medication in response to the question "Is your child currently taking any medication? (>14 days) (NO/YES) Which? __________".

Covariates

Information on maternal age, smoking during pregnancy, asthma, education, and child's sex was collected via questionnaire completed by the mother within the first 8 weeks after delivery. Maternal age was included as a continuous variable. Maternal smoking status during pregnancy was classified into three groups: non-smoker, stopped smoking in early pregnancy, and smoked throughout pregnancy. Reported doctor diagnosed maternal asthma was included as a dichotomous variable. Maternal educational level was categorized into three groups based on years of education: low = basic schooling only or less than 10 yrs.; medium = secondary schooling of

10 to less than 12 yrs; high = completion of college, university or at least 12 years of secondary schooling. Child's sex was included as a dichotomous variable.

The current analyses include the children who had DNA methylation measurements, school-age asthma and covariate data (n=382). Batch effects were accounted for by including categorized variable plate in the analyses.

DNA Methylation Data

In the CHOP study, epigenome-wide DNA methylation was measured with the Illumina Infinium HumanMethylation450K Bead Chip (HM450K) array in 384 children of age 5.5 years (Illumina Inc., San Diego, USA). Briefly, genomic DNA was extracted from peripheral blood cells from buffy coats, bisulfite converted (800 ng) with the EZ-96 DNA Methylation Kit (Zymo Research, Irvine, Ca; USA) and finally hybridized on the HM450K arrays at the Genome Analysis Center of Helmholtz Zentrum Muenchen, Munich, Germany. Details on pre-processing, normalization and quality control were previously described[9]. In brief, raw methylation data were pre-processed and normalized according to the approach of Touleimat and Tost[4] with the modification of a beta-mixture quantile normalization (BMIQ) step[11]. Quality control was conducted according to standard criteria: Retaining only probes with signals from ≥3 beads, detection *p*-values≤0.01 and samples with ≥80% significant probe methylation signals per sample. In addition, color bias correction and background adjustment were conducted with R-package lumi. However, except for identified cross-binding probes[12], no probe filtering according to proximity of CpG site with SNPs of minor allele frequency ≥5% within 50bp or probes on the X and Y chromosomes were conducted. In total, 431 313 CpG methylation values for n= 384 children of age 5.5 years were available for EWAS analysis before potential trimming of calculated beta-values and 429948 after trimming. The final sample for the CHOP study in the school-age asthma EWAS analyses comprised 429948 CpG methylation values for n=382 children after removing any missing in phenotype and covariates (described below). In the CHOP analysis sample mean age (sd; range) of DNA-methylation measurement was 5.5 (0.07; 0.82) years.

Acknowledgements

The research of the CHOP study reported herein was partially supported by the Commission of the European Community, specific RTD Programme "Quality of Life and Management of Living Resources," within the 5th Framework Programme (research grant nos. QLRT-2001-00389 and QLK1-CT-2002-30582); the 6th Framework Programme contract no. 007036 (FP6-007036); the European Union's Seventh Framework Programme Project EarlyNutrition under grant agreement no. 289346 (FP7-289346), the Horizon 2020 research and innovation programme DYNAHEALTH (no. 633595) and the European Research Council Advanced Grant META-GROWTH (ERC-2012-AdG – no. 322605). Additional support from the German Ministry of Education and Research, Berlin (Grant Nr. 01 GI 0825) and the University of Munich Innovative Research Priority Project MC-Health is gratefully acknowledged. This manuscript does not necessarily reflect the views of the Commission and in no way anticipates the future policy in this area. The funders of this study had no role in study design, data collection, data analysis, data interpretation, decision to publish, or preparation of the manuscript.

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*CHS*

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Study population

The Children's Health Study (CHS) is a population-based prospective cohort study from age 5 onwards in Southern California, which has been described in detail elsewhere[13]. The study protocol was approved by the University of Southern California Institutional Review Board and informed, written consent and assent were provided by the parents and children respectively. A total of 5341 children were recruited, all of whom were born between 1995 and 1997 and are currently being followed until age 18.

Based on the availability of newborn bloodspots archived by the state of California, a subset of 273 children was selected for a sub-study in which epigenome-wide DNA methylation was assessed in newborn bloodspots. Multiple births were excluded from analyses (7 subjects).

Phenotype data

*Asthma*

We classified asthma based on responses to the following questions completed by the parents when the child was 5-10 years of age (if multiple, the year close to age 6-7 window was chosen). Children were classified as having asthma if the parent responded "yes" to the following question – "Has a doctor ever diagnosed this child as having asthma?". Further, the child was classified as asthmatic only if the parent also responded YES to either of the three following questions – "Has your child had wheezing or whistling in the chest in the last 12 months?" OR "In the last 12 months, has your child required medication for asthma or wheezing?" OR "In the last 12 months, has your child taken any other medication for asthma or wheezing except for controller and rescue medication?". The control group was NEVER asthma.

Covariates

Information on maternal smoking during pregnancy, asthma and education were obtained from parent-completed questionnaires at study entry when the subjects were around 6 years old. Child's sex and maternal age at delivery were obtained from California birth certificates. Maternal age was included as a continuous variable. Maternal smoking status during pregnancy and maternal asthma were both included as dichotomous variables. Maternal educational level was categorized into three groups based on years of education: less than or finished high school, some college or completed college, and some graduate training. Child's sex was included as a dichotomous variable. Ancestry was assessed from CHS genome-wide genotypic data using the program STRUCTURE from a set of ancestral informative markers that were scaled to represent the proportion of African American, Asian, Native American and white admixture[14]. We additionally corrected the analyses for batch effect by including the Illumina Infinium HumanMethylation450 BeadChip plate number (n=3).

The current analyses include the children who had DNA methylation measurements, school-age asthma and covariate data (N=229).

DNA Methylation Data

Methylation was measured using the Infinium HumanMethylation450 BeadChip (HM450). Laboratory personnel performing DNA methylation analysis were blinded to study subject information. DNA was extracted from whole blood cells using the QiaAmp DNA blood kit (Qiagen Inc, Valencia, CA) and stored at -80 degrees Celcius. 700-1000ng of genomic DNA from each sample was treated with bisulfite using the EZ-96 DNA Methylation Kit™ (Zymo Research, Irvine, CA, USA), according to the manufacturer's recommended protocol and eluted in 18 μl. The results of the Infinium HumanMethylation450 BeadChip (HM450) were compiled for each locus as previously described and were reported as beta (β) values[15]. A normal-exponential background correction with dye bias correction was applied to the raw intensities at the array level to reduce background noise[16]. We then normalized each sample's methylation values to have the same quantiles to address sample to sample variability[4]. CpG loci on the HM450 array were removed from analyses if they were on the X and Y chromosomes, or if they contained SNPs, deletions, repeats, or if they have more than 10% missing values, leaving a total of 384,310 probes for analysis. Beta values were considered as outliers and were removed if they fall below Quartile 1-3×IQR or above Quartile 3+3×IQR.

Acknowledgements

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*EDEN*

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Study population

The EDEN (Etude des Déterminants pré et post natals du développement et de la santé de l'Enfant) study is a prospective Birth Cohort Study (https://eden.vjf.inserm.fr/), which has been described in detail elsewhere[17]. Pregnant women seen for a prenatal visit at the departments of Obstetrics and Gynecology of the University Hospital of Nancy and Poitiers before their twenty-fourth week of amenorrhea were invited to participate. Enrollment started in February 2003 in Poitiers and September 2003 in Nancy; it lasted 27 months in each centre. Among eligible women, 55% (2002 women) accepted to participate. The study has been approved by the ethical committees « Comité Consultatif pour la Protection des Personnes dans la Recherche Biomédicale », Le Kremlin-Bicêtre University hospital, and « Commission Nationale de l'Informatique et des Libertés ».

Phenotype Data

*Asthma*

Asthma was defined based on responses to a questionnaire completed by the mother when the child was five years of age. Children were classified as having asthma if the mother responded "yes" to the following questions – "Has your child ever been diagnosed by a doctor as having asthma". Further, the child was classified as asthmatic only if the mother also responded YES to either of the three following questions: 1) Has your child had asthma in the past 12 months? 2) Has your child had medication for asthma in the past 12 months? 3) Wheezing in the last 12 months.

DNA Methylation Data

DNA was extracted from 150 cord blood samples. Amplified and genomic DNA samples are now stored in 96-well plates at -80°C. More than 40 single nucleotide polymorphisms (SNPs) have been genotyped either from genomic or from amplified DNA. The samples underwent bisulfite treatment using the EZ-96 DNA Methylation kit (Zymo Research Corporation, Irvine, USA), and were subsequently processed with the Illumina Infinium Human Methylation 450 BeadChip (Illumina Inc., San Diego, USA). In total, 439,306 CpGs are available in children with DNA measurements.

Acknowledgements

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*GALA II*

Study Population

The Genes-environments and Admixture in Latino Americans (GALA II) study is a case-control study initiated in 2008 designed to investigate genetic, behavioral, social, and environmental determinants of asthma risk and morbidity among children aged 8-21 years, as previously described in detail[18-20]. The study used identical protocols to recruit nearly 5000 Latinos (age 8-21) from 5 recruitment centers across the US (San Francisco Bay area; Houston, TX; Chicago, IL; New York, NY; and Puerto Rico). The study was approved by each of the five sites' institutional review boards, and all subjects provided informed consent/assent. Trained interviewers' bilingual in English and Spanish administered questionnaires to participants' parents/caretakers to obtain basic socio-demographic information, medical histories, and environmental exposures, such as exposure to tobacco smoke at various time points.

Phenotype Data

*Asthma*

In GALA II, childhood asthma is defined as having reported physician-diagnosed asthma plus at least two symptoms of coughing, wheezing, or shortness of breath in the 2 years preceding recruitment. Outcomes for all subjects were assessed at time of recruitment (baseline assessment). Eligible control subjects must not have had a reported history of asthma, lung disease, or chronic illness, and no reported symptoms of coughing, wheezing, or shortness of breath in the 2 years prior to enrollment. Exclusion criteria for asthma cases and controls included subjects who were in the third trimester of pregnancy, current smokers, or had at least a 10 pack-year smoking history. All subjects were aged 8-21 years at time of recruitment. Therefore, age of asthma onset and current asthma status were both asked at ages 8-21. Selection of subjects was limited to participants who were aged 8 to 10 years old. The current analyses include 193 children who had whole blood DNA methylation measurements and data on school-age asthma.

Covariates

The age of the participant and the participant's mother were both treated as continuous variables. Categorical variables included the child's ethnicity (Mexican, Puerto Rican, and Other Latino), sex (male/female), mother's asthma status (ever/never) and maternal educational achievement (less than high school, high school or equivalent, some college, college graduate or higher). Maternal smoking during pregnancy was classified into one of three categories: non-smoker, stopped smoking in early pregnancy, and smoked throughout pregnancy. Lastly, we also included measures of Native American and African genetic ancestry using ADMIXTURE[21] to account for the mixed ancestry of Latinos.

DNA Methylation Data

After examining DNA for complete bisulfite conversion of DNA (Zymo Research, Irvine, CA), we randomized the samples onto the Illumina Infinium HumanMethylation450 BeadChip (Illumina Inc., San Diego, USA). Raw genome-wide methylation data were loaded in the R package minfi and assessed for basic quality control metrics, including determination of poorly performing probes with insignificant detection p-values above background control probes (i.e., detection p-value >0.01). Probes with a single nucleotide polymorphism in the single base extension site were excluded. Since our study population included males and females, we also removed the X and Y chromosomes from the raw methylation values. A total of 321,509 methylation loci were included for analysis. We corrected for batch (microarray chip) effect using the ComBat function in the R package SVA (surrogate variable analysis) and performed SWAN normalization to correct for intra-array differences between Illumina Type I and Type II probes[22, 23].

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*Generation R*

Study Population

The Generation R Study is a population-based prospective cohort study from fetal life onwards in Rotterdam, the Netherlands[24, 25]. Assessments in pregnant women and children consisted of physical examinations, fetal ultrasounds, biological samples, and questionnaires. All children were born between April 2002 and January 2006. The study has been approved by the Medical Ethical Committee of the Erasmus University Medical Center and written consent was obtained from participating parents of their children.

DNA methylation

DNA was extracted from cord blood samples of 979 Caucasian children. Using the EZ-96 DNA-methylation kit (Shallow-well) (Zymo Research Corporation, Irvine, USA), 500 ng DNA per sample underwent bisulfite conversion. Samples were transferred onto 96-well plates in a random order. Samples were processed with Illumina's Infinium HumanMethylation450 BeadChip (Illumina Inc., San Diego, USA). Quality control of analyzed samples was performed using standardized criteria. Samples were excluded due to sample call rate <99% (n=7) or poor bisulfite conversion (n=1). In addition, 2 samples were excluded because of a gender mismatch and 1 sample because of a retracted informed consent, leaving a total of 969 samples in the statistical analysis. Probes with a single nucleotide polymorphism in the single base extension site with a frequency of >1% in the GoNLv4 reference panel were excluded, as were probes with non-optimal binding (non-mapping or mapping multiple times to either the normal or the bisulphite-converted genome), resulting in the exclusion of 49,564 probes, leaving a total of 436,013 probes in the analysis. Data were normalized with DASES normalization using a pipeline adapted from that developed by Touleimat and Tost[4]. DASES normalization includes background adjustment, between-array normalization applied to type I and type II probes separately, and dye bias correction applied to type I and type II probes separately. DASES is based on the DASEN method, but adds the dye bias correction, which is not included in DASEN[26]. Beta-values were calculated for all CpG sites.

## Phenotype Data

*Asthma*

Information about asthma (no; yes) was collected by questionnaires at the ages 4 and 6 years. Response rates for these questionnaires were 73% and 68%, respectively. Asthma was defined by a "yes" response to the following two questions on the questionnaire at age 6 years: 'Was your child ever diagnosed with asthma by a doctor? AND 'Did your child ever suffer from chest wheezing? [never, 1-3 times, >4 times]. Non-cases were children without report of asthma at either follow-up time.

## Covariates

Information on maternal age, parity, asthma, maternal education and maternal smoking during pregnancy was collected by questionnaires at enrollment. Maternal age was used as a continuous covariate. Parity was categorized into nulli- and multiparity. Maternal education was categorized into lower or normal (none, primary or secondary education) and higher (more than secondary education). Maternal smoking during pregnancy was assessed by questionnaires in early (<18 weeks gestational age), mid (18-25 weeks gestational age) and late (>25 weeks gestational age) pregnancy. In each trimester, pregnant women were asked whether they had smoked and if so, how much. Maternal smoking during pregnancy was categorized into no smoking during pregnancy, smoking during first trimester only, and continued smoking during pregnancy. Analyses were additionally adjusted for batch effects by adding plate number (11 categories) as a covariate.

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*GOYA*

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Study Population

The Genome-Wide Population-based Association Study of Extremely Overweight Young Adults (GOYA) study has been described previously by Paternoster et al.[27, 28]. It is based on the Danish National Birth Cohort (DNBC) that included 92,000 pregnant women and their pregnancies during 1996-2002. Of 67,853 women who had given birth to a live born infant, 67,853 had provided a blood sample during pregnancy and had BMI information available, 3.6% of these women with the largest residuals from the regression of BMI on age and parity (all entered as continuous variables) were selected for GOYA. The BMI for these 2451 women ranged from 32.6 to 64.4. From the remaining cohort, a random sample of similar size (2,450) was also selected. DNA methylation data were generated for the offspring of 1000 mothers in the GOYA study. Study "cases" had mothers with a BMI>32 and "controls" were sampled from the normal BMI distribution (can include mothers with a BMI>32). All participants in the DNBC gave written informed consent and the collection and use of their data has ethics approval.

Phenotype data

*Asthma*

Information on asthma was obtained from a questionnaire completed by the mothers at 7 years after birth and defined as asthma ever (diagnosed by a doctor).

Covariates

Data on maternal parity, socio-economic status, smoking and pre-pregnancy body mass index were collected via a telephone interview at around 16 weeks' gestation. Maternal age was derived from the mother's report of her own date of birth. Newborn sex and gestational age at birth were extracted from birth records. Socioeconomic status was defined using maternal education or occupation: 1) manager/long or medium education, 2) work requiring a short training period, or skilled manual labor, 3) unskilled or public service. Parity was categorized for this study as nulliparous or parous. Maternal smoking in pregnancy was defined as any smoking in pregnancy or no smoking in pregnancy. We restricted the analysis to GOYA controls, i.e. mothers sampled from the normal BMI distribution.

DNA Methylation measurements

Cord blood was collected according to standard procedures, spun and frozen at -80˚C. DNA methylation analysis and data pre-processing were performed at the University of Bristol. Following extraction, DNA was bisulfite converted using the Zymo EZ DNA MethylationTM kit (Zymo, Irvine, CA). Following conversion, the genome-wide methylation status of over 485,000 CpG sites was measured using the Illumina Infinium® HumanMethylation450k BeadChip assay according to the standard protocol. The arrays were scanned using an

Illumina iScan and initial quality review was assessed using GenomeStudio (version 2011.1). The level of methylation is expressed as a "Beta" value (β-value), ranging from 0 (no cytosine methylation) to 1 (complete cytosine methylation). Samples were distributed across slides using a semi-random approach to minimize the possibility of confounding by batch effects. Samples failing quality control (average probe detection p-value ≥ 0.01) were repeated. As an additional quality control step genotype probes on the HumanMethylation450k were compared between samples from the same individual and against SNP-chip data to identify and remove any sample mismatches. Data were normalized using the functional normalization approach in the Minfi R package. We removed probes that had a detection p-value >0.05 for >5% of samples, probes on the X or Y chromosomes and SNPs (rs probes). 473864 probes remained. Batch correction was done using 10 surrogate variables generated using the sva package in R and included these in models.

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*ICAC*

Study Population

The Inner-City Asthma Consortium EPIGEN population consisted of inner-city children aged 6-12 years with atopy and persistent asthma (cases) and without atopy or asthma (healthy controls). The cases and controls were recruited by six sites of the Inner-City Asthma Consortium (Boston; Washington, DC; Denver; New York; Dallas; and Detroit) from census tracts that contain at least 20% of households below the U.S. government poverty level[29].

Phenotype data

*Asthma*

Cases of asthma were required to meet the following criteria: 1) a physician diagnosis of asthma; 2) persistent or uncontrolled disease as defined by the National Asthma Education and Prevention Program[30]; 3) physiologic evidence of asthma ($FEV_1$ < 85% predicted, or $FEV_1$/FVC ratio < 85% and bronchodilator responsiveness (≥ 12%), or $PC_{20}$ < 8 mg/ml of methacholine); and 4) positive prick skin-test to as least one of a panel of indoor aeroallergens (i.e. dust mite, cockroach, mold, cat, dog, rat, or mouse). Controls were required to have: 1) no medical history of asthma, rhinitis, sinusitis, and atopic dermatitis; 2) an $FEV_1$ > 85% predicted; and 3) no positive prick skin-tests.

DNA Methylation

Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood using the Ficoll density gradient separation. DNA was isolated from the PBMCs using the AllPrep DNA/RNA kit (Qiagen, Germantown, MD), and purity was assessed using a NanoDrop spectrophotometer (Thermo Scientific, Wilmington, DE). We used Illumina's Infinium Human Methylation 450k BeadChip on bisulfite-treated samples. 0.85-1.00 µg DNA were bisulfite converted using the Zymo EZ DNA Methylation kit (Zymo Research, Orange, CA). Each conversion assay included a commercially available positive and negative control sample. Bisulfite converted samples formed the input for the Illumina Infinium Methylation assay using the Human Methylation 450k BeadChips (Illumina Inc, San Diego, CA). The labeling, hybridization, and scanning procedures were performed on the iScan system. All samples were assayed once (no technical replicates) with 194 arrays performed in 3 batches.

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*INMA –contributed analysis of gene expression in relation to methylation*

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Study population

The INMA—INfancia y Medio Ambiente— (Environment and Childhood) Project is a network of birth cohorts in Spain that aims to study the role of environmental pollutants in air, water and diet during pregnancy and early childhood in relation to child growth and development[31]. Mothers were enrolled at week 12 of pregnancy from 1997 to 2008 in seven regions of Spain (Flix, Granada, Menorca, Asturias, Gipuzkoa, Sabadell and Valencia). The cohort consisted of 3,768 children at birth. During the follow-up visits information on environmental exposures and health outcomes (reproductive, growth and obesity, lung function, allergies and neurodevelopment) were assessed through questionnaires, biomarker measurements, clinical data, and physical exploration. The study website contains details of the design and data available in INMA project (http://www.proyectoinma.org/). The study was approved by the Ethical Committees of each participating center and written consent was obtained from parents. The present study uses data only from the Sabadell birth subcohort.

DNA Methylation Data

Cord blood and whole blood collected at age 4y was extracted using the Chemagen kit (Perkin Elmer). DNA concentration was determined by a NanoDrop spectrophotometer (Thermo Scientific) and with the Quant-iT PicoGreen dsDNA Assay Kit (Life Technologies).

Blood methylation data were produced in two laboratories: the Genome Analysis Facility of the University Medical Center Groningen (UMCG) in Holland as part of the MeDALL project (0y and 4y), and the Bellvitge Biomedical Research Institute (IDIBELL) in Barcelona as part of the BREATHE project (0y). Both laboratories randomized the samples in batches and followed the Illumina protocol for the Infinium HumanMethylation450 BeadChip. Briefly, 500 ng of DNA was bisulfite-converted using the EZ 96-DNA methylation kit, and DNA methylation was measured through hybridization on the BeadChips. BeadChips were scanned with an Illumina iScan and image data were uploaded into the Methylation Module of Illumina's analysis software GenomeStudio and converted in β-values.

Two blood samples with overall low quality (MethylAid package[32]), and three blood samples discordant for sex (shinyMethyl package[33]) were removed during the quality control. After applying a stringent detection p-value[34] of $1.10 \times 10^{-16}$, 18 blood samples with a call rate <98% were excluded. Data were normalized with the functional normalization method implemented in the minfi package[35]. 7,136 probes with a call rate <95%, control probes and probes designed to detect genetic polymorphisms were removed. ComBat was applied to eliminate laboratory batch effects, without removing age differences by keeping age in the statistical model (Johnson, Li, and Rabinovic 2007). Finally, one of the 12 duplicated samples was excluded. The final dataset consisted of 476,946 probes and 616 samples (391 at age 0y and 209 at age 4y, 185 of them paired 0-4y).

Gene expression data

At age 4 years, whole blood was collected in PAXGene tubes and extracted using the kit recommended by the company. All samples had an RNA Integrity Number higher (RIN) than 7.

Gene expression data were obtained using the Affymetrix HTA 2.0 array at the European Institute for Systems Biology and Medicine in Lyon, France. Gene expression was normalized using the Expression Console Software from Affymetrix and probes were clustered to the transcript level using the version 35 of Affymetrix annotation. In addition, Affymetrix transcript clusters were mapped to gene symbols. Four samples were excluded because there were sex discrepancies (N=4). The final sample size was 124 (113 of them have DNA methylation at 0y and 112 at 4y).

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A full roster of the INMA Project Investigators can be found at http://www.proyectoinma.org/presentacion-inma/listado-investigadores/en_listado-investigadores.html.

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*IoW – analysis of gene expression and methylation data*

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Study population

This is the Isle of Wight (IoW) 3rd Generation Study[36]. The recruitment of newborns started from April 2010. Data used in the analyses were from infants born between April 2010 to May 2014. In total, 200 newborns were recruited such that at least one of their parents is in the IoW birth cohort (IoW F1) and the recruitment is ongoing.

DNA Methylation Data

We measured epigenome-wide DNA methylation of 192 newborns using DNA extracted from cord blood. One thousand ng DNA per sample underwent bisulfite conversion using the EZ-96 DNA Methylation kit (Shallow) (Zymo Research Corporation, Irvine, USA). Samples were processed with the Illumina Infinium HumanMethylation450 BeadChip (n = 129) and Illumina MethylationEPIC Beadchips (n = 63). "CPACOR" method by Lehne, et al. [34] has been used in normalization of the beta values. The 65 single nucleotide polymorphism (SNP) markers were removed. Illumina Background Correction was applied to the intensity values. The CpGs with set intensity values with detection p-value $\geq 10^{-16}$ was set as missing and removed in the further analysis. Samples exhibiting call rate <98% were excluded. Quantile normalization on intensity values was applied by incorporating control probe adjustment and reduction of global correlation. Also, DNA methylation from the 192 subjects were measured in seven batches. The R function ComBat (package sva)[37] built upon an empirical Bayes framework was used to remove batch effects. Beta-values were calculated for all CpG sites. After pre-processing a total 399, 383 CpG sites were remained for subsequent studies.

Gene expression data

We analyzed data from 157 matching cord blood samples between methylation data and gene expression (Agilent one-color microarray, Agilent Technologies, Santa Clara, CA). The pre-processing was performed with Limma [38] in the R statistical computing environment [39]. Raw idat files are read into R with the read.miamages function with the source set to Agilent. Background correction was performed with the function backgroundCorrect using the method “normexp” [40]. This method fits a convolution of normal and exponential distributions to the foreground intensities with the background probe intensities set as a covariate. The expected signal, given the foreground observed, is then set as the corrected intensity measures. Normalization is then performed with the normalizeBetweenArrays function and the method is set to “quantile”. Data is then converted to log2 transformed data for further analysis. Filtering is performed to remove lowly expressed probes that are close to the background level. Negative control probes are also removed from the data.

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*MoBa1 & MoBa2*

Study Population

Participants represent two subsets of mother-offspring pairs from the national Norwegian Mother and Child Cohort Study (MoBa)[41-43]. The years of birth for MoBa participants ranged from 1999-2009. MoBa mothers provided written informed consent. Each subset is referred to here as MoBa1 and MoBa2. MoBa1 is a subset of a larger study within MoBa that included a cohort random sample and cases of asthma at age three years[44]. We previously reported an association between maternal smoking during pregnancy and differential DNA methylation in MoBa1 newborns[45]. We subsequently measured DNA methylation in additional newborns (MoBa2) in the same laboratory (Illumina, San Diego, CA)[46]. MoBa2 included a cohort random sample plus cases of asthma at age seven years and non-asthmatic controls. Years of birth were 2002-2004 for children in MoBa1 and 2000-2005 for MoBa2. Both studies were approved by the Regional Committee for Ethics in Medical Research, Norway and were approved by the Institutional Review Board of the National Institute of Environmental Health Sciences, USA.

Phenotype data

*Asthma*

MoBa1 participants were originally selected for analysis of methylation based on asthma status at age 3 years (current asthma with use of inhaled asthma medications) along with a cohort random sample. Individuals whose parent responded to the follow-up questionnaire at age 7 years were included in the current study. Asthma was defined at age 7 according to the ideal definition, i.e. as doctor diagnosed asthma and one of current asthma, asthma symptoms in the past year, or medication for asthma in the past year. The reference group excluded children whose mother had reported asthma at age 3 but not at age 7.

MoBa2 was selected on asthma case/noncase status based on the questionnaire at age 7 years, therefore school-age asthma is defined by this selection variable. There were additional approximately 200 subjects selected because they had measurement of plasma folate available and these are excluded from the analysis. Asthma was previously defined as current asthma (symptoms in the last year) AND medication for asthma in the past year. The control group is NEVER asthma.

Covariates

For both datasets, information on maternal age, smoking during pregnancy, asthma, education, and child's sex was collected via questionnaires completed by the mother or from birth registry records as previously described [44]. Maternal age was included as a continuous variable. Maternal smoking status during pregnancy was classified into three groups: non-smoker, stopped smoking in early pregnancy, and smoked throughout pregnancy. Maternal asthma was included as a dichotomous variable. Maternal educational level was categorized into four groups based on years of education: less than high school/secondary school, high school/secondary school completion, some college or university, or 4 years of college/university or more. Child's sex was included as a dichotomous variable.

DNA Methylation Data

Details of the DNA methylation measurements and quality control for the MoBa1 participants were previously described[45] and the same protocol was implemented for the MoBa2 participants. Briefly, umbilical cord blood samples were collected and frozen at birth at -80°C. All biological material was obtained from the Biobank of the MoBa study[43]. Bisulfite conversion was performed using the EZ-96 DNA Methylation kit (Zymo Research Corporation, Irvine, CA) and DNA methylation was measured at 485,577 CpGs in cord blood using Illumina's Infinium HumanMethylation450 BeadChip[47]. Raw intensity (.idat) files were handled in R using the *minfi* package to calculate the methylation level at each CpG as the beta-value (β=intensity of the methylated allele (M)/(intensity of the unmethylated allele (U) + intensity of the methylated allele (M) + 100)) and the data were exported for quality control and processing. Probe and sample-specific quality control was performed in the MoBa1 and MoBa2 datasets separately. Similar protocols were applied to MoBa1 and Moba2, as follows: Control probes (N=65) and probes on X (N=11 230) and Y (N=416) chromosomes were excluded in both datasets. Remaining CpGs missing > 10% of methylation data were also removed (N=20 in MoBa1, none in MoBa2). Samples indicated by Illumina to have failed or have an average detection p-value across all probes < 0.05 (N=49 MoBa1, N=35 MoBa2) and samples with gender mismatch (N=13 MoBa1, N=8 MoBa2) were also removed. For MoBa1 and MoBa2, we accounted for the two different probe designs by applying the intra-array normalization strategy Beta Mixture Quantile dilation (BMIQ)[11]. The Empirical Bayes method via *ComBat* was applied separately in each dataset for batch correction using the *sva* package in *R*[37].

The following number of samples passed the above quality control: 1,068 for MoBa1 and 685 for MoBa2. Samples determined to be ancestry outliers based on principal components analysis of Illumina HumanCore genotype data were excluded from analyses (12 in MoBa1; 5 in MoBa2). The current analyses include the children who had cord blood DNA methylation measurements, school-age asthma and covariate data (N=661 from MoBa1; N=456 from MoBa2), and each dataset was analysed independently.

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*NEST*

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Study Population

NEST is a multiethnic birth cohort designed to identify the effects of early exposures on epigenetic profiles and phenotypic outcomes. Pregnant women were recruited from prenatal clinics serving Duke University Hospital and Durham Regional Hospital Obstetrics facilities in Durham, North Carolina from April 2005 to July 2009. Gestational age at enrollment ranged from 6 to 42 weeks (median 30 weeks). Eligibility criteria were women aged 18 years or older, English speaking, pregnant, and an intention to use one of the two obstetrics facilities. Among these, women infected with HIV or intending to give up custody of the offspring of index pregnancy were excluded. Current smokers were targeted for the first ~200 participants. Of the 1101 women who met eligibility criteria and were approached, 895 (81%) were enrolled and umbilical cord blood was collected from 741 infants. This study was approved by the Duke Institutional Review Board. Additional details about NEST may be found in previous publications[48, 49].

## Phenotype Data

*Asthma*

Asthma was defined based on a combination of medical records and survey responses. The survey included the following two questions which were used to identify asthma diagnoses: 1) "What was the outcome of your child's doctor visits? Normal or concerns. If there were Concerns, what were they?" and 2) "Was your child diagnosed with any condition by his/her doctor? Yes or No. If Yes, please specify". Parental reports of asthma in these questions were classified as asthma cases, otherwise if the parent said there were no diagnoses or concerns they were classified as not having asthma. Medical records were further used to refine and supplement survey data. Medical billing codes related to asthma (i.e. ICD 9 493.XX codes) and the number of encounters were used to identify children with asthma among those with recent visits. This was checked against a review of the child's full medical records to ensure accuracy. The age at which the asthma diagnosis was reported varies; however, it ranges from five to nine years.

## Covariates

The sex of the child was collected from medical records following delivery. Maternal smoking status, socioeconomic status (education), age, asthma, and race were reported by the mother on a questionnaire completed during pregnancy. Maternal age was included as a continuous variable. Maternal smoking status during pregnancy was classified into three groups: non-smoker, stopped smoking in early pregnancy, and smoked throughout pregnancy. Maternal asthma was included as a dichotomous variable. Maternal educational level was categorized into 3 groups: high school education/GED or less, some college, or college degree or higher.

## DNA Methylation Data

Genomic DNA from buffy coat specimens was extracted from umbilical cord blood using Puregene Reagents (Qiagen, Valencia, CA). Bisulfite conversion was performed using the EZ-96 DNA Methylation Kit (Zymo Research Corporation) and DNA methylation was measured at 485577 CpGs using Illumina Infinium HumanMethylation450 BeadChip (Illumina Inc., San Diego, USA). Illumina's GenomeStudio Methylation module version 1.0 (Illumina Inc.) was used to calculate the methylation level at each CpG as the beta value. Probe and sample-specific quality control was performed in the NEST cohort using a similar approach to MoBa1 and MoBa2 cohorts. Specifically, control probes (N=65) and probes on X (N=11 230) and Y (N=416) chromosomes were excluded as well as CpGs missing > 10% of methylation data. Samples indicated by Illumina to have failed or have an average detection p-value across all probes < 0.05 and samples with gender mismatch were also removed. The two different probe designs by applying the intra-array normalization strategy Beta Mixture Quantile dilation (BMIQ)[11]. The Empirical Bayes method via ComBat was applied for batch correction using the sva package in R[37]. The current analyses include the children who had cord blood DNA methylation measurements, school-age asthma and covariate data (N= 213 from NEST).

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*NFBC 1986*

Study Population

The Northern Finland Birth Cohort 1986 (NFBC 1986) is a prospective population-based birth cohort which consists of 99% of all children who were born in the provinces of Oulu and Lapland in Northern Finland between 1 July 1985 and 30 June 1986. 9,203 live-born individuals entered the study[50]. At the age of 16, the subjects living in the original target area or in the capital area (n=9,215) were invited to participate in a follow-up study including a clinical examination. 7344 participants attend the study in year 2001/2002, of which 5654 completed the postal questionnaire, the clinical examination and provided a blood sample.

Ethical approval was obtained from the ethical committee of the Northern Ostrobothnia Hospital District and all participants gave written informed consent. The Finnish Ministry of Social Affairs and Health has granted permission to use register data and patient records. Participants' interviews and postal questionnaires were completed/returned from the 24th gestational week onwards with data since 12-16th gestational week. Both the course of pregnancy and delivery, and also complications, were confirmed from patient records, as was the neonatal outcome. Follow-ups of children have been conducted at the age of 6-12 months, 7-8 years and 14-16 years. DNA methylation was measured on 566 randomly selected subjects.

Phenotype Data

*Asthma*

In the Northern Finland Birth Cohort 1986, asthma was defined based on the following questions asked on questionnaire completed by the child at an age of 16 years. Children were classified as having asthma if they responded "yes" to both of the following questions – "Have you ever had any of the following respiratory and/or allergic symptoms or illnesses? - Asthma (Diagnosed or treated by a doctor)". Further, the child was classified as asthmatic only if the child also responded with occasionally or regularly to the following question "How often do you take the following medicines at the present? - Asthma medication".

Covariates

SES was defined based on the question asked on questionnaire completed by the mother during pregnancy. "Your own school attendance: 1= less than 6 years primary school, 2=7-8 years primary school,3= 9-10 years primary school, 4 =vocational school or college 6-12 months, 5 =vocational school or college > 1 years, 6 =matriculation, no vocational schooling, 7=matriculation + college, 8=matriculation, university studies not finished, 9=university degree". This was recoded according to the leaving age of school education: 1= before 16 years, 2= 16 to 19 years old, 3 = older than 19 years.

DNA Methylation Data

Methylation of genomic DNA was quantified using the Illumina HumanMethylation450 array according to manufacturer's instructions. Bisulfite conversion of genomic DNA was performed using the EZ DNA methylation kit according to manufacturer's instructions (Zymo Research, Orange, CA). DNA methylation was recoded on Illumina HumanMethlation450K array for 566 randomly selected subjects. To account for batch effects in the data, beta values underwent a functional normalization approach described by Fortin *et al*.[51] using the first 10 PCs of the Illumina 450K array control probes. This approach includes subset quantile normalization of the data and normal-exponential out-of-band background correction.

24 technical replicates were excluded. 18 samples did not reach a call rate of >95% applying a detection p-value filter of $1x10^{-16}$. We excluded 7 samples with gender inconsistency, no sample was outlying from the overall data structure (1st PC score of the DNA methylation values outside mean +/- 4SD). DNA methylation data of 517 samples with 466290 autosomal probes (call rate filter 95%) each were available for analysis.

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*PIAMA*

Study Population

PIAMA (Prevention and Incidence of Asthma and Mite Allergy) is a birth cohort study of children born in 1996-1997 in the Netherlands. Details of the study design have been published previously[51]. In brief, 10,232 pregnant women completed a validated screening questionnaire at their prenatal health care clinic (n=52). Based on this screening, 7,862 women were invited to participate, of whom 4,146 women agreed and gave informed consent. The study started with 3,963 newborns. Questionnaire based follow-up of the children took place at 3 months of age, yearly from 1 to 8 years of age, and at 11, 14, and 16 years of age, with clinical investigations at ages 4, 8, 12 and 16 years. Whole blood DNA was extracted of children who provided a blood sample at ages 4, 8 and 16 years.

At the age of 16 years, nasal epithelial cells were collected in two study centers (Groningen and Utrecht) by brushing the lateral area underneath the right inferior turbinate. Brushes were placed in screw-cap Eppendorf tubes and stored at -80oC until further processing. DNA was extracted from nasal brushes using DNA investigator kits (Qiagen, Benelux BV, Venlo, the Netherlands), followed by precipitation-based concentration using GlycoBlue (Ambion). DNA (500ng) was bisulphite-converted using EZ 96-DNA methylation kits (Zymo Research), following manufacturer's standard protocols. After verification of bisulphite conversion using Sanger

Sequencing, DNA concentration was normalized and samples were randomized to avoid batch effects. One standard DNA sample per chip was included in this step for quality control.

The Medical Ethical Committees of the participating institutes approved the study, and the parents and legal guardians of all participants as well as the participants themselves gave written informed consent.

Phenotype Data

*Asthma*

Asthma was defined based on the questionnaire completed by the mother when the child was eight years of age.

Children were classified as having asthma if the mother responded "yes" to the question – "Has your child ever been diagnosed by a doctor as having asthma". Further, the child was classified as asthmatic only if the mother also responded YES to either of the three following questions: 1) "whether a child had asthma in the past 12 months?", 2) "Has your child had medication for respiratory or lung problems?", or 3) Wheezing in the last 12 months

Covariates

Information on maternal age, smoking during pregnancy, asthma, education, and child's sex was collected via questionnaires completed by the mother. Maternal age was included as a continuous variable. Maternal smoking status during pregnancy was classified into three groups: non-smoker, stopped smoking in early pregnancy, and smoked throughout pregnancy. Maternal asthma was included as a dichotomous variable. Maternal educational level was categorized into three groups based on years of education: 1=primary school, lower vocational or lower secondary education; 2=intermediate vocational education or intermediate/higher secondary; 3=higher vocational education and university (high). Child's sex was included as a dichotomous variable.

DNA Methylation Data

Details of the DNA methylation measurements and quality control for the PIAMA participants were previously described[52]. Briefly, peripheral blood samples were collected from all consenting cohort participants and DNA was extracted using the QIAamp blood kit (Qiagen or equivalent protocols), followed by precipitation-based concentration using GlycoBlue (Ambion). DNA concentration was determined by Nanodrop measurement and Picogreen quantification. 500 ng of DNA was bisulphite-converted using the EZ 96-DNA methylation kit (Zymo Research), following the manufacturer's standard protocol. After verification of the bisulphite conversion step using Sanger Sequencing, genome-wide DNA methylation was measured using the Illumina Infinium HumanMethylation450 BeadChip. After normalization of the concentration, the samples were randomized to avoid batch effects. Standard male and female DNA samples were included in this step as control samples. DNA methylation data were pre-processed in R with the Bioconductor package Minfi[35], using the original IDAT files extracted from the HiScanSQ scanner. Samples that did not provide significant methylation signals in more than 10% of probes (detection P=0.01) were excluded from further analysis. Samples were also excluded in cases of low staining efficiency, low single base extension efficiency, low stripping efficiency of DNA from probes after single base extension, poor hybridization performance, poor bisulphite conversion and high negative control probe staining. Further, we used the 65 SNP probes to check for concordances between paired DNA samples from the sample individual and assessed the methylation distribution of the X-chromosome to verify gender. Paired samples with Pearson correlation coefficients <0.9 were regarded as sample mix-ups and were excluded from the study. In probe filtering[12], we excluded probes on sex chromosomes, probes that mapped on multi-loci, the 65 random SNPs assay and probes that contained SNPs at the target CpG sites with a minor allele frequency >10%. Finally, we implemented “DASEN”[26] to perform signal correction and normalization. After quality control, 226 samples and 439,306 autosomal probes remained for further analysis.

For nasal epithelium, in total 479 nasal epithelium DNA samples were hybridized to the Infinium HumanMethylation450 BeadChip array (Illumina, San Diego, CA). DNA methylation data were pre-processed with Bioconductor package Minfi3, using the original IDAT files from the HiScanSQ scanner. Samples with call rate <99% were removed. We used 65 SNP probes to check for concordance between paired DNA samples (nasal and blood DNA samples from the same subjects were hybridized in the same experiments); paired samples with Pearson correlation coefficient <0.9 were excluded, as were probes on sex chromosomes, probes that mapped to multiple loci, 65 SNP-probes, and probes containing SNPs at the target CpG sites with a MAF>5%. “DASEN” was used to perform signal correction and normalization. After QC, 455 samples and 436,824 probes remained.

Acknowledgements

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*Raine Study*

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Study Population

The Western Australian Pregnancy Cohort (Raine) Study (http://www.rainestudy.org.au) is a longitudinal Australian birth cohort that has serially assessed the offspring of 2900 pregnant women from 18 weeks' gestation in utero. Follow-up of the offspring has been undertaken at 1, 2, 3, 5, 8, 10, 14, 17, and 24 years[53, 54]. DNA was extracted from whole blood samples (n=1137) obtained at 17-year-old follow up.

Asthma

Asthma was ascertained at 6- and 17-year-old follow up time-points, by questionnaire answered by the primary care-giver. At the 6-year-old follow up, asthma was defined as a prior doctor diagnosis or prior wheeze or asthma medication in last 12 months. At 17 years it was defined by presence of wheeze in last 12 months. For the current analysis, asthma was defined as asthma diagnosis by age 17 years plus wheeze in the past 12 months reported at that same time point. Children with report of asthma at age 6, but not at age 17 were excluded from the comparison group.

DNA Methylation Data

Bisulphite conversion was prepared from whole blood cells by standard phenol:chloroform extraction and ethanol precipitation. Processing of the Illumina Infinium HumanMethylation450 BeadChips was carried out by the Centre for Molecular Medicine and Therapeutics (CMMT) http://www.cmmt.ubc.ca. The raw IDAT files were imported into R using the rnb.run.import() function available in the *RnBeads* package. Two packages were used to perform quality control checks of the samples; *shinyMethyl*[33] and *MethylAid*[32]. Three samples were evident as outliers based on the output from *shinyMethyl* and *MethylAid*. Gender was inferred using the rnb.execute.gender.prediction() function available in the *RnBeads* package[55]. When predicted gender was compared to known gender there was a single discrepancy. 58 of the samples were run in duplicate or triplicate and the 65 SNP probes present on the BeadChip were used to assess genetic similarity between these individuals as a check for sample mix-ups. The rnb.plot.snp.heatmap() function available in the *RnBeads* package was used to produce a heatmap of $\beta$ values. One contaminated sample was excluded based on this plot. Intentional SNP probes (n=65), sex chromosome probes (n=11,648) and probes with a detection *p*-value greater than 0.05 in any sample (n=10,777) were removed. A further 160 probes with low bead counts (bead counts less than 3 in more than 5% of samples) were removed.

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*SLSJ – Analysis of asthma in relation to methylation in purified eosinophils*

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Study Population

The families (1394 individuals distributed in 271 families) included in the Saguenay-Lac-Saint-Jean asthma familial cohort[56] were recruited through probands with documented allergic asthma. To be included in the study, a family needs to fulfill these criteria: the two parents must be available for clinical assessment, one parent must be unaffected and all grand-parents must be of French-Canadian origin. Clinical evaluation (measures of lung function: forced expiratory volume in 1 s ($FEV_1$) and methacholine challenge ($PC_{20}$)), white blood cell counts, skin prick test for allergy and a standardized questionnaire were completed for all individuals.

Acknowledgements

The Saguenay-Lac-Saint-Jean asthma familial cohort was supported by Laprise grants from the Canadian Institute of Health Research (CIHR).

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*STOPPA*

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Study Population

The Swedish Twin study On Prediction and Prevention of Asthma (STOPPA) is a twin cohort study including n=752 individuals[57]. Study participants were selected from an on-going data collection within the Child and Adolescent Twin study in Sweden (CATSS)[58] based on the pair's asthma status. Approximately one third each of asthma concordant (ACC), asthma discordant (ADC) and healthy concordant (HCC) pairs took part in clinical examinations including questionnaires, lung function testing (spirometry with reversibility test and fractional exhaled nitric oxide, FeNO) and collection of biosamples. The twins were 9-14 years old at the time of invitation to the study.

The study population has been linked to the Swedish population-based Medical Birth Register for information on pregnancy and delivery outcomes, the National Patient Register for all in- and outpatient diagnoses and the Swedish Prescribed Drug Register for data on prescribed drugs since 2005. Biosamples include whole blood (collected in 4 ml EDTA tubes and stored at -80°C) from n=708 twins. Further details regarding STOPPA have been provided in a separate publication[57].

Phenotype Data

*Asthma*

In STOPPA, childhood asthma is defined based on the following sources;

1) **Questionnaires** to parents and children distributed at the clinical examinations within STOPPA.
2) **A telephone interview** with the study participants' parents when the children were 9 years of age (within the Child and Adolescent Twin Study in Sweden, CATSS)
3) **Population-based register data** covering asthma diagnoses in in- and outpatient care (National Patient Register, NPR) and dispensed asthma medication (Swedish Prescribed Drug Register, SPDR).
    a) The presence of an asthma diagnosis prior to the clinical examination, from either the STOPPA questionnaires (parent -reported), the CATSS telephone interview (parent-reported), or that had been recorded in the NPR.

and

b) At least one of the following:
    *i)* Yes to *"Does your child have asthma?"* (STOPPA parent questionnaire) or *"Do you have asthma?"* (STOPPA twin questionnaire)

ii) Yes to "Has your child had wheezing or whistled breathing at some point during the last 12 months?" (STOPPA parent questionnaire) or "Have you had wheezing or whistled breathing at some point during the last 12 months?" (STOPPA twin questionnaire)
iii) Yes to "Does your child currently take any asthma medication? (STOPPA parent questionnaire)
iv) During the year prior to the clinical examination in STOPPA, the child fulfilled either of the following validated[59] asthma medication combinations in the SPDR:
    (1) Two or more dispenses of inhaled corticosteroids (ICS, ATC code R03BA), fixed combinations of selective beta-2-agonists and ICS (β2-ICS, ATC code R03AK), or Leukotriene Receptor Antagonists (LTRA, ATC code R03DC).
    (2) Three or more dispenses of selective beta-2-agonists (β2, ATC code R03AC), ICS, β2 + ICS or LTRA, within one year.

The **reference group** for school age asthma were those who answered No to *"Has your child ever had wheezing or whistled breathing?"* (STOPPA parent questionnaire). There was no question regarding asthma ever in STOPPA.

DNA Methylation Data

DNA was extracted from whole blood using the Chemagic Star 400 kit (PerkinElmer chemagen, Baesweiler, Aachen, Germany) according to a standardized protocol. Samples allocation was performed by complete randomization of samples between analysis plates and chips, with the exception that samples from twin pairs were kept within the same chip to allow for within-pair comparisons free of batch effects. Laboratory analyses took place at the Mutation Analysis Facility (MAF), Karolinska Institutet, Stockholm, Sweden, using the Infinium HumanMethylation450 Beadchip Kit (Illumina, Inc., San Diego, California, USA).

Quality control, sample and probe filtering were performed using RnBeads[55]. Predicted gender and phenotype-based sex were compared and matched for all samples. Probes were filtered out due to overlap with single nucleotide polymorphisms or specific nucleotide contexts, unreliable measurements (defined as detection p-values > $5x10^{-8}$), or location on sex chromosomes, leaving approximately 455,000 CpG probes for final analyses when using the full data set. The methylation data were normalized using the dasen method, which includes background adjustment and separate between-array normalization of Type I and Type II probes[26]. Methylation at each CpG site was expressed as beta values.

To allow for all twins to be retained within the sample, generalized estimating equation (GEE) models are generally used in analyses using STOPPA data. By specifying twin pairs as clusters, the GEE method produces robust standard errors and corrects for within-cluster (i.e. within-pair) correlations. The parameter estimates themselves are not affected. For these analyses the R package drgee is used[60].

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## 2. Meta-Analysis Details

### 2.1. PACE Consortium

The Pregnancy and Childhood Epigenetics (PACE) Consortium is an international consortium of cohorts with Illumina Infinium HumanMethylation450 BeadChip (450K) data measured at birth (ie: in newborns) or in childhood[61].

The studies participating in the prospective analysis of newborn DNA methylation data in relation to the development of asthma are: the Avon Longitudinal Study of Parents and Children (ALSPAC), the Children's Health Study (CHS), Etudes des Déterminants pré et postnatals précoces du développement et de la santé de l'Enfant (EDEN, the Generation R Study, the Genome-Wide Population-based Association Study of Extremely Overweight Young Adults (GOYA) study (part of the Danish National Birth Cohort), Infancia y Medio Ambiente (INMA), the Isle of Wight (IoW) study, two independent datasets from the Norwegian Mother and Child Cohort Study (MoBa1 and MoBa2), and the Newborn Epigenetics Study (NEST).

The studies participating in the cross-sectional analyses of asthma in relation to DNA methylation measured in childhood are two independent cohorts from the Children's Allergy Environment Stockholm Epidemiology study (BAMSE; BAMSE-EpiGene and BAMSE-MeDALL), the European Childhood Obesity Project (CHOP) Study, the Genes-environments and Admixture in Latino Americans (GALA II) study, the Inner City Asthma Consortium (ICAC), the Northern Finish Birth Cohort (NFBC 1986), the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study, the Western Australian Pregnancy Cohort (Raine) Study, and the Swedish Twin Study on Prediction and Prevention of Asthma (STOPPA).

### 2.2. Harmonization of Childhood Asthma and Wheeze Outcomes

We developed a common definition of asthma to be generated from questionnaire data by each cohort. Asthma cases were children with doctor diagnosis of asthma and report of at least one of the following: (a) current asthma, (b) asthma (or asthma symptoms such as wheeze) in the past year, or (c) asthma medication use in the last year. The time point for the assessment of asthma was school age – defined as at least 5 years of age. Controls were children that had never had asthma. Details of cohort specific definitions are provided in the previous section.

### 2.3 Methylation Data Measurements and Quality Control

DNA methylation was measured either in newborns or older children using the Illumina 450K platform. All cohorts analyzed untransformed beta values. Cohorts performed their preferred quality control and normalization methods (see previous section). We had previously found that different pre-processing or normalization methods do not have an effect on meta-analysis results[46]. Cohorts corrected for batch effects in their data using ComBat[62] or by including a batch covariate in their models. To reduce the impact of severe outliers in the methylation data on the meta-analysis, all cohorts trimmed the methylation beta values by removing, for each CpG, observations more than three times the interquartile range below the 25$^{th}$ percentile or above the 75$^{th}$ percentile (outer fences)[63].

Cohorts retained all CpGs that passed quality control and did not remove CpGs that were included on lists of polymorphic, SNP, or non-specific probes such as in Chen, et al. [12]. Instead these were evaluated post-hoc in the meta-analysis results. The distribution of all individual significant CpGs that appear on these lists were visually assessed for multi-modality in three of the larger cohorts (MoBa1, Generation R, and STOPPA).

### 2.3. Cohort Specific Statistical Analyses

The association of methylation and asthma was assessed using logistic regression. Covariates included in the adjusted models were maternal age (continuous), maternal smoking status (did not smoke during pregnancy, smoked early then quit, smoked throughout pregnancy), maternal asthma (yes or no), child's sex, and maternal socioeconomic status (generally categorical maternal education). As noted above, Cohorts corrected for batch effects in their data using ComBat[62] or by including a batch covariate in their models. Cohorts that have oversampled or selected on a phenotype included this selection variable in the analysis. We also adjusted for potential confounding by cell type using estimated cell type proportions calculated using the Houseman method[64] from either the cord blood cell type reference panel[65] for newborn cohorts (CD8T, CD4T, NK, Bcell, Mono, Gran, and nRBC) or the adult blood cell type reference panel[66] for cohorts with older children (CD8T, CD4T, NK, Bcell, Mono, Eos, and Neu). A crude model with adjustment only for optional batch, ancestry, and selection covariates was also done. The primary models presented include adjustment for covariates as well as cell type.

### 2.4. Meta-analyses Methods

We performed inverse variance-weighted fixed effects meta-analysis with METAL[67] and accounted for multiple testing by controlling for the false discovery rate (FDR) at 0.05[68]. As a sensitivity analysis, we also performed random effects meta-analysis using the METASOFT tool[69].

### 2.5. Enhanced CpG Annotation

The official gene name was noted for each CpG via Illumina's genome coordinate 40. As in Joubert, et al. [46], we enhanced the annotation provided by Illumina by using the UCSC Genome Browser (including data the RefSeq and Ensembl databases) to identify the UCSC Known Gene. UCSC genes occasionally differ from the Illumina annotation file RefSeq genes. All of the annotations use the human February 2009 (GRCh37/hg19) assembly. UCSC Known Gene annotations include nearest genes within 10 Mb of each CpG and thus fill in gene names missing in the Illumina annotation file.

### 2.6. Analysis of Differentially Methylated Regions

Differentially methylated regions (DMRs) were assessed via two methods, comb-p[70] and DMRcate[71]. Among the available methods, these two accept p-values as input, and thus can be used in the context of meta-analysis. Comb-p and DMRcate use different algorithms to identify significantly differentially methylated regions. Comb-p uses a one-step Šidák correction method for multiple comparisons[72], while DMRcate uses an FDR method[68]. Each method requires the input of parameters to be used in selecting the regions and these were chosen such that they were most similar to each other as detailed below. To reduce false positives, we only considered a DMR to be statistically significant if it was statistically significant in both packages, according to the definition used in each. DMRcate annotates CpGs using the UCSC Refgene in the Illumina annotation file.

For Comb-p, the input parameters found in Online Repository Methods Table 1 were used. For DMRcate, the input parameters found in Online Repository Methods Table 2 were used.

### 2.7. Lookup of significant DNA methylation findings in previous literature

We performed a literature review of all DNA methylation and asthma association studies to identify genes reported as differentially methylated in relation to asthma or wheeze. The literature review was performed using the below PubMed search terms (originally on June 3, 2016 and updated 1/12/2018): (((((("Asthma"[Majr]))) OR (((((airways hyper responsiveness[Title/Abstract]) OR airway reactivity[Title/Abstract]) OR bronchodilator response[Title/Abstract]) OR asthma[Title/Abstract]) OR wheez*[Title/Abstract] OR FENO[Title/Abstract]))) AND (((("Methylation"[Majr]) OR "DNA Methylation"[Majr])) OR ((methylation[Title/Abstract]) OR DNA methylation[Title/Abstract])))

We additionally identified genes related to asthma in genome-wide association study (GWAS) results in the GWAS catalog[73](p-value<$5x10^{-8}$; downloaded 6/29/2016) and updated subsequently using the Genome-Wide Repository of Associations Between SNPs and Phenotypes (GRASP) database[74](p-value<$1x10^{-8}$; downloaded 3/7/2017). We updated the literature review on 01/12/2018 to include novel loci identified in the largest GWAS meta-analysis of asthma to date[75].

### 2.8. Functional follow-up of significant DNA methylation findings

#### *2.8.1. Analysis of DNA Methylation in relation to Expression of Nearby Genes*

To identify associations between methylation levels and the expression levels of nearby genes (cis-eQTMs) we analyzed methylation and blood gene expression available in the same subjects from several sources. The association of gene expression with methylation was assessed within a 500kb window for each individual CpG (+/-250kb from the CpG). For differential methylated regions, we used a window 250kb up- and down-stream of the end and start site of each region.

There were five datasets available with expression and methylation measured in the blood from the same subjects at different periods of the life course. The largest dataset was adults with 3,096 samples from four cohorts in the Netherlands (Biobank-Based Integrative Omics Studies (BIOS) consortium) in which gene expression was assessed by RNA-Seq[76, 77]). The BAMSE study consisted of 248 samples from older children (16 years) in which gene expression was assessed using the Affymetrix Human Transcriptome Array (HTA 2.0)[78]. From the INMA study we analyzed 112 samples with methylation in cord blood and 113 samples with methylation at age 4 years, both compared to gene expression measured at age four also using the Affymetrix Human Transcriptome Array (HTA 2.0) (Affymetrix, Inc, Santa Clara, CA) (ref). From the IoW cohort we analyzed paired methylation and gene expression data from cord blood samples from 158 newborns where gene expression was measured using the Agilent one-color microarray (Agilent Technologies, Santa Clara, C). In all of these studies, linear regression analysis took into account cohort specific joint sources of variability (age, gender, differential cell counts, batch effects for both methylation and gene expression). Additionally, we assessed correlation between gene expression and methylation in 38 cord blood samples from Mexican newborns deposited in Gene Expression Omnibus (GEO) [GSE62924 for methylation[79], GSE48354 for gene expression measured using the Affymetrix HTA 2.0 Array[80]]. For this study, Pearson correlation coefficients were calculated because covariates were not available for linear regression analysis. Given the modest size of the studies of newborns or children, we report association based on nominal significant (P<0.05). For the much larger BIOS study of adults, the FDR was used to account for multiple testing. In all studies, methylation was measured using the Ilumina450K array.

### 2.8.2. Functional Annotation

Functional annotation was done using tracks customized to DNA methylation in the UCSC Genome Browser. See Online Repository Methods Table 3 for detail on specific tracks. We examined regions to which the genome-wide significant individual CpGs annotated as well as the significant differentially methylated regions (DMRs).

### 2.8.3. Search for Druggable Targets

We matched the list of genes to which our asthma-associated CpGs and DMRs annotated against the ChEMBL database (v22.1, updated on November 15, 2016)[81] to identify genes as targets of approved drugs or drugs in development. In addition, we used the Ingenuity Pathway Analysis[82] (IPA, www.ingenuity.com, content of 2017-06-22) to identify drug targets and upstream regulators of the gene lists. We reported the upstream regulators in the following categories, biologic drug, chemical - endogenous mammalian, chemical - kinase inhibitor, chemical – other, chemical drug, chemical reagent, and chemical toxicant.

### 2.8.4. Identification of tissue and cell specific signals using eFORGE

To identify tissue or cell type specific signals in EWAS results, we used eFORGE software[83]. Input for eFORGE was a list of FDR significant CpGs: 9 CpGs for newborn analysis and 179 for older kids analysis. We examined enrichments for DNase I hypersensitive sites (DHSs) or histone marks. The software provides DHS data from the Roadmap Epigenomics, ENCODE, and BLUEPRINT projects; five separate histone marks (H3K27me3, H3K36me3, H3K4me3, H3K9me3, and H3K4me1) from the Roadmap Epigenomics project. We used default options (proximity distance to filter out nearby CpGs = 1 kb, the number of background CpG sets = 1000) to run the analyses.

### 2.8.5. Pathway Analysis

We performed pathway and network analyses using Ingenuity Pathway Analysis (IPA) ((QIAGEN Inc., HTTPS://WWW.QIAGENBIOINFORMATICS.COM/PRODUCTS/INGENUITY-PATHWAY-ANALYSIS)[82].

## 3. Online Repository Methods Tables

Online Repository Methods Table 1: Input parameters used in the comb-p algorithm

| Parameter | Value | Description |
|---|---|---|
| **dist** | 1000 | Maximum distance to search for adjacent peaks. |
| **seed** | 0.05 | A value must be at least this large/small in order to seed a region. |
| **region-filter-p** | 0.01 | Maximum adjusted region-level p-value to be reported in final output. |
| **region-filter-n** | 2 | Require at least this number of probes for a region to be reported in final output. |

Online Repository Methods Table 2: Input parameters used in the DMRcate

| Parameter | Value | Description |
|---|---|---|
| **lambda** | 1000 | Gaussian kernel bandwidth for smoothed-function estimation. Gaps ≥ lambda between significant CpG sites will be in separate DMRs. |
| **C** | 2 | Scaling factor for bandwidth. Gaussian kernel is calculated where lambda/C = sigma. Empirical testing shows that, for 450k data when lambda = 1000, near-optimal prediction of sequencing-derived DMRs is obtained when C is approximately 2. |
| **pcutoff** | 0.01 | p-value cutoff to determine DMRs. |
| **min.cpgs** | 2 | Minimum number of consecutive CpGs constituting a DMR. |

Supplementary Methods Table 3: UCSC Genome Browser customized track details.

| Category | Label | Description |
|---|---|---|
| Our EWAS results | CpGs | CpGs included in the meta-analysis: red – p-value < FDR; light blue – FDR ≤ p-value < 0.001; royal blue – 0.001 ≤ p-value < 0.05; black – p-value ≥ 0.05 |
| | DMRs | Significant DMRs |
| UCSC Genes | Gene Name | UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics) |
| Human mRNAs | Human mRNAs | Human mRNAs from GenBank |
| CpG Islands | CpG Islands | Islands<300 bases are light green |

| | | |
|---|---|---|
| SNP | Common SNPs | Simple Nucleotide Polymorphisms (dbSNP 147) found in ≥ 1% of samples<br><br>(https://genome.ucsc.edu/cgi-bin/hgTrackUi?g=snp147Common&hgsid=560497663_3Vf9tNVA6AoTDdnAgU0NTbvVGlc8&db=hg19)<br><br>- SNP feature for color specification<br><br>Unknown and intron: black; Coding-synonymous: green; Coding – non-synonymous: red; untranslated: blue, Splice site: red |
| | SNPs | Sequences in scientific articles (https://genome.ucsc.edu/cgi-bin/hgTrackUi?hgsid=560497663_3Vf9tNVA6AoTDdnAgU0NTbvVGlc8&g=pubs)<br><br>- Filter articles by keywords in abstract, title or authors: 'lung' |
| DNaseI Hypersensitivity Site | Master DNaseI HS | DNaseI Hypersensitive Site Master List (125 cell types) from ENCODE/Analysis |
| DNaseI Hypersensitivity Site<br><br>Open chromatin | FL DNase 76 46,<br><br>FL DNase 27 17,<br><br>FL DNase 48 07,<br><br>FL DNase 90 85,<br><br>FL DNase 47 66,<br><br>FL DNase 66 24,<br><br>FL DNase 66 51,<br><br>FL DNase 84 09,<br><br>FL DNase 84 20,<br><br>FL DNase 65 27,<br><br>FL DNase 99 61,<br><br>FL DNase 19 73 | DNase Hypersensitivity Raw Signal from REMC/UW: Fetal Lung |
| | H1-hESC Syn PK | H1-hESC DNaseI/FAIRE/ChIP Synthesis from ENCODE/OpenChrom. |

| | | |
|---|---|---|
| | | - Open Chromatin (OC) code (detection assay) and color (level of validation determined by its OC Code and its statistical significance) are below.<br><br>Validated, OC Code=1, Black; Open Chromatin, OC Code = 2 or 3, Blue; DNase, OC Code = 2, Blue (high significance), Green (low significance); FAIRE, OC Code = 3, Blue (high significance), Dark Red (low significance); ChIP-seq, OC Code = 4, Pink |
| Chromatin State Segmentation | NHLF ChromHMM | NHLF Chromatin State Segmentation by HMM from ENCODE/Broad.<br><br>The fifteen states of the HMM, associated segment color, and annotations are below.<br><br>State 1 - Bright Red - Active Promoter<br><br>State 2 - Light Red -Weak Promoter<br><br>State 3 - Purple - Inactive/poised Promoter<br><br>State 4 - Orange - Strong enhancer<br><br>State 5 - Orange - Strong enhancer<br><br>State 6 - Yellow - Weak/poised enhancer<br><br>State 7 - Yellow - Weak/poised enhancer<br><br>State 8 - Blue - Insulator<br><br>State 9 - Dark Green - Transcriptional transition<br><br>State 10 - Dark Green - Transcriptional elongation<br><br>State 11 - Light Green - Weak transcribed<br><br>State 12 - Gray - Polycomb-repressed<br><br>State 13 - Light Gray - Heterochromatin; low signal<br><br>State 14 - Light Gray - Repetitive/Copy Number Variation<br><br>State 15 - Light Gray - Repetitive/Copy Number Variation |

| | | |
|---|---|---|
| Chromatin State Segmentation<br><br>Histone Modification | LNG | Chromatin State Segmentations from the cell types used by Roadmap Consortium.<br><br>The HMM states, associated color, and annotations are below.<br><br>State 1 - Red - TssA (Active_TSS)<br><br>State 2 - OrangeRed - TssAFlnk (Flanking_Active_TSS)<br><br>State 3 - LimeGreen - TxFlnk (Transcr_at_gene_5_and_3primer)<br><br>State 4 - Green - Tx (Strong_transcription)<br><br>State 5 - DarkGreen - TxWk (Weak_transcription)<br><br>State 6 - GreenYellow - EnhG (Genic_enhancers)<br><br>State 7 - Yellow - Enh (Enhancers)<br><br>State 8 - MediumAquamarine - ZNF/Rpts (ZNF_genes&repeats)<br><br>State 9 - PaleTurquoise - Het (Heterochromatin)<br><br>State 10 - IndianRed - TssBiv (Bivalent/Poised_TSS)<br><br>State 11 - DarkSalmon - BivFlnk (Flanking_Bivalent_TSS/Enh)<br><br>State 12 - DarkKhaki - EnhBiv (Bivalent_Enhancer)<br><br>State 13 - Silver - ReprPC (Repressed_PolyComb)<br><br>State 14 - Gainsboro - ReprPCWk (Weak_Repressed_PolyComb)<br><br>State 15 - White - Quies (Quiescent/Low) |
| | Lung H3K27ac 01 61,<br><br>Lung H3K27ac 02 48,<br><br>Lung H3K36me3 01 64,<br><br>Lung H3K36me3 02 14, | Histone Modification by ChIP-seq from REMC/UCSD: Lung |

| | | |
|---|---|---|
| | Lung H3K4me1 01 66,<br><br>Lung H3K4me1 02 98,<br><br>Lung H3K4me3 02 33,<br><br>Lung H3K9me3 01 84,<br><br>Lung H3K9me3 02 49,<br><br>Lung Input 01 53,<br><br>Lung Input 02 61,<br><br>Lung Input 02 96 | |
| Genomic Footprinting | FL DGF 66 24 | Digital Genomic Footprinting (HOTSPOT_SCORE=0.5004 Pcnt=20): Fetal Lung |
| Gene expression | GTEx | Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors) – subset of 4 tissues: Whole Blood, Lung, Cells – EBV-transformed lymphocytes, and Cells – Transformed fibroblasts |
| | Lung F YFC4 | GTEx RNA-seq read coverage for female donor sample YFC4 (20-49 years): Lung |
| | wholBlood F YFC4 | GTEx RNA-seq read coverage for female donor sample YFC4 (20-49 years): Whole Blood |
| | Lung M ZPU1 | GTEx RNA-seq read coverage for male donor sample ZPU1 (20-49 years): Lung |
| | wholBlood M ZPU1 | GTEx RNA-seq read coverage for male donor sample ZPU1 (20-49 years): Whole Blood |
| | Lung mRNA | RNA-seq signal from REMC: Lung |
| Transcription Factor Binding Sites (TFBS) | | Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs – subset of asthma-related TFBS: ATF1, ATF2, BCLAF1, CREB1, E2F1, EBF1, ELK1, EP300, ETS1, FOS, GABPA, GATA1, GATA3, GTF2B, HDAC1, HDAC6, HMGN3, HSF1, IRF4, JUN, KDM5A, MAFF, MYBL2, MYC, NFATC1, NFYB, NR3C1, RAD21, RELA, RUNX3, RXRA, SIN3A, SP1, SP2, SPI1, SRF, STAT1, STAT3, STAT5A, TBP, TFAP2A, UBTF, USF1, USF2, YY1 |

## 4. Online Repository Figure Legends

Figure E1: Forest plots of 9 significant CpGs from the meta-analysis of asthma in relation to newborn methylation with adjustment for covariates and cell type. These plots show the number of cases and non-cases and odds ratios (OR) and 95% confidence intervals (95% CI) for a one percent change in methylation for each cohort along with the meta-analysis results.

Figure E2: Leave out one plots for the 9 significant CpGs from the meta-analysis of asthma in relation to newborn methylation with adjustment for covariates and cell type. These plots show the untransformed regression coefficients and 95% confidence intervals for the meta-analysis of all studies and then for the meta-analysis repeated leaving each labelled cohort out, one at a time.

Figure E3. Forest plots of 179 significant CpGs from the meta-analysis of asthma in relation to methylation in children with adjustment for covariates and cell type. These plots show the number of cases and noncases and odds ratios (OR) and 95% confidence intervals (95% CI) for a one percent change in methylation for each cohort along with the meta-analysis results.

Figure E4. Leave out one plots for the 179 significant CpGs from the meta-analysis of asthma in relation to childhood methylation with adjustment for covariates and cell type. These plots show the untransformed regression coefficients and 95% confidence intervals for the meta-analysis of all studies and then for the meta-analysis repeated leaving each labelled cohort out, one at a time.

Figure E5: Functional annotation plots of 7 significant CpGs (A-I) from the meta-analysis of asthma in relation to newborn methylation with adjustment for covariates and cell type. Custom track titled “CpGs (Newborns)” show the location of the significant CpG (red) in relation to other nearby CpGs (red – p-value < FDR; light blue – FDR ≤ p-value < 0.001; royal blue – 0.001 ≤ p-value < 0.05; black – p-value ≥ 0.05).

(A) cg21486411 – CLNS1A
(B) cg16792002 – MAML2
(C) cg13427149 – GPATCH2; SPATA17
(D) cg17333211 – SCOC; LOC100129858
(E) cg02331902 – RP11-213H15.3; AK091866 (near LUCAT1)
(F) cg13289553 – SUB1
(G) cg07156990 – WDR20

Figure E6: Functional annotation plots of 34 CpGs non-singleton significant CpGs corresponding to 13 genes from the meta-analysis of asthma in relation to childhood methylation with adjustment for covariates and cell type. Custom track titled “CpGs (Older Kids)” show the location of the significant CpG (red) in relation to other nearby CpGs (red – p-value < FDR; light blue – FDR ≤ p-value < 0.001; royal blue – 0.001 ≤ p-value < 0.05; black – p-value ≥ 0.05). Custom track titled “DMRs (Older Kids)” indicates the location of the significant differentially methylated region.

Figure E7: Tissue and cell type specific enrichment pattern of CpGs significantly associated (FDR < 0.05) with asthma in relation to childhood methylation.

(A) DNase1 sites (probably transcription factor binding sites) in cell lines for H3K4me1 on Roadmap Epigenomics Project (Consolidated data)
(B) DNase1 sites (probably transcription factor binding sites) in cell lines for H3K36me3 on Roadmap Epigenomics Project (Consolidated data)

Figure E8: A heatmap is drawn using the categories of disease and biological functions, significant at p-value cutoff of 0.05 in at either newborns or children. All the categories as well as the genes are hierarchically clustered. The genes involved in newborns are colored as red and those in children as orange.

Figure E9: Density distributions of 9 significant CpGs in 2 cohorts, (A) MoBa1 and (B) Generation R from the meta-analysis of asthma in relation to newborn methylation with adjustment for covariates and cell type.

(A) MoBa1
(B) Generation R

Figure E10: Density distributions of 34 non-singleton CpGs in STOPPA from the meta-analysis of asthma in relation to childhood methylation with adjustment for covariates and cell type. Distributions of all 179 CpGs were checked (not shown).

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*Table E1* *Descriptive statistics of covariates for each cohort*

| Methylation Age Group | Cohort | Ancestry* | Total N | N cases | N controls | Age at Asthma Phenotyping (SD) | Mean maternal age (SD) | N any smoking in pregnancy | N no smoking in pregnancy | N smoking in early pregnancy | N smoking throughout pregnancy | N maternal asthma | N boys | N girls | N SES group1 ** (low) | N SES group2 ** | N SES group3 ** | N SES group4 ** (high) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Newborns | ALSPAC | EU | 688 | 88 | 600 | 7.63 (0.11) | 30.30 (4.23) | 75 | 613 | 19 | 56 | 81 | 337 | 351 | 62 | 296 | 330 | |
| | CHS | M | 229 | 39 | 190 | 6.40 (0.58) | 29.50 (5.72) | 17 | 212 | | | 21 | 91 | 138 | 75 | 121 | 33 | |
| | EDEN | EU | 150 | 34 | 116 | 5.65 (0.12) | 30.80 (5.00) | 36 | 114 | 13 | 23 | 14 | 87 | 63 | 8 | 94 | 48 | |
| | Generation R | EU | 661 | 37 | 624 | 6.20 (0.50) | 31.80 (4.00) | 162 | 499 | 64 | 98 | 46 | 344 | 317 | 239 | 422 | | |
| | GOYA | EU | 507 | 37 | 470 | 7.20 (0.12) | 29.50 (4.00) | 112 | 395 | 44 | 68 | | 250 | 257 | 50 | 169 | 288 | |
| | MoBa1 | EU | 666 | 149 | 517 | 7.14 (0.14) | 29.99 (4.28) | 175 | 491 | 88 | 87 | 68 | 347 | 319 | 44 | 223 | 296 | 103 |
| | MoBa2 | EU | 458 | 239 | 219 | 7.20 (0.28) | 30.20 (4.61) | 103 | 355 | 68 | 35 | 59 | 264 | 194 | 40 | 156 | 171 | 91 |
| | NEST | M | 213 | 45 | 168 | 7.00 (1.13) | 28.78 (6.41) | 73 | 140 | 24 | 49 | 38 | 109 | 104 | 78 | 62 | 73 | |
| Children | BAMSE EpiGene | EU | 307 | 93 | 214 | 8.33 (0.52) | 30.94 (4.32) | 31 | 276 | 3 | 28 | 34 | 160 | 147 | 45 | 262 | | |
| | BAMSE MeDALL | EU | 214 | 47 | 167 | 8.37 (0.37) | 31.32 (4.48) | 25 | 189 | 5 | 20 | 20 | 120 | 94 | 37 | 177 | | |
| | CHOP | EU | 382 | 19 | 363 | 7.10 (0.29) | 32.01 (4.24) | 76 | 306 | 18 | 58 | 11 | 183 | 199 | 68 | 200 | 114 | |
| | GALA II | M | 193 | 106 | 87 | 9.31 (0.83) | 35.03 (6.72) | 19 | 174 | 12 | 7 | 31 | 108 | 85 | 88 | 43 | 41 | 21 |
| | ICAC | AA | 187 | 92 | 95 | 9.19 (1.92) | | | | | | 8 | 96 | 91 | 147 | 40 | | |
| | NFBC 1986 | EU | 413 | 17 | 396 | 16.00 (0.38) | 29.05 (5.03) | 96 | 317 | 57 | 39 | 24 | 191 | 222 | 30 | 252 | 131 | |
| | PIAMA | EU | 197 | 15 | 182 | 8.06 (0.28) | 30.51 (3.60) | 35 | 162 | 17 | 18 | 161 | 99 | 98 | 37 | 90 | 70 | |
| | Raine Study | EU | 509 | 105 | 404 | 17.01 (0.23) | 29.66(5.73) | 130 | 379 | 51 | 79 | 69 | 248 | 261 | 51 | 109 | 140 | 209 |
| | STOPPA | EU | 460 | 137 | 323 | 12.54 (1.47) | 31.21 (4.68) | 37 | 423 | | | 65 | 244 | 216 | 21 | 119 | 105 | 215 |

* EU = European Ancestry; M = Mixed Ancestry; AA = African American Ancestry

** SES = Socioeconomic Status; each cohort used their best estimate for SES, often maternal education level.

*Table E2 All CpGs within the significant differentially methylated regions in analysis of asthma in relation to newborn methylation. Sorted by chromosomal position*

| DMR chr:pos | N CpGs (N nominal*) | CpG | CpG Position | p-value |
|---|---|---|---|---|
| chr1:1296093-1296489 | 2 (2) | cg13354934 | 1296093 | 3.68E-05 |
| | | cg14375163 | 1296488 | 1.39E-02 |
| chr1:59280290-59280842 | 5 (5) | cg17826530 | 59280290 | 9.13E-03 |
| | | cg20593826 | 59280370 | 1.01E-02 |
| | | cg08731696 | 59280489 | 6.71E-03 |
| | | cg02951357 | 59280619 | 8.05E-03 |
| | | cg16037711 | 59280841 | 2.64E-02 |
| chr1:220263017-220263699 | 11 (8) | cg17009631 | 220263017 | 2.00E-02 |
| | | cg06854438 | 220263111 | 6.35E-02 |
| | | cg07017209 | 220263177 | 3.77E-02 |
| | | cg10818272 | 220263189 | 1.14E-01 |
| | | cg23274377 | 220263237 | 3.69E-02 |
| | | cg00578530 | 220263239 | 7.47E-03 |
| | | cg04168050 | 220263278 | 1.36E-03 |
| | | cg00784308 | 220263509 | 7.05E-03 |
| | | cg20243626 | 220263520 | 5.86E-01 |
| | | cg11379360 | 220263525 | 4.77E-02 |
| | | cg00719685 | 220263698 | 1.19E-02 |
| chr2:202097062-202097608 | 5 (3) | cg04048517 | 202097062 | 2.34E-01 |
| | | cg02878216 | 202097093 | 3.99E-05 |
| | | cg19448993 | 202097129 | 7.28E-03 |
| | | cg24410214 | 202097173 | 9.46E-05 |
| | | cg20608990 | 202097607 | 2.44E-01 |
| chr2:235004843-235005012 | 2 (2) | cg03259207 | 235004843 | 8.92E-04 |
| | | cg27534679 | 235005011 | 1.70E-04 |
| chr3:194188646-194189444 | 3 (3) | cg08059402 | 194188646 | 1.66E-03 |
| | | cg13959207 | 194188988 | 5.29E-04 |
| | | cg15977148 | 194189443 | 2.24E-02 |
| chr4:113218385-113218525 | 3 (3) | cg17445830 | 113218385 | 5.05E-03 |
| | | cg15299279 | 113218437 | 9.35E-05 |
| | | cg16292983 | 113218524 | 3.83E-03 |
| chr5:64777678-64778186 | 10 (6) | cg02577849 | 64777678 | 1.03E-01 |
| | | cg24184449 | 64777750 | 3.14E-02 |
| | | cg24166172 | 64777777 | 5.49E-02 |
| | | cg10642820 | 64777786 | 3.16E-02 |
| | | cg14700821 | 64777802 | 3.89E-02 |
| | | cg10944144 | 64777807 | 8.20E-01 |
| | | cg19927028 | 64777838 | 1.15E-02 |
| | | cg14793753 | 64778097 | 8.76E-02 |
| | | cg18140645 | 64778147 | 4.28E-02 |
| | | cg26688155 | 64778185 | 5.08E-05 |
| chr5:81573780-81574461 | 11 (7) | cg08341821 | 81573780 | 2.60E-02 |
| | | cg07833035 | 81573845 | 3.44E-01 |
| | | cg27310251 | 81574067 | 4.83E-02 |
| | | cg04645034 | 81574156 | 1.14E-03 |
| | | cg01556715 | 81574292 | 2.30E-03 |
| | | cg14916917 | 81574294 | 9.71E-03 |
| | | cg26986558 | 81574325 | 2.46E-01 |
| | | cg17724054 | 81574408 | 1.90E-02 |
| | | cg05002974 | 81574439 | 5.25E-01 |
| | | cg10681725 | 81574453 | 1.71E-01 |
| | | cg10425506 | 81574460 | 1.26E-02 |
| chr5:158526108-158526694 | 6 (4) | cg27347265 | 158526108 | 3.41E-01 |
| | | cg07256113 | 158526263 | 1.11E-01 |
| | | cg17036833 | 158526332 | 1.17E-03 |
| | | cg05530568 | 158526614 | 8.00E-03 |
| | | cg17009297 | 158526642 | 2.41E-03 |
| | | cg04217450 | 158526693 | 1.36E-03 |
| chr6:291687-292824 | 9 (6) | cg07332563 | 291687 | 5.62E-02 |
| | | cg21548813 | 291882 | 4.10E-03 |
| | | cg03395511 | 291903 | 3.20E-03 |
| | | cg15383120 | 291909 | 2.50E-03 |
| | | cg18110333 | 292329 | 1.45E-02 |
| | | cg05064044 | 292385 | 1.96E-03 |
| | | cg11235426 | 292522 | 5.30E-02 |
| | | cg01516881 | 292596 | 2.73E-02 |

| | | | | |
|---|---|---|---|---|
| | | cg26668828 | 292823 | 2.24E-01 |
| chr6:26234819-26235610 | 9 (4) | cg24036126 | 26234819 | 5.76E-01 |
| | | cg23705973 | 26235061 | 7.83E-04 |
| | | cg24855943 | 26235224 | 4.05E-04 |
| | | cg21085190 | 26235254 | 4.47E-01 |
| | | cg15689967 | 26235287 | 5.50E-02 |
| | | cg25267285 | 26235290 | 1.08E-01 |
| | | cg03761746 | 26235311 | 3.46E-02 |
| | | cg25091056 | 26235462 | 9.14E-04 |
| | | cg10638657 | 26235609 | 1.49E-01 |
| chr6:29648161-29649085 | 22 (19) | cg25978138 | 29648161 | 2.28E-01 |
| | | cg11747594 | 29648225 | 1.20E-02 |
| | | cg15708526 | 29648271 | 1.02E-03 |
| | | cg04071440 | 29648275 | 8.85E-02 |
| | | cg08022281 | 29648345 | 4.94E-02 |
| | | cg10648573 | 29648348 | 2.82E-02 |
| | | cg12644888 | 29648360 | 2.14E-02 |
| | | cg22494932 | 29648379 | 5.72E-04 |
| | | cg25699073 | 29648381 | 1.91E-03 |
| | | cg07134666 | 29648400 | 2.28E-02 |
| | | cg00588198 | 29648452 | 1.67E-02 |
| | | cg16885113 | 29648507 | 9.60E-03 |
| | | cg20228636 | 29648525 | 2.17E-02 |
| | | cg11383134 | 29648590 | 9.34E-03 |
| | | cg03198009 | 29648604 | 3.17E-02 |
| | | cg03449857 | 29648623 | 2.62E-02 |
| | | cg15570656 | 29648628 | 4.84E-02 |
| | | cg02157626 | 29648736 | 1.57E-02 |
| | | cg13835168 | 29648756 | 1.70E-01 |
| | | cg08041448 | 29648901 | 4.61E-02 |
| | | cg24100841 | 29649024 | 3.15E-02 |
| | | cg19636627 | 29649084 | 1.12E-02 |
| chr6:31055396-31055503 | 5 (5) | cg15583958 | 31055396 | 1.17E-03 |
| | | cg09470958 | 31055471 | 2.45E-03 |
| | | cg15625467 | 31055486 | 2.15E-03 |
| | | cg17077639 | 31055492 | 1.28E-02 |
| | | cg26138460 | 31055502 | 1.11E-02 |
| chr6:32799997-32801050 | 13 (9) | cg01283574 | 32799997 | 4.94E-02 |
| | | cg11752893 | 32800103 | 3.97E-02 |
| | | cg12121080 | 32800427 | 4.22E-01 |
| | | cg13600652 | 32800429 | 4.20E-01 |
| | | cg12644497 | 32800444 | 3.24E-02 |
| | | cg00720839 | 32800486 | 3.65E-03 |
| | | cg16026549 | 32800519 | 1.16E-02 |
| | | cg12761728 | 32800523 | 6.14E-03 |
| | | cg07015256 | 32800541 | 4.81E-03 |
| | | cg24813704 | 32800549 | 1.45E-02 |
| | | cg21359558 | 32800563 | 1.76E-02 |
| | | cg09187413 | 32800591 | 1.99E-01 |
| | | cg24469596 | 32801049 | 5.08E-01 |
| chr7:87974722-87975316 | 4 (3) | cg27221053 | 87974722 | 9.90E-06 |
| | | cg03673737 | 87974733 | 1.02E-02 |
| | | cg10649525 | 87974756 | 2.58E-03 |
| | | cg23857078 | 87975315 | 3.80E-01 |
| chr7:106694832-106695007 | 2 (2) | cg22214581 | 106694832 | 2.16E-05 |
| | | cg15154519 | 106695006 | 5.00E-03 |
| chr7:158045980-158046359 | 6 (5) | cg27200869 | 158045980 | 2.98E-02 |
| | | cg16571642 | 158045996 | 1.01E-02 |
| | | cg06715136 | 158046025 | 1.37E-03 |
| | | cg02770061 | 158046166 | 6.25E-03 |
| | | cg06400119 | 158046222 | 3.70E-02 |
| | | cg10473311 | 158046358 | 6.17E-02 |
| chr8:33370172-33371226 | 9 (7) | cg26948599 | 33370172 | 2.41E-01 |
| | | cg04340421 | 33370637 | 1.06E-02 |
| | | cg13529074 | 33370659 | 5.59E-03 |
| | | cg11008718 | 33370666 | 9.01E-03 |
| | | cg19906737 | 33370681 | 2.21E-02 |
| | | cg22610784 | 33370693 | 5.02E-04 |
| | | cg08328324 | 33370759 | 2.07E-02 |

| | | | | |
|---|---|---|---|---|
| | | cg18030007 | 33370902 | 3.70E-03 |
| | | cg07516225 | 33371225 | 5.06E-01 |
| chr8:127889010-127889296 | 4 (4) | cg22056468 | 127889010 | 3.38E-05 |
| | | cg02411950 | 127889025 | 1.93E-03 |
| | | cg26726325 | 127889050 | 1.86E-03 |
| | | cg21238284 | 127889295 | 8.78E-03 |
| chr10:65028929-65029169 | 5 (4) | cg22492966 | 65028929 | 2.66E-04 |
| | | cg14534336 | 65028980 | 1.67E-01 |
| | | cg09254098 | 65029020 | 2.07E-03 |
| | | cg16951385 | 65029115 | 2.10E-02 |
| | | cg27596707 | 65029168 | 2.86E-02 |
| chr10:71871364-71871634 | 4 (3) | cg17523282 | 71871364 | 1.13E-03 |
| | | cg03096811 | 71871388 | 3.52E-04 |
| | | cg02735204 | 71871463 | 1.08E-02 |
| | | cg09777856 | 71871633 | 1.58E-01 |
| chr11:268923-269469 | 5 (4) | cg02443306 | 268923 | 1.29E-02 |
| | | cg13185005 | 268950 | 8.48E-03 |
| | | cg10308673 | 268976 | 8.30E-04 |
| | | cg11546385 | 269375 | 9.60E-02 |
| | | cg02563407 | 269468 | 4.39E-02 |
| chr11:107328442-107328915 | 10 (5) | cg20965478 | 107328442 | 1.25E-01 |
| | | cg25435332 | 107328525 | 9.88E-02 |
| | | cg12301744 | 107328559 | 1.20E-01 |
| | | cg02558537 | 107328586 | 5.82E-01 |
| | | cg25102621 | 107328605 | 4.11E-02 |
| | | cg19998148 | 107328636 | 3.96E-02 |
| | | cg07444288 | 107328657 | 6.96E-04 |
| | | cg23880829 | 107328671 | 1.98E-01 |
| | | cg10872513 | 107328690 | 1.04E-03 |
| | | cg12578959 | 107328914 | 1.80E-04 |
| chr12:58329764-58330116 | 5 (4) | cg14878686 | 58329764 | 8.22E-04 |
| | | cg09932636 | 58329862 | 7.64E-02 |
| | | cg02175503 | 58329896 | 1.14E-02 |
| | | cg22764591 | 58329936 | 2.25E-02 |
| | | cg06537201 | 58330115 | 1.41E-03 |
| chr12:74931289-74932008 | 10 (8) | cg15612392 | 74931289 | 6.83E-04 |
| | | cg04707531 | 74931420 | 1.34E-02 |
| | | cg20100969 | 74931493 | 1.20E-03 |
| | | cg21144006 | 74931510 | 1.79E-02 |
| | | cg16403677 | 74931512 | 9.90E-04 |
| | | cg17824173 | 74931535 | 1.14E-02 |
| | | cg01865610 | 74931554 | 4.38E-02 |
| | | cg22232397 | 74931695 | 4.11E-01 |
| | | cg23311950 | 74931760 | 4.46E-02 |
| | | cg23798332 | 74932007 | 9.00E-01 |
| chr13:31618695-31618744 | 2 (2) | cg07321753 | 31618695 | 4.11E-03 |
| | | cg10670748 | 31618743 | 3.12E-06 |
| chr13:108953659-108954055 | 2 (2) | cg11726530 | 108953659 | 3.67E-04 |
| | | cg16929959 | 108954054 | 1.40E-03 |
| chr14:69341139-69341739 | 4 (4) | cg00000289 | 69341139 | 2.40E-02 |
| | | cg11072851 | 69341430 | 7.39E-03 |
| | | cg27036347 | 69341603 | 8.09E-04 |
| | | cg01707795 | 69341738 | 7.18E-03 |
| chr16:20774873-20775353 | 5 (4) | cg06478823 | 20774873 | 8.35E-02 |
| | | cg10060338 | 20774960 | 6.01E-03 |
| | | cg10078415 | 20775011 | 4.98E-03 |
| | | cg00394823 | 20775166 | 4.45E-03 |
| | | cg21644826 | 20775352 | 2.13E-02 |
| chr17:21029189-21029296 | 2 (2) | cg19360316 | 21029189 | 1.87E-04 |
| | | cg06582708 | 21029295 | 5.92E-04 |
| chr17:74667833-74668253 | 6 (4) | cg04684864 | 74667833 | 1.12E-03 |
| | | cg03874568 | 74667923 | 9.02E-01 |
| | | cg09326547 | 74667999 | 1.70E-03 |
| | | cg05121093 | 74668089 | 3.13E-04 |
| | | cg09509528 | 74668195 | 1.29E-06 |
| | | cg17177017 | 74668252 | 4.56E-01 |
| chr18:47813745-47815431 | 11 (8) | cg27250841 | 47813745 | 2.22E-02 |
| | | cg22433261 | 47813856 | 1.25E-02 |
| | | cg00418882 | 47814150 | 1.31E-03 |

| | | | | |
|---|---|---|---|---|
| | | cg13423076 | 47814178 | 3.38E-02 |
| | | cg07675399 | 47814227 | 3.78E-01 |
| | | cg20016845 | 47814312 | 3.63E-01 |
| | | cg02159718 | 47814464 | 5.65E-02 |
| | | cg27419474 | 47814612 | 1.63E-02 |
| | | cg21134610 | 47815407 | 1.42E-02 |
| | | cg15632775 | 47815417 | 7.91E-03 |
| | | cg11871295 | 47815430 | 2.30E-02 |
| chr21:36421467-36421956 | 6 (3) | cg01519261 | 36421467 | 5.67E-02 |
| | | cg04915566 | 36421472 | 3.92E-04 |
| | | cg13030790 | 36421503 | 4.93E-01 |
| | | cg15242225 | 36421857 | 5.48E-04 |
| | | cg19836199 | 36421941 | 1.48E-03 |
| | | cg08443845 | 36421955 | 1.19E-01 |
| chr22:24372913-24374013 | 12 (7) | cg20007245 | 24372913 | 1.61E-02 |
| | | cg04824771 | 24372921 | 1.86E-01 |
| | | cg24565820 | 24372926 | 3.84E-02 |
| | | cg10150615 | 24372951 | 5.24E-01 |
| | | cg18538332 | 24372958 | 7.44E-01 |
| | | cg23131131 | 24373011 | 8.83E-02 |
| | | cg25703541 | 24373054 | 7.83E-03 |
| | | cg02953382 | 24373134 | 2.88E-03 |
| | | cg04234412 | 24373322 | 5.03E-03 |
| | | cg12419862 | 24373484 | 8.06E-05 |
| | | cg09033563 | 24373618 | 3.54E-04 |
| | | cg21256200 | 24374012 | 4.33E-01 |

* p-value<0.05

*Table E3* *Nine significant (FDR<0.05) CpGs from the meta-analysis of asthma in relation to newborn methylation with adjustment for covariates and cell type, and look up of results for same CpGs without cell type adjustment and without any adjustment*

| CpG | chr:pos | UCSC RefGene Name | UCSC Known Gene* | Covariates + Cell Type | | | | | Covariates | | Crude | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | OR** (CI) | P-value | HetPVal | RE OR** (CI) | RE p-value | OR** (CI) | P-value | OR** (CI) | P-value |
| cg21486411 | chr11:77348243 | *CLNS1A* | *CLNS1A* | 1.13 (1.08,1.18) | 3.43E-07 | 0.3090 | | | 1.11 (1.06,1.15) | 1.97E-06 | 1.10 (1.05,1.14) | 8.35E-06 |
| cg16792002 | chr11:95788886 | *MAML2* | *Mir_548* | 0.95 (0.93,0.97) | 5.59E-07 | 0.7276 | | | 0.95 (0.94,0.97) | 2.67E-06 | 0.96 (0.94,0.98) | 5.05E-05 |
| ch.11.109687686R | chr11:110182476 | | | 1.08 (1.05,1.11) | 7.06E-07 | 0.3949 | | | 1.05 (1.03,1.08) | 5.29E-05 | 1.05 (1.02,1.07) | 2.50E-04 |
| cg13427149 | chr1:217804379 | *GPATCH2;SPATA17* | *GPATCH2* | 1.19 (1.11,1.27) | 8.04E-07 | 0.8095 | | | 1.17 (1.10,1.25) | 4.51E-07 | 1.15 (1.08,1.22) | 8.26E-06 |
| cg17333211 | chr4:141294016 | *SCOC* | *LOC100129858* | 1.13 (1.08,1.19) | 8.25E-07 | 0.4246 | | | 1.10 (1.05,1.15) | 5.24E-05 | 1.08 (1.04,1.13) | 1.52E-04 |
| cg02331902 | chr5:90610303 | | *AK091866* | 1.12 (1.07,1.18) | 8.37E-07 | 0.9151 | | | 1.10 (1.05,1.14) | 5.27E-05 | 1.09 (1.05,1.13) | 4.03E-05 |
| cg13289553 | chr5:32585524 | *SUB1* | *SUB1* | 1.14 (1.08,1.20) | 8.68E-07 | 0.0392 | 1.13 (1.04,1.23) | 4.00E-03 | 1.10 (1.04,1.15) | 8.80E-05 | 1.10 (1.05,1.15) | 1.02E-04 |
| ch.6.1218502R | chr6:51250028 | | | 1.27 (1.15,1.39) | 9.32E-07 | 0.7301 | | | 1.16 (1.06,1.26) | 1.06E-03 | 1.13 (1.04,1.23) | 3.55E-03 |
| cg07156990 | chr14:102685678 | *WDR20* | *WDR20* | 0.87 (0.83,0.92) | 9.54E-07 | 0.2642 | | | 0.89 (0.85,0.94) | 6.02E-06 | 0.89 (0.85,0.94) | 7.18E-06 |

* Annotation based on UCSC Known Gene also fills in nearest gene within 10 MB.

** Odds ratio of developing asthma for a 1% absolute increase in methylation.

*Table E4* *Genes previously associated with childhood asthma identified from literature review in either methylation or GWAS of asthma.*

| | | | | | |
|---|---|---|---|---|---|
| ADAM17 | FCER2 | IL2RA | LOC105373951 | NOTCH4 | SLC38A6 |
| ADRB2 | FLJ41481 | IL2RB | LOC105374811 | NPSR1 | SMAD3 |
| AHR | FOXP2 | IL33 | LOC105375647 | NRG1 | SNTB1 |
| AK5 | FOXP3 | IL4 | LOC105375922 | NTF3 | STAC2 |
| AKAP6 | GATA3 | IL4R | LOC105375976 | OR51A7 | STARD3 |
| ALOX12 | GC | IL5 | LOC105376400 | ORMDL1 | STAT6 |
| ARG1 | GSDMA | IL6 | LOC105376583 | ORMDL3 | SYNM |
| ARG2 | GSDMB | IL6R | LOC105376673 | PAPLN | TBCD |
| ARMC10 | GTF3AP1 | INPP4B | LOC105376928 | PBX2 | TBX21 |
| BRD2 | HCG23 | KCNH1 | LOC105377623 | PDE4D | TBX5 |
| BTNL2 | HERC2 | KCNQ4 | LOC105377670 | PGAP3 | TCAP |
| C11orf30 | HGC6.3 | KIAA1244 | LOC105377671 | PNMT | TENM3 |
| C1orf53 | HLA-DOA | KIAA1598 | LOC105378906 | PPP3CA | TET1 |
| C6orf10 | HLA-DPA1 | LCE5A | LOC105378907 | PSMD3 | TGFB1 |
| CCDC40 | HLA-DQA1 | LEP | LOC105379121 | PYHIN1 | TLR1 |
| CCL5 | HLA-DQA2 | LIF | LOC105379200 | PYY2 | TNFa |
| CDC14B | HLA-DQB1 | LINC01565 | LOC284661 | RAD50 | TNXB |
| CDH17 | HLA-DRA | LOC100130207 | LOC727896 | RAM19A4 | TOP2A |
| CDHR3 | HLA-DRB1 | LOC100131635 | LOC727896;LPIN2 | RANBP6 | TSLP |
| CDK2 | HLA-DRB5 | LOC100216346 | LOC90246 | RAP2B | TUSC3 |
| CHI3L1 | HNMT | LOC100996770 | LPIN2 | RBP1 | TYRP1 |
| CLEC16A | HPSE2 | LOC101927335 | LRRC3C | RNA5SP299 | USP38 |
| COL12A1 | HTATIP2 | LOC101928813 | MAX | RNA5SP508 | WDR36 |
| CRB1 | HTR5A | LOC101928947 | ME1 | RORA | ZFPM1 |
| CRNN | IKZF3 | LOC101929163 | MED24 | RPL21P96 | ZNF432 |
| CTD-2350J17.1 | IKZF4 | LOC101929497 | MIR8084 | RPS3AP21 | ZNF614 |
| CUX1 | IL13 | LOC102725019 | MLLT3 | RTP2 | ZNF616 |
| DDIT4L | IL18R1 | LOC102725082 | MMP13 | SCARB1 | ZNF680 |
| DENND1B | IL18RAP | LOC105369165 | MNAT1 | SEC22B | ZNF841 |
| ERBB2 | IL1R2 | LOC105369563 | MTUS1 | SH2B3 | ZNF90P3 |
| ETS1 | IL1RL1 | LOC105371272 | NCRNA00250 | SIX4 | ZPBP2 |
| FAM110B | IL1RL2 | LOC105371273 | NEK6 | SLC26A5 | |
| FBXL7 | IL2 site 1 | LOC105373949 | NHEJ1 | SLC30A8 | |

*Table E5* *The 179 CpGs significantly differentially methylated in childhood in relation to asthma (FDR<0.05) along with the look-up of their associations with newborn methylation.*

| CpG | chr:pos | UCSC RefGene Name | UCSC Known Gene* | Childhood Methylation | | | | | | | Newborn Methylation | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Coef | SE | OR** (CI) | p-value | HetPVal | RE OR** (CI) | RE P-value | Coef | SE | OR** (CI) | P-value | |
| cg06315149 | chr1:2036398 | *PRKCZ* | *PRKCZ* | -11.88 | 2.63 | 0.89 (0.84,0.93) | 6.08E-06 | 0.2363 | | | -0.04 | 1.44 | 1.00 (0.97,1.03) | 0.9791 | |
| cg13066938 | chr1:6341140 | *ACOT7* | *ACOT7* | -9.14 | 2.12 | 0.91 (0.88,0.95) | 1.67E-05 | 0.0457 | 0.92 (0.86,0.98) | 1.21E-02 | -0.17 | 0.70 | 1.00 (0.98,1.01) | 0.8084 | |
| cg21220721 | chr1:6341230 | *ACOT7* | *ACOT7* | -6.32 | 1.10 | 0.94 (0.92,0.96) | 1.02E-08 | 0.0049 | 0.94 (0.90,0.98) | 1.73E-03 | -1.99 | 1.68 | 0.98 (0.95,1.01) | 0.2363 | |
| cg09249800 | chr1:6341287 | *ACOT7* | *ACOT7* | -13.20 | 2.31 | 0.88 (0.84,0.92) | 1.19E-08 | 0.2057 | | | -0.28 | 1.65 | 1.00 (0.97,1.03) | 0.8653 | |
| cg11699125 | chr1:6341327 | *ACOT7* | *ACOT7* | -10.23 | 1.66 | 0.90 (0.87,0.93) | 7.54E-10 | 0.1397 | | | -0.65 | 1.25 | 0.99 (0.97,1.02) | 0.6033 | |
| cg18783781 | chr1:9599067 | *SLC25A33* | *SLC25A33* | -10.56 | 2.36 | 0.90 (0.86,0.94) | 7.45E-06 | 0.0424 | 0.91 (0.85,0.98) | 1.39E-02 | 0.37 | 0.84 | 1.00 (0.99,1.02) | 0.6572 | |
| cg02171825 | chr1:26517586 | *CATSPER4* | *CATSPER4* | -13.19 | 2.97 | 0.88 (0.83,0.93) | 9.01E-06 | 0.5951 | | | -0.44 | 2.27 | 1.00 (0.95,1.04) | 0.8476 | |
| cg01942646 | chr1:27240694 | *NR0B2* | *NR0B2* | -13.02 | 2.70 | 0.88 (0.83,0.93) | 1.45E-06 | 0.4145 | | | -1.43 | 1.69 | 0.99 (0.95,1.02) | 0.3966 | |
| cg16263722 | chr1:29523841 | *MECR* | *MECR* | -11.15 | 2.15 | 0.89 (0.86,0.93) | 2.14E-07 | 0.4042 | | | -1.31 | 1.29 | 0.99 (0.96,1.01) | 0.3117 | |
| cg11987455 | chr1:43290834 | *ERMAP* | *ERMAP* | -11.98 | 2.42 | 0.89 (0.85,0.93) | 7.55E-07 | 0.5742 | | | 0.74 | 1.45 | 1.01 (0.98,1.04) | 0.6099 | |
| cg11683482 | chr1:44678623 | *DMAP1* | *DMAP1* | -10.92 | 2.01 | 0.90 (0.86,0.93) | 5.39E-08 | 0.0067 | 0.88 (0.82,0.95) | 5.26E-04 | 0.55 | 1.03 | 1.01 (0.99,1.03) | 0.5965 | |
| cg12643917 | chr1:44715958 | *ERI3* | *ERI3* | -11.13 | 2.51 | 0.89 (0.85,0.94) | 8.98E-06 | 0.5525 | | | -0.51 | 1.38 | 0.99 (0.97,1.02) | 0.7101 | |
| cg26252077 | chr1:61607055 | *NFIA* | *NFIA* | -12.78 | 2.28 | 0.88 (0.84,0.92) | 2.18E-08 | 0.0388 | 0.88 (0.82,0.95) | 9.20E-04 | -1.20 | 1.49 | 0.99 (0.96,1.02) | 0.4204 | |
| cg10704177 | chr1:62209607 | *INADL* | *INADL* | -10.42 | 2.01 | 0.90 (0.87,0.94) | 2.25E-07 | 0.0135 | 0.90 (0.84,0.96) | 2.12E-03 | 0.44 | 1.25 | 1.00 (0.98,1.03) | 0.7225 | |
| cg01445399 | chr1:87596934 | *LOC339524* | *LOC339524* | -9.37 | 2.18 | 0.91 (0.87,0.95) | 1.72E-05 | 0.3217 | | | -0.91 | 1.12 | 0.99 (0.97,1.01) | 0.4179 | |
| cg19805160 | chr1:159870731 | *CCDC19* | *CCDC19* | -11.37 | 2.43 | 0.89 (0.85,0.94) | 2.85E-06 | 0.0611 | | | 2.62 | 1.32 | 1.03 (1.00,1.05) | 0.0477 | *** |
| cg09332506 | chr1:160309220 | *COPA* | *NCSTN* | -15.15 | 3.10 | 0.86 (0.81,0.91) | 1.00E-06 | 0.5562 | | | -2.36 | 2.82 | 0.98 (0.92,1.03) | 0.4040 | |
| cg17971251 | chr1:177907297 | *SEC16B* | *SEC16B* | -14.63 | 2.55 | 0.86 (0.82,0.91) | 9.52E-09 | 0.1650 | | | 1.55 | 1.94 | 1.02 (0.98,1.05) | 0.4245 | |
| cg26033504 | chr1:201458737 | *CSRP1* | *CSRP1* | -9.70 | 2.15 | 0.91 (0.87,0.95) | 6.35E-06 | 0.0006 | 0.91 (0.83,0.99) | 3.21E-02 | 1.69 | 1.46 | 1.02 (0.99,1.05) | 0.2466 | |
| cg04895895 | chr1:231005895 | *C1orf198* | *C1orf198* | -12.21 | 2.68 | 0.89 (0.84,0.93) | 5.26E-06 | 0.0314 | 0.91 (0.83,0.99) | 2.35E-02 | 0.07 | 1.38 | 1.00 (0.97,1.03) | 0.9581 | |
| cg02473287 | chr2:9752386 | *YWHAQ* | *YWHAQ* | -10.99 | 2.46 | 0.90 (0.85,0.94) | 8.00E-06 | 0.0334 | 0.90 (0.83,0.97) | 5.96E-03 | -0.80 | 1.41 | 0.99 (0.97,1.02) | 0.5700 | |
| cg10142874 | chr2:11917623 | *LPIN1* | *LPIN1* | -11.55 | 2.36 | 0.89 (0.85,0.93) | 1.04E-06 | 0.0355 | 0.89 (0.82,0.95) | 1.10E-03 | 0.67 | 1.91 | 1.01 (0.97,1.05) | 0.7262 | |
| cg26752663 | chr2:25142016 | *ADCY3* | *ADCY3* | 11.13 | 2.33 | 1.12 (1.07,1.17) | 1.79E-06 | 0.0551 | | | 1.44 | 1.01 | 1.01 (0.99,1.03) | 0.1525 | |
| cg00043800 | chr2:74612144 | *LOC100189589* | *LOC100189589* | -9.47 | 2.17 | 0.91 (0.87,0.95) | 1.32E-05 | 0.6044 | | | -1.68 | 1.23 | 0.98 (0.96,1.01) | 0.1715 | |
| cg17988187 | chr2:74612222 | *LOC100189589* | *LOC100189589* | -11.04 | 2.27 | 0.90 (0.86,0.94) | 1.21E-06 | 0.0403 | 0.89 (0.83,0.96) | 2.28E-03 | -1.90 | 1.51 | 0.98 (0.95,1.01) | 0.2068 | |
| cg12077754 | chr2:75089669 | *HK2* | *HK2* | -7.90 | 1.72 | 0.92 (0.89,0.96) | 4.56E-06 | 0.3634 | | | 0.55 | 1.13 | 1.01 (0.98,1.03) | 0.6295 | |
| cg22674082 | chr2:98585733 | *TMEM131* | *TMEM131* | -12.20 | 2.81 | 0.89 (0.84,0.94) | 1.44E-05 | 0.1191 | | | -0.54 | 1.51 | 0.99 (0.97,1.02) | 0.7220 | |
| cg00327263 | chr2:120019111 | *STEAP3* | *STEAP3* | -10.70 | 2.40 | 0.90 (0.86,0.94) | 8.00E-06 | 0.1989 | | | -0.25 | 1.17 | 1.00 (0.97,1.02) | 0.8333 | |
| cg25950520 | chr2:121036760 | *RALB* | *RALB* | -16.28 | 3.74 | 0.85 (0.79,0.91) | 1.31E-05 | 0.4625 | | | -2.66 | 2.64 | 0.97 (0.92,1.03) | 0.3140 | |
| cg00213281 | chr2:149639822 | *KIF5C;MIR1978* | *JA429504* | -12.85 | 2.65 | 0.88 (0.83,0.93) | 1.24E-06 | 0.1106 | | | 2.13 | 1.43 | 1.02 (0.99,1.05) | 0.1365 | |
| cg02494549 | chr2:161798364 | | *TANK* | -14.66 | 2.80 | 0.86 (0.82,0.91) | 1.56E-07 | 0.0096 | 0.88 (0.80,0.98) | 1.52E-02 | -1.16 | 1.93 | 0.99 (0.95,1.03) | 0.5488 | |
| cg01310029 | chr3:3152374 | *IL5RA* | *IL5RA* | -11.12 | 2.42 | 0.89 (0.85,0.94) | 4.18E-06 | 0.3101 | | | 0.94 | 1.52 | 1.01 (0.98,1.04) | 0.5358 | |
| cg10159529 | chr3:3152530 | *IL5RA* | *IL5RA* | -10.82 | 2.36 | 0.90 (0.86,0.94) | 4.48E-06 | 0.1419 | | | 0.44 | 1.49 | 1.00 (0.98,1.03) | 0.7688 | |
| cg25224369 | chr3:12918528 | | *DQ581328* | -10.53 | 2.36 | 0.90 (0.86,0.94) | 7.75E-06 | 0.0265 | 0.89 (0.83,0.96) | 3.58E-03 | -2.38 | 1.25 | 0.98 (0.95,1.00) | 0.0564 | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| cg07386061 | chr3:52492874 | *NISCH* | *NISCH* | -8.93 | 1.83 | 0.91 (0.88,0.95) | 1.00E-06 | 0.3566 | | | 0.70 | 1.21 | 1.01 (0.98,1.03) | 0.5622 | |
| cg17890764 | chr3:52864816 | *ITIH4* | *ITIH4* | -9.95 | 2.03 | 0.91 (0.87,0.94) | 8.95E-07 | 0.0503 | | | 0.99 | 1.08 | 1.01 (0.99,1.03) | 0.3571 | |
| cg07410597 | chr3:66404129 | *SLC25A26* | *LRIG1* | -12.48 | 2.43 | 0.88 (0.84,0.93) | 2.70E-07 | 0.1875 | | | 0.69 | 1.78 | 1.01 (0.97,1.04) | 0.6968 | |
| cg04217850 | chr3:66428294 | *SLC25A26* | *LRIG1* | -13.23 | 2.80 | 0.88 (0.83,0.93) | 2.35E-06 | 0.0001 | 0.85 (0.76,0.96) | 8.68E-03 | -0.50 | 1.95 | 0.99 (0.96,1.03) | 0.7967 | |
| cg06070625 | chr3:69812798 | *MITF* | *MITF* | -10.54 | 2.32 | 0.90 (0.86,0.94) | 5.36E-06 | 0.0079 | 0.91 (0.84,0.99) | 3.24E-02 | -0.15 | 1.74 | 1.00 (0.97,1.03) | 0.9327 | |
| cg06391412 | chr3:71295684 | *FOXP1* | *FOXP1* | -13.39 | 2.26 | 0.87 (0.84,0.91) | 3.00E-09 | 0.2689 | | | 1.92 | 1.40 | 1.02 (0.99,1.05) | 0.1697 | |
| cg20263733 | chr3:130616293 | *ATP2C1* | *ATP2C1* | -14.20 | 2.81 | 0.87 (0.82,0.92) | 4.26E-07 | 0.1056 | | | -2.60 | 2.57 | 0.97 (0.93,1.02) | 0.3123 | |
| cg09423651 | chr3:136618442 | *NCK1* | *NCK1* | -12.74 | 2.88 | 0.88 (0.83,0.93) | 9.72E-06 | 0.8604 | | | -5.22 | 1.88 | 0.95 (0.91,0.98) | 0.0056 | *** |
| cg08698681 | chr3:171091657 | *TNIK* | *TNIK* | -12.14 | 2.67 | 0.89 (0.84,0.93) | 5.52E-06 | 0.1997 | | | -1.74 | 1.67 | 0.98 (0.95,1.02) | 0.2978 | |
| cg25636075 | chr3:185217761 | *TMEM41A* | *TMEM41A* | -14.50 | 3.19 | 0.87 (0.81,0.92) | 5.59E-06 | 0.4020 | | | -0.69 | 1.46 | 0.99 (0.97,1.02) | 0.6350 | |
| cg02803925 | chr3:195974300 | *PCYT1A* | *PCYT1A* | -14.57 | 2.97 | 0.86 (0.82,0.92) | 9.27E-07 | 0.5322 | | | -5.06 | 3.23 | 0.95 (0.89,1.01) | 0.1179 | |
| cg04077085 | chr4:9937674 | *SLC2A9* | *SLC2A9* | -14.84 | 2.96 | 0.86 (0.81,0.91) | 5.34E-07 | 0.4046 | | | 4.07 | 1.74 | 1.04 (1.01,1.08) | 0.0198 | *** |
| cg18912470 | chr4:57848125 | *POLR2B* | *POLR2B* | -9.85 | 2.03 | 0.91 (0.87,0.94) | 1.23E-06 | 0.3294 | | | 0.27 | 1.51 | 1.00 (0.97,1.03) | 0.8575 | |
| cg26396815 | chr4:102878132 | *BANK1* | *BANK1* | -11.95 | 2.74 | 0.89 (0.84,0.94) | 1.24E-05 | 0.3019 | | | 0.73 | 1.85 | 1.01 (0.97,1.04) | 0.6918 | |
| cg20866785 | chr4:148733880 | *ARHGAP10* | *Metazoa_SRP* | -9.27 | 2.16 | 0.91 (0.87,0.95) | 1.70E-05 | 0.1982 | | | 0.36 | 1.65 | 1.00 (0.97,1.04) | 0.8267 | |
| cg16362140 | chr5:10708717 | *DAP* | *DAP* | -10.14 | 2.09 | 0.90 (0.87,0.94) | 1.17E-06 | 0.0078 | 0.91 (0.85,0.98) | 1.57E-02 | -2.27 | 1.33 | 0.98 (0.95,1.00) | 0.0877 | |
| cg22588983 | chr5:38783142 | | *AK126213* | -15.64 | 3.60 | 0.86 (0.80,0.92) | 1.35E-05 | 0.7202 | | | 1.60 | 2.44 | 1.02 (0.97,1.07) | 0.5120 | |
| cg00944309 | chr5:60142446 | | *ELOVL7* | -10.74 | 2.12 | 0.90 (0.86,0.94) | 4.03E-07 | 0.0674 | | | 1.67 | 1.63 | 1.02 (0.98,1.05) | 0.3032 | |
| cg14978242 | chr5:79501131 | *SERINC5* | *SERINC5* | -7.74 | 1.80 | 0.93 (0.89,0.96) | 1.74E-05 | 0.3326 | | | 2.48 | 1.19 | 1.03 (1.00,1.05) | 0.0374 | *** |
| cg09565310 | chr5:112541553 | *MCC* | *MCC* | -11.68 | 2.50 | 0.89 (0.85,0.93) | 3.10E-06 | 0.0920 | | | -2.16 | 1.55 | 0.98 (0.95,1.01) | 0.1640 | |
| cg08969102 | chr5:133563532 | | *PPP2CA* | -8.91 | 2.06 | 0.91 (0.88,0.95) | 1.54E-05 | 0.1870 | | | -0.89 | 1.20 | 0.99 (0.97,1.01) | 0.4559 | |
| cg21627181 | chr6:25754190 | *SLC17A4* | *SLC17A4* | -10.14 | 2.37 | 0.90 (0.86,0.95) | 1.90E-05 | 0.0424 | 0.90 (0.84,0.97) | 4.22E-03 | -0.38 | 1.80 | 1.00 (0.96,1.03) | 0.8313 | |
| cg09597192 | chr6:32141591 | *AGPAT1* | *PPT2* | -12.53 | 2.73 | 0.88 (0.84,0.93) | 4.29E-06 | 0.0134 | 0.88 (0.80,0.96) | 6.09E-03 | 0.12 | 1.48 | 1.00 (0.97,1.03) | 0.9355 | |
| cg06426027 | chr6:33232644 | *VPS52* | *VPS52* | -18.72 | 3.96 | 0.83 (0.77,0.90) | 2.32E-06 | 0.6621 | | | -1.25 | 1.99 | 0.99 (0.95,1.03) | 0.5316 | |
| cg18460809 | chr6:57048049 | *BAG2* | *BAG2* | -11.60 | 2.32 | 0.89 (0.85,0.93) | 6.05E-07 | 0.0535 | | | -2.84 | 1.53 | 0.97 (0.94,1.00) | 0.0631 | |
| cg15961693 | chr6:139689053 | | *CITED2* | -11.72 | 2.68 | 0.89 (0.84,0.94) | 1.22E-05 | 0.1694 | | | -1.77 | 1.79 | 0.98 (0.95,1.02) | 0.3237 | |
| cg26774971 | chr6:158994407 | *TMEM181* | *TMEM181* | -10.23 | 2.39 | 0.90 (0.86,0.95) | 1.88E-05 | 0.0615 | | | 0.46 | 1.83 | 1.00 (0.97,1.04) | 0.8032 | |
| cg05477517 | chr6:164531576 | | *AK093114* | -13.14 | 2.62 | 0.88 (0.83,0.92) | 5.42E-07 | 0.0055 | 0.87 (0.79,0.96) | 5.86E-03 | -2.04 | 1.51 | 0.98 (0.95,1.01) | 0.1771 | |
| cg15304012 | chr6:166876490 | *RPS6KA2* | *RPS6KA2* | 8.11 | 1.89 | 1.08 (1.04,1.13) | 1.86E-05 | 0.1151 | | | -0.23 | 1.05 | 1.00 (0.98,1.02) | 0.8266 | |
| cg19851574 | chr6:167178233 | *RPS6KA2* | *RPS6KA2* | -4.71 | 1.01 | 0.95 (0.94,0.97) | 3.42E-06 | 0.2116 | | | -0.82 | 0.64 | 0.99 (0.98,1.00) | 0.1955 | |
| cg03329755 | chr6:167189272 | *RPS6KA2* | *RPS6KA2* | -8.91 | 1.97 | 0.91 (0.88,0.95) | 6.14E-06 | 0.2372 | | | -1.50 | 1.82 | 0.99 (0.95,1.02) | 0.4102 | |
| cg25270424 | chr7:24965657 | *OSBPL3* | *OSBPL3* | -14.53 | 2.88 | 0.86 (0.82,0.92) | 4.75E-07 | 0.3966 | | | -0.63 | 2.02 | 0.99 (0.96,1.03) | 0.7538 | |
| cg04321303 | chr7:44107504 | | *PGAM2* | -9.36 | 2.00 | 0.91 (0.88,0.95) | 2.72E-06 | 0.0422 | 0.91 (0.85,0.96) | 1.84E-03 | -0.16 | 1.25 | 1.00 (0.97,1.02) | 0.8994 | |
| cg02435538 | chr7:75507337 | *RHBDD2* | *RHBDD2* | -10.68 | 2.16 | 0.90 (0.86,0.94) | 7.37E-07 | 0.1305 | | | -0.70 | 1.05 | 0.99 (0.97,1.01) | 0.5045 | |
| cg13007207 | chr7:105279391 | *ATXN7L1* | *ATXN7L1* | 22.95 | 5.36 | 1.26 (1.13,1.40) | 1.87E-05 | 0.1715 | | | -5.33 | 2.80 | 0.95 (0.80,1.00) | 0.0566 | |
| cg17947765 | chr7:117857964 | | *ANKRD7* | -14.71 | 3.36 | 0.86 (0.81,0.92) | 1.17E-05 | 0.1488 | | | -2.04 | 2.73 | 0.98 (0.93,1.03) | 0.4551 | |
| cg14678084 | chr7:127627251 | *SND1* | *SND1-IT1* | -17.96 | 3.69 | 0.84 (0.78,0.90) | 1.17E-06 | 0.0463 | 0.82 (0.73,0.92) | 7.30E-04 | -1.00 | 2.06 | 0.99 (0.95,1.03) | 0.6291 | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| cg05184016 | chr7:149543136 | *ZNF862* | *BC045757* | -16.07 | 2.89 | 0.85 (0.80,0.90) | 2.74E-08 | 0.0470 | 0.85 (0.78,0.93) | 2.28E-04 | -1.86 | 2.10 | 0.98 (0.94,1.02) | 0.3759 |
| cg07970948 | chr7:149543165 | *ZNF862* | *BC045757* | -9.41 | 1.74 | 0.91 (0.88,0.94) | 6.39E-08 | 0.0567 | | | -0.74 | 1.23 | 0.99 (0.97,1.02) | 0.5436 |
| cg06558622 | chr7:149543177 | *ZNF862* | *BC045757* | -12.58 | 2.13 | 0.88 (0.85,0.92) | 3.39E-09 | 0.6337 | | | -1.04 | 1.36 | 0.99 (0.96,1.02) | 0.4429 |
| cg24576940 | chr7:150648283 | *KCNH2* | *KCNH2* | -14.05 | 3.28 | 0.87 (0.81,0.93) | 1.83E-05 | 0.3610 | | | -0.30 | 1.26 | 1.00 (0.97,1.02) | 0.8088 |
| cg23147443 | chr7:150649655 | *KCNH2* | *KCNH2* | -11.54 | 2.42 | 0.89 (0.85,0.93) | 1.83E-06 | 0.6492 | | | -0.59 | 0.65 | 0.99 (0.98,1.01) | 0.3585 |
| cg18666454 | chr7:150651937 | *KCNH2* | *KCNH2* | -11.32 | 2.15 | 0.89 (0.86,0.93) | 1.46E-07 | 0.5027 | | | -0.93 | 0.87 | 0.99 (0.97,1.01) | 0.2858 |
| cg02596233 | chr7:150970209 | *SMARCD3* | *SMARCD3* | -14.99 | 2.89 | 0.86 (0.81,0.91) | 2.11E-07 | 0.0041 | 0.89 (0.79,0.99) | 3.75E-02 | 0.72 | 2.35 | 1.01 (0.96,1.05) | 0.7604 |
| cg23706836 | chr8:6407997 | *ANGPT2;MCPH1* | *ANGPT2* | -8.80 | 1.76 | 0.92 (0.88,0.95) | 5.63E-07 | 0.0080 | 0.92 (0.86,0.98) | 6.91E-03 | -1.69 | 1.26 | 0.98 (0.96,1.01) | 0.1795 |
| cg21919729 | chr8:11719367 | *CTSB* | *CTSB* | -8.01 | 1.71 | 0.92 (0.89,0.95) | 3.03E-06 | 0.1753 | | | -0.26 | 1.32 | 1.00 (0.97,1.02) | 0.8422 |
| cg03437605 | chr8:22847209 | *RHOBTB2* | *RHOBTB2* | -13.92 | 2.62 | 0.87 (0.83,0.92) | 1.05E-07 | 0.3078 | | | 1.54 | 1.83 | 1.02 (0.98,1.05) | 0.4002 |
| cg22816343 | chr8:26243601 | *BNIP3L* | *BNIP3L* | -11.80 | 2.49 | 0.89 (0.85,0.93) | 2.12E-06 | 0.0804 | | | 0.13 | 1.57 | 1.00 (0.97,1.03) | 0.9339 |
| cg23205629 | chr8:33421410 | *RNF122* | *RNF122* | -9.10 | 2.05 | 0.91 (0.88,0.95) | 9.28E-06 | 0.1432 | | | 1.40 | 1.31 | 1.01 (0.99,1.04) | 0.2863 |
| cg10815420 | chr8:105599835 | *LRP12* | *LRP12* | -15.10 | 2.93 | 0.86 (0.81,0.91) | 2.66E-07 | 0.9000 | | | 0.33 | 2.03 | 1.00 (0.96,1.04) | 0.8719 |
| cg02133716 | chr8:128981622 | *PVT1* | *MIR1205* | -16.57 | 3.37 | 0.85 (0.79,0.91) | 8.64E-07 | 0.3547 | | | 0.91 | 1.72 | 1.01 (0.98,1.04) | 0.5991 |
| cg00736681 | chr8:134546052 | *ST3GAL1* | *ST3GAL1* | -10.18 | 2.14 | 0.90 (0.87,0.94) | 1.93E-06 | 0.1431 | | | 0.29 | 1.87 | 1.00 (0.97,1.04) | 0.8753 |
| cg09377531 | chr8:141046469 | *TRAPPC9* | *AX748239* | -10.41 | 1.83 | 0.90 (0.87,0.93) | 1.23E-08 | 0.0578 | | | 1.38 | 1.25 | 1.01 (0.99,1.04) | 0.2705 |
| cg14025883 | chr9:5436224 | *C9orf46* | *C9orf46* | -11.76 | 2.39 | 0.89 (0.85,0.93) | 8.42E-07 | 0.1487 | | | 0.88 | 1.28 | 1.01 (0.98,1.03) | 0.4934 |
| cg01499988 | chr9:35755346 | *MSMP* | *MSMP* | -12.47 | 2.62 | 0.88 (0.84,0.93) | 2.01E-06 | 0.5397 | | | 0.04 | 1.50 | 1.00 (0.97,1.03) | 0.9794 |
| cg13482814 | chr9:82183332 | | *TLE4* | -12.32 | 2.69 | 0.88 (0.84,0.93) | 4.74E-06 | 0.0662 | | | -1.36 | 2.02 | 0.99 (0.95,1.03) | 0.5015 |
| cg13576859 | chr9:97403129 | *FBP1* | *FBP1* | -8.69 | 2.00 | 0.92 (0.88,0.95) | 1.37E-05 | 0.0438 | 0.91 (0.86,0.97) | 3.67E-03 | -0.82 | 1.20 | 0.99 (0.97,1.02) | 0.4951 |
| cg20503329 | chr9:101705792 | *COL15A1* | *COL15A1* | -19.24 | 4.13 | 0.82 (0.76,0.89) | 3.10E-06 | 0.0285 | 0.83 (0.73,0.96) | 8.80E-03 | -4.73 | 2.76 | 0.95 (0.80,1.01) | 0.0861 |
| cg00045753 | chr9:123630545 | *PHF19* | *PHF19* | -12.84 | 2.95 | 0.88 (0.83,0.93) | 1.32E-05 | 0.0388 | 0.88 (0.80,0.97) | 7.24E-03 | -2.38 | 1.24 | 0.98 (0.95,1.00) | 0.0548 |
| cg13458609 | chr9:130608923 | *ENG* | *ENG* | -12.05 | 2.22 | 0.89 (0.85,0.93) | 5.74E-08 | 0.2476 | | | 0.37 | 1.41 | 1.00 (0.98,1.03) | 0.7930 |
| cg13835688 | chr9:130859454 | *SLC25A25* | *SLC25A25* | -11.63 | 1.97 | 0.89 (0.86,0.93) | 3.33E-09 | 0.0364 | 0.89 (0.83,0.95) | 2.62E-04 | 0.05 | 1.29 | 1.00 (0.98,1.03) | 0.9718 |
| cg13628444 | chr9:134883788 | *MED27* | *MED27* | -12.04 | 2.44 | 0.89 (0.85,0.93) | 7.76E-07 | 0.2127 | | | -1.51 | 1.69 | 0.98 (0.95,1.02) | 0.3701 |
| cg13850063 | chr9:138362321 | | *AK096249* | -24.77 | 4.56 | 0.78 (0.71,0.85) | 5.49E-08 | 0.0736 | | | -1.65 | 2.28 | 0.98 (0.94,1.03) | 0.4696 |
| cg14011077 | chr9:138362327 | | *AK096249* | -15.12 | 2.61 | 0.86 (0.82,0.90) | 7.02E-09 | 0.6429 | | | -0.53 | 2.10 | 0.99 (0.95,1.04) | 0.7997 |
| cg06958964 | chr10:45494806 | *C10orf25;ZNF22* | *ZNF22* | -15.96 | 3.42 | 0.85 (0.80,0.91) | 2.97E-06 | 0.7645 | | | 1.25 | 2.68 | 1.01 (0.96,1.07) | 0.6400 |
| cg25854298 | chr10:73936754 | *ASCC1* | *ASCC1* | -11.91 | 2.68 | 0.89 (0.84,0.94) | 8.74E-06 | 0.2139 | | | -0.89 | 1.29 | 0.99 (0.97,1.02) | 0.4901 |
| cg04973995 | chr10:74057977 | | *DDIT4* | -7.83 | 1.78 | 0.92 (0.89,0.96) | 1.10E-05 | 0.3720 | | | 0.10 | 2.08 | 1.00 (0.96,1.04) | 0.9632 |
| cg00366037 | chr10:76781121 | *MYST4* | *KAT6B* | -12.66 | 2.92 | 0.88 (0.83,0.93) | 1.45E-05 | 0.9001 | | | 0.14 | 2.10 | 1.00 (0.96,1.04) | 0.9473 |
| cg22235258 | chr11:34675402 | *EHF* | *EHF* | -13.03 | 3.02 | 0.88 (0.83,0.93) | 1.61E-05 | 0.1041 | | | -1.23 | 2.47 | 0.99 (0.94,1.04) | 0.6194 |
| cg24459209 | chr11:57148215 | *PRG3* | *PRG3* | -15.30 | 2.86 | 0.86 (0.81,0.91) | 8.52E-08 | 0.8292 | | | 0.70 | 1.75 | 1.01 (0.97,1.04) | 0.6907 |
| cg15700636 | chr11:57156050 | *PRG2* | *PRG2* | -11.65 | 2.25 | 0.89 (0.85,0.93) | 2.35E-07 | 0.0146 | 0.89 (0.83,0.96) | 2.61E-03 | 0.28 | 1.51 | 1.00 (0.97,1.03) | 0.8533 |
| cg08773180 | chr11:57157607 | *PRG2* | *PRG2* | -11.66 | 2.23 | 0.89 (0.85,0.93) | 1.77E-07 | 0.0409 | 0.88 (0.83,0.95) | 5.02E-04 | -1.98 | 1.66 | 0.98 (0.95,1.01) | 0.2336 |
| cg12819873 | chr11:57157632 | *PRG2* | *PRG2* | -10.83 | 2.45 | 0.90 (0.86,0.94) | 9.55E-06 | 0.2663 | | | -0.42 | 1.88 | 1.00 (0.96,1.03) | 0.8246 |
| cg27533472 | chr11:59856225 | *MS4A2* | *MS4A2* | -19.27 | 4.18 | 0.82 (0.76,0.90) | 4.09E-06 | 0.3282 | | | -3.27 | 3.38 | 0.97 (0.91,1.03) | 0.3334 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| cg25087851 | chr11:60623918 | *GPR44* | *PTGDR2* | -11.86 | 2.10 | 0.89 (0.85,0.93) | 1.69E-08 | 0.2450 | | | -0.76 | 1.43 | 0.99 (0.97,1.02) | 0.5940 | |
| cg13233042 | chr11:63432489 | *ATL3* | *ATL3* | -13.01 | 2.81 | 0.88 (0.83,0.93) | 3.59E-06 | 0.1843 | | | 1.36 | 1.76 | 1.01 (0.98,1.05) | 0.4387 | |
| cg05300717 | chr11:65546210 | *DKFZp761E198* | *DKFZp761E198* | -15.35 | 2.48 | 0.86 (0.82,0.90) | 6.51E-10 | 0.1399 | | | -0.94 | 2.38 | 0.99 (0.95,1.04) | 0.6930 | |
| cg15219163 | chr11:70842128 | *SHANK2* | *SHANK2* | 15.93 | 3.71 | 1.17 (1.09,1.26) | 1.80E-05 | 0.4823 | | | 1.13 | 1.53 | 1.01 (0.98,1.04) | 0.4600 | |
| cg24368962 | chr11:111570978 | *SIK2* | *DQ599327* | -15.79 | 3.26 | 0.85 (0.80,0.91) | 1.28E-06 | 0.0010 | 0.86 (0.75,0.99) | 3.43E-02 | -0.90 | 4.14 | 0.99 (0.91,1.07) | 0.8277 | |
| cg19434937 | chr12:7104184 | *LPCAT3* | *EMG1* | -8.95 | 1.86 | 0.91 (0.88,0.95) | 1.55E-06 | 0.0382 | 0.92 (0.86,0.97) | 3.25E-03 | -1.33 | 1.28 | 0.99 (0.96,1.01) | 0.2976 | |
| cg03014680 | chr12:10122522 | *CLEC12A* | *CLEC12A* | -8.84 | 1.86 | 0.92 (0.88,0.95) | 2.14E-06 | 0.2674 | | | -1.85 | 1.28 | 0.98 (0.96,1.01) | 0.1477 | |
| cg09447105 | chr12:15126020 | *PDE6H* | *PDE6H* | -13.27 | 2.68 | 0.88 (0.83,0.92) | 7.60E-07 | 0.0074 | 0.89 (0.81,0.97) | 1.22E-02 | 0.89 | 1.51 | 1.01 (0.98,1.04) | 0.5557 | |
| cg24028828 | chr12:56694932 | *CS* | *CS* | -13.71 | 2.88 | 0.87 (0.82,0.92) | 1.99E-06 | 0.5495 | | | 1.11 | 1.44 | 1.01 (0.98,1.04) | 0.4374 | |
| cg21498475 | chr12:113737469 | *SLC24A6* | *SLC24A6* | -10.40 | 2.29 | 0.90 (0.86,0.94) | 5.44E-06 | 0.0297 | 0.90 (0.84,0.97) | 6.21E-03 | -0.75 | 1.52 | 0.99 (0.96,1.02) | 0.6193 | |
| cg10065736 | chr12:117440120 | *FBXW8* | *AK055849* | -10.22 | 1.94 | 0.90 (0.87,0.94) | 1.41E-07 | 0.1856 | | | -1.02 | 1.16 | 0.99 (0.97,1.01) | 0.3790 | |
| cg03131767 | chr12:123446272 | *ABCB9* | *ABCB9* | -11.72 | 2.36 | 0.89 (0.85,0.93) | 7.21E-07 | 0.1245 | | | 0.15 | 1.41 | 1.00 (0.97,1.03) | 0.9145 | |
| cg19928703 | chr13:30143971 | *SLC7A1* | *SLC7A1* | -11.71 | 2.68 | 0.89 (0.84,0.94) | 1.21E-05 | 0.4460 | | | 1.26 | 1.97 | 1.01 (0.97,1.05) | 0.5223 | |
| cg07908654 | chr13:41631052 | | *TRNA_Glu* | -11.47 | 2.23 | 0.89 (0.85,0.93) | 2.60E-07 | 0.1662 | | | -0.55 | 1.50 | 0.99 (0.97,1.02) | 0.7142 | |
| cg24818699 | chr13:43355514 | *C13orf30* | *C13orf30* | -13.92 | 3.13 | 0.87 (0.82,0.93) | 8.53E-06 | 0.2994 | | | 2.02 | 2.31 | 1.02 (0.98,1.07) | 0.3828 | |
| cg08770358 | chr13:48876684 | *RB1* | *BC039553* | -16.86 | 3.88 | 0.84 (0.78,0.91) | 1.42E-05 | 0.9019 | | | 1.35 | 2.03 | 1.01 (0.97,1.05) | 0.5072 | |
| cg00222125 | chr13:53226144 | *SUGT1* | *SUGT1* | -10.12 | 2.33 | 0.90 (0.86,0.95) | 1.43E-05 | 0.8730 | | | 2.93 | 1.19 | 1.03 (1.01,1.05) | 0.0138 | *** |
| cg11770323 | chr13:80066032 | *NDFIP2* | *NDFIP2* | -9.41 | 2.08 | 0.91 (0.87,0.95) | 5.86E-06 | 0.0916 | | | -0.23 | 1.35 | 1.00 (0.97,1.02) | 0.8630 | |
| cg25479097 | chr13:113305704 | *C13orf35* | *C13orf35* | -12.19 | 2.48 | 0.89 (0.84,0.93) | 9.11E-07 | 0.1731 | | | 1.36 | 1.57 | 1.01 (0.98,1.05) | 0.3861 | |
| cg18368116 | chr14:21436271 | | *RNASE2* | -11.80 | 2.58 | 0.89 (0.84,0.93) | 4.93E-06 | 0.2402 | | | 0.58 | 2.10 | 1.01 (0.97,1.05) | 0.7820 | |
| cg08077807 | chr14:62001072 | *PRKCH* | *PRKCH* | -16.27 | 3.08 | 0.85 (0.80,0.90) | 1.29E-07 | 0.6743 | | | -2.93 | 2.14 | 0.97 (0.93,1.01) | 0.1708 | |
| cg04933530 | chr14:77419754 | | *IRF2BPL* | -11.70 | 2.20 | 0.89 (0.85,0.93) | 1.02E-07 | 0.4659 | | | -0.12 | 1.47 | 1.00 (0.97,1.03) | 0.9368 | |
| cg01901579 | chr14:95615731 | *DICER1* | *DICER1* | -9.29 | 2.05 | 0.91 (0.88,0.95) | 5.86E-06 | 0.0257 | 0.91 (0.85,0.97) | 5.84E-03 | 0.10 | 1.44 | 1.00 (0.97,1.03) | 0.9473 | |
| cg16409452 | chr14:100610186 | *EVL* | *AX747103* | -9.84 | 1.96 | 0.91 (0.87,0.94) | 4.89E-07 | 0.2881 | | | -2.62 | 0.75 | 0.97 (0.96,0.99) | 0.0005 | *** |
| cg14084609 | chr14:100610407 | *EVL* | *AX747103* | -12.03 | 2.03 | 0.89 (0.85,0.92) | 2.96E-09 | 0.3931 | | | -0.68 | 0.93 | 0.99 (0.98,1.01) | 0.4653 | |
| cg18550847 | chr14:100610570 | *EVL* | *AX747103* | -9.38 | 1.89 | 0.91 (0.88,0.94) | 7.10E-07 | 0.1220 | | | -0.07 | 0.55 | 1.00 (0.99,1.01) | 0.8948 | |
| cg01000631 | chr14:100610667 | | *EVL* | -9.86 | 1.81 | 0.91 (0.87,0.94) | 4.88E-08 | 0.0153 | 0.90 (0.84,0.96) | 8.40E-04 | 0.38 | 0.49 | 1.00 (0.99,1.01) | 0.4364 | |
| cg05875066 | chr14:104625249 | *KIF26A* | *KIF26A* | -13.75 | 2.63 | 0.87 (0.83,0.92) | 1.77E-07 | 0.1313 | | | -0.23 | 0.58 | 1.00 (0.99,1.01) | 0.6869 | |
| cg18817654 | chr15:39485138 | | *C15orf54* | -14.23 | 3.06 | 0.87 (0.82,0.92) | 3.41E-06 | 0.1330 | | | 2.59 | 3.18 | 1.03 (0.96,1.09) | 0.4151 | |
| cg25939647 | chr15:40173065 | *GPR176* | *GPR176* | -9.35 | 1.96 | 0.91 (0.88,0.95) | 1.91E-06 | 0.0607 | | | 2.37 | 1.67 | 1.02 (0.99,1.06) | 0.1553 | |
| cg07177867 | chr15:52030746 | *LYSMD2* | *LYSMD2* | -10.62 | 2.44 | 0.90 (0.86,0.94) | 1.29E-05 | 0.2360 | | | 0.44 | 1.14 | 1.00 (0.98,1.03) | 0.7032 | |
| cg11266582 | chr15:64275853 | *DAPK2* | *DAPK2* | -11.58 | 2.68 | 0.89 (0.85,0.94) | 1.52E-05 | 0.0761 | | | -3.00 | 2.29 | 0.97 (0.93,1.02) | 0.1904 | |
| cg10387956 | chr15:72646210 | *HEXA* | *BC034424* | -9.63 | 2.05 | 0.91 (0.87,0.95) | 2.72E-06 | 0.0368 | 0.90 (0.85,0.96) | 2.27E-03 | -0.44 | 1.33 | 1.00 (0.97,1.02) | 0.7430 | |
| cg23387863 | chr15:77472416 | *SGK269* | *AX747193* | -9.78 | 2.03 | 0.91 (0.87,0.94) | 1.51E-06 | 0.0407 | 0.92 (0.86,0.97) | 5.65E-03 | 1.28 | 1.53 | 1.01 (0.98,1.04) | 0.4017 | |
| cg04497992 | chr16:616212 | *NHLRC4* | *C16orf11* | -10.13 | 2.13 | 0.90 (0.87,0.94) | 1.92E-06 | 0.1859 | | | -1.08 | 1.82 | 0.99 (0.95,1.03) | 0.5532 | |
| cg08067346 | chr16:25011481 | *ARHGAP17* | *DQ583809* | -10.13 | 2.35 | 0.90 (0.86,0.95) | 1.60E-05 | 0.0093 | 0.92 (0.85,1.00) | 4.91E-02 | 0.66 | 1.44 | 1.01 (0.98,1.04) | 0.6467 | |
| cg26134665 | chr16:31021544 | *STX1B* | *STX1B* | -8.66 | 1.96 | 0.92 (0.88,0.95) | 9.50E-06 | 0.3601 | | | -0.73 | 1.43 | 0.99 (0.97,1.02) | 0.6118 | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| cg09147843 | chr16:53467612 | *RBL2* | *RBL2* | -11.57 | 2.60 | 0.89 (0.85,0.94) | 8.89E-06 | 0.0427 | 0.91 (0.84,0.99) | 3.27E-02 | 1.67 | 1.61 | 1.02 (0.99,1.05) | 0.2982 |
| cg01998785 | chr16:55542709 | *LPCAT2* | *LPCAT2* | -9.91 | 1.99 | 0.91 (0.87,0.94) | 6.17E-07 | 0.0594 | | | -0.74 | 0.94 | 0.99 (0.97,1.01) | 0.4310 |
| cg27383865 | chr16:84075870 | *SLC38A8* | *SLC38A8* | 10.35 | 2.41 | 1.11 (1.06,1.16) | 1.73E-05 | 0.0300 | 1.12 (1.04,1.21) | 4.24E-03 | -1.72 | 1.71 | 0.98 (0.95,1.02) | 0.3171 |
| cg08640475 | chr16:85551478 | | *KIAA0182* | -7.97 | 1.69 | 0.92 (0.89,0.95) | 2.36E-06 | 0.0577 | | | -0.63 | 1.01 | 0.99 (0.97,1.01) | 0.5372 |
| cg10099827 | chr16:85551514 | | *KIAA0182* | -8.05 | 1.66 | 0.92 (0.89,0.95) | 1.32E-06 | 0.2595 | | | -0.35 | 1.10 | 1.00 (0.98,1.02) | 0.7509 |
| cg08940169 | chr16:88540241 | *ZFPM1* | *ZFPM1* | -9.73 | 1.90 | 0.91 (0.87,0.94) | 2.93E-07 | 0.1990 | | | -1.50 | 1.56 | 0.99 (0.96,1.02) | 0.3346 |
| cg04983687 | chr16:88558223 | *ZFPM1* | *ZFPM1* | -7.76 | 1.21 | 0.93 (0.80,0.95) | 1.33E-10 | 0.1560 | | | -0.54 | 1.10 | 0.99 (0.97,1.02) | 0.6259 |
| cg20315954 | chr17:15137304 | *PMP22* | *PMP22* | -12.65 | 2.73 | 0.88 (0.84,0.93) | 3.58E-06 | 0.1377 | | | -0.55 | 1.68 | 0.99 (0.96,1.03) | 0.7436 |
| cg20885063 | chr17:17939419 | *ATPAF2* | *ATPAF2* | -10.94 | 2.24 | 0.90 (0.86,0.94) | 1.06E-06 | 0.1305 | | | -0.30 | 1.34 | 1.00 (0.97,1.02) | 0.8197 |
| cg14611258 | chr17:17946468 | *C17orf39* | *C17orf39* | -11.70 | 2.59 | 0.89 (0.85,0.94) | 6.41E-06 | 0.0120 | 0.89 (0.82,0.97) | 1.06E-02 | 2.35 | 1.53 | 1.02 (0.99,1.05) | 0.1254 |
| cg19468946 | chr17:37922297 | *IKZF3* | *IKZF3* | 8.35 | 1.93 | 1.09 (1.05,1.13) | 1.50E-05 | 0.9004 | | | -0.34 | 0.96 | 1.00 (0.98,1.02) | 0.7268 |
| cg21723861 | chr17:39686628 | | *KRT19* | -14.05 | 2.68 | 0.87 (0.82,0.92) | 1.59E-07 | 0.4059 | | | -0.59 | 1.59 | 0.99 (0.96,1.03) | 0.7077 |
| cg00170714 | chr17:40724562 | *MLX;PSMC3IP* | *PSMC3IP* | -12.13 | 2.24 | 0.89 (0.85,0.93) | 6.15E-08 | 0.1413 | | | 0.58 | 1.50 | 1.01 (0.98,1.04) | 0.6985 |
| cg25173129 | chr17:56269410 | *EPX* | *EPX* | -12.40 | 2.51 | 0.88 (0.84,0.93) | 8.09E-07 | 0.0960 | | | 1.23 | 1.76 | 1.01 (0.98,1.05) | 0.4845 |
| cg02970679 | chr17:56269818 | *EPX* | *EPX* | -13.35 | 2.73 | 0.88 (0.83,0.92) | 9.99E-07 | 0.1576 | | | -3.60 | 1.90 | 0.96 (0.93,1.00) | 0.0584 |
| cg17374802 | chr17:56270828 | *EPX* | *EPX* | -10.55 | 2.22 | 0.90 (0.86,0.94) | 2.06E-06 | 0.0543 | | | -1.40 | 1.25 | 0.99 (0.96,1.01) | 0.2630 |
| cg17041511 | chr17:61509620 | | *CYB561* | -9.62 | 2.19 | 0.91 (0.87,0.95) | 1.15E-05 | 0.4396 | | | -0.74 | 1.38 | 0.99 (0.97,1.02) | 0.5905 |
| cg22312249 | chr17:72779428 | *TMEM104* | *TMEM104* | -9.31 | 2.09 | 0.91 (0.87,0.95) | 8.73E-06 | 0.1446 | | | -0.66 | 1.16 | 0.99 (0.97,1.02) | 0.5724 |
| cg09705784 | chr17:76565232 | *DNAH17* | *DNAH17* | -9.15 | 1.74 | 0.91 (0.88,0.94) | 1.50E-07 | 0.0185 | 0.87 (0.82,0.93) | 3.95E-05 | 0.94 | 1.31 | 1.01 (0.98,1.04) | 0.4743 |
| cg06725287 | chr17:80533762 | *FOXK2* | *FOXK2* | -13.56 | 2.54 | 0.87 (0.83,0.92) | 9.07E-08 | 0.3875 | | | -0.26 | 0.81 | 1.00 (0.98,1.01) | 0.7504 |
| cg13054523 | chr17:81055722 | | *METRNL* | -13.94 | 2.45 | 0.87 (0.83,0.91) | 1.20E-08 | 0.1336 | | | -0.60 | 1.81 | 0.99 (0.96,1.03) | 0.7400 |
| cg18337287 | chr19:930871 | *ARID3A* | *ARID3A* | -15.13 | 2.81 | 0.86 (0.81,0.91) | 7.21E-08 | 0.2100 | | | -0.07 | 1.36 | 1.00 (0.97,1.03) | 0.9583 |
| cg12104982 | chr19:5592815 | *SAFB2* | *SAFB2* | -15.43 | 2.91 | 0.86 (0.81,0.91) | 1.13E-07 | 0.2578 | | | 2.89 | 3.25 | 1.03 (0.97,1.10) | 0.3750 |
| cg10644885 | chr19:11687621 | *ACP5* | *ACP5* | -15.00 | 2.29 | 0.86 (0.82,0.90) | 5.77E-11 | 0.2290 | | | -0.84 | 1.17 | 0.99 (0.97,1.01) | 0.4712 |
| cg02359181 | chr19:34860339 | *GPI* | *GPI* | -12.75 | 2.72 | 0.88 (0.83,0.93) | 2.68E-06 | 0.0204 | 0.89 (0.82,0.97) | 1.15E-02 | -0.80 | 1.51 | 0.99 (0.96,1.02) | 0.5938 |
| cg20673965 | chr19:44220148 | *IRGC* | *IRGC* | -11.06 | 2.43 | 0.90 (0.85,0.94) | 5.54E-06 | 0.2895 | | | -0.61 | 1.57 | 0.99 (0.96,1.02) | 0.6983 |
| cg26979537 | chr19:48016860 | *NAPA* | *NAPA* | -18.55 | 3.83 | 0.83 (0.77,0.90) | 1.31E-06 | 0.5977 | | | 1.53 | 3.53 | 1.02 (0.95,1.09) | 0.6642 |
| cg21073212 | chr20:30866501 | *KIF3B* | *KIF3B* | -7.94 | 1.85 | 0.92 (0.89,0.96) | 1.79E-05 | 0.3531 | | | -0.41 | 1.15 | 1.00 (0.97,1.02) | 0.7204 |
| cg20226253 | chr20:34022914 | *GDF5* | *GDF5OS* | -14.37 | 3.28 | 0.87 (0.81,0.92) | 1.15E-05 | 0.0008 | 0.87 (0.77,0.99) | 3.62E-02 | 2.61 | 1.54 | 1.03 (1.00,1.06) | 0.0901 |
| cg21045547 | chr20:35422703 | *C20orf117* | *KIAA0889* | -11.71 | 2.57 | 0.89 (0.85,0.94) | 5.32E-06 | 0.2887 | | | -0.37 | 0.62 | 1.00 (0.98,1.01) | 0.5521 |
| cg13792581 | chr20:43590115 | *TOMM34* | *TOMM34* | -13.71 | 3.15 | 0.87 (0.82,0.93) | 1.34E-05 | 0.2441 | | | 0.40 | 1.69 | 1.00 (0.97,1.04) | 0.8132 |
| cg13197551 | chr20:60709957 | *LSM14B* | *LSM14B* | -15.40 | 3.14 | 0.86 (0.81,0.91) | 9.23E-07 | 0.7768 | | | -1.03 | 2.73 | 0.99 (0.94,1.04) | 0.7063 |
| cg18042632 | chr21:42520902 | *C21orf130* | *LINC00323* | -8.87 | 1.86 | 0.92 (0.88,0.95) | 1.87E-06 | 0.6020 | | | 1.36 | 1.38 | 1.01 (0.99,1.04) | 0.3245 |
| cg18879389 | chr21:43771120 | *TFF2* | *TFF2* | -13.79 | 2.84 | 0.87 (0.82,0.92) | 1.21E-06 | 0.5763 | | | -1.17 | 1.31 | 0.99 (0.96,1.01) | 0.3730 |

* Annotation based on UCSC Known Gene also fills in nearest gene within 10 MB.

** Odds ratio of developing asthma for a 1% absolute increase in methylation.

*** Significant nominal (<0.05) p-value

Table E6 *Lookup of 179 CpGs differentially methylated in blood in childhood in two studies of nasal methylation: PIAMA and ICAC*

| CpG | chr:position | UCSC RefGene Name | UCSC Known Gene* | PACE Discovery (N=647 cases) | | PIAMA Look-Up in Nasal (N= 37 cases) | | ICAC Look-Up in Nasal (N=36 cases) | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | OR (CI) | P-value | Direction of Effect Concordant with PACE | P-value | Direction of Effect Concordant with PACE | P-value |
| cg06315149 | chr1:2036398 | *PRKCZ* | *PRKCZ* | 0.89 (0.84,0.93) | 6.08E-06 | yes | 5.66E-01 | yes | 3.40E-01 |
| cg13066938 | chr1:6341140 | *ACOT7* | *ACOT7* | 0.91 (0.88,0.95) | 1.67E-05 | yes | 1.88E-01 | yes | 2.39E-01 |
| cg21220721 | chr1:6341230 | *ACOT7* | *ACOT7* | 0.94 (0.92,0.96) | 1.02E-08 | yes | 1.09E-01 | yes | 1.14E-05 |
| cg09249800 | chr1:6341287 | *ACOT7* | *ACOT7* | 0.88 (0.84,0.92) | 1.19E-08 | NA | NA | yes | 1.40E-06 |
| cg11699125 | chr1:6341327 | *ACOT7* | *ACOT7* | 0.90 (0.87,0.93) | 7.54E-10 | yes | 5.80E-03 | yes | 1.19E-04 |
| cg18783781 | chr1:9599067 | *SLC25A33* | *SLC25A33* | 0.90 (0.86,0.94) | 7.45E-06 | no | 3.71E-01 | yes | 3.33E-02 |
| cg02171825 | chr1:26517586 | *CATSPER4* | *CATSPER4* | 0.88 (0.83,0.93) | 9.01E-06 | no | 9.17E-01 | yes | 1.82E-03 |
| cg01942646 | chr1:27240694 | *NR0B2* | *NR0B2* | 0.88 (0.83,0.93) | 1.45E-06 | yes | 7.50E-01 | yes | 6.98E-02 |
| cg16263722 | chr1:29523841 | *MECR* | *MECR* | 0.89 (0.86,0.93) | 2.14E-07 | yes | 4.54E-02 | yes | 2.92E-03 |
| cg11987455 | chr1:43290834 | *ERMAP* | *ERMAP* | 0.89 (0.85,0.93) | 7.55E-07 | no | 8.81E-01 | yes | 9.29E-04 |
| cg11683482 | chr1:44678623 | *DMAP1* | *DMAP1* | 0.90 (0.86,0.93) | 5.39E-08 | yes | 4.67E-01 | yes | 1.39E-01 |
| cg12643917 | chr1:44715958 | *ERI3* | *ERI3* | 0.89 (0.85,0.94) | 8.98E-06 | yes | 1.96E-01 | yes | 4.28E-04 |
| cg26252077 | chr1:61607055 | *NFIA* | *NFIA* | 0.88 (0.84,0.92) | 2.18E-08 | yes | 2.24E-01 | yes | 2.89E-02 |
| cg10704177 | chr1:62209607 | *INADL* | *INADL* | 0.90 (0.87,0.94) | 2.25E-07 | yes | 3.16E-01 | yes | 1.77E-02 |
| cg01445399 | chr1:87596934 | *LOC339524* | *LOC339524* | 0.91 (0.87,0.95) | 1.72E-05 | yes | 1.48E-02 | yes | 2.15E-03 |
| cg19805160 | chr1:159870731 | *CCDC19* | *CCDC19* | 0.89 (0.85,0.94) | 2.85E-06 | yes | 1.69E-01 | yes | 1.55E-02 |
| cg09332506 | chr1:160309220 | *COPA* | *NCSTN* | 0.86 (0.81,0.91) | 1.00E-06 | yes | 1.34E-01 | yes | 2.64E-03 |
| cg17971251 | chr1:177907297 | *SEC16B* | *SEC16B* | 0.86 (0.82,0.91) | 9.52E-09 | yes | 1.33E-01 | yes | 5.66E-03 |
| cg26033504 | chr1:201458737 | *CSRP1* | *CSRP1* | 0.91 (0.87,0.95) | 6.35E-06 | no | 5.99E-01 | yes | 3.52E-02 |
| cg04895895 | chr1:231005895 | *C1orf198* | *C1orf198* | 0.89 (0.84,0.93) | 5.26E-06 | yes | 9.29E-01 | yes | 8.06E-02 |
| cg02473287 | chr2:9752386 | *YWHAQ* | *YWHAQ* | 0.90 (0.85,0.94) | 8.00E-06 | no | 7.98E-01 | yes | 1.39E-02 |
| cg10142874 | chr2:11917623 | *LPIN1* | *LPIN1* | 0.89 (0.85,0.93) | 1.04E-06 | yes | 6.74E-01 | yes | 5.26E-04 |
| cg26752663 | chr2:25142016 | *ADCY3* | *ADCY3* | 1.12 (1.07,1.17) | 1.79E-06 | no | 1.51E-01 | yes | 3.88E-03 |
| cg00043800 | chr2:74612144 | *LOC100189589* | *LOC100189589* | 0.91 (0.87,0.95) | 1.32E-05 | no | 4.21E-01 | yes | 3.66E-03 |
| cg17988187 | chr2:74612222 | *LOC100189589* | *LOC100189589* | 0.90 (0.86,0.94) | 1.21E-06 | yes | 6.80E-01 | yes | 3.17E-03 |
| cg12077754 | chr2:75089669 | *HK2* | *HK2* | 0.92 (0.89,0.96) | 4.56E-06 | yes | 6.02E-01 | yes | 1.08E-04 |
| cg22674082 | chr2:98585733 | *TMEM131* | *TMEM131* | 0.89 (0.84,0.94) | 1.44E-05 | no | 2.89E-01 | yes | 2.19E-03 |
| cg00327263 | chr2:120019111 | *STEAP3* | *STEAP3* | 0.90 (0.86,0.94) | 8.00E-06 | no | 9.08E-02 | yes | 5.62E-02 |
| cg25950520 | chr2:121036760 | *RALB* | *RALB* | 0.85 (0.79,0.91) | 1.31E-05 | yes | 2.01E-01 | yes | 1.58E-01 |
| cg00213281 | chr2:149639822 | *KIF5C;MIR1978* | *JA429504* | 0.88 (0.83,0.93) | 1.24E-06 | yes | 8.98E-03 | yes | 2.24E-05 |
| cg02494549 | chr2:161798364 | | *TANK* | 0.86 (0.82,0.91) | 1.56E-07 | yes | 6.51E-02 | yes | 2.56E-05 |
| cg01310029 | chr3:3152374 | *IL5RA* | *IL5RA* | 0.89 (0.85,0.94) | 4.18E-06 | yes | 7.91E-02 | yes | 6.09E-04 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| cg10159529 | chr3:3152530 | *IL5RA* | *IL5RA* | 0.90 (0.86,0.94) | 4.48E-06 | yes | 1.69E-01 | yes | 3.77E-02 |
| cg25224369 | chr3:12918528 | | *DQ581328* | 0.90 (0.86,0.94) | 7.75E-06 | yes | 8.13E-01 | yes | 3.03E-03 |
| cg07386061 | chr3:52492874 | *NISCH* | *NISCH* | 0.91 (0.88,0.95) | 1.00E-06 | yes | 5.27E-01 | yes | 4.22E-02 |
| cg17890764 | chr3:52864816 | *ITIH4* | *ITIH4* | 0.91 (0.87,0.94) | 8.95E-07 | yes | 5.33E-02 | yes | 1.90E-02 |
| cg07410597 | chr3:66404129 | *SLC25A26* | *LRIG1* | 0.88 (0.84,0.93) | 2.70E-07 | yes | 2.12E-01 | yes | 8.38E-02 |
| cg04217850 | chr3:66428294 | *SLC25A26* | *LRIG1* | 0.88 (0.83,0.93) | 2.35E-06 | no | 2.70E-01 | yes | 9.42E-03 |
| cg06070625 | chr3:69812798 | *MITF* | *MITF* | 0.90 (0.86,0.94) | 5.36E-06 | yes | 1.72E-01 | yes | 2.88E-01 |
| cg06391412 | chr3:71295684 | *FOXP1* | *FOXP1* | 0.87 (0.84,0.91) | 3.00E-09 | yes | 1.03E-01 | no | 9.59E-01 |
| cg20263733 | chr3:130616293 | *ATP2C1* | *ATP2C1* | 0.87 (0.82,0.92) | 4.26E-07 | yes | 3.63E-02 | yes | 3.80E-04 |
| cg09423651 | chr3:136618442 | *NCK1* | *NCK1* | 0.88 (0.83,0.93) | 9.72E-06 | yes | 6.47E-02 | yes | 6.71E-06 |
| cg08698681 | chr3:171091657 | *TNIK* | *TNIK* | 0.89 (0.84,0.93) | 5.52E-06 | yes | 7.36E-01 | yes | 5.54E-03 |
| cg25636075 | chr3:185217761 | *TMEM41A* | *TMEM41A* | 0.87 (0.81,0.92) | 5.59E-06 | yes | 5.90E-01 | yes | 1.15E-01 |
| cg02803925 | chr3:195974300 | *PCYT1A* | *PCYT1A* | 0.86 (0.82,0.92) | 9.27E-07 | no | 5.10E-01 | yes | 1.45E-03 |
| cg04077085 | chr4:9937674 | *SLC2A9* | *SLC2A9* | 0.86 (0.81,0.91) | 5.34E-07 | yes | 9.54E-01 | yes | 1.65E-04 |
| cg18912470 | chr4:57848125 | *POLR2B* | *POLR2B* | 0.91 (0.87,0.94) | 1.23E-06 | no | 8.94E-01 | no | 6.94E-01 |
| cg26396815 | chr4:102878132 | *BANK1* | *BANK1* | 0.89 (0.84,0.94) | 1.24E-05 | yes | 7.85E-01 | yes | 6.99E-04 |
| cg20866785 | chr4:148733880 | *ARHGAP10* | *Metazoa_SRP* | 0.91 (0.87,0.95) | 1.70E-05 | no | 4.11E-01 | yes | 4.87E-03 |
| cg16362140 | chr5:10708717 | *DAP* | *DAP* | 0.90 (0.87,0.94) | 1.17E-06 | yes | 5.48E-01 | yes | 6.81E-04 |
| cg22588983 | chr5:38783142 | | *AK126213* | 0.86 (0.80,0.92) | 1.35E-05 | yes | 2.06E-01 | yes | 6.09E-03 |
| cg00944309 | chr5:60142446 | | *ELOVL7* | 0.90 (0.86,0.94) | 4.03E-07 | yes | 1.25E-02 | yes | 9.53E-04 |
| cg14978242 | chr5:79501131 | *SERINC5* | *SERINC5* | 0.93 (0.89,0.96) | 1.74E-05 | no | 5.80E-01 | yes | 2.02E-02 |
| cg09565310 | chr5:112541553 | *MCC* | *MCC* | 0.89 (0.85,0.93) | 3.10E-06 | yes | 2.27E-01 | yes | 1.39E-01 |
| cg08969102 | chr5:133563532 | | *PPP2CA* | 0.91 (0.88,0.95) | 1.54E-05 | yes | 1.93E-01 | yes | 3.90E-03 |
| cg21627181 | chr6:25754190 | *SLC17A4* | *SLC17A4* | 0.90 (0.86,0.95) | 1.90E-05 | yes | 2.43E-01 | yes | 3.77E-02 |
| cg09597192 | chr6:32141591 | *AGPAT1* | *PPT2* | 0.88 (0.84,0.93) | 4.29E-06 | yes | 1.44E-02 | yes | 6.25E-03 |
| cg06426027 | chr6:33232644 | *VPS52* | *VPS52* | 0.83 (0.77,0.90) | 2.32E-06 | yes | 4.81E-01 | yes | 6.43E-02 |
| cg18460809 | chr6:57048049 | *BAG2* | *BAG2* | 0.89 (0.85,0.93) | 6.05E-07 | no | 9.91E-01 | yes | 3.55E-03 |
| cg15961693 | chr6:139689053 | | *CITED2* | 0.89 (0.84,0.94) | 1.22E-05 | yes | 7.14E-01 | yes | 1.71E-02 |
| cg26774971 | chr6:158994407 | *TMEM181* | *TMEM181* | 0.90 (0.86,0.95) | 1.88E-05 | no | 8.94E-01 | yes | 1.50E-03 |
| cg05477517 | chr6:164531576 | | *AK093114* | 0.88 (0.83,0.92) | 5.42E-07 | no | 8.79E-01 | yes | 1.28E-06 |
| cg15304012 | chr6:166876490 | *RPS6KA2* | *RPS6KA2* | 1.08 (1.04,1.13) | 1.86E-05 | yes | 4.78E-01 | no | 5.98E-01 |
| cg19851574 | chr6:167178233 | *RPS6KA2* | *RPS6KA2* | 0.95 (0.94,0.97) | 3.42E-06 | yes | 2.34E-01 | yes | 9.92E-03 |
| cg03329755 | chr6:167189272 | *RPS6KA2* | *RPS6KA2* | 0.91 (0.88,0.95) | 6.14E-06 | yes | 1.94E-01 | yes | 2.81E-02 |
| cg25270424 | chr7:24965657 | *OSBPL3* | *OSBPL3* | 0.86 (0.82,0.92) | 4.75E-07 | yes | 1.83E-01 | yes | 5.42E-02 |
| cg04321303 | chr7:44107504 | | *PGAM2* | 0.91 (0.88,0.95) | 2.72E-06 | yes | 3.49E-01 | yes | 2.11E-02 |
| cg02435538 | chr7:75507337 | *RHBDD2* | *RHBDD2* | 0.90 (0.86,0.94) | 7.37E-07 | no | 6.48E-01 | yes | 3.60E-03 |
| cg13007207 | chr7:105279391 | *ATXN7L1* | *ATXN7L1* | 1.26 (1.13,1.40) | 1.87E-05 | no | 1.04E-01 | yes | 9.82E-01 |
| cg17947765 | chr7:117857964 | | *ANKRD7* | 0.86 (0.81,0.92) | 1.17E-05 | yes | 4.12E-01 | yes | 1.23E-01 |
| cg14678084 | chr7:127627251 | *SND1* | *SND1-IT1* | 0.84 (0.78,0.90) | 1.17E-06 | no | 7.92E-01 | yes | 1.92E-03 |
| cg05184016 | chr7:149543136 | *ZNF862* | *BC045757* | 0.85 (0.80,0.90) | 2.74E-08 | yes | 1.84E-01 | yes | 1.38E-06 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| cg07970948 | chr7:149543165 | *ZNF862* | *BC045757* | 0.91 (0.88,0.94) | 6.39E-08 | yes | 2.04E-02 | yes | 1.51E-06 |
| cg06558622 | chr7:149543177 | *ZNF862* | *BC045757* | 0.88 (0.85,0.92) | 3.39E-09 | yes | 4.12E-02 | yes | 1.01E-07 |
| cg24576940 | chr7:150648283 | *KCNH2* | *KCNH2* | 0.87 (0.81,0.93) | 1.83E-05 | yes | 2.26E-02 | yes | 1.91E-03 |
| cg23147443 | chr7:150649655 | *KCNH2* | *KCNH2* | 0.89 (0.85,0.93) | 1.83E-06 | NA | NA | yes | 1.96E-03 |
| cg18666454 | chr7:150651937 | *KCNH2* | *KCNH2* | 0.89 (0.86,0.93) | 1.46E-07 | yes | 4.46E-01 | yes | 5.80E-04 |
| cg02596233 | chr7:150970209 | *SMARCD3* | *SMARCD3* | 0.86 (0.81,0.91) | 2.11E-07 | no | 8.17E-01 | yes | 1.07E-01 |
| cg23706836 | chr8:6407997 | *ANGPT2;MCPH1* | *ANGPT2* | 0.92 (0.88,0.95) | 5.63E-07 | yes | 2.98E-02 | yes | 3.03E-02 |
| cg21919729 | chr8:11719367 | *CTSB* | *CTSB* | 0.92 (0.89,0.95) | 3.03E-06 | yes | 1.76E-01 | yes | 1.05E-01 |
| cg03437605 | chr8:22847209 | *RHOBTB2* | *RHOBTB2* | 0.87 (0.83,0.92) | 1.05E-07 | yes | 4.00E-01 | yes | 5.92E-02 |
| cg22816343 | chr8:26243601 | *BNIP3L* | *BNIP3L* | 0.89 (0.85,0.93) | 2.12E-06 | no | 8.60E-01 | yes | 1.59E-05 |
| cg23205629 | chr8:33421410 | *RNF122* | *RNF122* | 0.91 (0.88,0.95) | 9.28E-06 | yes | 1.29E-01 | yes | 5.57E-01 |
| cg10815420 | chr8:105599835 | *LRP12* | *LRP12* | 0.86 (0.81,0.91) | 2.66E-07 | yes | 2.98E-01 | yes | 2.51E-01 |
| cg02133716 | chr8:128981622 | *PVT1* | *MIR1205* | 0.85 (0.79,0.91) | 8.64E-07 | yes | 3.91E-01 | yes | 3.47E-04 |
| cg00736681 | chr8:134546052 | *ST3GAL1* | *ST3GAL1* | 0.90 (0.87,0.94) | 1.93E-06 | yes | 6.89E-01 | yes | 8.95E-01 |
| cg09377531 | chr8:141046469 | *TRAPPC9* | *AX748239* | 0.90 (0.87,0.93) | 1.23E-08 | yes | 1.87E-01 | yes | 3.13E-05 |
| cg14025883 | chr9:5436224 | *C9orf46* | *C9orf46* | 0.89 (0.85,0.93) | 8.42E-07 | yes | 5.90E-02 | yes | 5.17E-05 |
| cg01499988 | chr9:35755346 | *MSMP* | *MSMP* | 0.88 (0.84,0.93) | 2.01E-06 | yes | 1.05E-01 | yes | 4.30E-03 |
| cg13482814 | chr9:82183332 | | *TLE4* | 0.88 (0.84,0.93) | 4.74E-06 | yes | 4.99E-01 | yes | 2.25E-04 |
| cg13576859 | chr9:97403129 | *FBP1* | *FBP1* | 0.92 (0.88,0.95) | 1.37E-05 | no | 8.87E-01 | yes | 2.39E-03 |
| cg20503329 | chr9:101705792 | *COL15A1* | *COL15A1* | 0.82 (0.76,0.89) | 3.10E-06 | yes | 3.35E-01 | yes | 1.70E-01 |
| cg00045753 | chr9:123630545 | *PHF19* | *PHF19* | 0.88 (0.83,0.93) | 1.32E-05 | yes | 4.29E-01 | yes | 1.52E-01 |
| cg13458609 | chr9:130608923 | *ENG* | *ENG* | 0.89 (0.85,0.93) | 5.74E-08 | yes | 3.81E-01 | yes | 5.87E-05 |
| cg13835688 | chr9:130859454 | *SLC25A25* | *SLC25A25* | 0.89 (0.86,0.93) | 3.33E-09 | yes | 1.90E-02 | yes | 9.77E-04 |
| cg13628444 | chr9:134883788 | *MED27* | *MED27* | 0.89 (0.85,0.93) | 7.76E-07 | yes | 3.70E-03 | yes | 3.48E-02 |
| cg13850063 | chr9:138362321 | | *AK096249* | 0.78 (0.71,0.85) | 5.49E-08 | yes | 8.89E-01 | yes | 7.10E-01 |
| cg14011077 | chr9:138362327 | | *AK096249* | 0.86 (0.82,0.90) | 7.02E-09 | yes | 9.10E-01 | yes | 4.25E-01 |
| cg06958964 | chr10:45494806 | *C10orf25;ZNF22* | *ZNF22* | 0.85 (0.80,0.91) | 2.97E-06 | no | 3.07E-01 | yes | 2.79E-02 |
| cg25854298 | chr10:73936754 | *ASCC1* | *ASCC1* | 0.89 (0.84,0.94) | 8.74E-06 | yes | 1.18E-01 | yes | 1.91E-03 |
| cg04973995 | chr10:74057977 | | *DDIT4* | 0.92 (0.89,0.96) | 1.10E-05 | yes | 5.68E-01 | yes | 8.10E-01 |
| cg00366037 | chr10:76781121 | *MYST4* | *KAT6B* | 0.88 (0.83,0.93) | 1.45E-05 | yes | 2.11E-01 | yes | 7.89E-03 |
| cg22235258 | chr11:34675402 | *EHF* | *EHF* | 0.88 (0.83,0.93) | 1.61E-05 | yes | 2.27E-01 | yes | 1.08E-03 |
| cg24459209 | chr11:57148215 | *PRG3* | *PRG3* | 0.86 (0.81,0.91) | 8.52E-08 | yes | 5.07E-02 | yes | 9.52E-03 |
| cg15700636 | chr11:57156050 | *PRG2* | *PRG2* | 0.89 (0.85,0.93) | 2.35E-07 | no | 8.75E-01 | yes | 1.59E-02 |
| cg08773180 | chr11:57157607 | *PRG2* | *PRG2* | 0.89 (0.85,0.93) | 1.77E-07 | no | 5.88E-01 | yes | 1.99E-04 |
| cg12819873 | chr11:57157632 | *PRG2* | *PRG2* | 0.90 (0.86,0.94) | 9.55E-06 | yes | 1.69E-01 | yes | 8.70E-03 |
| cg27533472 | chr11:59856225 | *MS4A2* | *MS4A2* | 0.82 (0.76,0.90) | 4.09E-06 | yes | 3.44E-01 | yes | 4.65E-01 |
| cg25087851 | chr11:60623918 | *GPR44* | *PTGDR2* | 0.89 (0.85,0.93) | 1.69E-08 | yes | 1.80E-01 | yes | 4.03E-02 |
| cg13233042 | chr11:63432489 | *ATL3* | *ATL3* | 0.88 (0.83,0.93) | 3.59E-06 | no | 4.50E-01 | yes | 1.82E-03 |
| cg05300717 | chr11:65546210 | *DKFZp761E198* | *DKFZp761E198* | 0.86 (0.82,0.90) | 6.51E-10 | yes | 4.86E-01 | yes | 1.41E-03 |
| cg15219163 | chr11:70842128 | *SHANK2* | *SHANK2* | 1.17 (1.09,1.26) | 1.80E-05 | yes | 4.61E-01 | no | 3.35E-01 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| cg24368962 | chr11:111570978 | *SIK2* | *DQ599327* | 0.85 (0.80,0.91) | 1.28E-06 | no | 7.04E-01 | yes | 3.32E-04 |
| cg19434937 | chr12:7104184 | *LPCAT3* | *EMG1* | 0.91 (0.88,0.95) | 1.55E-06 | yes | 3.37E-01 | yes | 1.82E-02 |
| cg03014680 | chr12:10122522 | *CLEC12A* | *CLEC12A* | 0.92 (0.88,0.95) | 2.14E-06 | yes | 3.27E-01 | yes | 2.36E-01 |
| cg09447105 | chr12:15126020 | *PDE6H* | *PDE6H* | 0.88 (0.83,0.92) | 7.60E-07 | yes | 1.90E-04 | yes | 6.53E-02 |
| cg24028828 | chr12:56694932 | *CS* | *CS* | 0.87 (0.82,0.92) | 1.99E-06 | yes | 6.15E-01 | yes | 2.71E-04 |
| cg21498475 | chr12:113737469 | *SLC24A6* | *SLC24A6* | 0.90 (0.86,0.94) | 5.44E-06 | yes | 2.79E-01 | yes | 2.43E-03 |
| cg10065736 | chr12:117440120 | *FBXW8* | *AK055849* | 0.90 (0.87,0.94) | 1.41E-07 | yes | 8.32E-01 | yes | 4.36E-01 |
| cg03131767 | chr12:123446272 | *ABCB9* | *ABCB9* | 0.89 (0.85,0.93) | 7.21E-07 | yes | 6.36E-01 | no | 8.41E-02 |
| cg19928703 | chr13:30143971 | *SLC7A1* | *SLC7A1* | 0.89 (0.84,0.94) | 1.21E-05 | yes | 2.32E-01 | yes | 3.45E-03 |
| cg07908654 | chr13:41631052 | | *TRNA_Glu* | 0.89 (0.85,0.93) | 2.60E-07 | yes | 1.68E-01 | yes | 1.89E-04 |
| cg24818699 | chr13:43355514 | *C13orf30* | *C13orf30* | 0.87 (0.82,0.93) | 8.53E-06 | no | 1.94E-01 | yes | 2.73E-02 |
| cg08770358 | chr13:48876684 | *RB1* | *BC039553* | 0.84 (0.78,0.91) | 1.42E-05 | yes | 3.50E-01 | yes | 8.73E-04 |
| cg00222125 | chr13:53226144 | *SUGT1* | *SUGT1* | 0.90 (0.86,0.95) | 1.43E-05 | yes | 9.45E-01 | yes | 2.95E-01 |
| cg11770323 | chr13:80066032 | *NDFIP2* | *NDFIP2* | 0.91 (0.87,0.95) | 5.86E-06 | yes | 1.80E-01 | yes | 1.85E-04 |
| cg25479097 | chr13:113305704 | *C13orf35* | *C13orf35* | 0.89 (0.84,0.93) | 9.11E-07 | no | 4.89E-01 | yes | 1.07E-02 |
| cg18368116 | chr14:21436271 | | *RNASE2* | 0.89 (0.84,0.93) | 4.93E-06 | yes | 2.16E-01 | yes | 6.19E-03 |
| cg08077807 | chr14:62001072 | *PRKCH* | *PRKCH* | 0.85 (0.80,0.90) | 1.29E-07 | no | 9.48E-01 | yes | 5.21E-04 |
| cg04933530 | chr14:77419754 | | *IRF2BPL* | 0.89 (0.85,0.93) | 1.02E-07 | yes | 3.88E-01 | yes | 8.35E-04 |
| cg01901579 | chr14:95615731 | *DICER1* | *DICER1* | 0.91 (0.88,0.95) | 5.86E-06 | yes | 7.73E-04 | yes | 2.91E-01 |
| cg16409452 | chr14:100610186 | *EVL* | *AX747103* | 0.91 (0.87,0.94) | 4.89E-07 | yes | 3.79E-01 | yes | 5.53E-03 |
| cg14084609 | chr14:100610407 | *EVL* | *AX747103* | 0.89 (0.85,0.92) | 2.96E-09 | yes | 1.97E-01 | yes | 6.81E-01 |
| cg18550847 | chr14:100610570 | *EVL* | *AX747103* | 0.91 (0.88,0.94) | 7.10E-07 | no | 1.00E+00 | yes | 2.36E-02 |
| cg01000631 | chr14:100610667 | | *EVL* | 0.91 (0.87,0.94) | 4.88E-08 | yes | 7.95E-01 | yes | 2.70E-02 |
| cg05875066 | chr14:104625249 | *KIF26A* | *KIF26A* | 0.87 (0.83,0.92) | 1.77E-07 | yes | 8.03E-01 | yes | 1.48E-02 |
| cg18817654 | chr15:39485138 | | *C15orf54* | 0.87 (0.82,0.92) | 3.41E-06 | yes | 5.33E-01 | no | 9.20E-01 |
| cg25939647 | chr15:40173065 | *GPR176* | *GPR176* | 0.91 (0.88,0.95) | 1.91E-06 | yes | 2.61E-01 | yes | 2.18E-03 |
| cg07177867 | chr15:52030746 | *LYSMD2* | *LYSMD2* | 0.90 (0.86,0.94) | 1.29E-05 | yes | 3.19E-03 | yes | 3.93E-02 |
| cg11266582 | chr15:64275853 | *DAPK2* | *DAPK2* | 0.89 (0.85,0.94) | 1.52E-05 | no | 5.22E-01 | yes | 1.57E-03 |
| cg10387956 | chr15:72646210 | *HEXA* | *BC034424* | 0.91 (0.87,0.95) | 2.72E-06 | no | 6.56E-01 | yes | 1.64E-03 |
| cg23387863 | chr15:77472416 | *SGK269* | *AX747193* | 0.91 (0.87,0.94) | 1.51E-06 | yes | 6.99E-01 | yes | 4.93E-03 |
| cg04497992 | chr16:616212 | *NHLRC4* | *C16orf11* | 0.90 (0.87,0.94) | 1.92E-06 | yes | 7.99E-01 | yes | 1.20E-01 |
| cg08067346 | chr16:25011481 | *ARHGAP17* | *DQ583809* | 0.90 (0.86,0.95) | 1.60E-05 | yes | 8.15E-02 | yes | 1.26E-02 |
| cg26134665 | chr16:31021544 | *STX1B* | *STX1B* | 0.92 (0.88,0.95) | 9.50E-06 | yes | 9.09E-01 | yes | 8.09E-01 |
| cg09147843 | chr16:53467612 | *RBL2* | *RBL2* | 0.89 (0.85,0.94) | 8.89E-06 | yes | 1.52E-01 | yes | 1.26E-03 |
| cg01998785 | chr16:55542709 | *LPCAT2* | *LPCAT2* | 0.91 (0.87,0.94) | 6.17E-07 | yes | 6.47E-01 | yes | 3.60E-03 |
| cg27383865 | chr16:84075870 | *SLC38A8* | *SLC38A8* | 1.11 (1.06,1.16) | 1.73E-05 | yes | 7.77E-01 | yes | 5.82E-01 |
| cg08640475 | chr16:85551478 | | *KIAA0182* | 0.92 (0.89,0.95) | 2.36E-06 | yes | 9.26E-02 | yes | 1.20E-04 |
| cg10099827 | chr16:85551514 | | *KIAA0182* | 0.92 (0.89,0.95) | 1.32E-06 | yes | 4.54E-02 | yes | 3.95E-04 |
| cg08940169 | chr16:88540241 | *ZFPM1* | *ZFPM1* | 0.91 (0.87,0.94) | 2.93E-07 | yes | 6.88E-02 | yes | 2.18E-05 |
| cg04983687 | chr16:88558223 | *ZFPM1* | *ZFPM1* | 0.93 (0.90,0.95) | 1.33E-10 | yes | 1.82E-02 | yes | 5.27E-10 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| cg20315954 | chr17:15137304 | *PMP22* | *PMP22* | 0.88 (0.84,0.93) | 3.58E-06 | no | 9.09E-01 | yes | 1.95E-02 |
| cg20885063 | chr17:17939419 | *ATPAF2* | *ATPAF2* | 0.90 (0.86,0.94) | 1.06E-06 | yes | 1.68E-01 | yes | 9.97E-03 |
| cg14611258 | chr17:17946468 | *C17orf39* | *C17orf39* | 0.89 (0.85,0.94) | 6.41E-06 | yes | 2.75E-01 | yes | 1.74E-03 |
| cg19468946 | chr17:37922297 | *IKZF3* | *IKZF3* | 1.09 (1.05,1.13) | 1.50E-05 | yes | 4.50E-01 | no | 5.77E-01 |
| cg21723861 | chr17:39686628 | | *KRT19* | 0.87 (0.82,0.92) | 1.59E-07 | yes | 4.81E-01 | yes | 1.26E-03 |
| cg00170714 | chr17:40724562 | *MLX;PSMC3IP* | *PSMC3IP* | 0.89 (0.85,0.93) | 6.15E-08 | no | 5.98E-01 | yes | 5.88E-02 |
| cg25173129 | chr17:56269410 | *EPX* | *EPX* | 0.88 (0.84,0.93) | 8.09E-07 | yes | 1.92E-01 | yes | 1.50E-01 |
| cg02970679 | chr17:56269818 | *EPX* | *EPX* | 0.88 (0.83,0.92) | 9.99E-07 | no | 5.25E-01 | yes | 1.74E-03 |
| cg17374802 | chr17:56270828 | *EPX* | *EPX* | 0.90 (0.86,0.94) | 2.06E-06 | no | 5.64E-01 | yes | 3.47E-02 |
| cg17041511 | chr17:61509620 | | *CYB561* | 0.91 (0.87,0.95) | 1.15E-05 | yes | 3.47E-02 | yes | 3.39E-02 |
| cg22312249 | chr17:72779428 | *TMEM104* | *TMEM104* | 0.91 (0.87,0.95) | 8.73E-06 | yes | 6.60E-01 | yes | 1.90E-03 |
| cg09705784 | chr17:76565232 | *DNAH17* | *DNAH17* | 0.91 (0.88,0.94) | 1.50E-07 | yes | 6.05E-02 | yes | 3.80E-03 |
| cg06725287 | chr17:80533762 | *FOXK2* | *FOXK2* | 0.87 (0.83,0.92) | 9.07E-08 | no | 3.20E-01 | yes | 1.26E-05 |
| cg13054523 | chr17:81055722 | | *METRNL* | 0.87 (0.83,0.91) | 1.20E-08 | yes | 3.92E-01 | yes | 4.40E-01 |
| cg18337287 | chr19:930871 | *ARID3A* | *ARID3A* | 0.86 (0.81,0.91) | 7.21E-08 | yes | 6.02E-01 | yes | 8.52E-05 |
| cg12104982 | chr19:5592815 | *SAFB2* | *SAFB2* | 0.86 (0.81,0.91) | 1.13E-07 | yes | 1.59E-02 | yes | 1.49E-04 |
| cg10644885 | chr19:11687621 | *ACP5* | *ACP5* | 0.86 (0.82,0.90) | 5.77E-11 | yes | 2.35E-01 | yes | 2.03E-03 |
| cg02359181 | chr19:34860339 | *GPI* | *GPI* | 0.88 (0.83,0.93) | 2.68E-06 | yes | 8.27E-01 | yes | 5.69E-04 |
| cg20673965 | chr19:44220148 | *IRGC* | *IRGC* | 0.90 (0.85,0.94) | 5.54E-06 | yes | 9.59E-01 | yes | 3.27E-02 |
| cg26979537 | chr19:48016860 | *NAPA* | *NAPA* | 0.83 (0.77,0.90) | 1.31E-06 | yes | 3.68E-01 | yes | 2.13E-01 |
| cg21073212 | chr20:30866501 | *KIF3B* | *KIF3B* | 0.92 (0.89,0.96) | 1.79E-05 | no | 7.85E-02 | yes | 4.58E-01 |
| cg20226253 | chr20:34022914 | *GDF5* | *GDF5OS* | 0.87 (0.81,0.92) | 1.15E-05 | yes | 8.43E-01 | yes | 2.12E-01 |
| cg21045547 | chr20:35422703 | *C20orf117* | *KIAA0889* | 0.89 (0.85,0.94) | 5.32E-06 | no | 9.41E-02 | yes | 4.39E-02 |
| cg13792581 | chr20:43590115 | *TOMM34* | *TOMM34* | 0.87 (0.82,0.93) | 1.34E-05 | yes | 3.61E-01 | yes | 3.10E-04 |
| cg13197551 | chr20:60709957 | *LSM14B* | *LSM14B* | 0.86 (0.81,0.91) | 9.23E-07 | yes | 5.26E-01 | yes | 1.21E-01 |
| cg18042632 | chr21:42520902 | *C21orf130* | *LINC00323* | 0.92 (0.88,0.95) | 1.87E-06 | no | 9.54E-01 | yes | 5.57E-03 |
| cg18879389 | chr21:43771120 | *TFF2* | *TFF2* | 0.87 (0.82,0.92) | 1.21E-06 | yes | 2.08E-01 | yes | 1.03E-01 |

* Annotation based on UCSC Known Gene also fills in nearest gene within 10 MB.

Table E7 *Lookup of 179 CpGs differentially methylated in blood in childhood relation to asthma, in an independent study of methylation in purified eosinophils (Eos) in relation to asthma.*



| CpG | chr:position | UCSC RefGene Name | UCSC Known Gene* | PACE Discovery (N=647 cases) | | Look-Up in Eos (N= 16 cases) | |
|---|---|---|---|---|---|---|---|
| | | | | OR (CI) | P-value | Direction of Effect Concordant with PACE | P-value |
| cg06315149 | chr1:2036398 | *PRKCZ* | *PRKCZ* | 0.89 (0.84,0.93) | 6.08E-06 | yes | 2.43E-02 |
| cg13066938 | chr1:6341140 | *ACOT7* | *ACOT7* | 0.91 (0.88,0.95) | 1.67E-05 | yes | 2.36E-02 |
| cg21220721 | chr1:6341230 | *ACOT7* | *ACOT7* | 0.94 (0.92,0.96) | 1.02E-08 | yes | 1.80E-02 |
| cg09249800 | chr1:6341287 | *ACOT7* | *ACOT7* | 0.88 (0.84,0.92) | 1.19E-08 | yes | 3.52E-02 |
| cg11699125 | chr1:6341327 | *ACOT7* | *ACOT7* | 0.90 (0.87,0.93) | 7.54E-10 | yes | 4.74E-02 |
| cg18783781 | chr1:9599067 | *SLC25A33* | *SLC25A33* | 0.90 (0.86,0.94) | 7.45E-06 | yes | 4.16E-02 |
| cg02171825 | chr1:26517586 | *CATSPER4* | *CATSPER4* | 0.88 (0.83,0.93) | 9.01E-06 | yes | 2.31E-02 |
| cg01942646 | chr1:27240694 | *NR0B2* | *NR0B2* | 0.88 (0.83,0.93) | 1.45E-06 | yes | 3.78E-02 |
| cg16263722 | chr1:29523841 | *MECR* | *MECR* | 0.89 (0.86,0.93) | 2.14E-07 | yes | 3.24E-02 |
| cg11987455 | chr1:43290834 | *ERMAP* | *ERMAP* | 0.89 (0.85,0.93) | 7.55E-07 | yes | 3.90E-02 |
| cg11683482 | chr1:44678623 | *DMAP1* | *DMAP1* | 0.90 (0.86,0.93) | 5.39E-08 | yes | 3.32E-02 |
| cg12643917 | chr1:44715958 | *ERI3* | *ERI3* | 0.89 (0.85,0.94) | 8.98E-06 | yes | 1.67E-02 |
| cg26252077 | chr1:61607055 | *NFIA* | *NFIA* | 0.88 (0.84,0.92) | 2.18E-08 | yes | 3.82E-02 |
| cg10704177 | chr1:62209607 | *INADL* | *INADL* | 0.90 (0.87,0.94) | 2.25E-07 | yes | 3.63E-02 |
| cg01445399 | chr1:87596934 | *LOC339524* | *LOC339524* | 0.91 (0.87,0.95) | 1.72E-05 | yes | 3.23E-02 |
| cg19805160 | chr1:159870731 | *CCDC19* | *CCDC19* | 0.89 (0.85,0.94) | 2.85E-06 | yes | 2.76E-02 |
| cg09332506 | chr1:160309220 | *COPA* | *NCSTN* | 0.86 (0.81,0.91) | 1.00E-06 | yes | 2.66E-02 |
| cg17971251 | chr1:177907297 | *SEC16B* | *SEC16B* | 0.86 (0.82,0.91) | 9.52E-09 | yes | 3.41E-02 |
| cg26033504 | chr1:201458737 | *CSRP1* | *CSRP1* | 0.91 (0.87,0.95) | 6.35E-06 | yes | 5.95E-02 |
| cg04895895 | chr1:231005895 | *C1orf198* | *C1orf198* | 0.89 (0.84,0.93) | 5.26E-06 | yes | 4.08E-02 |
| cg02473287 | chr2:9752386 | *YWHAQ* | *YWHAQ* | 0.90 (0.85,0.94) | 8.00E-06 | yes | 3.18E-02 |
| cg10142874 | chr2:11917623 | *LPIN1* | *LPIN1* | 0.89 (0.85,0.93) | 1.04E-06 | yes | 3.75E-02 |
| cg26752663 | chr2:25142016 | *ADCY3* | *ADCY3* | 1.12 (1.07,1.17) | 1.79E-06 | yes | 3.75E-01 |
| cg00043800 | chr2:74612144 | *LOC100189589* | *LOC100189589* | 0.91 (0.87,0.95) | 1.32E-05 | yes | 5.14E-02 |
| cg17988187 | chr2:74612222 | *LOC100189589* | *LOC100189589* | 0.90 (0.86,0.94) | 1.21E-06 | yes | 2.62E-02 |
| cg12077754 | chr2:75089669 | *HK2* | *HK2* | 0.92 (0.89,0.96) | 4.56E-06 | yes | 3.41E-02 |
| cg22674082 | chr2:98585733 | *TMEM131* | *TMEM131* | 0.89 (0.84,0.94) | 1.44E-05 | yes | 2.99E-02 |
| cg00327263 | chr2:120019111 | *STEAP3* | *STEAP3* | 0.90 (0.86,0.94) | 8.00E-06 | yes | 9.15E-02 |
| cg25950520 | chr2:121036760 | *RALB* | *RALB* | 0.85 (0.79,0.91) | 1.31E-05 | yes | 5.60E-02 |
| cg00213281 | chr2:149639822 | *KIF5C;MIR1978* | *JA429504* | 0.88 (0.83,0.93) | 1.24E-06 | yes | 2.29E-02 |
| cg02494549 | chr2:161798364 | | *TANK* | 0.86 (0.82,0.91) | 1.56E-07 | yes | 5.16E-02 |
| cg01310029 | chr3:3152374 | *IL5RA* | *IL5RA* | 0.89 (0.85,0.94) | 4.18E-06 | yes | 3.68E-02 |
| cg10159529 | chr3:3152530 | *IL5RA* | *IL5RA* | 0.90 (0.86,0.94) | 4.48E-06 | yes | 3.12E-02 |
| cg25224369 | chr3:12918528 | | *DQ581328* | 0.90 (0.86,0.94) | 7.75E-06 | yes | 4.65E-02 |
| cg07386061 | chr3:52492874 | *NISCH* | *NISCH* | 0.91 (0.88,0.95) | 1.00E-06 | yes | 3.81E-02 |
| cg17890764 | chr3:52864816 | *ITIH4* | *ITIH4* | 0.91 (0.87,0.94) | 8.95E-07 | yes | 9.14E-02 |
| cg07410597 | chr3:66404129 | *SLC25A26* | *LRIG1* | 0.88 (0.84,0.93) | 2.70E-07 | yes | 3.02E-02 |
| cg04217850 | chr3:66428294 | *SLC25A26* | *LRIG1* | 0.88 (0.83,0.93) | 2.35E-06 | yes | 4.53E-02 |
| cg06070625 | chr3:69812798 | *MITF* | *MITF* | 0.90 (0.86,0.94) | 5.36E-06 | yes | 2.97E-02 |
| cg06391412 | chr3:71295684 | *FOXP1* | *FOXP1* | 0.87 (0.84,0.91) | 3.00E-09 | yes | 2.70E-02 |
| cg20263733 | chr3:130616293 | *ATP2C1* | *ATP2C1* | 0.87 (0.82,0.92) | 4.26E-07 | yes | 5.11E-02 |
| cg09423651 | chr3:136618442 | *NCK1* | *NCK1* | 0.88 (0.83,0.93) | 9.72E-06 | yes | 3.98E-02 |
| cg08698681 | chr3:171091657 | *TNIK* | *TNIK* | 0.89 (0.84,0.93) | 5.52E-06 | yes | 2.04E-02 |
| cg25636075 | chr3:185217761 | *TMEM41A* | *TMEM41A* | 0.87 (0.81,0.92) | 5.59E-06 | yes | 2.23E-02 |
| cg02803925 | chr3:195974300 | *PCYT1A* | *PCYT1A* | 0.86 (0.82,0.92) | 9.27E-07 | yes | 3.86E-02 |
| cg04077085 | chr4:9937674 | *SLC2A9* | *SLC2A9* | 0.86 (0.81,0.91) | 5.34E-07 | yes | 3.42E-02 |
| cg18912470 | chr4:57848125 | *POLR2B* | *POLR2B* | 0.91 (0.87,0.94) | 1.23E-06 | yes | 3.57E-02 |
| cg26396815 | chr4:102878132 | *BANK1* | *BANK1* | 0.89 (0.84,0.94) | 1.24E-05 | yes | 3.87E-02 |
| cg20866785 | chr4:148733880 | *ARHGAP10* | *Metazoa_SRP* | 0.91 (0.87,0.95) | 1.70E-05 | yes | 6.39E-02 |
| cg16362140 | chr5:10708717 | *DAP* | *DAP* | 0.90 (0.87,0.94) | 1.17E-06 | yes | 3.66E-02 |
| cg22588983 | chr5:38783142 | | *AK126213* | 0.86 (0.80,0.92) | 1.35E-05 | yes | 4.05E-02 |
| cg00944309 | chr5:60142446 | | *ELOVL7* | 0.90 (0.86,0.94) | 4.03E-07 | yes | 4.96E-02 |
| cg14978242 | chr5:79501131 | *SERINC5* | *SERINC5* | 0.93 (0.89,0.96) | 1.74E-05 | yes | 2.47E-02 |
| cg09565310 | chr5:112541553 | *MCC* | *MCC* | 0.89 (0.85,0.93) | 3.10E-06 | yes | 3.03E-02 |
| cg08969102 | chr5:133563532 | | *PPP2CA* | 0.91 (0.88,0.95) | 1.54E-05 | yes | 3.31E-02 |
| cg21627181 | chr6:25754190 | *SLC17A4* | *SLC17A4* | 0.90 (0.86,0.95) | 1.90E-05 | yes | 3.21E-02 |
| cg09597192 | chr6:32141591 | *AGPAT1* | *PPT2* | 0.88 (0.84,0.93) | 4.29E-06 | yes | 1.99E-02 |
| cg06426027 | chr6:33232644 | *VPS52* | *VPS52* | 0.83 (0.77,0.90) | 2.32E-06 | yes | 1.87E-02 |
| cg18460809 | chr6:57048049 | *BAG2* | *BAG2* | 0.89 (0.85,0.93) | 6.05E-07 | yes | 3.41E-02 |
| cg15961693 | chr6:139689053 | | *CITED2* | 0.89 (0.84,0.94) | 1.22E-05 | yes | 3.02E-02 |
| cg26774971 | chr6:158994407 | *TMEM181* | *TMEM181* | 0.90 (0.86,0.95) | 1.88E-05 | yes | 3.08E-02 |
| cg05477517 | chr6:164531576 | | *AK093114* | 0.88 (0.83,0.92) | 5.42E-07 | yes | 4.58E-02 |
| cg15304012 | chr6:166876490 | *RPS6KA2* | *RPS6KA2* | 1.08 (1.04,1.13) | 1.86E-05 | yes | 2.13E-01 |
| cg19851574 | chr6:167178233 | *RPS6KA2* | *RPS6KA2* | 0.95 (0.94,0.97) | 3.42E-06 | yes | 3.76E-02 |
| cg03329755 | chr6:167189272 | *RPS6KA2* | *RPS6KA2* | 0.91 (0.88,0.95) | 6.14E-06 | yes | 3.04E-02 |
| cg25270424 | chr7:24965657 | *OSBPL3* | *OSBPL3* | 0.86 (0.82,0.92) | 4.75E-07 | yes | 4.69E-02 |
| cg04321303 | chr7:44107504 | | *PGAM2* | 0.91 (0.88,0.95) | 2.72E-06 | yes | 3.02E-02 |
| cg02435538 | chr7:75507337 | *RHBDD2* | *RHBDD2* | 0.90 (0.86,0.94) | 7.37E-07 | yes | 6.15E-02 |

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|---|---|---|---|---|---|---|---|
| cg13007207 | chr7:105279391 | *ATXN7L1* | *ATXN7L1* | 1.26 (1.13,1.40) | 1.87E-05 | yes | 6.20E-01 |
| cg17947765 | chr7:117857964 | | *ANKRD7* | 0.86 (0.81,0.92) | 1.17E-05 | yes | 1.41E-01 |
| cg14678084 | chr7:127627251 | *SND1* | *SND1-IT1* | 0.84 (0.78,0.90) | 1.17E-06 | yes | 1.57E-02 |
| cg05184016 | chr7:149543136 | *ZNF862* | *BC045757* | 0.85 (0.80,0.90) | 2.74E-08 | yes | 4.56E-02 |
| cg07970948 | chr7:149543165 | *ZNF862* | *BC045757* | 0.91 (0.88,0.94) | 6.39E-08 | yes | 3.05E-02 |
| cg06558622 | chr7:149543177 | *ZNF862* | *BC045757* | 0.88 (0.85,0.92) | 3.39E-09 | yes | 4.61E-02 |
| cg24576940 | chr7:150648283 | *KCNH2* | *KCNH2* | 0.87 (0.81,0.93) | 1.83E-05 | yes | 3.44E-02 |
| cg23147443 | chr7:150649655 | *KCNH2* | *KCNH2* | 0.89 (0.85,0.93) | 1.83E-06 | yes | 2.39E-02 |
| cg18666454 | chr7:150651937 | *KCNH2* | *KCNH2* | 0.89 (0.86,0.93) | 1.46E-07 | yes | 2.53E-02 |
| cg02596233 | chr7:150970209 | *SMARCD3* | *SMARCD3* | 0.86 (0.81,0.91) | 2.11E-07 | yes | 2.55E-02 |
| cg23706836 | chr8:6407997 | *ANGPT2;MCPH1* | *ANGPT2* | 0.92 (0.88,0.95) | 5.63E-07 | yes | 3.33E-02 |
| cg21919729 | chr8:11719367 | *CTSB* | *CTSB* | 0.92 (0.89,0.95) | 3.03E-06 | yes | 4.45E-02 |
| cg03437605 | chr8:22847209 | *RHOBTB2* | *RHOBTB2* | 0.87 (0.83,0.92) | 1.05E-07 | yes | 6.06E-02 |
| cg22816343 | chr8:26243601 | *BNIP3L* | *BNIP3L* | 0.89 (0.85,0.93) | 2.12E-06 | yes | 5.31E-02 |
| cg23205629 | chr8:33421410 | *RNF122* | *RNF122* | 0.91 (0.88,0.95) | 9.28E-06 | yes | 4.96E-02 |
| cg10815420 | chr8:105599835 | *LRP12* | *LRP12* | 0.86 (0.81,0.91) | 2.66E-07 | yes | 9.38E-02 |
| cg02133716 | chr8:128981622 | *PVT1* | *MIR1205* | 0.85 (0.79,0.91) | 8.64E-07 | yes | 2.62E-02 |
| cg00736681 | chr8:134546052 | *ST3GAL1* | *ST3GAL1* | 0.90 (0.87,0.94) | 1.93E-06 | yes | 2.41E-02 |
| cg09377531 | chr8:141046469 | *TRAPPC9* | *AX748239* | 0.90 (0.87,0.93) | 1.23E-08 | yes | 4.19E-02 |
| cg14025883 | chr9:5436224 | *C9orf46* | *C9orf46* | 0.89 (0.85,0.93) | 8.42E-07 | yes | 2.96E-02 |
| cg01499988 | chr9:35755346 | *MSMP* | *MSMP* | 0.88 (0.84,0.93) | 2.01E-06 | yes | 3.59E-02 |
| cg13482814 | chr9:82183332 | | *TLE4* | 0.88 (0.84,0.93) | 4.74E-06 | yes | 2.99E-02 |
| cg13576859 | chr9:97403129 | *FBP1* | *FBP1* | 0.92 (0.88,0.95) | 1.37E-05 | yes | 2.46E-02 |
| cg20503329 | chr9:101705792 | *COL15A1* | *COL15A1* | 0.82 (0.76,0.89) | 3.10E-06 | yes | 2.35E-02 |
| cg00045753 | chr9:123630545 | *PHF19* | *PHF19* | 0.88 (0.83,0.93) | 1.32E-05 | yes | 3.10E-02 |
| cg13458609 | chr9:130608923 | *ENG* | *ENG* | 0.89 (0.85,0.93) | 5.74E-08 | yes | 4.21E-02 |
| cg13835688 | chr9:130859454 | *SLC25A25* | *SLC25A25* | 0.89 (0.86,0.93) | 3.33E-09 | yes | 2.66E-02 |
| cg13628444 | chr9:134883788 | *MED27* | *MED27* | 0.89 (0.85,0.93) | 7.76E-07 | yes | 3.53E-02 |
| cg13850063 | chr9:138362321 | | *AK096249* | 0.78 (0.71,0.85) | 5.49E-08 | yes | 3.02E-02 |
| cg14011077 | chr9:138362327 | | *AK096249* | 0.86 (0.82,0.90) | 7.02E-09 | yes | 3.48E-02 |
| cg06958964 | chr10:45494806 | *C10orf25;ZNF22* | *ZNF22* | 0.85 (0.80,0.91) | 2.97E-06 | yes | 4.05E-02 |
| cg25854298 | chr10:73936754 | *ASCC1* | *ASCC1* | 0.89 (0.84,0.94) | 8.74E-06 | yes | 2.58E-02 |
| cg04973995 | chr10:74057977 | | *DDIT4* | 0.92 (0.89,0.96) | 1.10E-05 | yes | 4.83E-01 |
| cg00366037 | chr10:76781121 | *MYST4* | *KAT6B* | 0.88 (0.83,0.93) | 1.45E-05 | yes | 4.11E-02 |
| cg22235258 | chr11:34675402 | *EHF* | *EHF* | 0.88 (0.83,0.93) | 1.61E-05 | yes | 4.94E-02 |
| cg24459209 | chr11:57148215 | *PRG3* | *PRG3* | 0.86 (0.81,0.91) | 8.52E-08 | yes | 2.74E-02 |
| cg15700636 | chr11:57156050 | *PRG2* | *PRG2* | 0.89 (0.85,0.93) | 2.35E-07 | yes | 3.13E-02 |
| cg08773180 | chr11:57157607 | *PRG2* | *PRG2* | 0.89 (0.85,0.93) | 1.77E-07 | yes | 2.40E-02 |
| cg12819873 | chr11:57157632 | *PRG2* | *PRG2* | 0.90 (0.86,0.94) | 9.55E-06 | yes | 4.33E-02 |
| cg27533472 | chr11:59856225 | *MS4A2* | *MS4A2* | 0.82 (0.76,0.90) | 4.09E-06 | yes | 2.21E-02 |
| cg25087851 | chr11:60623918 | *GPR44* | *PTGDR2* | 0.89 (0.85,0.93) | 1.69E-08 | yes | 3.14E-02 |
| cg13233042 | chr11:63432489 | *ATL3* | *ATL3* | 0.88 (0.83,0.93) | 3.59E-06 | yes | 4.19E-02 |
| cg05300717 | chr11:65546210 | *DKFZp761E198* | *DKFZp761E198* | 0.86 (0.82,0.90) | 6.51E-10 | yes | 1.25E-02 |
| cg15219163 | chr11:70842128 | *SHANK2* | *SHANK2* | 1.17 (1.09,1.26) | 1.80E-05 | no | 1.09E-01 |
| cg24368962 | chr11:111570978 | *SIK2* | *DQ599327* | 0.85 (0.80,0.91) | 1.28E-06 | yes | 3.42E-02 |
| cg19434937 | chr12:7104184 | *LPCAT3* | *EMG1* | 0.91 (0.88,0.95) | 1.55E-06 | yes | 3.88E-02 |
| cg03014680 | chr12:10122522 | *CLEC12A* | *CLEC12A* | 0.92 (0.88,0.95) | 2.14E-06 | yes | 4.57E-02 |
| cg09447105 | chr12:15126020 | *PDE6H* | *PDE6H* | 0.88 (0.83,0.92) | 7.60E-07 | yes | 2.92E-02 |
| cg24028828 | chr12:56694932 | *CS* | *CS* | 0.87 (0.82,0.92) | 1.99E-06 | yes | 2.24E-02 |
| cg21498475 | chr12:113737469 | *SLC24A6* | *SLC24A6* | 0.90 (0.86,0.94) | 5.44E-06 | yes | 2.10E-02 |
| cg10065736 | chr12:117440120 | *FBXW8* | *AK055849* | 0.90 (0.87,0.94) | 1.41E-07 | yes | 1.71E-02 |
| cg03131767 | chr12:123446272 | *ABCB9* | *ABCB9* | 0.89 (0.85,0.93) | 7.21E-07 | yes | 3.09E-02 |
| cg19928703 | chr13:30143971 | *SLC7A1* | *SLC7A1* | 0.89 (0.84,0.94) | 1.21E-05 | yes | 2.82E-02 |
| cg07908654 | chr13:41631052 | | *TRNA_Glu* | 0.89 (0.85,0.93) | 2.60E-07 | yes | 4.01E-02 |
| cg24818699 | chr13:43355514 | *C13orf30* | *C13orf30* | 0.87 (0.82,0.93) | 8.53E-06 | yes | 8.31E-02 |
| cg08770358 | chr13:48876684 | *RB1* | *BC039553* | 0.84 (0.78,0.91) | 1.42E-05 | yes | 4.03E-02 |
| cg00222125 | chr13:53226144 | *SUGT1* | *SUGT1* | 0.90 (0.86,0.95) | 1.43E-05 | yes | 9.65E-01 |
| cg11770323 | chr13:80066032 | *NDFIP2* | *NDFIP2* | 0.91 (0.87,0.95) | 5.86E-06 | yes | 3.73E-02 |
| cg25479097 | chr13:113305704 | *C13orf35* | *C13orf35* | 0.89 (0.84,0.93) | 9.11E-07 | yes | 2.49E-02 |
| cg18368116 | chr14:21436271 | | *RNASE2* | 0.89 (0.84,0.93) | 4.93E-06 | yes | 2.25E-02 |
| cg08077807 | chr14:62001072 | *PRKCH* | *PRKCH* | 0.85 (0.80,0.90) | 1.29E-07 | yes | 4.37E-02 |
| cg04933530 | chr14:77419754 | | *IRF2BPL* | 0.89 (0.85,0.93) | 1.02E-07 | yes | 2.64E-02 |
| cg01901579 | chr14:95615731 | *DICER1* | *DICER1* | 0.91 (0.88,0.95) | 5.86E-06 | yes | 3.61E-02 |
| cg16409452 | chr14:100610186 | *EVL* | *AX747103* | 0.91 (0.87,0.94) | 4.89E-07 | yes | 2.12E-02 |
| cg14084609 | chr14:100610407 | *EVL* | *AX747103* | 0.89 (0.85,0.92) | 2.96E-09 | yes | 3.24E-02 |
| cg18550847 | chr14:100610570 | *EVL* | *AX747103* | 0.91 (0.88,0.94) | 7.10E-07 | yes | 2.85E-02 |
| cg01000631 | chr14:100610667 | | *EVL* | 0.91 (0.87,0.94) | 4.88E-08 | yes | 2.75E-02 |
| cg05875066 | chr14:104625249 | *KIF26A* | *KIF26A* | 0.87 (0.83,0.92) | 1.77E-07 | yes | 5.64E-02 |
| cg18817654 | chr15:39485138 | | *C15orf54* | 0.87 (0.82,0.92) | 3.41E-06 | yes | 7.10E-02 |
| cg25939647 | chr15:40173065 | *GPR176* | *GPR176* | 0.91 (0.88,0.95) | 1.91E-06 | yes | 2.83E-02 |
| cg07177867 | chr15:52030746 | *LYSMD2* | *LYSMD2* | 0.90 (0.86,0.94) | 1.29E-05 | yes | 3.26E-02 |
| cg11266582 | chr15:64275853 | *DAPK2* | *DAPK2* | 0.89 (0.85,0.94) | 1.52E-05 | yes | 2.56E-02 |
| cg10387956 | chr15:72646210 | *HEXA* | *BC034424* | 0.91 (0.87,0.95) | 2.72E-06 | yes | 4.78E-02 |
| cg23387863 | chr15:77472416 | *SGK269* | *AX747193* | 0.91 (0.87,0.94) | 1.51E-06 | yes | 5.29E-02 |
| cg04497992 | chr16:616212 | *NHLRC4* | *C16orf11* | 0.90 (0.87,0.94) | 1.92E-06 | yes | 4.10E-02 |
| cg08067346 | chr16:25011481 | *ARHGAP17* | *DQ583809* | 0.90 (0.86,0.95) | 1.60E-05 | yes | 2.70E-02 |

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|---|---|---|---|---|---|---|---|
| cg26134665 | chr16:31021544 | *STX1B* | *STX1B* | 0.92 (0.88,0.95) | 9.50E-06 | yes | 7.87E-01 |
| cg09147843 | chr16:53467612 | *RBL2* | *RBL2* | 0.89 (0.85,0.94) | 8.89E-06 | yes | 5.72E-02 |
| cg01998785 | chr16:55542709 | *LPCAT2* | *LPCAT2* | 0.91 (0.87,0.94) | 6.17E-07 | yes | 3.52E-02 |
| cg27383865 | chr16:84075870 | *SLC38A8* | *SLC38A8* | 1.11 (1.06,1.16) | 1.73E-05 | no | 2.63E-01 |
| cg08640475 | chr16:85551478 | | *KIAA0182* | 0.92 (0.89,0.95) | 2.36E-06 | yes | 1.99E-01 |
| cg10099827 | chr16:85551514 | | *KIAA0182* | 0.92 (0.89,0.95) | 1.32E-06 | yes | 1.48E-01 |
| cg08940169 | chr16:88540241 | *ZFPM1* | *ZFPM1* | 0.91 (0.87,0.94) | 2.93E-07 | yes | 3.33E-02 |
| cg04983687 | chr16:88558223 | *ZFPM1* | *ZFPM1* | 0.93 (0.90,0.95) | 1.33E-10 | yes | 3.29E-02 |
| cg20315954 | chr17:15137304 | *PMP22* | *PMP22* | 0.88 (0.84,0.93) | 3.58E-06 | yes | 1.89E-02 |
| cg20885063 | chr17:17939419 | *ATPAF2* | *ATPAF2* | 0.90 (0.86,0.94) | 1.06E-06 | yes | 3.13E-02 |
| cg14611258 | chr17:17946468 | *C17orf39* | *C17orf39* | 0.89 (0.85,0.94) | 6.41E-06 | yes | 3.89E-02 |
| cg19468946 | chr17:37922297 | *IKZF3* | *IKZF3* | 1.09 (1.05,1.13) | 1.50E-05 | yes | 4.02E-01 |
| cg21723861 | chr17:39686628 | | *KRT19* | 0.87 (0.82,0.92) | 1.59E-07 | yes | 2.68E-02 |
| cg00170714 | chr17:40724562 | *MLX;PSMC3IP* | *PSMC3IP* | 0.89 (0.85,0.93) | 6.15E-08 | yes | 3.55E-02 |
| cg25173129 | chr17:56269410 | *EPX* | *EPX* | 0.88 (0.84,0.93) | 8.09E-07 | yes | 2.54E-02 |
| cg02970679 | chr17:56269818 | *EPX* | *EPX* | 0.88 (0.83,0.92) | 9.99E-07 | yes | 2.37E-02 |
| cg17374802 | chr17:56270828 | *EPX* | *EPX* | 0.90 (0.86,0.94) | 2.06E-06 | yes | 2.64E-02 |
| cg17041511 | chr17:61509620 | | *CYB561* | 0.91 (0.87,0.95) | 1.15E-05 | yes | 3.37E-02 |
| cg22312249 | chr17:72779428 | *TMEM104* | *TMEM104* | 0.91 (0.87,0.95) | 8.73E-06 | yes | 3.19E-02 |
| cg09705784 | chr17:76565232 | *DNAH17* | *DNAH17* | 0.91 (0.88,0.94) | 1.50E-07 | yes | 2.96E-02 |
| cg06725287 | chr17:80533762 | *FOXK2* | *FOXK2* | 0.87 (0.83,0.92) | 9.07E-08 | yes | 5.71E-02 |
| cg13054523 | chr17:81055722 | | *METRNL* | 0.87 (0.83,0.91) | 1.20E-08 | yes | 2.07E-02 |
| cg18337287 | chr19:930871 | *ARID3A* | *ARID3A* | 0.86 (0.81,0.91) | 7.21E-08 | yes | 3.51E-02 |
| cg12104982 | chr19:5592815 | *SAFB2* | *SAFB2* | 0.86 (0.81,0.91) | 1.13E-07 | yes | 1.55E-02 |
| cg10644885 | chr19:11687621 | *ACP5* | *ACP5* | 0.86 (0.82,0.90) | 5.77E-11 | yes | 1.85E-02 |
| cg02359181 | chr19:34860339 | *GPI* | *GPI* | 0.88 (0.83,0.93) | 2.68E-06 | yes | 3.91E-02 |
| cg20673965 | chr19:44220148 | *IRGC* | *IRGC* | 0.90 (0.85,0.94) | 5.54E-06 | yes | 3.81E-02 |
| cg26979537 | chr19:48016860 | *NAPA* | *NAPA* | 0.83 (0.77,0.90) | 1.31E-06 | yes | 3.93E-02 |
| cg21073212 | chr20:30866501 | *KIF3B* | *KIF3B* | 0.92 (0.89,0.96) | 1.79E-05 | yes | 2.48E-02 |
| cg20226253 | chr20:34022914 | *GDF5* | *GDF5OS* | 0.87 (0.81,0.92) | 1.15E-05 | yes | 4.10E-02 |
| cg21045547 | chr20:35422703 | *C20orf117* | *KIAA0889* | 0.89 (0.85,0.94) | 5.32E-06 | yes | 2.86E-02 |
| cg13792581 | chr20:43590115 | *TOMM34* | *TOMM34* | 0.87 (0.82,0.93) | 1.34E-05 | yes | 2.74E-02 |
| cg13197551 | chr20:60709957 | *LSM14B* | *LSM14B* | 0.86 (0.81,0.91) | 9.23E-07 | yes | 2.25E-02 |
| cg18042632 | chr21:42520902 | *C21orf130* | *LINC00323* | 0.92 (0.88,0.95) | 1.87E-06 | yes | 1.91E-02 |
| cg18879389 | chr21:43771120 | *TFF2* | *TFF2* | 0.87 (0.82,0.92) | 1.21E-06 | yes | 1.57E-01 |

*Table E8* *Association of methylation with gene expression in different datasets: (A) CpGs differentially methylated in newborns in relation to asthma; (B) Regions differentially methylated (DMRs) in newborns in relation to asthma development; (C) CpGs differentially methylated in childhood in relation to asthma; (D) Regions differentially methylated (DMRs) in older children in relation to school aged asthma.*

*(A)*

| List of CpGs* | chr:pos | UCSC RefGene Name | UCSC Known Gene** | Significant*** (Y) association with gene expression in | | | | | | N datasets showing association (max 6) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | GEO (N=38) cord blood | IoW (N=157) cord blood | INMA (N=113) cord blood | INMA (N=112) 4-year-olds | BAMSE (N=248) 16-year-olds | BIOS (N=3,096) adults | |
| cg13427149 | chr1:217804379 | *GPATCH2;SPATA17* | *GPATCH2* | N | N | N | N | Y | Y | 2 |
| cg17333211 | chr4:141294016 | *SCOC* | *LOC100129858* | N | Y | N | N | N | Y | 2 |
| cg13289553 | chr5:32585524 | *SUB1* | *SUB1* | N | N | Y | Y | N | N | 2 |
| cg02331902 | chr5:90610303 | | *AK091866* | Y | N | Y | N | N | Y | 3 |
| ch.6.1218502R | chr6:51250028 | | | N | NA | NA | NA | NA | N | 0 |
| cg21486411 | chr11:77348243 | *CLNS1A* | *CLNS1A* | N | NA | Y | Y | N | N | 2 |
| cg16792002 | chr11:95788886 | *MAML2* | *Mir_548* | N | N | N | N | N | N | 0 |
| ch.11.109687686R | chr11:110182476 | | | N | NA | NA | NA | NA | N | 0 |
| cg07156990 | chr14:102685678 | *WDR20* | *WDR20* | Y | Y | N | Y | N | N | 3 |
| CpGs associated with gene expression in at least one of the datasets. | | | | | | | | | | 6 |

* ch probes (ch.11.109687686R and ch.6.1218502R) have been reported to be cross hybridizing and thus UCSC Known Gene is intentionally left blank.
** UCSC Known Gene fills in nearest genes for those missing gene annotation in the UCSC RefGene Name column.
*** P-value < 0.05 in the smaller GEO, IoW, INMA and BAMSE datasets and FDR < 0.05 in the larger BIOS dataset.

*(B)*

| DMR chr:pos | Gene Name | Significant* (Y) correlation with gene expression in | | | | | | N datasets showing association (max 5) |
|---|---|---|---|---|---|---|---|---|
| | | GEO (N=38) cord blood | IoW (N=157) cord blood | INMA (N=113) cord blood | INMA (N=112) 4-year-olds | BAMSE (N=248) 16-year-olds | BIOS (3,096) adults | |
| chr1:1296093-1296489 | *MXRA8* | Y | NA | Y | Y | N | Y | 4 |
| chr1:59280290-59280842 | *LINC01135* | N | NA | Y | Y | Y | Y | 4 |
| chr1:220263017-220263699 | *BPNT1;RNU5F-1* | Y | NA | Y | Y | N | Y | 4 |
| chr2:202097062-202097608 | *CASP8* | N | NA | N | Y | Y | Y | 3 |
| chr2:235004843-235005012 | *SPP2* | Y | NA | NA | NA | N | N | 1 |
| chr3:194188646-194189444 | *ATP13A3* | N | NA | N | N | Y | Y | 2 |
| chr4:113218385-113218525 | *ALPK1* | N | NA | N | N | Y | Y | 2 |
| chr5:64777678-64778186 | *ADAMTS6* | Y | NA | N | Y | N | Y | 3 |
| chr5:81573780-81574461 | *RPS23* | N | NA | N | Y | N | Y | 2 |
| chr5:158526108-158526694 | *EBF1* | Y | NA | Y | Y | Y | Y | 5 |
| chr6:291687-292824 | *DUSP22* | N | NA | Y | Y | Y | Y | 4 |
| chr6:26234819-26235610 | *HIST1H1D* | N | NA | Y | Y | Y | Y | 4 |
| chr6:29648161-29649085 | *ZFP57* | Y | NA | Y | Y | Y | Y | 5 |
| chr6:31055396-31055503 | *C6orf15* | Y | NA | Y | N | N | Y | 3 |
| chr6:32799997-32801050 | *TAP2* | Y | NA | N | N | N | Y | 2 |
| chr7:87974722-87975316 | *STEAP4* | Y | NA | N | N | N | Y | 2 |
| chr7:106694832-106695007 | *PRKAR2B* | N | NA | N | N | N | Y | 1 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| chr7:158045980-158046359 | *PTPRN2* | N | NA | N | N | NA | Y | 1 |
| chr8:33370172-33371226 | *TTI2* | N | NA | Y | Y | N | Y | 3 |
| chr8:127889010-127889296 | *PCAT1* | N | NA | N | Y | NA | N | 1 |
| chr10:65028929-65029169 | *JMJD1C* | N | NA | Y | N | N | N | 1 |
| chr10:71871364-71871634 | *H2AFY2* | N | NA | Y | Y | N | N | 2 |
| chr11:268923-269469 | *NLRP6* | N | NA | Y | Y | N | Y | 3 |
| chr11:107328442-107328915 | *CWF19L2* | N | NA | N | N | N | Y | 1 |
| chr12:58329764-58330116 | *LOC100506844* | Y | NA | Y | Y | N | Y | 4 |
| chr12:74931289-74932008 | *ATXN7L3B* | N | NA | N | N | NA | Y | 1 |
| chr13:31618695-31618744 | *TEX26* | N | NA | Y | N | N | N | 1 |
| chr13:108953659-108954055 | *TNFSF13B* | Y | NA | N | N | Y | Y | 3 |
| chr14:69341139-69341739 | *ACTN1* | N | NA | Y | Y | Y | Y | 4 |
| chr16:20774873-20775353 | *ACSM3* | Y | NA | N | N | Y | Y | 3 |
| chr17:21029189-21029296 | *DHRS7B* | N | NA | Y | Y | N | Y | 3 |
| chr17:74667833-74668253 | *LOC105274304* | Y | NA | N | N | N | Y | 2 |
| chr18:47813745-47815431 | *CXXC1* | Y | NA | N | N | N | Y | 2 |
| chr21:36421467-36421956 | *RUNX1* | N | NA | N | N | NA | Y | 1 |
| chr22:24372913-24374013 | *LOC391322* | Y | NA | N | N | Y | Y | 3 |
| DMRs associated with gene expression in at least one of the datasets. | | | | | | | | 35 |

* P-value < 0.05 in the smaller GEO, IoW, INMA and BAMSE datasets and FDR < 0.05 in the larger BIOS dataset.

*(C)*

| CpG | chr:pos | UCSC RefGene Name | UCSC Known Gene* | Significant** (Y) correlation with gene expression in | | | | | | N datasets showing association (max 6) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | GEO (N=38) cord blood | IoW (N=157) cord blood | INMA (N=113) cord blood | INMA (N=112) 4-year-olds | BAMSE (N=248) 16-year-olds | BIOS (3,096) adults | |
| cg06315149 | chr1:2036398 | *PRKCZ* | *PRKCZ* | N | Y | Y | N | Y | Y | 4 |
| cg13066938 | chr1:6341140 | *ACOT7* | *ACOT7* | Y | Y | N | N | Y | Y | 4 |
| cg21220721 | chr1:6341230 | *ACOT7* | *ACOT7* | Y | N | Y | Y | Y | Y | 5 |
| cg09249800 | chr1:6341287 | *ACOT7* | *ACOT7* | Y | N | Y | Y | NA | Y | 4 |
| cg11699125 | chr1:6341327 | *ACOT7* | *ACOT7* | Y | Y | Y | Y | Y | Y | 6 |
| cg18783781 | chr1:9599067 | *SLC25A33* | *SLC25A33* | Y | Y | N | Y | Y | Y | 5 |
| cg02171825 | chr1:26517586 | *CATSPER4* | *CATSPER4* | Y | N | Y | Y | Y | Y | 5 |
| cg01942646 | chr1:27240694 | *NR0B2* | *NR0B2* | Y | N | Y | N | Y | Y | 4 |
| cg16263722 | chr1:29523841 | *MECR* | *MECR* | Y | N | Y | N | N | Y | 3 |
| cg11987455 | chr1:43290834 | *ERMAP* | *ERMAP* | Y | Y | Y | Y | N | Y | 5 |
| cg11683482 | chr1:44678623 | *DMAP1* | *DMAP1* | Y | N | N | Y | Y | Y | 4 |
| cg12643917 | chr1:44715958 | *ERI3* | *ERI3* | Y | NA | N | N | N | Y | 2 |
| cg26252077 | chr1:61607055 | *NFIA* | *NFIA* | N | NA | N | N | N | Y | 1 |
| cg10704177 | chr1:62209607 | *INADL* | *INADL* | N | N | N | N | Y | Y | 2 |
| cg01445399 | chr1:87596934 | *LOC339524* | *LOC339524* | N | N | Y | N | N | Y | 2 |
| cg19805160 | chr1:159870731 | *CCDC19* | *CCDC19* | Y | NA | N | Y | Y | Y | 4 |
| cg09332506 | chr1:160309220 | *COPA* | *NCSTN* | Y | Y | Y | N | Y | Y | 5 |
| cg17971251 | chr1:177907297 | *SEC16B* | *SEC16B* | N | N | N | N | N | Y | 1 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| cg26033504 | chr1:201458737 | *CSRP1* | *CSRP1* | Y | Y | Y | Y | Y | Y | 6 |
| cg04895895 | chr1:231005895 | *C1orf198* | *C1orf198* | Y | Y | Y | N | N | Y | 4 |
| cg02473287 | chr2:9752386 | *YWHAQ* | *YWHAQ* | N | Y | N | Y | Y | Y | 4 |
| cg10142874 | chr2:11917623 | *LPIN1* | *LPIN1* | N | Y | N | Y | N | N | 2 |
| cg26752663 | chr2:25142016 | *ADCY3* | *ADCY3* | Y | N | N | N | Y | Y | 3 |
| cg00043800 | chr2:74612144 | *LOC100189589* | *LOC100189589* | Y | Y | Y | Y | Y | Y | 6 |
| cg17988187 | chr2:74612222 | *LOC100189589* | *LOC100189589* | Y | Y | Y | Y | Y | Y | 6 |
| cg12077754 | chr2:75089669 | *HK2* | *HK2* | N | Y | N | Y | N | Y | 3 |
| cg22674082 | chr2:98585733 | *TMEM131* | *TMEM131* | N | N | N | N | Y | Y | 2 |
| cg00327263 | chr2:120019111 | *STEAP3* | *STEAP3* | Y | NA | Y | N | N | Y | 3 |
| cg25950520 | chr2:121036760 | *RALB* | *RALB* | N | N | N | N | N | N | 0 |
| cg00213281 | chr2:149639822 | *KIF5C;MIR1978* | *JA429504* | Y | N | N | N | Y | Y | 3 |
| cg02494549 | chr2:161798364 | | *TANK* | N | NA | N | N | N | Y | 1 |
| cg01310029 | chr3:3152374 | *IL5RA* | *IL5RA* | Y | Y | N | Y | Y | Y | 5 |
| cg10159529 | chr3:3152530 | *IL5RA* | *IL5RA* | Y | Y | N | Y | Y | Y | 5 |
| cg25224369 | chr3:12918528 | | *DQ581328* | N | N | Y | Y | Y | Y | 4 |
| cg07386061 | chr3:52492874 | *NISCH* | *NISCH* | Y | Y | Y | Y | N | Y | 5 |
| cg17890764 | chr3:52864816 | *ITIH4* | *ITIH4* | Y | N | N | Y | N | Y | 3 |
| cg07410597 | chr3:66404129 | *SLC25A26* | *LRIG1* | Y | N | N | N | N | Y | 2 |
| cg04217850 | chr3:66428294 | *SLC25A26* | *LRIG1* | N | N | Y | N | N | Y | 2 |
| cg06070625 | chr3:69812798 | *MITF* | *MITF* | N | N | N | N | N | Y | 1 |
| cg06391412 | chr3:71295684 | *FOXP1* | *FOXP1* | N | N | N | N | N | Y | 1 |
| cg20263733 | chr3:130616293 | *ATP2C1* | *ATP2C1* | Y | N | N | N | Y | Y | 3 |
| cg09423651 | chr3:136618442 | *NCK1* | *NCK1* | Y | N | Y | N | N | Y | 3 |
| cg08698681 | chr3:171091657 | *TNIK* | *TNIK* | N | N | N | N | Y | Y | 2 |
| cg25636075 | chr3:185217761 | *TMEM41A* | *TMEM41A* | Y | N | Y | Y | N | N | 3 |
| cg02803925 | chr3:195974300 | *PCYT1A* | *PCYT1A* | Y | Y | N | N | Y | Y | 4 |
| cg04077085 | chr4:9937674 | *SLC2A9* | *SLC2A9* | Y | Y | Y | Y | N | Y | 5 |
| cg18912470 | chr4:57848125 | *POLR2B* | *POLR2B* | Y | N | N | N | N | Y | 2 |
| cg26396815 | chr4:102878132 | *BANK1* | *BANK1* | Y | N | N | N | N | Y | 2 |
| cg20866785 | chr4:148733880 | *ARHGAP10* | *Metazoa_SRP* | N | N | N | Y | Y | Y | 3 |
| cg16362140 | chr5:10708717 | *DAP* | *DAP* | Y | Y | Y | Y | N | Y | 5 |
| cg22588983 | chr5:38783142 | | *AK126213* | Y | N | N | N | N | Y | 2 |
| cg00944309 | chr5:60142446 | | *ELOVL7* | Y | N | N | N | N | Y | 2 |
| cg14978242 | chr5:79501131 | *SERINC5* | *SERINC5* | N | Y | Y | Y | N | Y | 4 |
| cg09565310 | chr5:112541553 | *MCC* | *MCC* | N | N | N | N | N | Y | 1 |
| cg08969102 | chr5:133563532 | | *PPP2CA* | N | Y | N | N | N | Y | 2 |
| cg21627181 | chr6:25754190 | *SLC17A4* | *SLC17A4* | N | N | N | Y | N | Y | 2 |
| cg09597192 | chr6:32141591 | *AGPAT1* | *PPT2* | Y | Y | Y | N | Y | Y | 5 |
| cg06426027 | chr6:33232644 | *VPS52* | *VPS52* | Y | Y | Y | N | Y | Y | 5 |
| cg18460809 | chr6:57048049 | *BAG2* | *BAG2* | Y | N | Y | Y | N | Y | 4 |
| cg15961693 | chr6:139689053 | | *CITED2* | Y | N | N | Y | N | Y | 3 |
| cg26774971 | chr6:158994407 | *TMEM181* | *TMEM181* | N | Y | Y | N | Y | N | 3 |
| cg05477517 | chr6:164531576 | | *AK093114* | N | NA | N | N | NA | NA | 0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| cg15304012 | chr6:166876490 | *RPS6KA2* | *RPS6KA2* | Y | Y | N | N | N | N | 2 |
| cg19851574 | chr6:167178233 | *RPS6KA2* | *RPS6KA2* | N | NA | Y | Y | Y | Y | 4 |
| cg03329755 | chr6:167189272 | *RPS6KA2* | *RPS6KA2* | N | N | Y | N | Y | Y | 3 |
| cg25270424 | chr7:24965657 | *OSBPL3* | *OSBPL3* | N | N | N | N | N | Y | 1 |
| cg04321303 | chr7:44107504 | | *PGAM2* | Y | N | N | N | Y | Y | 3 |
| cg02435538 | chr7:75507337 | *RHBDD2* | *RHBDD2* | Y | N | N | N | N | Y | 2 |
| cg13007207 | chr7:105279391 | *ATXN7L1* | *ATXN7L1* | N | N | N | N | Y | N | 1 |
| cg17947765 | chr7:117857964 | | *ANKRD7* | Y | N | Y | Y | Y | N | 4 |
| cg14678084 | chr7:127627251 | *SND1* | *SND1-IT1* | N | NA | N | Y | Y | N | 2 |
| cg05184016 | chr7:149543136 | *ZNF862* | *BC045757* | Y | Y | Y | Y | Y | Y | 6 |
| cg07970948 | chr7:149543165 | *ZNF862* | *BC045757* | Y | Y | Y | Y | Y | Y | 6 |
| cg06558622 | chr7:149543177 | *ZNF862* | *BC045757* | Y | NA | N | Y | Y | Y | 4 |
| cg24576940 | chr7:150648283 | *KCNH2* | *KCNH2* | Y | Y | Y | N | N | Y | 4 |
| cg23147443 | chr7:150649655 | *KCNH2* | *KCNH2* | Y | Y | N | N | NA | Y | 3 |
| cg18666454 | chr7:150651937 | *KCNH2* | *KCNH2* | Y | N | Y | N | N | Y | 3 |
| cg02596233 | chr7:150970209 | *SMARCD3* | *SMARCD3* | Y | NA | N | N | Y | Y | 3 |
| cg23706836 | chr8:6407997 | *ANGPT2;MCPH1* | *ANGPT2* | N | NA | N | N | Y | Y | 2 |
| cg21919729 | chr8:11719367 | *CTSB* | *CTSB* | Y | Y | Y | Y | Y | Y | 6 |
| cg03437605 | chr8:22847209 | *RHOBTB2* | *RHOBTB2* | Y | N | Y | N | N | Y | 3 |
| cg22816343 | chr8:26243601 | *BNIP3L* | *BNIP3L* | Y | N | N | N | N | Y | 2 |
| cg23205629 | chr8:33421410 | *RNF122* | *RNF122* | Y | N | Y | Y | Y | Y | 5 |
| cg10815420 | chr8:105599835 | *LRP12* | *LRP12* | Y | Y | N | N | Y | Y | 4 |
| cg02133716 | chr8:128981622 | *PVT1* | *MIR1205* | Y | N | N | N | N | N | 1 |
| cg00736681 | chr8:134546052 | *ST3GAL1* | *ST3GAL1* | N | N | Y | N | N | N | 1 |
| cg09377531 | chr8:141046469 | *TRAPPC9* | *AX748239* | N | N | N | Y | N | Y | 2 |
| cg14025883 | chr9:5436224 | *C9orf46* | *C9orf46* | N | N | N | Y | Y | N | 2 |
| cg01499988 | chr9:35755346 | *MSMP* | *MSMP* | Y | Y | N | N | N | Y | 3 |
| cg13482814 | chr9:82183332 | | *TLE4* | N | NA | Y | N | N | N | 1 |
| cg13576859 | chr9:97403129 | *FBP1* | *FBP1* | Y | N | Y | Y | Y | Y | 5 |
| cg20503329 | chr9:101705792 | *COL15A1* | *COL15A1* | Y | N | N | Y | Y | Y | 4 |
| cg00045753 | chr9:123630545 | *PHF19* | *PHF19* | Y | Y | N | Y | N | Y | 4 |
| cg13458609 | chr9:130608923 | *ENG* | *ENG* | Y | N | N | Y | Y | Y | 4 |
| cg13835688 | chr9:130859454 | *SLC25A25* | *SLC25A25* | Y | Y | Y | N | Y | Y | 5 |
| cg13628444 | chr9:134883788 | *MED27* | *MED27* | N | Y | Y | N | N | Y | 3 |
| cg13850063 | chr9:138362321 | | *AK096249* | N | N | Y | N | N | Y | 2 |
| cg14011077 | chr9:138362327 | | *AK096249* | Y | N | N | Y | Y | Y | 4 |
| cg06958964 | chr10:45494806 | *C10orf25;ZNF22* | *ZNF22* | Y | N | Y | Y | Y | Y | 5 |
| cg25854298 | chr10:73936754 | *ASCC1* | *ASCC1* | Y | Y | Y | N | Y | Y | 5 |
| cg04973995 | chr10:74057977 | | *DDIT4* | N | N | Y | N | N | Y | 2 |
| cg00366037 | chr10:76781121 | *MYST4* | *KAT6B* | Y | N | N | N | N | Y | 2 |
| cg22235258 | chr11:34675402 | *EHF* | *EHF* | N | N | Y | Y | Y | Y | 4 |
| cg24459209 | chr11:57148215 | *PRG3* | *PRG3* | Y | N | Y | Y | Y | Y | 5 |
| cg15700636 | chr11:57156050 | *PRG2* | *PRG2* | Y | Y | Y | N | Y | Y | 5 |
| cg08773180 | chr11:57157607 | *PRG2* | *PRG2* | Y | NA | Y | Y | Y | Y | 5 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| cg12819873 | chr11:57157632 | *PRG2* | *PRG2* | Y | Y | Y | Y | Y | Y | 6 |
| cg27533472 | chr11:59856225 | *MS4A2* | *MS4A2* | Y | N | N | N | Y | Y | 3 |
| cg25087851 | chr11:60623918 | *GPR44* | *PTGDR2* | Y | Y | Y | Y | Y | Y | 6 |
| cg13233042 | chr11:63432489 | *ATL3* | *ATL3* | Y | NA | N | Y | Y | Y | 4 |
| cg05300717 | chr11:65546210 | *DKFZp761E198* | *DKFZp761E198* | N | N | Y | N | Y | Y | 3 |
| cg15219163 | chr11:70842128 | *SHANK2* | *SHANK2* | N | NA | N | N | N | NA | 0 |
| cg24368962 | chr11:111570978 | *SIK2* | *DQ599327* | Y | N | N | Y | Y | Y | 4 |
| cg19434937 | chr12:7104184 | *LPCAT3* | *EMG1* | Y | Y | Y | Y | Y | Y | 6 |
| cg03014680 | chr12:10122522 | *CLEC12A* | *CLEC12A* | Y | Y | Y | Y | Y | Y | 6 |
| cg09447105 | chr12:15126020 | *PDE6H* | *PDE6H* | Y | Y | Y | N | N | Y | 4 |
| cg24028828 | chr12:56694932 | *CS* | *CS* | Y | N | N | Y | Y | Y | 4 |
| cg21498475 | chr12:113737469 | *SLC24A6* | *SLC24A6* | N | Y | Y | N | Y | N | 3 |
| cg10065736 | chr12:117440120 | *FBXW8* | *AK055849* | N | Y | N | N | Y | Y | 3 |
| cg03131767 | chr12:123446272 | *ABCB9* | *ABCB9* | Y | Y | Y | N | Y | Y | 5 |
| cg19928703 | chr13:30143971 | *SLC7A1* | *SLC7A1* | N | N | N | Y | Y | Y | 3 |
| cg07908654 | chr13:41631052 | | *TRNA_Glu* | Y | N | N | Y | N | Y | 3 |
| cg24818699 | chr13:43355514 | *C13orf30* | *C13orf30* | N | N | Y | Y | Y | N | 3 |
| cg08770358 | chr13:48876684 | *RB1* | *BC039553* | Y | NA | N | N | Y | N | 2 |
| cg00222125 | chr13:53226144 | *SUGT1* | *SUGT1* | Y | N | N | Y | N | N | 2 |
| cg11770323 | chr13:80066032 | *NDFIP2* | *NDFIP2* | Y | N | N | Y | Y | Y | 4 |
| cg25479097 | chr13:113305704 | *C13orf35* | *C13orf35* | Y | N | N | N | N | Y | 2 |
| cg18368116 | chr14:21436271 | | *RNASE2* | Y | Y | N | Y | Y | Y | 5 |
| cg08077807 | chr14:62001072 | *PRKCH* | *PRKCH* | N | N | N | Y | N | Y | 2 |
| cg04933530 | chr14:77419754 | | *IRF2BPL* | Y | N | N | Y | Y | N | 3 |
| cg01901579 | chr14:95615731 | *DICER1* | *DICER1* | Y | N | N | N | N | Y | 2 |
| cg16409452 | chr14:100610186 | *EVL* | *AX747103* | N | N | Y | N | Y | Y | 3 |
| cg14084609 | chr14:100610407 | *EVL* | *AX747103* | Y | N | Y | N | N | Y | 3 |
| cg18550847 | chr14:100610570 | *EVL* | *AX747103* | Y | N | Y | Y | N | Y | 4 |
| cg01000631 | chr14:100610667 | | *EVL* | N | N | Y | Y | N | Y | 3 |
| cg05875066 | chr14:104625249 | *KIF26A* | *KIF26A* | N | N | Y | Y | Y | Y | 4 |
| cg18817654 | chr15:39485138 | | *C15orf54* | Y | NA | N | N | NA | N | 1 |
| cg25939647 | chr15:40173065 | *GPR176* | *GPR176* | Y | Y | Y | N | Y | Y | 5 |
| cg07177867 | chr15:52030746 | *LYSMD2* | *LYSMD2* | Y | Y | Y | Y | N | Y | 5 |
| cg11266582 | chr15:64275853 | *DAPK2* | *DAPK2* | Y | N | N | N | N | Y | 2 |
| cg10387956 | chr15:72646210 | *HEXA* | *BC034424* | N | Y | Y | Y | Y | N | 4 |
| cg23387863 | chr15:77472416 | *SGK269* | *AX747193* | Y | N | N | N | N | Y | 2 |
| cg04497992 | chr16:616212 | *NHLRC4* | *C16orf11* | Y | N | N | Y | Y | Y | 4 |
| cg08067346 | chr16:25011481 | *ARHGAP17* | *DQ583809* | Y | NA | N | Y | Y | Y | 4 |
| cg26134665 | chr16:31021544 | *STX1B* | *STX1B* | Y | Y | Y | Y | Y | Y | 6 |
| cg09147843 | chr16:53467612 | *RBL2* | *RBL2* | N | N | Y | N | N | Y | 2 |
| cg01998785 | chr16:55542709 | *LPCAT2* | *LPCAT2* | Y | Y | N | Y | N | Y | 4 |
| cg27383865 | chr16:84075870 | *SLC38A8* | *SLC38A8* | N | NA | Y | Y | N | Y | 3 |
| cg08640475 | chr16:85551478 | | *KIAA0182* | N | N | N | N | N | Y | 1 |
| cg10099827 | chr16:85551514 | | *KIAA0182* | Y | Y | N | Y | N | Y | 4 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| cg08940169 | chr16:88540241 | *ZFPM1* | *ZFPM1* | N | Y | Y | N | Y | Y | 4 |
| cg04983687 | chr16:88558223 | *ZFPM1* | *ZFPM1* | Y | Y | Y | Y | Y | Y | 6 |
| cg20315954 | chr17:15137304 | *PMP22* | *PMP22* | N | Y | Y | Y | Y | Y | 5 |
| cg20885063 | chr17:17939419 | *ATPAF2* | *ATPAF2* | Y | N | N | Y | N | Y | 3 |
| cg14611258 | chr17:17946468 | *C17orf39* | *C17orf39* | Y | N | N | N | Y | Y | 3 |
| cg19468946 | chr17:37922297 | *IKZF3* | *IKZF3* | Y | Y | Y | Y | Y | Y | 6 |
| cg21723861 | chr17:39686628 | | *KRT19* | Y | Y | Y | Y | Y | Y | 6 |
| cg00170714 | chr17:40724562 | *MLX;PSMC3IP* | *PSMC3IP* | Y | Y | Y | Y | Y | Y | 6 |
| cg25173129 | chr17:56269410 | *EPX* | *EPX* | Y | NA | Y | Y | N | Y | 4 |
| cg02970679 | chr17:56269818 | *EPX* | *EPX* | Y | N | Y | N | N | Y | 3 |
| cg17374802 | chr17:56270828 | *EPX* | *EPX* | Y | N | Y | N | N | Y | 3 |
| cg17041511 | chr17:61509620 | | *CYB561* | N | N | N | N | N | Y | 1 |
| cg22312249 | chr17:72779428 | *TMEM104* | *TMEM104* | Y | Y | Y | Y | Y | Y | 6 |
| cg09705784 | chr17:76565232 | *DNAH17* | *DNAH17* | N | N | N | N | N | Y | 1 |
| cg06725287 | chr17:80533762 | *FOXK2* | *FOXK2* | Y | N | Y | Y | N | Y | 4 |
| cg13054523 | chr17:81055722 | | *METRNL* | N | N | Y | N | Y | Y | 3 |
| cg18337287 | chr19:930871 | *ARID3A* | *ARID3A* | N | Y | Y | Y | Y | Y | 5 |
| cg12104982 | chr19:5592815 | *SAFB2* | *SAFB2* | N | Y | N | Y | N | Y | 3 |
| cg10644885 | chr19:11687621 | *ACP5* | *ACP5* | N | Y | N | Y | Y | Y | 4 |
| cg02359181 | chr19:34860339 | *GPI* | *GPI* | Y | N | N | Y | Y | Y | 4 |
| cg20673965 | chr19:44220148 | *IRGC* | *IRGC* | Y | N | Y | Y | Y | Y | 5 |
| cg26979537 | chr19:48016860 | *NAPA* | *NAPA* | Y | Y | N | N | N | Y | 3 |
| cg21073212 | chr20:30866501 | *KIF3B* | *KIF3B* | N | N | Y | Y | N | Y | 3 |
| cg20226253 | chr20:34022914 | *GDF5* | *GDF5OS* | Y | Y | N | Y | Y | Y | 5 |
| cg21045547 | chr20:35422703 | *C20orf117* | *KIAA0889* | Y | Y | N | Y | Y | Y | 5 |
| cg13792581 | chr20:43590115 | *TOMM34* | *TOMM34* | Y | Y | Y | Y | Y | Y | 6 |
| cg13197551 | chr20:60709957 | *LSM14B* | *LSM14B* | N | N | Y | Y | Y | Y | 4 |
| cg18042632 | chr21:42520902 | *C21orf130* | *LINC00323* | Y | N | Y | Y | Y | Y | 5 |
| cg18879389 | chr21:43771120 | *TFF2* | *TFF2* | Y | Y | N | Y | N | Y | 4 |
| CpGs associated with gene expression in at least one of the datasets. | | | | | | | | | | 176 |

* UCSC Known Gene fills in nearest genes for those missing gene annotation in the UCSC RefGene Name column.
** P-value < 0.05 in the smaller GEO, IoW, INMA and BAMSE datasets and FDR < 0.05 in the larger BIOS dataset.

*(D)*

| DMR | Gene Name | Significant* (Y) correlation with gene expression in | | | | | | N datasets showing association (max 5) |
|---|---|---|---|---|---|---|---|---|
| | | GEO (N=38) cord blood | IoW (N=157) cord blood | INMA (N=113) cord blood | INMA (N=112) 4-year-olds | BAMSE (N=248) 16-year-olds | BIOS (3,096) adults | |
| chr1:2036283-2036644 | *PRKCZ* | Y | NA | Y | N | Y | Y | 4 |
| chr1:87596820-87596935 | *LINC01140* | N | NA | N | N | N | Y | 1 |
| chr1:161575716-161576323 | *HSPA7* | Y | NA | Y | N | Y | Y | 5 |
| chr1:209979111-209979780 | *IRF6* | Y | NA | Y | N | Y | Y | 4 |
| chr2:11917490-11917788 | *LPIN1* | N | NA | N | N | N | Y | 1 |
| chr2:149639612-149640260 | *KIF5C* | Y | NA | NA | NA | Y | Y | 3 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| chr3:3151795-3152917 | *IL5RA* | N | NA | Y | N | Y | Y | 3 |
| chr3:195974258-195974330 | *PCYT1A* | Y | NA | Y | N | Y | Y | 4 |
| chr5:38445220-38446193 | *EGFLAM* | N | NA | N | N | N | NA | 1 |
| chr5:132008525-132009631 | *IL4* | N | NA | Y | N | Y | Y | 3 |
| chr6:112688010-112688931 | *RFPL4B* | N | NA | Y | Y | Y | NA | 3 |
| chr6:166876490-166877039 | *RPS6KA2;RPS6KA2-IT1* | N | NA | N | N | N | Y | 1 |
| chr7:65419185-65419289 | *VKORC1L1* | Y | NA | Y | Y | Y | Y | 5 |
| chr7:149543136-149543178 | *ZNF862* | Y | NA | Y | Y | Y | Y | 5 |
| chr7:156735383-156735657 | *NOM1* | N | NA | Y | N | N | N | 1 |
| chr8:832917-833049 | *ERICH1-AS1;DLGAP2* | N | NA | N | N | NA | Y | 1 |
| chr8:141046436-141046853 | *TRAPPC9* | N | NA | N | N | N | Y | 1 |
| chr9:130859454-130859607 | *SLC25A25* | Y | NA | Y | N | Y | Y | 5 |
| chr9:138362321-138362505 | *PPP1R26-AS1* | N | NA | Y | N | N | Y | 2 |
| chr11:59856225-59856359 | *MS4A2* | Y | NA | Y | Y | Y | Y | 5 |
| chr11:65545808-65547173 | *AP5B1* | Y | NA | Y | Y | Y | Y | 5 |
| chr11:69291998-69292065 | *LINC01488* | N | NA | Y | N | Y | Y | 3 |
| chr12:15125458-15126021 | *PDE6H* | Y | NA | Y | Y | N | Y | 4 |
| chr14:100610071-100610668 | *EVL* | Y | NA | Y | Y | Y | Y | 5 |
| chr15:64275810-64275854 | *DAPK2* | N | NA | N | N | N | Y | 1 |
| chr15:99443213-99443667 | *IGF1R* | Y | NA | Y | N | N | Y | 2 |
| chr16:615709-616221 | *PRR35* | Y | NA | Y | Y | Y | Y | 5 |
| chr16:875257-875627 | *PRR25* | Y | NA | Y | Y | Y | Y | 5 |
| chr16:85551478-85551749 | *GSE1* | N | NA | N | N | N | Y | 1 |
| chr16:88539861-88540397 | *ZFPM1* | N | NA | Y | Y | Y | Y | 3 |
| chr17:56269410-56270829 | *EPX* | Y | NA | Y | Y | N | Y | 4 |
| chr17:78682785-78683458 | *RPTOR* | N | NA | Y | Y | Y | Y | 3 |
| chr19:50553682-50554511 | *LOC400710* | Y | NA | Y | N | Y | Y | 4 |
| chr19:51961666-51961938 | *SIGLEC8* | Y | NA | Y | Y | Y | Y | 5 |
| chr20:35503832-35504554 | *TLDC2* | Y | NA | Y | Y | Y | Y | 5 |
| chr21:42520365-42520903 | *LINC00323* | Y | NA | N | Y | Y | Y | 5 |
| DMRs associated with gene expression in at least one of the datasets. | | | | | | | | 36 |

* P-value < 0.05 in the smaller GEO, IoW, INMA and BAMSE datasets and FDR < 0.05 in the larger BIOS dataset.

*Table E9: Significantly enriched canonical pathways, diseases and biological functions from Ingenuity Pathway Analysis based on CpGs and regions differentially methylated in newborns in relation to asthma*

***CANONICAL PATHWAYS***

| Category | Genes | P-value |
|---|---|---|
| Granzyme B Signaling | CASP8, | 0.029512092 |
| Granzyme A Signaling | HIST1H1D, | 0.031622777 |
| D-myo-inositol (1,4,5)-trisphosphate Degradation | BPNT1, | 0.033113112 |
| Protein Kinase A Signaling | HIST1H1D,PRKAR2B,DUSP22 | 0.034673685 |
| Inflammasome pathway | CASP8, | 0.037153523 |
| eNOS Signaling | PRKAR2B,CASP8 | 0.038904514 |
| Superpathway of D-myo-inositol (1,4,5)-trisphosphate Metabolism | BPNT1, | 0.044668359 |
| Tumoricidal Function of Hepatic Natural Killer Cells | CASP8, | 0.044668359 |
| Sertoli Cell-Sertoli Cell Junction Signaling | PRKAR2B,ACTN1 | 0.044668359 |
| NF-kB Signaling | TNFSF13B,CASP8 | 0.045708819 |

***DISEASES AND BIOLOGICAL FUNCTIONS***

| Category | Disease and Biological Function* | P-value | Genes |
|---|---|---|---|
| Cellular Development | Arrest in differentiation of leukocytes | 9.96E-06 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Arrest in differentiation of myeloid cells | 2.07E-05 | RUNX1,CASP8 |
| | Arrest in differentiation of leukemia cells | 3.44E-05 | RUNX1,CASP8 |
| | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Expansion of leukocytes | 0.000965 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Differentiation of neutrophils | 0.00271 | DHRS7B,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Expansion of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Differentiation of phagocytes | 0.00322 | DHRS7B,EBF1,RUNX1,CASP8 |
| | Thrombopoiesis | 0.00325 | ACTN1,CASP8 |
| | Hematopoiesis in embryo | 0.00517 | RUNX1,CASP8 |
| | Expansion of lymphocytes | 0.00735 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of hematopoietic progenitor cells | 0.00811 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of antigen presenting cells | 0.0107 | EBF1,RUNX1,CASP8 |
| | Expansion of hematopoietic progenitor cells | 0.0109 | EBF1,RUNX1 |
| | Proliferation of leukemia cell lines | 0.0141 | PRKAR2B,RUNX1,CASP8 |
| | Development of hematopoietic progenitor cells | 0.0194 | TNFSF13B,EBF1,RUNX1 |
| | Proliferation of hematopoietic progenitor cells | 0.0223 | EBF1,RUNX1,JMJD1C |
| | Differentiation of embryonic stem cells | 0.0225 | RUNX1,H2AFY2 |
| | Differentiation of myeloid leukocytes | 0.023 | DHRS7B,RUNX1,CASP8 |
| | Maturation of lymphocytes | 0.026 | TNFSF13B,RUNX1 |
| | Formation of osteoclasts | 0.0297 | EBF1,RUNX1 |

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|---|---|---|---|
| | Proliferation of B lymphocytes | 0.0302 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of macrophages | 0.0341 | RUNX1,CASP8 |
| | Commitment of cells | 0.0373 | EBF1,RUNX1 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| | Expansion of T lymphocytes | 0.0443 | TNFSF13B,CASP8 |
| | Differentiation of leukemia cell lines | 0.0456 | PRKAR2B,RUNX1 |
| | Proliferation of keratinocytes | 0.0498 | RUNX1,STEAP4 |
| Cellular Growth and Proliferation | Arrest in differentiation of leukocytes | 9.96E-06 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Arrest in differentiation of myeloid cells | 2.07E-05 | RUNX1,CASP8 |
| | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Expansion of leukocytes | 0.000965 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Expansion of lymphatic system cells | 0.00098 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Differentiation of neutrophils | 0.00271 | DHRS7B,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Expansion of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Differentiation of phagocytes | 0.00322 | DHRS7B,EBF1,RUNX1,CASP8 |
| | Thrombopoiesis | 0.00325 | ACTN1,CASP8 |
| | Hematopoiesis in embryo | 0.00517 | RUNX1,CASP8 |
| | Expansion of lymphocytes | 0.00735 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of hematopoietic progenitor cells | 0.00811 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of antigen presenting cells | 0.0107 | EBF1,RUNX1,CASP8 |
| | Expansion of hematopoietic progenitor cells | 0.0109 | EBF1,RUNX1 |
| | Proliferation of leukemia cell lines | 0.0141 | PRKAR2B,RUNX1,CASP8 |
| | Development of hematopoietic progenitor cells | 0.0194 | TNFSF13B,EBF1,RUNX1 |
| | Proliferation of hematopoietic progenitor cells | 0.0223 | EBF1,RUNX1,JMJD1C |
| | Differentiation of myeloid leukocytes | 0.023 | DHRS7B,RUNX1,CASP8 |
| | Formation of osteoclasts | 0.0297 | EBF1,RUNX1 |
| | Proliferation of B lymphocytes | 0.0302 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of macrophages | 0.0341 | RUNX1,CASP8 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| | Expansion of T lymphocytes | 0.0443 | TNFSF13B,CASP8 |
| | Proliferation of keratinocytes | 0.0498 | RUNX1,STEAP4 |
| Hematological System Development and Function | Arrest in differentiation of leukocytes | 9.96E-06 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Arrest in differentiation of myeloid cells | 2.07E-05 | RUNX1,CASP8 |
| | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Survival of pre-B lymphocytes | 0.00093 | TNFSF13B,EBF1 |
| | Expansion of leukocytes | 0.000965 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Survival of hematopoietic cells | 0.00131 | TNFSF13B,EBF1,RUNX1 |

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|---|---|---|---|
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Activation of B lymphocytes | 0.0026 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of neutrophils | 0.00271 | DHRS7B,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Expansion of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Differentiation of phagocytes | 0.00322 | DHRS7B,EBF1,RUNX1,CASP8 |
| | Thrombopoiesis | 0.00325 | ACTN1,CASP8 |
| | Abnormal morphology of thymus gland | 0.00331 | HIST1H1D,RUNX1,CASP8 |
| | Quantity of myeloid progenitor cells | 0.00369 | RUNX1,CASP8 |
| | Activation of lymphocytes | 0.00432 | TNFSF13B,EBF1,RUNX1,DUSP22,CASP8 |
| | Hematopoiesis in embryo | 0.00517 | RUNX1,CASP8 |
| | Expansion of lymphocytes | 0.00735 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of hematopoietic progenitor cells | 0.00811 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Cell viability of lymphocytes | 0.0093 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of antigen presenting cells | 0.0107 | EBF1,RUNX1,CASP8 |
| | Expansion of hematopoietic progenitor cells | 0.0109 | EBF1,RUNX1 |
| | Abnormal morphology of lymphoid organ | 0.0113 | HIST1H1D,TNFSF13B,RUNX1,CASP8 |
| | Quantity of marginal-zone B lymphocytes | 0.0133 | TNFSF13B,CASP8 |
| | Abnormal morphology of enlarged lymph node | 0.0147 | TNFSF13B,CASP8 |
| | Development of hematopoietic progenitor cells | 0.0194 | TNFSF13B,EBF1,RUNX1 |
| | Proliferation of hematopoietic progenitor cells | 0.0223 | EBF1,RUNX1,JMJD1C |
| | Differentiation of myeloid leukocytes | 0.023 | DHRS7B,RUNX1,CASP8 |
| | Quantity of hematopoietic progenitor cells | 0.0239 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Maturation of lymphocytes | 0.026 | TNFSF13B,RUNX1 |
| | Quantity of pre-B lymphocytes | 0.0271 | TNFSF13B,EBF1 |
| | Proliferation of B lymphocytes | 0.0302 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of macrophages | 0.0341 | RUNX1,CASP8 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| | Expansion of T lymphocytes | 0.0443 | TNFSF13B,CASP8 |
| | T cell homeostasis | 0.0472 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Activation of T lymphocytes | 0.0474 | RUNX1,DUSP22,CASP8 |
| | Abnormal morphology of enlarged spleen | 0.0488 | TNFSF13B,CASP8 |
| Hematopoiesis | Arrest in differentiation of leukocytes | 9.96E-06 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Arrest in differentiation of myeloid cells | 2.07E-05 | RUNX1,CASP8 |
| | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Differentiation of neutrophils | 0.00271 | DHRS7B,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |

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|---|---|---|---|
| | Differentiation of phagocytes | 0.00322 | DHRS7B,EBF1,RUNX1,CASP8 |
| | Thrombopoiesis | 0.00325 | ACTN1,CASP8 |
| | Quantity of myeloid progenitor cells | 0.00369 | RUNX1,CASP8 |
| | Hematopoiesis in embryo | 0.00517 | RUNX1,CASP8 |
| | Differentiation of hematopoietic progenitor cells | 0.00811 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of antigen presenting cells | 0.0107 | EBF1,RUNX1,CASP8 |
| | Expansion of hematopoietic progenitor cells | 0.0109 | EBF1,RUNX1 |
| | Development of hematopoietic progenitor cells | 0.0194 | TNFSF13B,EBF1,RUNX1 |
| | Proliferation of hematopoietic progenitor cells | 0.0223 | EBF1,RUNX1,JMJD1C |
| | Differentiation of myeloid leukocytes | 0.023 | DHRS7B,RUNX1,CASP8 |
| | Quantity of hematopoietic progenitor cells | 0.0239 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Quantity of pre-B lymphocytes | 0.0271 | TNFSF13B,EBF1 |
| | Differentiation of macrophages | 0.0341 | RUNX1,CASP8 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| Lymphoid Tissue Structure and Development | Arrest in differentiation of leukocytes | 9.96E-06 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Expansion of leukocytes | 0.000965 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Expansion of lymphatic system cells | 0.00098 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Frequency of B lymphocytes | 0.00176 | TNFSF13B,RUNX1 |
| | Differentiation of neutrophils | 0.00271 | DHRS7B,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Expansion of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Differentiation of phagocytes | 0.00322 | DHRS7B,EBF1,RUNX1,CASP8 |
| | Abnormal morphology of thymus gland | 0.00331 | HIST1H1D,RUNX1,CASP8 |
| | Quantity of myeloid progenitor cells | 0.00369 | RUNX1,CASP8 |
| | Quantity of bone marrow cells | 0.00627 | EBF1,RUNX1,CASP8 |
| | Expansion of lymphocytes | 0.00735 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of antigen presenting cells | 0.0107 | EBF1,RUNX1,CASP8 |
| | Abnormal morphology of lymphoid organ | 0.0113 | HIST1H1D,TNFSF13B,RUNX1,CASP8 |
| | Quantity of marginal-zone B lymphocytes | 0.0133 | TNFSF13B,CASP8 |
| | Abnormal morphology of enlarged lymph node | 0.0147 | TNFSF13B,CASP8 |
| | Differentiation of myeloid leukocytes | 0.023 | DHRS7B,RUNX1,CASP8 |
| | Maturation of lymphocytes | 0.026 | TNFSF13B,RUNX1 |
| | Quantity of pre-B lymphocytes | 0.0271 | TNFSF13B,EBF1 |
| | Proliferation of B lymphocytes | 0.0302 | TNFSF13B,EBF1,CASP8 |
| | Differentiation of macrophages | 0.0341 | RUNX1,CASP8 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| | Expansion of T lymphocytes | 0.0443 | TNFSF13B,CASP8 |

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|---|---|---|---|
| | Abnormal morphology of enlarged spleen | 0.0488 | TNFSF13B,CASP8 |
| Tissue Development | Arrest in differentiation of leukocytes | 9.96E-06 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Arrest in differentiation of myeloid cells | 2.07E-05 | RUNX1,CASP8 |
| | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Differentiation of neutrophils | 0.00271 | DHRS7B,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Differentiation of phagocytes | 0.00322 | DHRS7B,EBF1,RUNX1,CASP8 |
| | Thrombopoiesis | 0.00325 | ACTN1,CASP8 |
| | Hematopoiesis in embryo | 0.00517 | RUNX1,CASP8 |
| | Activation of osteoclasts | 0.00667 | EBF1,RUNX1 |
| | Differentiation of hematopoietic progenitor cells | 0.00811 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of antigen presenting cells | 0.0107 | EBF1,RUNX1,CASP8 |
| | Formation of coronary vessel | 0.0122 | ADAMTS6,RUNX1 |
| | Development of hematopoietic progenitor cells | 0.0194 | TNFSF13B,EBF1,RUNX1 |
| | Differentiation of myeloid leukocytes | 0.023 | DHRS7B,RUNX1,CASP8 |
| | Formation of osteoclasts | 0.0297 | EBF1,RUNX1 |
| | Differentiation of macrophages | 0.0341 | RUNX1,CASP8 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| | Proliferation of keratinocytes | 0.0498 | RUNX1,STEAP4 |
| Cancer | Arrest in differentiation of leukemia cells | 3.44E-05 | RUNX1,CASP8 |
| | Apoptosis of leukemia cells | 0.000605 | TNFSF13B,RUNX1,CASP8 |
| | Type M4 acute myeloid leukemia | 0.00648 | RUNX1,STEAP4 |
| | Precursor B-cell acute lymphoblastic leukemia | 0.0264 | EBF1,RUNX1 |
| | Cecum adenocarcinoma | 0.028 | ATP13A3,TAP2,MXRA8,STEAP4 |
| | Oral tumor | 0.0329 | ATP13A3,ADAMTS6,EBF1,WDR20,DUSP22,STEAP4,CASP8 |
| Organismal Injury and Abnormalities | Arrest in differentiation of leukemia cells | 3.44E-05 | RUNX1,CASP8 |
| | Apoptosis of leukemia cells | 0.000605 | TNFSF13B,RUNX1,CASP8 |
| | Hemopericardium | 0.00127 | RUNX1,CASP8 |
| | Primary Sjögren syndrome | 0.00258 | TNFSF13B,TAP2 |
| | Abnormal morphology of thymus gland | 0.00331 | HIST1H1D,RUNX1,CASP8 |
| | Insulin-dependent diabetes mellitus | 0.00339 | TNFSF13B,C6orf15,ADAMTS6,TAP2,ZFP57 |
| | Advanced stage peripheral arterial disease | 0.00367 | SUB1,RUNX1,CASP8 |
| | Intermediate disease stage peripheral arterial disease | 0.00426 | SUB1,RUNX1,CASP8 |
| | Inflammation of joint | 0.00508 | TNFSF13B,C6orf15,ADAMTS6,TAP2,PTPRN2,STEAP4,CASP8,JMJD1C |
| | Type M4 acute myeloid leukemia | 0.00648 | RUNX1,STEAP4 |
| | Non-traumatic arthropathy | 0.00682 | TNFSF13B,C6orf15,ADAMTS6,TAP2,PTPRN2,STEAP4,JMJD1C |
| | Hereditary bleeding disorder | 0.00813 | RUNX1,ACTN1 |
| | Abnormal morphology of lymphoid organ | 0.0113 | HIST1H1D,TNFSF13B,RUNX1,CASP8 |

| | | | |
|---|---|---|---|
| | Rheumatoid arthritis | 0.0135 | TNFSF13B,C6orf15,TAP2,PTPRN2,STEAP4,JMJD1C |
| | Abnormal morphology of enlarged lymph node | 0.0147 | TNFSF13B,CASP8 |
| | Autosomal recessive immunodeficiency | 0.0228 | TAP2,CASP8 |
| | Precursor B-cell acute lymphoblastic leukemia | 0.0264 | EBF1,RUNX1 |
| | Cecum adenocarcinoma | 0.028 | ATP13A3,TAP2,MXRA8,STEAP4 |
| | Oral tumor | 0.0329 | ATP13A3,ADAMTS6,EBF1,WDR20,DUSP22,STEAP4,CASP8 |
| | Hepatic steatosis | 0.0351 | PRKAR2B,EBF1,STEAP4 |
| | Abnormal morphology of enlarged spleen | 0.0488 | TNFSF13B,CASP8 |
| Tumor Morphology | Arrest in differentiation of leukemia cells | 3.44E-05 | RUNX1,CASP8 |
| | Apoptosis of leukemia cells | 0.000605 | TNFSF13B,RUNX1,CASP8 |
| Embryonic Development | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Remodeling of vitelline vessel | 0.0034 | RUNX1,CASP8 |
| | Hematopoiesis in embryo | 0.00517 | RUNX1,CASP8 |
| | Formation of coronary vessel | 0.0122 | ADAMTS6,RUNX1 |
| | Abnormal morphology of yolk sac | 0.0192 | HIST1H1D,CASP8 |
| | Differentiation of embryonic stem cells | 0.0225 | RUNX1,H2AFY2 |
| | Abnormal morphology of vitelline vessel | 0.0228 | HIST1H1D,CASP8 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| Humoral Immune Response | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Activation of B lymphocytes | 0.0026 | TNFSF13B,EBF1,CASP8 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Expansion of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Quantity of marginal-zone B lymphocytes | 0.0133 | TNFSF13B,CASP8 |
| | Quantity of pre-B lymphocytes | 0.0271 | TNFSF13B,EBF1 |
| | Proliferation of B lymphocytes | 0.0302 | TNFSF13B,EBF1,CASP8 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| Organ Development | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Formation of coronary vessel | 0.0122 | ADAMTS6,RUNX1 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| | Proliferation of keratinocytes | 0.0498 | RUNX1,STEAP4 |
| Organismal Development | Differentiation of pre-B lymphocytes | 0.000128 | TNFSF13B,EBF1,RUNX1 |
| | Differentiation of B lymphocytes | 0.00163 | TNFSF13B,EBF1,RUNX1,CASP8 |

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|---|---|---|---|
| | Differentiation of pro-B lymphocytes | 0.00176 | EBF1,RUNX1 |
| | Arrest in differentiation of B lymphocytes | 0.00297 | TNFSF13B,EBF1 |
| | Paleness of liver | 0.00297 | RUNX1,BPNT1 |
| | Thrombopoiesis | 0.00325 | ACTN1,CASP8 |
| | Abnormal morphology of thymus gland | 0.00331 | HIST1H1D,RUNX1,CASP8 |
| | Hematopoiesis in embryo | 0.00517 | RUNX1,CASP8 |
| | Formation of coronary vessel | 0.0122 | ADAMTS6,RUNX1 |
| | Differentiation of embryonic stem cells | 0.0225 | RUNX1,H2AFY2 |
| | Abnormal morphology of vitelline vessel | 0.0228 | HIST1H1D,CASP8 |
| | Development of artery | 0.0357 | ADAMTS6,RUNX1 |
| | Development of B lymphocytes | 0.0373 | TNFSF13B,EBF1 |
| | Morphology of liver | 0.0479 | RUNX1,BPNT1,STEAP4 |
| | Abnormal morphology of enlarged spleen | 0.0488 | TNFSF13B,CASP8 |
| Connective Tissue Development and Function | Quantity of adipose tissue | 0.000387 | C6orf15,PRKAR2B,EBF1,STEAP4,CASP8 |
| | Thrombopoiesis | 0.00325 | ACTN1,CASP8 |
| | Quantity of connective tissue | 0.00366 | C6orf15,PRKAR2B,EBF1,RUNX1,STEAP4,CASP8 |
| | Activation of osteoclasts | 0.00667 | EBF1,RUNX1 |
| | Quantity of subcutaneous fat | 0.00667 | EBF1,STEAP4 |
| | Formation of osteoclasts | 0.0297 | EBF1,RUNX1 |
| | Proliferation of keratinocytes | 0.0498 | RUNX1,STEAP4 |
| Tissue Morphology | Quantity of adipose tissue | 0.000387 | C6orf15,PRKAR2B,EBF1,STEAP4,CASP8 |
| | Abnormal morphology of thymus gland | 0.00331 | HIST1H1D,RUNX1,CASP8 |
| | Remodeling of vitelline vessel | 0.0034 | RUNX1,CASP8 |
| | Quantity of connective tissue | 0.00366 | C6orf15,PRKAR2B,EBF1,RUNX1,STEAP4,CASP8 |
| | Quantity of myeloid progenitor cells | 0.00369 | RUNX1,CASP8 |
| | Quantity of bone marrow cells | 0.00627 | EBF1,RUNX1,CASP8 |
| | Quantity of subcutaneous fat | 0.00667 | EBF1,STEAP4 |
| | Abnormal morphology of lymphoid organ | 0.0113 | HIST1H1D,TNFSF13B,RUNX1,CASP8 |
| | Quantity of marginal-zone B lymphocytes | 0.0133 | TNFSF13B,CASP8 |
| | Abnormal morphology of enlarged lymph node | 0.0147 | TNFSF13B,CASP8 |
| | Abnormal morphology of yolk sac | 0.0192 | HIST1H1D,CASP8 |
| | Abnormal morphology of vitelline vessel | 0.0228 | HIST1H1D,CASP8 |
| | Quantity of hematopoietic progenitor cells | 0.0239 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Quantity of pre-B lymphocytes | 0.0271 | TNFSF13B,EBF1 |
| | Abnormal morphology of membrane tissue | 0.0479 | HIST1H1D,NLRP6 |
| | Abnormal morphology of enlarged spleen | 0.0488 | TNFSF13B,CASP8 |
| Cell Death and Survival | Apoptosis of leukemia cells | 0.000605 | TNFSF13B,RUNX1,CASP8 |
| | Apoptosis of lymphoma cell lines | 0.000705 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Survival of pre-B lymphocytes | 0.00093 | TNFSF13B,EBF1 |
| | Survival of hematopoietic cells | 0.00131 | TNFSF13B,EBF1,RUNX1 |

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|---|---|---|---|
| | Cell death of macrophage cancer cell lines | 0.00465 | RUNX1,CASP8 |
| | Cell viability of blood cells | 0.00486 | TNFSF13B,EBF1,RUNX1,CASP8 |
| | Cell death of motor neurons | 0.0077 | RUNX1,CASP8 |
| | Cell viability of lymphocytes | 0.0093 | TNFSF13B,EBF1,CASP8 |
| | Cell viability of leukemia cell lines | 0.0109 | TNFSF13B,JMJD1C |
| | Apoptosis of myeloma cell lines | 0.0127 | TNFSF13B,CASP8 |
| | Killing of cells | 0.0135 | TNFSF13B,RUNX1,CASP8 |
| | Killing of tumor cell lines | 0.0173 | RUNX1,CASP8 |
| | Apoptosis of T lymphocytes | 0.0257 | TNFSF13B,RUNX1,CASP8 |
| | Apoptosis of leukemia cell lines | 0.0289 | TNFSF13B,RUNX1,CASP8 |
| | Apoptosis of thymocytes | 0.0309 | RUNX1,CASP8 |
| | Apoptosis of B lymphocytes | 0.0313 | TNFSF13B,CASP8 |
| | Cell viability | 0.0323 | TNFSF13B,EBF1,RUNX1,CLNS1A,PTPRN2,DUSP22,CASP8,JMJD1C |
| Organismal Survival | Viability | 0.000756 | RUNX1,CXXC1,CASP8 |
| | Organismal death | 0.0244 | HIST1H1D,TNFSF13B,EBF1,RUNX1,CLNS1A,SUB1,CXXC1,NLRP6,ZFP57,PTPRN2,BPNT1,CASP8 |
| Cardiovascular Disease | Hemopericardium | 0.00127 | RUNX1,CASP8 |
| | Advanced stage peripheral arterial disease | 0.00367 | SUB1,RUNX1,CASP8 |
| | Intermediate disease stage peripheral arterial disease | 0.00426 | SUB1,RUNX1,CASP8 |
| Connective Tissue Disorders | Inflammation of joint | 0.00508 | TNFSF13B,C6orf15,ADAMTS6,TAP2,PTPRN2,STEAP4,CASP8,JMJD1C |
| | Non-traumatic arthropathy | 0.00682 | TNFSF13B,C6orf15,ADAMTS6,TAP2,PTPRN2,STEAP4,JMJD1C |
| | Rheumatoid arthritis | 0.0135 | TNFSF13B,C6orf15,TAP2,PTPRN2,STEAP4,JMJD1C |
| Immunological Disease | Primary Sjögren syndrome | 0.00258 | TNFSF13B,TAP2 |
| | Abnormal morphology of thymus gland | 0.00331 | HIST1H1D,RUNX1,CASP8 |
| | Insulin-dependent diabetes mellitus | 0.00339 | TNFSF13B,C6orf15,ADAMTS6,TAP2,ZFP57 |
| | Systemic autoimmune syndrome | 0.00418 | TNFSF13B,C6orf15,ADAMTS6,TAP2,ZFP57,PTPRN2,STEAP4,CASP8,JMJD1C |
| | Type M4 acute myeloid leukemia | 0.00648 | RUNX1,STEAP4 |
| | Abnormal morphology of lymphoid organ | 0.0113 | HIST1H1D,TNFSF13B,RUNX1,CASP8 |
| | Rheumatoid arthritis | 0.0135 | TNFSF13B,C6orf15,TAP2,PTPRN2,STEAP4,JMJD1C |
| | Abnormal morphology of enlarged lymph node | 0.0147 | TNFSF13B,CASP8 |
| | Immunodeficiency | 0.0165 | TNFSF13B,TAP2,CASP8 |
| | Autosomal recessive immunodeficiency | 0.0228 | TAP2,CASP8 |
| | Precursor B-cell acute lymphoblastic leukemia | 0.0264 | EBF1,RUNX1 |
| | Primary immunodeficiency disorder | 0.0447 | TAP2,CASP8 |
| | Abnormal morphology of enlarged spleen | 0.0488 | TNFSF13B,CASP8 |
| Inflammatory Disease | Inflammation of joint | 0.00508 | TNFSF13B,C6orf15,ADAMTS6,TAP2,PTPRN2,STEAP4,CASP8,JMJD1C |
| | Rheumatoid arthritis | 0.0135 | TNFSF13B,C6orf15,TAP2,PTPRN2,STEAP4,JMJD1C |
| Skeletal and Muscular Disorders | Inflammation of joint | 0.00508 | TNFSF13B,C6orf15,ADAMTS6,TAP2,PTPRN2,STEAP4,CASP8,JMJD1C |
| | Non-traumatic arthropathy | 0.00682 | TNFSF13B,C6orf15,ADAMTS6,TAP2,PTPRN2,STEAP4,JMJD1C |
| | Rheumatoid arthritis | 0.0135 | TNFSF13B,C6orf15,TAP2,PTPRN2,STEAP4,JMJD1C |
| Hematological Disease | Type M4 acute myeloid leukemia | 0.00648 | RUNX1,STEAP4 |

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|---|---|---|---|
| | Hereditary bleeding disorder | 0.00813 | RUNX1,ACTN1 |
| | Precursor B-cell acute lymphoblastic leukemia | 0.0264 | EBF1,RUNX1 |
| Cardiovascular System Development and Function | Formation of coronary vessel | 0.0122 | ADAMTS6,RUNX1 |
| | Development of artery | 0.0357 | ADAMTS6,RUNX1 |
| Cell Cycle | Binding of protein binding site | 0.0283 | EBF1,RUNX1,SUB1 |
| | Binding of DNA | 0.0404 | TNFSF13B,EBF1,RUNX1,SUB1 |
| Cellular Function and Maintenance | T cell homeostasis | 0.0472 | TNFSF13B,EBF1,RUNX1,CASP8 |
| Developmental Disorder | Dysmorphogenesis | 0.0173 | HIST1H1D,CXXC1 |
| | Abnormal morphology of yolk sac | 0.0192 | HIST1H1D,CASP8 |
| | Abnormal morphology of vitelline vessel | 0.0228 | HIST1H1D,CASP8 |
| Hereditary Disorder | Hereditary bleeding disorder | 0.00813 | RUNX1,ACTN1 |
| | Autosomal recessive immunodeficiency | 0.0228 | TAP2,CASP8 |
| Cellular Movement | Cell movement of leukemia cell lines | 0.0438 | RUNX1,ACTN1 |
| Gastrointestinal Disease | Primary Sjögren syndrome | 0.00258 | TNFSF13B,TAP2 |
| | Insulin-dependent diabetes mellitus | 0.00339 | TNFSF13B,C6orf15,ADAMTS6,TAP2,ZFP57 |
| | Cecum adenocarcinoma | 0.028 | ATP13A3,TAP2,MXRA8,STEAP4 |
| | Oral tumor | 0.0329 | ATP13A3,ADAMTS6,EBF1,WDR20,DUSP22,STEAP4,CASP8 |
| | Hepatic steatosis | 0.0351 | PRKAR2B,EBF1,STEAP4 |
| Organ Morphology | Paleness of liver | 0.00297 | RUNX1,BPNT1 |
| | Abnormal morphology of thymus gland | 0.00331 | HIST1H1D,RUNX1,CASP8 |
| | Abnormal morphology of lymphoid organ | 0.0113 | HIST1H1D,TNFSF13B,RUNX1,CASP8 |
| | Abnormal morphology of enlarged lymph node | 0.0147 | TNFSF13B,CASP8 |
| | Morphology of liver | 0.0479 | RUNX1,BPNT1,STEAP4 |
| | Abnormal morphology of enlarged spleen | 0.0488 | TNFSF13B,CASP8 |
| Inflammatory Response | Activation of B lymphocytes | 0.0026 | TNFSF13B,EBF1,CASP8 |
| | Activation of lymphocytes | 0.00432 | TNFSF13B,EBF1,RUNX1,DUSP22,CASP8 |
| | Inflammation of joint | 0.00508 | TNFSF13B,C6orf15,ADAMTS6,TAP2,PTPRN2,STEAP4,CASP8,JMJD1C |
| | Rheumatoid arthritis | 0.0135 | TNFSF13B,C6orf15,TAP2,PTPRN2,STEAP4,JMJD1C |
| | Activation of T lymphocytes | 0.0474 | RUNX1,DUSP22,CASP8 |
| Cell-mediated Immune Response | T cell homeostasis | 0.0472 | TNFSF13B,EBF1,RUNX1,CASP8 |
| Metabolic Disease | Insulin-dependent diabetes mellitus | 0.00339 | TNFSF13B,C6orf15,ADAMTS6,TAP2,ZFP57 |
| | Glucose metabolism disorder | 0.0166 | TNFSF13B,C6orf15,ADAMTS6,TAP2,EBF1,ZFP57,STEAP4,CASP8 |
| | DNA repair-deficiency disorder | 0.0264 | TAP2,RUNX1 |
| | Hepatic steatosis | 0.0351 | PRKAR2B,EBF1,STEAP4 |
| Endocrine System Disorders | Insulin-dependent diabetes mellitus | 0.00339 | TNFSF13B,C6orf15,ADAMTS6,TAP2,ZFP57 |
| Ophthalmic Disease | Primary Sjögren syndrome | 0.00258 | TNFSF13B,TAP2 |
| Cell-To-Cell Signaling and Interaction | Activation of B lymphocytes | 0.0026 | TNFSF13B,EBF1,CASP8 |
| | Activation of lymphocytes | 0.00432 | TNFSF13B,EBF1,RUNX1,DUSP22,CASP8 |
| | Activation of osteoclasts | 0.00667 | EBF1,RUNX1 |
| | Activation of T lymphocytes | 0.0474 | RUNX1,DUSP22,CASP8 |

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|---|---|---|---|
| Immune Cell Trafficking | Activation of B lymphocytes | 0.0026 | TNFSF13B,EBF1,CASP8 |
| | Activation of lymphocytes | 0.00432 | TNFSF13B,EBF1,RUNX1,DUSP22,CASP8 |
| | Activation of T lymphocytes | 0.0474 | RUNX1,DUSP22,CASP8 |
| Digestive System Development and Function | Paleness of liver | 0.00297 | RUNX1,BPNT1 |
| | Morphology of liver | 0.0479 | RUNX1,BPNT1,STEAP4 |
| Hepatic System Development and Function | Paleness of liver | 0.00297 | RUNX1,BPNT1 |
| | Morphology of liver | 0.0479 | RUNX1,BPNT1,STEAP4 |
| Endocrine System Development and Function | Glucose tolerance | 0.00374 | PRKAR2B,PTPRN2,STEAP4,CASP8 |
| Gene Expression | Transcription of RNA | 0.00648 | HIST1H1D,PRKAR2B,EBF1,RUNX1,SUB1,CXXC1,H2AFY2,ZFP57,DUSP22,CASP8,JMJD1C |
| | Transcription | 0.00708 | HIST1H1D,TNFSF13B,PRKAR2B,EBF1,RUNX1,SUB1,CXXC1,H2AFY2,ZFP57,DUSP22,CASP8,JMJD1C |
| | Expression of RNA | 0.0109 | HIST1H1D,PRKAR2B,EBF1,RUNX1,SUB1,CXXC1,RPS23,H2AFY2,ZFP57,DUSP22,CASP8,JMJD1C |
| | Transcription of DNA | 0.0163 | HIST1H1D,EBF1,RUNX1,SUB1,CXXC1,H2AFY2,ZFP57,DUSP22,JMJD1C |
| | Binding of protein binding site | 0.0283 | EBF1,RUNX1,SUB1 |
| | Activation of DNA endogenous promoter | 0.0371 | HIST1H1D,EBF1,RUNX1,SUB1,H2AFY2,ZFP57,DUSP22 |
| | Binding of DNA | 0.0404 | TNFSF13B,EBF1,RUNX1,SUB1 |
| Skeletal and Muscular System Development and Function | Activation of osteoclasts | 0.00667 | EBF1,RUNX1 |
| | Formation of osteoclasts | 0.0297 | EBF1,RUNX1 |
| Hair and Skin Development and Function | Proliferation of keratinocytes | 0.0498 | RUNX1,STEAP4 |
| Carbohydrate Metabolism | Uptake of D-glucose | 0.0133 | TNFSF13B,EBF1,STEAP4 |
| Lipid Metabolism | Concentration of lipid | 0.0197 | PRKAR2B,RUNX1,PTPRN2,BPNT1,STEAP4,CASP8 |
| | Quantity of sphingolipid | 0.0222 | RUNX1,CASP8 |
| | Concentration of cholesterol | 0.0342 | PRKAR2B,BPNT1,STEAP4 |
| Small Molecule Biochemistry | Incorporation of thymidine | 0.0125 | TNFSF13B,PRKAR2B |
| | Uptake of D-glucose | 0.0133 | TNFSF13B,EBF1,STEAP4 |
| | Concentration of lipid | 0.0197 | PRKAR2B,RUNX1,PTPRN2,BPNT1,STEAP4,CASP8 |
| | Quantity of sphingolipid | 0.0222 | RUNX1,CASP8 |
| | Concentration of cholesterol | 0.0342 | PRKAR2B,BPNT1,STEAP4 |
| Molecular Transport | Uptake of D-glucose | 0.0133 | TNFSF13B,EBF1,STEAP4 |
| | Concentration of lipid | 0.0197 | PRKAR2B,RUNX1,PTPRN2,BPNT1,STEAP4,CASP8 |
| | Quantity of sphingolipid | 0.0222 | RUNX1,CASP8 |
| | Concentration of cholesterol | 0.0342 | PRKAR2B,BPNT1,STEAP4 |
| DNA Replication, Recombination, and Repair | Incorporation of thymidine | 0.0125 | TNFSF13B,PRKAR2B |
| | DNA damage | 0.0131 | EBF1,RUNX1,CASP8 |
| Nucleic Acid Metabolism | Incorporation of thymidine | 0.0125 | TNFSF13B,PRKAR2B |
| Protein Synthesis | Quantity of leptin in blood | 0.0253 | PRKAR2B,STEAP4 |
| Hepatic System Disease | Hepatic steatosis | 0.0351 | PRKAR2B,EBF1,STEAP4 |
| Post-Translational Modification | Dephosphorylation of protein | 0.0286 | PTPRN2,DUSP22 |
| Cell Signaling | I-kappaB kinase/NF-kappaB cascade | 0.0369 | NLRP6,CASP8 |

*Table E10: Significantly enriched canonical pathways, diseases and biological functions from Ingenuity Pathway Analysis based on CpGs and regions differentially methylated in older children relation to asthma*

***CANONICAL PATHWAYS***

| Category | Genes | P-value |
|---|---|---|
| p70S6K Signaling | RALB,YWHAQ,IL4,PRKCH,PRKCZ,PPP2CA | 0.000870964 |
| Glycolysis I | FBP1,PGAM2,GPI | 0.000954993 |
| Gluconeogenesis I | FBP1,PGAM2,GPI | 0.001096478 |
| mTOR Signaling | RALB,RPTOR,RPS6KA2,DDIT4,PRKCH,PRKCZ,PPP2CA | 0.00128825 |
| ERK5 Signaling | RALB,YWHAQ,RPS6KA2,PRKCZ | 0.002630268 |
| Glioma Signaling | IGF1R,RALB,RBL2,PRKCH,PRKCZ | 0.002951209 |
| UDP-N-acetyl-D-galactosamine Biosynthesis II | HK2,GPI | 0.003467369 |
| ErbB4 Signaling | RALB,NCSTN,PRKCH,PRKCZ | 0.003548134 |
| Myc Mediated Apoptosis Signaling | IGF1R,RALB,YWHAQ,PRKCZ | 0.003548134 |
| Fc Epsilon RI Signaling | RALB,IL4,PRKCH,PRKCZ,MS4A2 | 0.003715352 |
| Growth Hormone Signaling | IGF1R,RPS6KA2,PRKCH,PRKCZ | 0.005011872 |
| HIPPO signaling | PATJ,YWHAQ,PRKCZ,PPP2CA | 0.005011872 |
| α-Adrenergic Signaling | RALB,ADCY3,PRKCH,PRKCZ | 0.006606934 |
| UVC-Induced MAPK Signaling | RALB,PRKCH,PRKCZ | 0.007079458 |
| Hepatic Cholestasis | ADCY3,IL4,PRKCH,PRKCZ,NR0B2 | 0.009549926 |
| ErbB Signaling | RALB,PRKCH,PRKCZ,NCK1 | 0.01023293 |
| Melanocyte Development and Pigmentation Signaling | RALB,ADCY3,RPS6KA2,MITF | 0.01023293 |
| IGF-1 Signaling | IGF1R,RALB,YWHAQ,PRKCZ | 0.013182567 |
| Synaptic Long Term Depression | IGF1R,RALB,PRKCH,PRKCZ,PPP2CA | 0.013803843 |
| RAR Activation | ADCY3,SMARCD3,PRKCH,PRKCZ,CITED2 | 0.018197009 |
| Natural Killer Cell Signaling | RALB,PRKCH,PRKCZ,NCK1 | 0.018197009 |
| PI3K/AKT Signaling | RALB,YWHAQ,PRKCZ,PPP2CA | 0.019952623 |
| Renin-Angiotensin Signaling | RALB,ADCY3,PRKCH,PRKCZ | 0.020417379 |
| Thrombopoietin Signaling | RALB,PRKCH,PRKCZ | 0.020417379 |
| Estrogen Receptor Signaling | POLR2B,RALB,MED27,NR0B2 | 0.023442288 |
| 14-3-3-mediated Signaling | RALB,YWHAQ,PRKCH,PRKCZ | 0.025703958 |
| P2Y Purigenic Receptor Signaling Pathway | RALB,ADCY3,PRKCH,PRKCZ | 0.027542287 |
| Breast Cancer Regulation by Stathmin1 | RALB,ADCY3,PRKCH,PRKCZ,PPP2CA | 0.028183829 |
| Insulin Receptor Signaling | RALB,RPTOR,PRKCZ,NCK1 | 0.029512092 |
| Angiopoietin Signaling | RALB,ANGPT2,NCK1 | 0.030902954 |
| CREB Signaling in Neurons | POLR2B,RALB,ADCY3,PRKCH,PRKCZ | 0.032359366 |
| Airway Inflammation in Asthma | IL4, | 0.032359366 |
| Role of NFAT in Cardiac Hypertrophy | IGF1R,RALB,ADCY3,PRKCH,PRKCZ | 0.034673685 |
| Erythropoietin Signaling | RALB,PRKCH,PRKCZ | 0.034673685 |
| IL-3 Signaling | RALB,PRKCH,PRKCZ | 0.034673685 |
| Macropinocytosis Signaling | RALB,PRKCH,PRKCZ | 0.034673685 |
| Prolactin Signaling | RALB,PRKCH,PRKCZ | 0.036307805 |
| Neuregulin Signaling | RALB,PRKCH,PRKCZ | 0.038904514 |
| Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes | PRKCH,PRKCZ,NCK1 | 0.039810717 |
| LPS-stimulated MAPK Signaling | RALB,PRKCH,PRKCZ | 0.040738028 |

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| NF-kB Activation by Viruses | RALB,PRKCH,PRKCZ | 0.040738028 |
| Dopamine-DARPP32 Feedback in cAMP Signaling | ADCY3,PRKCH,PRKCZ,PPP2CA | 0.040738028 |
| Rapoport-Luebering Glycolytic Shunt | PGAM2, | 0.040738028 |
| Trehalose Degradation II (Trehalase) | HK2, | 0.040738028 |
| HER-2 Signaling in Breast Cancer | RALB,PRKCH,PRKCZ | 0.041686938 |
| VEGF Family Ligand-Receptor Interactions | RALB,PRKCH,PRKCZ | 0.041686938 |
| Mechanisms of Viral Exit from Host Cells | PRKCH,PRKCZ | 0.044668359 |
| Triacylglycerol Biosynthesis | LPIN1,LPCAT2 | 0.044668359 |
| Ceramide Signaling | RALB,PRKCZ,PPP2CA | 0.044668359 |
| Tight Junction Signaling | PATJ,NAPA,PRKCZ,PPP2CA | 0.045708819 |
| eNOS Signaling | ADCY3,SLC7A1,PRKCH,PRKCZ | 0.046773514 |
| PPAR Signaling | RALB,CITED2,NR0B2 | 0.046773514 |
| GDP-mannose Biosynthesis | GPI, | 0.047863009 |
| Opioid Signaling Pathway | RALB,ADCY3,RPS6KA2,PRKCH,PRKCZ | 0.047863009 |
| GNRH Signaling | RALB,ADCY3,PRKCH,PRKCZ | 0.048977882 |

***DISEASES AND BIOLOGICAL FUNCTIONS***

| Category | Disease and Biological Function* | P-value | Genes |
|---|---|---|---|
| Cell-To-Cell Signaling and Interaction | Activation of basophils | 1.97E-07 | PRG2,PTGDR2,IL4,EPX,PRG3 |
| | Activation of myeloid cells | 0.000194 | IRF6,PRG2,PTGDR2,SIGLEC8,ANGPT2,FOXP1,TFF2,IL4,METRNL,IL5RA,EPX,PRG3 |
| | Activation of granulocytes | 0.000552 | PRG2,PTGDR2,IL4,IL5RA,EPX,PRG3 |
| | Inflammatory response of tumor cell lines | 0.00136 | CTSB,ENG |
| | Activation of phagocytes | 0.00156 | IRF6,PRG2,SIGLEC8,ANGPT2,FOXP1,TFF2,IL4,METRNL,EPX,RNASE2,PRG3 |
| | Activation of eosinophils | 0.00168 | PTGDR2,IL4,IL5RA |
| | Immune response of tumor cell lines | 0.00263 | RALB,DICER1,FOXP1,CTSB,IL4,ENG |
| | Activation of mast cells | 0.00304 | PRG2,SIGLEC8,IL4,EPX |
| | Activation of cells | 0.00308 | PRG2,TANK,SIGLEC8,PTGDR2,ANGPT2,FOXP1,DDIT4,IL4,METRNL,IL5RA,PRG3,CLEC12A,IRF6,RPTOR,TFF2,EPX,PRKCZ,NCK1,BANK1,RNASE2,PPP2CA |
| | Contact growth inhibition | 0.00341 | IGF1R,RBL2,IL4,IKZF3,PRKCZ,GPI |
| | Priming of synaptic vesicles | 0.00653 | NAPA,STX1B |
| | Recruitment of muscle cells | 0.00653 | IL4,ENG |
| | Activation of blood cells | 0.00675 | PRG2,SIGLEC8,PTGDR2,ANGPT2,FOXP1,IL4,METRNL,IL5RA,PRG3,IRF6,RPTOR,TFF2,EPX,NCK1,BANK1,RNASE2 |
| | Detachment of cells | 0.00719 | IGF1R,ANGPT2,NAPA,ENG |
| | Activation of Th2 cells | 0.00742 | PTGDR2,IL4 |
| | Activation of leukocytes | 0.00789 | PRG2,PTGDR2,SIGLEC8,ANGPT2,FOXP1,IL4,METRNL,IL5RA,PRG3,IRF6,TFF2,EPX,BANK1,NCK1,RNASE2 |
| | Fusion of myotube | 0.00836 | IGF1R,IL4 |
| | Fusion of plasma membrane | 0.0138 | RALB,NAPA |
| | Stimulation of epithelial cells | 0.0151 | IL4,EPX |
| Hematological System Development and Function | Activation of basophils | 1.97E-07 | PRG2,PTGDR2,IL4,EPX,PRG3 |
| | Activation of myeloid cells | 0.000194 | IRF6,PRG2,PTGDR2,SIGLEC8,ANGPT2,FOXP1,TFF2,IL4,METRNL,IL5RA,EPX,PRG3 |
| | Proliferation of B lymphocytes | 0.000195 | TANK,LPIN1,RPTOR,DICER1,PCYT1A,RBL2,IL4,IL5RA,IKZF3,PRKCZ,BANK1 |
| | Abnormal morphology of eosinophils | 0.000199 | PRG2,EPX |
| | Activation of granulocytes | 0.000552 | PRG2,PTGDR2,IL4,IL5RA,EPX,PRG3 |
| | Quantity of naive B cells | 0.000656 | IL4,IKZF3 |
| | Abnormal morphology of reticulocytes | 0.000979 | SLC7A1,STEAP3 |

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| | Quantity of B-1 lymphocytes | 0.00101 | RPTOR,IL4,IL5RA,ARID3A,BANK1 |
| | Morphology of lymph follicle | 0.00112 | IL4,IKZF3,PRKCZ,TLE4,BANK1,PPT2 |
| | Proliferation of lymphocytes | 0.00119 | TANK,SLC7A1,RBL2,IL4,IL5RA,IKZF3,IRF6,IGF1R,NCSTN,LPIN1,RPTOR,DICER1,PCYT1A,PRKCH,PRKCZ,BANK1,NCK1,GPI |
| | Migration of basophils | 0.00136 | PTGDR2,ENG |
| | Activation of phagocytes | 0.00156 | IRF6,PRG2,SIGLEC8,ANGPT2,FOXP1,TFF2,IL4,METRNL,EPX,RNASE2,PRG3 |
| | Granulopoiesis | 0.00159 | IGF1R,ZFPM1,RALB,SIGLEC8,IL4,CITED2 |
| | Activation of eosinophils | 0.00168 | PTGDR2,IL4,IL5RA |
| | Morphology of granulocytes | 0.00246 | PRG2,IL4,EPX |
| | Homing of Th2 cells | 0.00287 | PTGDR2,IL4 |
| | Activation of mast cells | 0.00304 | PRG2,SIGLEC8,IL4,EPX |
| | Quantity of blood cells | 0.00333 | TANK,SIGLEC8,PTGDR2,SLC7A1,RBL2,BNIP3L,IL4,IL5RA,IKZF3,IRF6,IGF1R,RPTOR,DICER1,CTSB,STEAP3,PRKCH,ARID3A,BANK1,TLE4,ST3GAL1,PPT2,PPP2CA |
| | Survival of follicular B lymphocytes | 0.00349 | DICER1,IL4 |
| | Myelopoiesis of leukocytes | 0.00393 | IGF1R,ZFPM1,RALB,SIGLEC8,FOXP1,IL4,CITED2 |
| | Quantity of B-1a lymphocytes | 0.00397 | RPTOR,ARID3A,BANK1 |
| | Quantity of B lymphocytes | 0.00447 | TANK,RPTOR,CTSB,IL4,IL5RA,PRKCH,IKZF3,ARID3A,BANK1,TLE4 |
| | Migration of B-lymphocyte derived cell lines | 0.00653 | PTGDR2,ENG |
| | Proliferation of germinal center B lymphocytes | 0.00653 | DICER1,IL4 |
| | Activation of blood cells | 0.00675 | PRG2,SIGLEC8,PTGDR2,ANGPT2,FOXP1,IL4,METRNL,IL5RA,PRG3,IRF6,RPTOR,TFF2,EPX,NCK1,BANK1,RNASE2 |
| | Quantity of myeloid cells | 0.0073 | IRF6,IGF1R,PTGDR2,SIGLEC8,RBL2,CTSB,IL4,IL5RA,ARID3A,TLE4,PPT2,PPP2CA |
| | Activation of Th2 cells | 0.00742 | PTGDR2,IL4 |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Activation of leukocytes | 0.00789 | PRG2,PTGDR2,SIGLEC8,ANGPT2,FOXP1,IL4,METRNL,IL5RA,PRG3,IRF6,TFF2,EPX,BANK1,NCK1,RNASE2 |
| | Quantity of leukocytes | 0.00815 | TANK,SIGLEC8,PTGDR2,RBL2,IL4,IL5RA,IKZF3,IRF6,IGF1R,RPTOR,DICER1,CTSB,PRKCH,ARID3A,BANK1,TLE4,ST3GAL1,PPT2,PPP2CA |
| | Development of PBMCs | 0.00836 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Cellular infiltration by granulocytes | 0.00869 | IRF6,PTGDR2,SIGLEC8,ANGPT2,DICER1,CTSB,IL4 |
| | Differentiation of eosinophils | 0.00936 | SIGLEC8,IL4 |
| | Leukopoiesis | 0.00985 | ZFPM1,SIGLEC8,FOXP1,RBL2,IL4,IL5RA,IKZF3,CITED2,NR0B2,IGF1R,RALB,RPTOR,DICER1,PRKCH,PRKCZ,ARID3A,TLE4 |
| | Hematopoiesis in embryo | 0.0114 | ZFPM1,ENG,ARID3A |
| | Migration of Langerhans cells | 0.0115 | RPTOR,IL4 |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |
| | Abnormal morphology of lymphoid organ | 0.0151 | BNIP3L,STEAP3,IL5RA,PRKCH,IKZF3,BANK1,TLE4,CITED2,PPT2 |
| | Morphology of lymphoid tissue | 0.0162 | RBL2,BNIP3L,STEAP3,IL4,IL5RA,PRKCH,IKZF3,PRKCZ,BANK1,TLE4,CITED2,PPT2 |
| Hypersensitivity Response | Activation of basophils | 1.97E-07 | PRG2,PTGDR2,IL4,EPX,PRG3 |
| | Abnormal morphology of eosinophils | 0.000199 | PRG2,EPX |
| | Migration of basophils | 0.00136 | PTGDR2,ENG |
| | Activation of eosinophils | 0.00168 | PTGDR2,IL4,IL5RA |
| | Activation of mast cells | 0.00304 | PRG2,SIGLEC8,IL4,EPX |
| | Degranulation of BMMC cells | 0.0126 | IL4,EHF |
| Immune Cell Trafficking | Activation of basophils | 1.97E-07 | PRG2,PTGDR2,IL4,EPX,PRG3 |

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| | Activation of granulocytes | 0.000552 | PRG2,PTGDR2,IL4,IL5RA,EPX,PRG3 |
| | Migration of basophils | 0.00136 | PTGDR2,ENG |
| | Activation of phagocytes | 0.00156 | IRF6,PRG2,SIGLEC8,ANGPT2,FOXP1,TFF2,IL4,METRNL,EPX,RNASE2,PRG3 |
| | Activation of eosinophils | 0.00168 | PTGDR2,IL4,IL5RA |
| | Homing of Th2 cells | 0.00287 | PTGDR2,IL4 |
| | Activation of mast cells | 0.00304 | PRG2,SIGLEC8,IL4,EPX |
| | Migration of B-lymphocyte derived cell lines | 0.00653 | PTGDR2,ENG |
| | Activation of Th2 cells | 0.00742 | PTGDR2,IL4 |
| | Activation of leukocytes | 0.00789 | PRG2,PTGDR2,SIGLEC8,ANGPT2,FOXP1,IL4,METRNL,IL5RA,PRG3,IRF6,TFF2,EPX,BANK1,NCK1,RNASE2 |
| | Cellular infiltration by granulocytes | 0.00869 | IRF6,PTGDR2,SIGLEC8,ANGPT2,DICER1,CTSB,IL4 |
| | Migration of Langerhans cells | 0.0115 | RPTOR,IL4 |
| Inflammatory Response | Activation of basophils | 1.97E-07 | PRG2,PTGDR2,IL4,EPX,PRG3 |
| | Activation of granulocytes | 0.000552 | PRG2,PTGDR2,IL4,IL5RA,EPX,PRG3 |
| | Inflammatory response of tumor cell lines | 0.00136 | CTSB,ENG |
| | Activation of phagocytes | 0.00156 | IRF6,PRG2,SIGLEC8,ANGPT2,FOXP1,TFF2,IL4,METRNL,EPX,RNASE2,PRG3 |
| | Activation of eosinophils | 0.00168 | PTGDR2,IL4,IL5RA |
| | Degranulation of cells | 0.00183 | ZFPM1,PRG2,RALB,LPIN1,DICER1,IL4,EHF,MS4A2 |
| | Immune response of tumor cell lines | 0.00263 | RALB,DICER1,FOXP1,CTSB,IL4,ENG |
| | Activation of mast cells | 0.00304 | PRG2,SIGLEC8,IL4,EPX |
| | Inflammatory response | 0.00327 | PRG2,DAPK2,PTGDR2,ANGPT2,FOXP1,IL4,METRNL,ENG,PRG3,CLEC12A,MS4A2,IRF6,RALB,DICER1,TFF2,CTSB,EPX,RNASE2 |
| | Activation of Th2 cells | 0.00742 | PTGDR2,IL4 |
| | Activation of leukocytes | 0.00789 | PRG2,PTGDR2,SIGLEC8,ANGPT2,FOXP1,IL4,METRNL,IL5RA,PRG3,IRF6,TFF2,EPX,BANK1,NCK1,RNASE2 |
| | Size of phagocytes | 0.0104 | RPTOR,IL4 |
| | Antiviral response | 0.0109 | SERINC5,DICER1,BNIP3L,IL4,DDIT4,RNASE2 |
| | Migration of Langerhans cells | 0.0115 | RPTOR,IL4 |
| | Degranulation of BMMC cells | 0.0126 | IL4,EHF |
| Carbohydrate Metabolism | Glycolysis of cells | 3.26E-06 | IGF1R,RPTOR,IL4,DDIT4,FBP1,PGAM2,HK2,CITED2,GPI |
| | Modification of glucose-6-phosphate | 0.000396 | HK2,GPI |
| | Flux of carbohydrate | 0.000846 | PCYT1A,PGAM2,GPI |
| | Flux of D-glucose | 0.000979 | PGAM2,GPI |
| | Metabolism of monosaccharide | 0.00479 | IGF1R,NISCH,FBP1,HK2,GPI |
| | Catabolism of proteoglycan | 0.00836 | CTSB,IL4 |
| | Metabolism of D-hexose | 0.00957 | IGF1R,NISCH,FBP1,HK2 |
| | Gluconeogenesis | 0.0102 | SOGA1,FBP1,PGAM2,NR0B2 |
| Cell Death and Survival | Cell death of epithelial cells | 3.54E-05 | PRG2,ITIH4,YWHAQ,RBL2,BNIP3L,IL4,ENG,MITF,CITED2,NR0B2,IGF1R,DICER1,CTSB,EPX,HK2,PMP22,PPP2CA |
| | Necrosis of epithelial tissue | 0.000119 | PRG2,ITIH4,YWHAQ,ANGPT2,RBL2,BNIP3L,IL4,ENG,MITF,CITED2,NR0B2,IGF1R,DICER1,CTSB,EPX,HK2,PMP22,PPP2CA |
| | Necrosis | 0.000612 | DAPK2,RBL2,BNIP3L,EHF,MITF,RALB,LRIG1,DICER1,ATP2C1,EMG1,PRKCH,NCK1,TLE4,GPI,DDIT4,ENG,CITED2,IGF1R,RPTOR,RPS6KA2,CS,PPT2,YWHAQ,SIGLEC8,FOXP1,RHOBTB2,NAPA,IKZF3,MS4A2,STEAP3,STX1B,EPX,PRKCZ,HK2,TLDC2,ST3GAL1,PMP22,PPP2CA,PRG2,ITIH4,TANK,PTGDR2,ANGPT2,IL4,IL5RA,NR0B2,CTSB,FOXK2,RNASE2 |
| | Cell death of connective tissue cells | 0.00255 | TANK,RBL2,BNIP3L,DDIT4,IL4,ENG,NR0B2,IGF1R,RALB,DICER1,RPS6KA2,CTSB,PRKCZ,NCK1,GPI |
| | Survival of follicular B lymphocytes | 0.00349 | DICER1,IL4 |
| | Apoptosis of hepatoma cell lines | 0.00391 | IGF1R,CTSB,IL4,PRKCZ,PPP2CA,NR0B2 |

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| | Cell death of blood cells | 0.004 | DAPK2,SIGLEC8,FOXP1,BNIP3L,DDIT4,IL4,IL5RA,IKZF3,MS4A2,LRIG1,RPTOR,DICER1,CTSB,PRKCZ,TLE4,ST3GAL1 |
| | Apoptosis of tumor | 0.00417 | IGF1R,ANGPT2 |
| | Cell death of lymphatic system cells | 0.00457 | LRIG1,DICER1,FOXP1,CTSB,BNIP3L,STEAP3,DDIT4,IL4,IL5RA,TLE4,ST3GAL1 |
| | Cell death of immune cells | 0.0054 | DAPK2,SIGLEC8,FOXP1,DDIT4,IL4,IL5RA,IKZF3,MS4A2,LRIG1,RPTOR,DICER1,CTSB,PRKCZ,TLE4,ST3GAL1 |
| | Cell death of lung cells | 0.00595 | IGF1R,PRG2,EPX |
| | Cell death of embryonic cell lines | 0.00617 | IGF1R,TANK,YWHAQ,RBL2,CTSB,BNIP3L,DDIT4,HK2,CITED2,PMP22 |
| | Apoptosis | 0.00701 | DAPK2,YWHAQ,SIGLEC8,FOXP1,RHOBTB2,RBL2,NAPA,BNIP3L,EHF,IKZF3,MITF,MS4A2,KCNH2,RALB,LRIG1,DICER1,ATP2C1,STEAP3,PRKCH,PRKCZ,HK2,NCK1,ST3GAL1,TLE4,GPI,PMP22,PPP2CA,ITIH4,ANGPT2,DAP,DDIT4,IL4,IL5RA,ENG,CITED2,NR0B2,IGF1R,NCSTN,RPTOR,RPS6KA2,CTSB,CS,FOXK2,PPT2 |
| | Cell death | 0.00769 | DAPK2,RBL2,BNIP3L,EHF,MITF,RALB,LRIG1,DICER1,ATP2C1,EMG1,PRKCH,NCK1,TLE4,GPI,DAP,DDIT4,ENG,PRG3,CITED2,IGF1R,RPTOR,RPS6KA2,CS,PPT2,YWHAQ,SIGLEC8,FOXP1,RHOBTB2,NAPA,IKZF3,MS4A2,KCNH2,KRT19,STEAP3,STX1B,EPX,PRKCZ,HK2,TLDC2,ST3GAL1,PMP22,PPP2CA,PRG2,ITIH4,TANK,PTGDR2,ANGPT2,IL4,IL5RA,NR0B2,NCSTN,CTSB,FOXK2,RNASE2 |
| | Cell death of mononuclear leukocytes | 0.00868 | LRIG1,DICER1,FOXP1,CTSB,DDIT4,IL4,IL5RA,TLE4,ST3GAL1,MS4A2 |
| | Apoptosis of hepatocytes | 0.00904 | ITIH4,DICER1,CTSB,IL4,NR0B2 |
| | Apoptosis of epithelial cells | 0.00929 | ITIH4,DICER1,RBL2,CTSB,IL4,ENG,MITF,NR0B2 |
| | Cell death of B lymphocytes | 0.01 | LRIG1,DICER1,FOXP1,CTSB,IL4 |
| | Cell viability of cancer cells | 0.0113 | IGF1R,RALB,IL4,MITF |
| | Cell death of pneumocytes | 0.0138 | PRG2,EPX |
| | Cell viability of muscle cell lines | 0.0138 | IGF1R,CTSB |
| | Cell viability of muscle cells | 0.015 | IGF1R,ANGPT2,HK2 |
| | Apoptosis of lymphatic system cells | 0.0163 | LRIG1,DICER1,FOXP1,BNIP3L,STEAP3,IL4,IL5RA,ST3GAL1,TLE4 |
| Organismal Injury and Abnormalities | Cell death of epithelial cells | 3.54E-05 | PRG2,ITIH4,YWHAQ,RBL2,BNIP3L,IL4,ENG,MITF,CITED2,NR0B2,IGF1R,DICER1,CTSB,EPX,HK2,PMP22,PPP2CA |
| | Necrosis of epithelial tissue | 0.000119 | PRG2,ITIH4,YWHAQ,ANGPT2,RBL2,BNIP3L,IL4,ENG,MITF,CITED2,NR0B2,IGF1R,DICER1,CTSB,EPX,HK2,PMP22,PPP2CA |
| | Inhibition of tumor cells | 0.000402 | DDIT4,IL4,HK2 |
| | Goiter | 0.000474 | IGF1R,KRT19,DICER1 |
| | Inhibition of mammary tumor cells | 0.000656 | IL4,HK2 |
| | Colony formation of tumor cells | 0.000996 | DICER1,RHOBTB2,CTSB,SUGT1 |
| | Immortalization of fibroblasts | 0.00122 | RBL2,PGAM2,ARID3A |
| | Abnormal ratio tissue | 0.00145 | KRT19,IL5RA,ENG,PRKCZ,MS4A2 |
| | Failure of heart looping | 0.00225 | NCSTN,RBL2,ENG |
| | Chronic idiopathic urticaria | 0.00231 | IL5RA,MS4A2 |
| | Growth of pancreatic endocrine tumor | 0.00287 | CTSB,ENG |
| | Metastasis of colorectal cancer cell lines | 0.00291 | IGF1R,DICER1,RPTOR |
| | Development of angioma | 0.00352 | ANGPT2,DICER1,IKZF3,KAT6B |
| | Precancerous condition | 0.00368 | IL4,ENG,PRKCH,ASCC1,PRKCZ |
| | Apoptosis of tumor | 0.00417 | IGF1R,ANGPT2 |
| | Nodular goiter | 0.00417 | KRT19,DICER1 |
| | Colony formation of cancer cells | 0.00426 | DICER1,CTSB,SUGT1 |
| | Follicular thyroid tumor | 0.00462 | KRT19,ANGPT2,CTSB,ENG |
| | Skin papilloma | 0.00523 | ATP2C1,ENG,PRKCH |
| | Damage of hepatocytes | 0.00569 | IGF1R,DICER1 |
| | Polyp | 0.00593 | IL5RA,ENG,PRKCZ,MS4A2 |

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| | Abnormal morphology of hair follicle | 0.00595 | IGF1R,DICER1,RBL2 |
| | Cell death of lung cells | 0.00595 | IGF1R,PRG2,EPX |
| | Abnormal morphology of epidermis | 0.00668 | IGF1R,LRIG1,DICER1,RBL2,CTSB |
| | Hydronephrosis | 0.00693 | IGF1R,SLC2A9,IL4,NFIA |
| | Diabetes mellitus | 0.0077 | ITIH4,COL15A1,FOXP1,SLC17A4,IL4,NISCH,IKZF3,CLEC12A,NR0B2,KCNH2,IGF1R,SLC2A9,LRIG1,PCYT1A,CTSB,MED27,FBP1,HK2,BANK1,DLGAP2,PPT2 |
| | Hereditary myopathy | 0.00857 | LPIN1,PTGDR2,AP5B1,BNIP3L,ENG,SLC25A33,KIF26A,ASCC1,ATPAF2,CYB561,PMP22,KCNH2 |
| | Apoptosis of hepatocytes | 0.00904 | ITIH4,DICER1,CTSB,IL4,NR0B2 |
| | Apoptosis of epithelial cells | 0.00929 | ITIH4,DICER1,RBL2,CTSB,IL4,ENG,MITF,NR0B2 |
| | Hemangioblastoma | 0.0104 | DICER1,IKZF3,KAT6B |
| | Polyposis | 0.0104 | IL5RA,ENG,MS4A2 |
| | Parakeratosis | 0.0104 | LRIG1,RBL2 |
| | Hemangioma | 0.0108 | IGF1R,ANGPT2,DICER1,IKZF3,KAT6B |
| | Juvenile dermatomyositis | 0.0109 | BNIP3L,ENG,CYB561 |
| | Neurodegeneration of cerebellum | 0.0109 | DICER1,CTSB,PPT2 |
| | Cell viability of cancer cells | 0.0113 | IGF1R,RALB,IL4,MITF |
| | Congenital malformation of brain | 0.0123 | RALB,KIF5C,RPTOR,DICER1,ATP2C1,EMG1,NFIA,CITED2,KIF3B |
| | Autosomal dominant Emery-Dreifuss muscular dystrophy | 0.0125 | BNIP3L,ENG,CYB561 |
| | Proliferation of ovarian cancer cells | 0.0126 | IGF1R,PPP2CA |
| | Lymphatic system tumor | 0.013 | FOXP1,RBL2,ATXN7L1,LPCAT2,IKZF3,BAG2,KCNH2,POLR2B,TRAPPC9,LPIN1,TNIK,LRIG1,ADCY3,DICER1,STEAP3,EGFLAM,PRKCZ,HK2,PPP2CA,ANGPT2,COL15A1,DAP,IL4,ENG,PSMC3IP,CITED2,IGF1R,RPTOR,ACP5,SHANK2,TMEM131,SMARCD3 |
| | Cell death of pneumocytes | 0.0138 | PRG2,EPX |
| | Injury of renal glomerulus | 0.0138 | ANGPT2,DICER1 |
| | Metastasis of tumor cell lines | 0.0145 | IGF1R,RALB,ANGPT2,RPTOR,DICER1,CTSB,GPI |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |
| | Familial pervasive developmental disorder | 0.0151 | FOXP1,SHANK2 |
| | Abnormal morphology of lymphoid organ | 0.0151 | BNIP3L,STEAP3,IL5RA,PRKCH,IKZF3,BANK1,TLE4,CITED2,PPT2 |
| | Neoplasia of leukocytes | 0.0156 | FOXP1,RBL2,ATXN7L1,LPCAT2,IKZF3,BAG2,MS4A2,KCNH2,TRAPPC9,LPIN1,TNIK,LRIG1,ADCY3,DICER1,STEAP3,EGFLAM,PRKCZ,HK2,PPP2CA,ANGPT2,COL15A1,DAP,IL4,ENG,PSMC3IP,CITED2,RPTOR,ACP5,SHANK2,TMEM131,SMARCD3 |
| | Barrett syndrome | 0.0156 | IL4,ENG,ASCC1 |
| Hematological Disease | Eosinophilia of tissue | 0.000145 | SIGLEC8,PTGDR2,IL4 |
| | Anisopoikilocytosis | 0.00231 | SLC7A1,STEAP3 |
| | Hypercholesterolemia | 0.00593 | ITIH4,LPIN1,RPTOR,NR0B2 |
| | Neoplasia of leukocytes | 0.0156 | FOXP1,RBL2,ATXN7L1,LPCAT2,IKZF3,BAG2,MS4A2,KCNH2,TRAPPC9,LPIN1,TNIK,LRIG1,ADCY3,DICER1,STEAP3,EGFLAM,PRKCZ,HK2,PPP2CA,ANGPT2,COL15A1,DAP,IL4,ENG,PSMC3IP,CITED2,RPTOR,ACP5,SHANK2,TMEM131,SMARCD3 |
| Immunological Disease | Eosinophilia of tissue | 0.000145 | SIGLEC8,PTGDR2,IL4 |
| | Abnormal morphology of eosinophils | 0.000199 | PRG2,EPX |
| | Chronic idiopathic urticaria | 0.00231 | IL5RA,MS4A2 |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |
| | Abnormal morphology of lymphoid organ | 0.0151 | BNIP3L,STEAP3,IL5RA,PRKCH,IKZF3,BANK1,TLE4,CITED2,PPT2 |

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| | Neoplasia of leukocytes | 0.0156 | FOXP1,RBL2,ATXN7L1,LPCAT2,IKZF3,BAG2,MS4A2,KCNH2,TRAPPC9,LPIN1,TNIK,LRIG1,ADCY3,DICER1,STEAP3,EGFLAM,PRKCZ,HK2,PPP2CA,ANGPT2,COL15A1,DAP,IL4,ENG,PSMC3IP,CITED2,RPTOR,ACP5,SHANK2,TMEM131,SMARCD3 |
| Lipid Metabolism | Release of leukotriene | 0.000186 | PRG2,IL4,PRG3,MS4A2 |
| | Release of eicosanoid | 0.000315 | IGF1R,PRG2,LPIN1,CTSB,IL4,PRG3,MS4A2 |
| | Release of leukotriene C4 | 0.00074 | PRG2,IL4,PRG3 |
| | Catabolism of fatty acid | 0.0151 | LPIN1,ACOT7 |
| Molecular Transport | Release of leukotriene | 0.000186 | PRG2,IL4,PRG3,MS4A2 |
| | Release of eicosanoid | 0.000315 | IGF1R,PRG2,LPIN1,CTSB,IL4,PRG3,MS4A2 |
| | Release of leukotriene C4 | 0.00074 | PRG2,IL4,PRG3 |
| | Flux of D-glucose | 0.000979 | PGAM2,GPI |
| | Priming of synaptic vesicles | 0.00653 | NAPA,STX1B |
| | Release of histamine | 0.00712 | PRG2,IL4,PRG3 |
| | Exocytosis by eukaryotic cells | 0.00842 | IGF1R,NAPA,IL4 |
| | Translocation of Ca2+ | 0.00936 | SLC8B1,ATP2C1 |
| Small Molecule Biochemistry | Release of leukotriene | 0.000186 | PRG2,IL4,PRG3,MS4A2 |
| | Release of eicosanoid | 0.000315 | IGF1R,PRG2,LPIN1,CTSB,IL4,PRG3,MS4A2 |
| | Modification of glucose-6-phosphate | 0.000396 | HK2,GPI |
| | Release of leukotriene C4 | 0.00074 | PRG2,IL4,PRG3 |
| | Flux of D-glucose | 0.000979 | PGAM2,GPI |
| | Release of histamine | 0.00712 | PRG2,IL4,PRG3 |
| | Catabolism of proteoglycan | 0.00836 | CTSB,IL4 |
| | Metabolism of D-hexose | 0.00957 | IGF1R,NISCH,FBP1,HK2 |
| | Catabolism of fatty acid | 0.0151 | LPIN1,ACOT7 |
| Cellular Development | Differentiation of tumor cell lines | 0.000186 | FOXP1,RBL2,IL4,IGF1R,TRAPPC9,DICER1,PCYT1A,ATP2C1,MCC,PRKCH,PRKCZ,NCK1,RNASE2 |
| | Proliferation of B lymphocytes | 0.000195 | TANK,LPIN1,RPTOR,DICER1,PCYT1A,RBL2,IL4,IL5RA,IKZF3,PRKCZ,BANK1 |
| | Colony formation of tumor cells | 0.000996 | DICER1,RHOBTB2,CTSB,SUGT1 |
| | Proliferation of lymphocytes | 0.00119 | TANK,SLC7A1,RBL2,IL4,IL5RA,IKZF3,IRF6,IGF1R,NCSTN,LPIN1,RPTOR,DICER1,PCYT1A,PRKCH,PRKCZ,BANK1,NCK1,GPI |
| | Immortalization of fibroblasts | 0.00122 | RBL2,PGAM2,ARID3A |
| | Granulopoiesis | 0.00159 | IGF1R,ZFPM1,RALB,SIGLEC8,IL4,CITED2 |
| | Myelination of cells | 0.00257 | SERINC5,DICER1,DDIT4,HEXA,PMP22 |
| | Myelopoiesis of leukocytes | 0.00393 | IGF1R,ZFPM1,RALB,SIGLEC8,FOXP1,IL4,CITED2 |
| | Colony formation of cancer cells | 0.00426 | DICER1,CTSB,SUGT1 |
| | Morphogenesis of neurons | 0.00452 | CSRP1,NFIA,HEXA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Delay in differentiation of cells | 0.0049 | IGF1R,ATP2C1,CTSB |
| | Proliferation of germinal center B lymphocytes | 0.00653 | DICER1,IL4 |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Proliferation of skeletal muscle cells | 0.00742 | IGF1R,ANGPT2 |
| | Development of PBMCs | 0.00836 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Proliferation of myofibroblasts | 0.00836 | CTSB,IL4 |
| | Axonogenesis | 0.00885 | IGF1R,ADCY3,DICER1,NFIA,PRKCZ,PMP22,PPP2CA |
| | Differentiation of eosinophils | 0.00936 | SIGLEC8,IL4 |

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| | Differentiation of neuroblastoma cell lines | 0.00936 | IGF1R,PCYT1A,ATP2C1 |
| | Epithelial-mesenchymal transition | 0.00951 | IGF1R,RPTOR,DICER1,SLC25A33,PRKCZ,GPI,PPP2CA |
| | Proliferation of liver cells | 0.00961 | IGF1R,ITIH4,DICER1,CTSB,IL4,CITED2 |
| | Neuritogenesis | 0.00966 | CSRP1,NFIA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Leukopoiesis | 0.00985 | ZFPM1,SIGLEC8,FOXP1,RBL2,IL4,IL5RA,IKZF3,CITED2,NR0B2,IGF1R,RALB,RPTOR,DICER1,PRKCH,PRKCZ,ARID3A,TLE4 |
| | Hematopoiesis in embryo | 0.0114 | ZFPM1,ENG,ARID3A |
| | Cell proliferation of fibroblasts | 0.0121 | IGF1R,NCSTN,CTSB,IL4,ENG,PGAM2,ARID3A,CITED2,GPI |
| | Proliferation of ovarian cancer cells | 0.0126 | IGF1R,PPP2CA |
| | Cell proliferation of tumor cell lines | 0.0128 | DAPK2,YWHAQ,DMAP1,FOXP1,RHOBTB2,RBL2,EHF,MITF,IRF6,RALB,TNIK,LRIG1,KRT19,FBXW8,STEAP3,PRKCH,PRKCZ,HK2,ARID3A,TLE4,PPP2CA,ELOVL7,ANGPT2,IL4,ENG,IGF1R,NCSTN,RPTOR,TFF2,CTSB |
| | Differentiation of keratinocytes | 0.0131 | IRF6,LPIN1,LRIG1,RBL2,PRKCH |
| | Proliferation of hepatocytes | 0.0137 | IGF1R,ITIH4,DICER1,IL4,CITED2 |
| | Myelination of axons | 0.0138 | DICER1,PMP22 |
| | Proliferation of endocrine cells | 0.0144 | IGF1R,ANGPT2,DICER1,TFF2 |
| Cellular Growth and Proliferation | Proliferation of B lymphocytes | 0.000195 | TANK,LPIN1,RPTOR,DICER1,PCYT1A,RBL2,IL4,IL5RA,IKZF3,PRKCZ,BANK1 |
| | Inhibition of tumor cells | 0.000402 | DDIT4,IL4,HK2 |
| | Inhibition of mammary tumor cells | 0.000656 | IL4,HK2 |
| | Colony formation of tumor cells | 0.000996 | DICER1,RHOBTB2,CTSB,SUGT1 |
| | Proliferation of lymphocytes | 0.00119 | TANK,SLC7A1,RBL2,IL4,IL5RA,IKZF3,IRF6,IGF1R,NCSTN,LPIN1,RPTOR,DICER1,PCYT1A,PRKCH,PRKCZ,BANK1,NCK1,GPI |
| | Proliferation of bone marrow cell lines | 0.00145 | IGF1R,RALB,RBL2,IL4,PPP2CA |
| | Granulopoiesis | 0.00159 | IGF1R,ZFPM1,RALB,SIGLEC8,IL4,CITED2 |
| | Colony formation of cells | 0.0021 | DMAP1,RHOBTB2,RBL2,BNIP3L,IL4,EHF,MITF,IGF1R,KRT19,DICER1,CTSB,SUGT1,PRKCZ,PPP2CA |
| | Myelination of cells | 0.00257 | SERINC5,DICER1,DDIT4,HEXA,PMP22 |
| | Contact growth inhibition | 0.00341 | IGF1R,RBL2,IL4,IKZF3,PRKCZ,GPI |
| | Myelopoiesis of leukocytes | 0.00393 | IGF1R,ZFPM1,RALB,SIGLEC8,FOXP1,IL4,CITED2 |
| | Colony formation of cancer cells | 0.00426 | DICER1,CTSB,SUGT1 |
| | Morphogenesis of neurons | 0.00452 | CSRP1,NFIA,HEXA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Proliferation of germinal center B lymphocytes | 0.00653 | DICER1,IL4 |
| | Colony formation of tumor cell lines | 0.00654 | IGF1R,KRT19,DMAP1,DICER1,RBL2,CTSB,IL4,EHF,MITF |
| | Proliferation of connective tissue cells | 0.00708 | RBL2,IL4,ENG,CITED2,IRF6,IGF1R,NCSTN,LRIG1,DICER1,CTSB,PRKCH,PGAM2,ARID3A,GPI |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Proliferation of skeletal muscle cells | 0.00742 | IGF1R,ANGPT2 |
| | Development of PBMCs | 0.00836 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Proliferation of myofibroblasts | 0.00836 | CTSB,IL4 |
| | Axonogenesis | 0.00885 | IGF1R,ADCY3,DICER1,NFIA,PRKCZ,PMP22,PPP2CA |
| | Differentiation of eosinophils | 0.00936 | SIGLEC8,IL4 |
| | Proliferation of epithelial cells | 0.00947 | IRF6,IGF1R,NCSTN,ITIH4,LRIG1,DICER1,RBL2,IL4,MCC,ENG,PRKCH,CITED2 |
| | Proliferation of liver cells | 0.00961 | IGF1R,ITIH4,DICER1,CTSB,IL4,CITED2 |
| | Neuritogenesis | 0.00966 | CSRP1,NFIA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Leukopoiesis | 0.00985 | ZFPM1,SIGLEC8,FOXP1,RBL2,IL4,IL5RA,IKZF3,CITED2,NR0B2,IGF1R,RALB,RPTOR,DICER1,PRKCH,PRKCZ,ARID3A,TLE4 |

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| | Hematopoiesis in embryo | 0.0114 | ZFPM1,ENG,ARID3A |
| | Cell proliferation of fibroblasts | 0.0121 | IGF1R,NCSTN,CTSB,IL4,ENG,PGAM2,ARID3A,CITED2,GPI |
| | Proliferation of heart cells | 0.0124 | DICER1,FOXP1,RBL2,CITED2 |
| | Colony formation of stomach cancer cell lines | 0.0126 | IGF1R,DMAP1 |
| | Proliferation of ovarian cancer cells | 0.0126 | IGF1R,PPP2CA |
| | Cell proliferation of tumor cell lines | 0.0128 | DAPK2,YWHAQ,DMAP1,FOXP1,RHOBTB2,RBL2,EHF,MITF,IRF6,RALB,TNIK,LRIG1,KRT19,FBXW8,STEAP3,PRKCH,PRKCZ,HK2,ARID3A,TLE4,PPP2CA,ELOVL7,ANGPT2,IL4,ENG,IGF1R,NCSTN,RPTOR,TFF2,CTSB |
| | Proliferation of hepatocytes | 0.0137 | IGF1R,ITIH4,DICER1,IL4,CITED2 |
| | Myelination of axons | 0.0138 | DICER1,PMP22 |
| | Proliferation of endocrine cells | 0.0144 | IGF1R,ANGPT2,DICER1,TFF2 |
| | Stimulation of epithelial cells | 0.0151 | IL4,EPX |
| Humoral Immune Response | Proliferation of B lymphocytes | 0.000195 | TANK,LPIN1,RPTOR,DICER1,PCYT1A,RBL2,IL4,IL5RA,IKZF3,PRKCZ,BANK1 |
| | Quantity of naive B cells | 0.000656 | IL4,IKZF3 |
| | Quantity of B-1 lymphocytes | 0.00101 | RPTOR,IL4,IL5RA,ARID3A,BANK1 |
| | Quantity of IgM | 0.00108 | TANK,IL4,IL5RA,IKZF3,ARID3A,BANK1 |
| | Quantity of B-1a lymphocytes | 0.00397 | RPTOR,ARID3A,BANK1 |
| | Quantity of IgA | 0.00404 | TANK,IL4,IL5RA,IKZF3 |
| | Quantity of B lymphocytes | 0.00447 | TANK,RPTOR,CTSB,IL4,IL5RA,PRKCH,IKZF3,ARID3A,BANK1,TLE4 |
| | Quantity of IgG1 | 0.0056 | TANK,IL4,IL5RA,IKZF3,ARID3A |
| | Proliferation of germinal center B lymphocytes | 0.00653 | DICER1,IL4 |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Quantity of IgG2a | 0.0124 | TANK,IL4,IKZF3,BANK1 |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |
| Lymphoid Tissue Structure and Development | Proliferation of B lymphocytes | 0.000195 | TANK,LPIN1,RPTOR,DICER1,PCYT1A,RBL2,IL4,IL5RA,IKZF3,PRKCZ,BANK1 |
| | Quantity of naive B cells | 0.000656 | IL4,IKZF3 |
| | Quantity of B-1 lymphocytes | 0.00101 | RPTOR,IL4,IL5RA,ARID3A,BANK1 |
| | Morphology of lymph follicle | 0.00112 | IL4,IKZF3,PRKCZ,TLE4,BANK1,PPT2 |
| | Proliferation of lymphocytes | 0.00119 | TANK,SLC7A1,RBL2,IL4,IL5RA,IKZF3,IRF6,IGF1R,NCSTN,LPIN1,RPTOR,DICER1,PCYT1A,PRKCH,PRKCZ,BANK1,NCK1,GPI |
| | Granulopoiesis | 0.00159 | IGF1R,ZFPM1,RALB,SIGLEC8,IL4,CITED2 |
| | Homing of Th2 cells | 0.00287 | PTGDR2,IL4 |
| | Myelopoiesis of leukocytes | 0.00393 | IGF1R,ZFPM1,RALB,SIGLEC8,FOXP1,IL4,CITED2 |
| | Quantity of B-1a lymphocytes | 0.00397 | RPTOR,ARID3A,BANK1 |
| | Quantity of B lymphocytes | 0.00447 | TANK,RPTOR,CTSB,IL4,IL5RA,PRKCH,IKZF3,ARID3A,BANK1,TLE4 |
| | Proliferation of germinal center B lymphocytes | 0.00653 | DICER1,IL4 |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Development of PBMCs | 0.00836 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Differentiation of eosinophils | 0.00936 | SIGLEC8,IL4 |
| | Leukopoiesis | 0.00985 | ZFPM1,SIGLEC8,FOXP1,RBL2,IL4,IL5RA,IKZF3,CITED2,NR0B2,IGF1R,RALB,RPTOR,DICER1,PRKCH,PRKCZ,ARID3A,TLE4 |
| | Quantity of lymph follicle | 0.0144 | IKZF3,ARID3A,PRKCZ,BANK1,TLE4 |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |

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| | Abnormal morphology of lymphoid organ | 0.0151 | BNIP3L,STEAP3,IL5RA,PRKCH,IKZF3,BANK1,TLE4,CITED2,PPT2 |
| | Morphology of lymphoid tissue | 0.0162 | RBL2,BNIP3L,STEAP3,IL4,IL5RA,PRKCH,IKZF3,PRKCZ,BANK1,TLE4,CITED2,PPT2 |
| Cell Morphology | Abnormal morphology of eosinophils | 0.000199 | PRG2,EPX |
| | Autophagy of tumor cell lines | 0.000208 | KIF5C,YWHAQ,RPTOR,DICER1,BNIP3L,DDIT4,MITF,CATSPER4 |
| | Morphology of blood cells | 0.000254 | ZFPM1,PRG2,SLC7A1,BNIP3L,IL4,IL5RA,MITF,CITED2,RPTOR,STEAP3,PRKCH,EPX,ARID3A,PRKCZ |
| | Autophagy | 0.00033 | DAPK2,KIF5C,YWHAQ,SOGA1,BNIP3L,DAP,DDIT4,ENG,MITF,CATSPER4,CLEC12A,IGF1R,RPTOR,DICER1 |
| | Conversion of placental cells | 0.000656 | SMARCD3,MITF |
| | Orientation of axons | 0.000656 | NFIA,PRKCZ |
| | Abnormal morphology of reticulocytes | 0.000979 | SLC7A1,STEAP3 |
| | Conversion of chondrocytes | 0.000979 | SMARCD3,MITF |
| | Autophagy of cells | 0.00111 | DAPK2,KIF5C,YWHAQ,RPTOR,DICER1,BNIP3L,DDIT4,ENG,MITF,CATSPER4 |
| | Morphology of thyroid cells | 0.00136 | IGF1R,CTSB |
| | Transepithelial electrical resistance of cells | 0.00168 | IL4,PRKCZ,PPP2CA |
| | Morphology of granulocytes | 0.00246 | PRG2,IL4,EPX |
| | Morphology of hematopoietic progenitor cells | 0.00341 | ZFPM1,SLC7A1,RPTOR,STEAP3,ARID3A,CITED2 |
| | Transepithelial electrical resistance of colorectal cancer cell lines | 0.00349 | IL4,PPP2CA |
| | Morphology of tumor cell lines | 0.00441 | IGF1R,IRF6,DICER1,RBL2,PRKCH,MITF,PRKCZ,GPI |
| | Morphogenesis of neurons | 0.00452 | CSRP1,NFIA,HEXA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Cell flattening of tumor cell lines | 0.00569 | RBL2,PRKCH |
| | Size of antigen presenting cells | 0.00653 | RPTOR,IL4 |
| | Reorganization of actin cytoskeleton | 0.00707 | LPIN1,TNIK,ATP2C1,ENG,PRKCZ |
| | Morphology of leukocytes | 0.0075 | PRG2,RPTOR,IL4,IL5RA,PRKCH,EPX,MITF,ARID3A,PRKCZ |
| | Axonogenesis | 0.00885 | IGF1R,ADCY3,DICER1,NFIA,PRKCZ,PMP22,PPP2CA |
| | Neuritogenesis | 0.00966 | CSRP1,NFIA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Size of phagocytes | 0.0104 | RPTOR,IL4 |
| | Abnormal morphology of hematopoietic progenitor cells | 0.0108 | ZFPM1,SLC7A1,STEAP3,ARID3A,CITED2 |
| | Reorganization of cytoskeleton | 0.0113 | LPIN1,TNIK,ATP2C1,ENG,PRKCZ,MS4A2 |
| | Permeability of colorectal cancer cell lines | 0.0115 | IL4,PPP2CA |
| | Enlargement of cells | 0.0118 | DAPK2,LPIN1,ANGPT2,DICER1,RPS6KA2,CTSB,IL4,PRKCH,PMP22 |
| | Myelination of axons | 0.0138 | DICER1,PMP22 |
| Cellular Function and Maintenance | Autophagy of tumor cell lines | 0.000208 | KIF5C,YWHAQ,RPTOR,DICER1,BNIP3L,DDIT4,MITF,CATSPER4 |
| | Autophagy | 0.00033 | DAPK2,KIF5C,YWHAQ,SOGA1,BNIP3L,DAP,DDIT4,ENG,MITF,CATSPER4,CLEC12A,IGF1R,RPTOR,DICER1 |
| | Autophagy of cells | 0.00111 | DAPK2,KIF5C,YWHAQ,RPTOR,DICER1,BNIP3L,DDIT4,ENG,MITF,CATSPER4 |
| | Organization of actin cytoskeleton | 0.00125 | RALB,LPIN1,TNIK,CSRP1,ATP2C1,ENG,EVL,PRKCZ,NCK1,GPI |
| | Cellular homeostasis | 0.00184 | ZFPM1,DAPK2,YWHAQ,FOXP1,SOGA1,RBL2,BNIP3L,SLC25A33,MITF,MS4A2,KCNH2,DICER1,ATP2C1,PRKCH,PRKCZ, GPI,PPP2CA,KIF5C,ANGPT2,SLC25A25,SLC8B1,DAP,DDIT4,IL4,IL5RA,ENG,CATSPER4,CLEC12A,NR0B2,IGF1R,NCSTN, RPTOR |
| | Instability of microtubules | 0.00417 | KIF5C,KIF3B |
| | Priming of synaptic vesicles | 0.00653 | NAPA,STX1B |
| | Reorganization of actin cytoskeleton | 0.00707 | LPIN1,TNIK,ATP2C1,ENG,PRKCZ |
| | Exocytosis by eukaryotic cells | 0.00842 | IGF1R,NAPA,IL4 |
| | Axonogenesis | 0.00885 | IGF1R,ADCY3,DICER1,NFIA,PRKCZ,PMP22,PPP2CA |

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| | Neuritogenesis | 0.00966 | CSRP1,NFIA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Reorganization of cytoskeleton | 0.0113 | LPIN1,TNIK,ATP2C1,ENG,PRKCZ,MS4A2 |
| | Permeability of colorectal cancer cell lines | 0.0115 | IL4,PPP2CA |
| | Myelination of axons | 0.0138 | DICER1,PMP22 |
| | Homeostasis of blood cells | 0.0139 | ZFPM1,FOXP1,RBL2,IL4,IL5RA,NR0B2,IGF1R,NCSTN,RPTOR,DICER1,PRKCH,PRKCZ,GPI |
| | Organization of cytoplasm | 0.0142 | SEC16B,CSRP1,SLC25A33,HEXA,MS4A2,LPIN1,RALB,TNIK,ADCY3,DICER1,FBXW8,ATP2C1,LRP12,PRKCH,PRKCZ,NCK1,GPI,PMP22,PPP2CA,KIF5C,ANGPT2,ENG,NFIA,ATL3,KIF3B,IGF1R,SHANK2,EVL |
| Cell Cycle | Arrest in G1 phase of keratinocytes | 0.000396 | LPIN1,PRKCH |
| | Homologous pairing of DNA | 0.000979 | EVL,PSMC3IP |
| | Arrest in cell cycle progression | 0.00225 | IGF1R,IRF6,KRT19,RPTOR,RBL2,DDIT4,EHF,PRKCH,PGAM2,MITF |
| | Arrest in cell cycle progression of tumor cell lines | 0.00341 | IGF1R,KRT19,RBL2,DDIT4,EHF,PRKCH |
| | Contact growth inhibition | 0.00341 | IGF1R,RBL2,IL4,IKZF3,PRKCZ,GPI |
| | Cell cycle progression of prostate cancer cell lines | 0.00341 | LRIG1,DDIT4,EHF |
| | Fission | 0.00426 | SEC16B,LPIN1,RPTOR |
| | Cell cycle progression of tumor cell lines | 0.00656 | IGF1R,KRT19,LRIG1,RHOBTB2,RBL2,DDIT4,EHF,PRKCH |
| | Cell cycle progression | 0.00868 | RHOBTB2,RBL2,DDIT4,IL4,EHF,MITF,IKZF3,CITED2,IRF6,IGF1R,LRIG1,KRT19,RPTOR,DICER1,RPS6KA2,SUGT1,PRKCH,PGAM2,PRKCZ,GPI,PPP2CA |
| | Arrest in cell cycle progression of prostate cancer cell lines | 0.0115 | DDIT4,EHF |
| Hair and Skin Development and Function | Arrest in G1 phase of keratinocytes | 0.000396 | LPIN1,PRKCH |
| | Transepithelial electrical resistance of cells | 0.00168 | IL4,PRKCZ,PPP2CA |
| | Transepithelial electrical resistance of colorectal cancer cell lines | 0.00349 | IL4,PPP2CA |
| | Differentiation of keratinocytes | 0.0131 | IRF6,LPIN1,LRIG1,RBL2,PRKCH |
| Cancer | Inhibition of tumor cells | 0.000402 | DDIT4,IL4,HK2 |
| | Inhibition of mammary tumor cells | 0.000656 | IL4,HK2 |
| | Transformation of prostate cancer cell lines | 0.000656 | IGF1R,DDIT4 |
| | Colony formation of tumor cells | 0.000996 | DICER1,RHOBTB2,CTSB,SUGT1 |
| | Immortalization of fibroblasts | 0.00122 | RBL2,PGAM2,ARID3A |
| | Growth of pancreatic endocrine tumor | 0.00287 | CTSB,ENG |
| | Metastasis of colorectal cancer cell lines | 0.00291 | IGF1R,DICER1,RPTOR |
| | Development of angioma | 0.00352 | ANGPT2,DICER1,IKZF3,KAT6B |
| | Precancerous condition | 0.00368 | IL4,ENG,PRKCH,ASCC1,PRKCZ |
| | Apoptosis of tumor | 0.00417 | IGF1R,ANGPT2 |
| | Colony formation of cancer cells | 0.00426 | DICER1,CTSB,SUGT1 |
| | Follicular thyroid tumor | 0.00462 | KRT19,ANGPT2,CTSB,ENG |
| | Skin papilloma | 0.00523 | ATP2C1,ENG,PRKCH |
| | Hyperplasia of cell lines | 0.00836 | IGF1R,IL4 |
| | Hemangioblastoma | 0.0104 | DICER1,IKZF3,KAT6B |
| | Polyposis | 0.0104 | IL5RA,ENG,MS4A2 |
| | Hemangioma | 0.0108 | IGF1R,ANGPT2,DICER1,IKZF3,KAT6B |
| | Cell viability of cancer cells | 0.0113 | IGF1R,RALB,IL4,MITF |
| | Proliferation of ovarian cancer cells | 0.0126 | IGF1R,PPP2CA |
| | Lymphatic system tumor | 0.013 | FOXP1,RBL2,ATXN7L1,LPCAT2,IKZF3,BAG2,KCNH2,POLR2B,TRAPPC9,LPIN1,TNIK,LRIG1,ADCY3,DICER1,STEAP3,EGF |

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| | | | LAM,PRKCZ,HK2,PPP2CA,ANGPT2,COL15A1,DAP,IL4,ENG,PSMC3IP,CITED2,IGF1R,RPTOR,ACP5,SHANK2,TMEM131,SMARCD3 |
| | Metastasis of tumor cell lines | 0.0145 | IGF1R,RALB,ANGPT2,RPTOR,DICER1,CTSB,GPI |
| | Neoplasia of leukocytes | 0.0156 | FOXP1,RBL2,ATXN7L1,LPCAT2,IKZF3,BAG2,MS4A2,KCNH2,TRAPPC9,LPIN1,TNIK,LRIG1,ADCY3,DICER1,STEAP3,EGFLAM,PRKCZ,HK2,PPP2CA,ANGPT2,COL15A1,DAP,IL4,ENG,PSMC3IP,CITED2,RPTOR,ACP5,SHANK2,TMEM131,SMARCD3 |
| | Barrett syndrome | 0.0156 | IL4,ENG,ASCC1 |
| Organismal Functions | Inhibition of tumor cells | 0.000402 | DDIT4,IL4,HK2 |
| | Inhibition of mammary tumor cells | 0.000656 | IL4,HK2 |
| Tumor Morphology | Inhibition of tumor cells | 0.000402 | DDIT4,IL4,HK2 |
| | Inhibition of mammary tumor cells | 0.000656 | IL4,HK2 |
| | Colony formation of tumor cells | 0.000996 | DICER1,RHOBTB2,CTSB,SUGT1 |
| | Colony formation of cancer cells | 0.00426 | DICER1,CTSB,SUGT1 |
| | Cell viability of cancer cells | 0.0113 | IGF1R,RALB,IL4,MITF |
| | Proliferation of ovarian cancer cells | 0.0126 | IGF1R,PPP2CA |
| Endocrine System Disorders | Goiter | 0.000474 | IGF1R,KRT19,DICER1 |
| | Growth of pancreatic endocrine tumor | 0.00287 | CTSB,ENG |
| | Nodular goiter | 0.00417 | KRT19,DICER1 |
| | Follicular thyroid tumor | 0.00462 | KRT19,ANGPT2,CTSB,ENG |
| | Diabetes mellitus | 0.0077 | ITIH4,COL15A1,FOXP1,SLC17A4,IL4,NISCH,IKZF3,CLEC12A,NR0B2,KCNH2,IGF1R,SLC2A9,LRIG1,PCYT1A,CTSB,MED27,FBP1,HK2,BANK1,DLGAP2,PPT2 |
| | Proliferation of ovarian cancer cells | 0.0126 | IGF1R,PPP2CA |
| Cellular Assembly and Organization | Orientation of axons | 0.000656 | NFIA,PRKCZ |
| | Organization of actin cytoskeleton | 0.00125 | RALB,LPIN1,TNIK,CSRP1,ATP2C1,ENG,EVL,PRKCZ,NCK1,GPI |
| | Instability of microtubules | 0.00417 | KIF5C,KIF3B |
| | Priming of synaptic vesicles | 0.00653 | NAPA,STX1B |
| | Reorganization of actin cytoskeleton | 0.00707 | LPIN1,TNIK,ATP2C1,ENG,PRKCZ |
| | Fusion of myotube | 0.00836 | IGF1R,IL4 |
| | Axonogenesis | 0.00885 | IGF1R,ADCY3,DICER1,NFIA,PRKCZ,PMP22,PPP2CA |
| | Neuritogenesis | 0.00966 | CSRP1,NFIA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Accumulation of lysosome | 0.0104 | IGF1R,CTSB |
| | Reorganization of cytoskeleton | 0.0113 | LPIN1,TNIK,ATP2C1,ENG,PRKCZ,MS4A2 |
| | Fusion of plasma membrane | 0.0138 | RALB,NAPA |
| | Myelination of axons | 0.0138 | DICER1,PMP22 |
| | Organization of cytoplasm | 0.0142 | SEC16B,CSRP1,SLC25A33,HEXA,MS4A2,LPIN1,RALB,TNIK,ADCY3,DICER1,FBXW8,ATP2C1,LRP12,PRKCH,PRKCZ,NCK1,GPI,PMP22,PPP2CA,KIF5C,ANGPT2,ENG,NFIA,ATL3,KIF3B,IGF1R,SHANK2,EVL |
| Nervous System Development and Function | Orientation of axons | 0.000656 | NFIA,PRKCZ |
| | Myelination of cells | 0.00257 | SERINC5,DICER1,DDIT4,HEXA,PMP22 |
| | Morphogenesis of neurons | 0.00452 | CSRP1,NFIA,HEXA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Migration of cerebellar granule cell | 0.00653 | IGF1R,NFIA |
| | Axonogenesis | 0.00885 | IGF1R,ADCY3,DICER1,NFIA,PRKCZ,PMP22,PPP2CA |
| | Neuritogenesis | 0.00966 | CSRP1,NFIA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Myelination of axons | 0.0138 | DICER1,PMP22 |
| Tissue Morphology | Quantity of naive B cells | 0.000656 | IL4,IKZF3 |

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| | Abnormal morphology of reticulocytes | 0.000979 | SLC7A1,STEAP3 |
| | Quantity of B-1 lymphocytes | 0.00101 | RPTOR,IL4,IL5RA,ARID3A,BANK1 |
| | Morphology of lymph follicle | 0.00112 | IL4,IKZF3,PRKCZ,TLE4,BANK1,PPT2 |
| | Quantity of blood cells | 0.00333 | TANK,SIGLEC8,PTGDR2,SLC7A1,RBL2,BNIP3L,IL4,IL5RA,IKZF3,IRF6,IGF1R,RPTOR,DICER1,CTSB,STEAP3,PRKCH,ARID3A,BANK1,TLE4,ST3GAL1,PPT2,PPP2CA |
| | Size of embryo | 0.00348 | ZFPM1,IGF1R,NCSTN,DICER1,RBL2,ATP2C1,ENG,CITED2,KIF3B,PPP2CA |
| | Quantity of B-1a lymphocytes | 0.00397 | RPTOR,ARID3A,BANK1 |
| | Contraction of vein | 0.00417 | DICER1,IL4 |
| | Quantity of B lymphocytes | 0.00447 | TANK,RPTOR,CTSB,IL4,IL5RA,PRKCH,IKZF3,ARID3A,BANK1,TLE4 |
| | Quantity of cells | 0.00532 | SIGLEC8,RBL2,BNIP3L,MITF,IKZF3,IRF6,KRT19,DICER1,ATP2C1,STEAP3,STX1B,PRKCH,ARID3A,TLE4,ST3GAL1,PMP22,PPP2CA,TANK,PTGDR2,KIF5C,ANGPT2,SLC7A1,IL4,IL5RA,ENG,NFIA,CITED2,IGF1R,RPTOR,TFF2,CTSB,BANK1,PPT2 |
| | Quantity of epithelial tissue | 0.00586 | IGF1R,ANGPT2,DICER1,TFF2,CTSB,MITF |
| | Quantity of myeloid cells | 0.0073 | IRF6,IGF1R,PTGDR2,SIGLEC8,RBL2,CTSB,IL4,IL5RA,ARID3A,TLE4,PPT2,PPP2CA |
| | Quantity of leukocytes | 0.00815 | TANK,SIGLEC8,PTGDR2,RBL2,IL4,IL5RA,IKZF3,IRF6,IGF1R,RPTOR,DICER1,CTSB,PRKCH,ARID3A,BANK1,TLE4,ST3GAL1,PPT2,PPP2CA |
| | Quantity of lymph follicle | 0.0144 | IKZF3,ARID3A,PRKCZ,BANK1,TLE4 |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |
| | Quantity of glandular epithelial cells | 0.0151 | DICER1,TFF2 |
| | Abnormal morphology of lymphoid organ | 0.0151 | BNIP3L,STEAP3,IL5RA,PRKCH,IKZF3,BANK1,TLE4,CITED2,PPT2 |
| | Morphology of lymphoid tissue | 0.0162 | RBL2,BNIP3L,STEAP3,IL4,IL5RA,PRKCH,IKZF3,PRKCZ,BANK1,TLE4,CITED2,PPT2 |
| Cardiovascular System Development and Function | Stroke volume index | 0.000656 | ANGPT2,ENG |
| | Muscularization of artery | 0.00287 | RPTOR,IL4 |
| | Ejection fraction of heart | 0.00316 | IGF1R,ANGPT2,ENG |
| | Contraction of vein | 0.00417 | DICER1,IL4 |
| | Proliferation of heart cells | 0.0124 | DICER1,FOXP1,RBL2,CITED2 |
| Organ Development | Stroke volume index | 0.000656 | ANGPT2,ENG |
| | Ejection fraction of heart | 0.00316 | IGF1R,ANGPT2,ENG |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Proliferation of skeletal muscle cells | 0.00742 | IGF1R,ANGPT2 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Proliferation of myofibroblasts | 0.00836 | CTSB,IL4 |
| | Proliferation of liver cells | 0.00961 | IGF1R,ITIH4,DICER1,CTSB,IL4,CITED2 |
| | Proliferation of heart cells | 0.0124 | DICER1,FOXP1,RBL2,CITED2 |
| | Differentiation of keratinocytes | 0.0131 | IRF6,LPIN1,LRIG1,RBL2,PRKCH |
| | Proliferation of hepatocytes | 0.0137 | IGF1R,ITIH4,DICER1,IL4,CITED2 |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |
| Hematopoiesis | Abnormal morphology of reticulocytes | 0.000979 | SLC7A1,STEAP3 |
| | Granulopoiesis | 0.00159 | IGF1R,ZFPM1,RALB,SIGLEC8,IL4,CITED2 |
| | Morphology of hematopoietic progenitor cells | 0.00341 | ZFPM1,SLC7A1,RPTOR,STEAP3,ARID3A,CITED2 |
| | Myelopoiesis of leukocytes | 0.00393 | IGF1R,ZFPM1,RALB,SIGLEC8,FOXP1,IL4,CITED2 |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Development of PBMCs | 0.00836 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Differentiation of eosinophils | 0.00936 | SIGLEC8,IL4 |

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| | Leukopoiesis | 0.00985 | ZFPM1,SIGLEC8,FOXP1,RBL2,IL4,IL5RA,IKZF3,CITED2,NR0B2,IGF1R,RALB,RPTOR,DICER1,PRKCH,PRKCZ,ARID3A,TLE4 |
| | Abnormal morphology of hematopoietic progenitor cells | 0.0108 | ZFPM1,SLC7A1,STEAP3,ARID3A,CITED2 |
| | Hematopoiesis in embryo | 0.0114 | ZFPM1,ENG,ARID3A |
| DNA Replication, Recombination, and Repair | Homologous pairing of DNA | 0.000979 | EVL,PSMC3IP |
| | Synthesis of genomic DNA | 0.0151 | IL4,PRKCH |
| Protein Synthesis | Quantity of IgM | 0.00108 | TANK,IL4,IL5RA,IKZF3,ARID3A,BANK1 |
| | Quantity of IgA | 0.00404 | TANK,IL4,IL5RA,IKZF3 |
| | Quantity of IgG1 | 0.0056 | TANK,IL4,IL5RA,IKZF3,ARID3A |
| | Quantity of IgG2a | 0.0124 | TANK,IL4,IKZF3,BANK1 |
| Gene Expression | Transcription of DNA | 0.00126 | ZFPM1,YWHAQ,DMAP1,FOXP1,EHF,MITF,IKZF3,POLR2B,IRF6,LPIN1,DICER1,MED27,FBP1,IRF2BPL,ASCC1,ARID3A,PHF19,NCK1,TLE4,PPP2CA,DAP,IL4,ENG,NFIA,PSMC3IP,CITED2,NR0B2,IGF1R,SMARCD3,FOXK2,KAT6B |
| | Expression of RNA | 0.00157 | SEC16B,ZFPM1,YWHAQ,DMAP1,FOXP1,RBL2,EHF,MITF,IKZF3,POLR2B,IRF6,NDFIP2,LPIN1,DICER1,ATP2C1,MED27,STX1B,FBP1,IRF2BPL,PRKCZ,ASCC1,ARID3A,PHF19,NCK1,TLE4,PPP2CA,TANK,DAP,IL4,ENG,NFIA,PSMC3IP,PRG3,CITED2,NR0B2,IGF1R,RPS6KA2,SMARCD3,FOXK2,KAT6B,BANK1 |
| | Transcription of RNA | 0.00175 | ZFPM1,YWHAQ,DMAP1,FOXP1,RBL2,EHF,MITF,IKZF3,POLR2B,IRF6,LPIN1,DICER1,ATP2C1,MED27,FBP1,IRF2BPL,PRKCZ,ASCC1,ARID3A,PHF19,NCK1,TLE4,PPP2CA,TANK,DAP,IL4,ENG,NFIA,PSMC3IP,CITED2,NR0B2,IGF1R,SMARCD3,FOXK2,KAT6B |
| | Transcription | 0.00196 | SEC16B,ZFPM1,YWHAQ,DMAP1,FOXP1,RBL2,EHF,MITF,IKZF3,POLR2B,IRF6,NDFIP2,LPIN1,DICER1,ATP2C1,MED27,STX1B,FBP1,IRF2BPL,PRKCZ,ASCC1,ARID3A,PHF19,NCK1,TLE4,PPP2CA,TANK,DAP,IL4,ENG,NFIA,PSMC3IP,CITED2,NR0B2,IGF1R,RPS6KA2,SMARCD3,FOXK2,KAT6B |
| | Activation of DNA endogenous promoter | 0.00599 | ZFPM1,DMAP1,IL4,EHF,ENG,MITF,NFIA,PSMC3IP,IKZF3,CITED2,NR0B2,POLR2B,IRF6,LPIN1,DICER1,MED27,FOXK2,FBP1,IRF2BPL,ARID3A,PHF19,NCK1,TLE4,PPP2CA |
| Cellular Movement | Migration of basophils | 0.00136 | PTGDR2,ENG |
| | Invasion of cells | 0.00279 | YWHAQ,ANGPT2,FOXP1,RHOBTB2,ENG,MITF,KCNH2,PLGRKT,IRF6,IGF1R,RALB,LRIG1,KRT19,ADCY3,RPTOR,DICER1,TFF2,CTSB,PRKCZ,ST3GAL1,GPI |
| | Homing of Th2 cells | 0.00287 | PTGDR2,IL4 |
| | Invasion of lymphoma cell lines | 0.00349 | PLGRKT,CTSB |
| | Cell movement of prostate cell lines | 0.0049 | IGF1R,ENG |
| | Cell movement | 0.00559 | DAPK2,SIGLEC8,FOXP1,RHOBTB2,EHF,MITF,KCNH2,PLGRKT,IRF6,PATJ,RALB,TNIK,LRIG1,KRT19,ADCY3,DICER1,LRP12,PRKCZ,NCK1,GPI,PMP22,PTGDR2,ANGPT2,DDIT4,IL4,IL5RA,NISCH,ENG,NFIA,CATSPER4,CITED2,IGF1R,RPTOR,ACP5,TFF2,CTSB,EVL,RNASE2,PPT2 |
| | Dissemination of tumor cells | 0.00653 | IGF1R,ANGPT2 |
| | Migration of B-lymphocyte derived cell lines | 0.00653 | PTGDR2,ENG |
| | Migration of cerebellar granule cell | 0.00653 | IGF1R,NFIA |
| | Recruitment of muscle cells | 0.00653 | IL4,ENG |
| | Migration of cells | 0.00752 | DAPK2,SIGLEC8,FOXP1,RHOBTB2,EHF,MITF,KCNH2,PLGRKT,IRF6,PATJ,RALB,KRT19,ADCY3,DICER1,LRP12,PRKCZ,NCK1,GPI,PMP22,PTGDR2,ANGPT2,DDIT4,IL4,NISCH,ENG,NFIA,CITED2,IGF1R,RPTOR,ACP5,TFF2,CTSB,EVL,RNASE2,PPT2 |
| | Cellular infiltration by granulocytes | 0.00869 | IRF6,PTGDR2,SIGLEC8,ANGPT2,DICER1,CTSB,IL4 |
| | Migration of myeloma cell lines | 0.00936 | IGF1R,RALB |
| | Invasion of carcinoma cell lines | 0.01 | IRF6,RALB,FOXP1,CTSB,MITF,PRKCZ,ST3GAL1 |
| | Invasion of tumor cell lines | 0.0109 | YWHAQ,FOXP1,MITF,IRF6,PLGRKT,IGF1R,RALB,KRT19,LRIG1,RPTOR,DICER1,CTSB,TFF2,PRKCZ,ST3GAL1,GPI |

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| | Migration of Langerhans cells | 0.0115 | RPTOR,IL4 |
| Endocrine System Development and Function | Morphology of thyroid cells | 0.00136 | IGF1R,CTSB |
| | Proliferation of endocrine cells | 0.0144 | IGF1R,ANGPT2,DICER1,TFF2 |
| Organ Morphology | Morphology of thyroid cells | 0.00136 | IGF1R,CTSB |
| | Abnormal morphology of hair follicle | 0.00595 | IGF1R,DICER1,RBL2 |
| | Abnormal morphology of epidermis | 0.00668 | IGF1R,LRIG1,DICER1,RBL2,CTSB |
| | Quantity of glandular epithelial cells | 0.0151 | DICER1,TFF2 |
| | Abnormal morphology of lymphoid organ | 0.0151 | BNIP3L,STEAP3,IL5RA,PRKCH,IKZF3,BANK1,TLE4,CITED2,PPT2 |
| Organismal Development | Morphology of thyroid cells | 0.00136 | IGF1R,CTSB |
| | Muscularization of artery | 0.00287 | RPTOR,IL4 |
| | Size of embryo | 0.00348 | ZFPM1,IGF1R,NCSTN,DICER1,RBL2,ATP2C1,ENG,CITED2,KIF3B,PPP2CA |
| | Morphogenesis of neurons | 0.00452 | CSRP1,NFIA,HEXA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Development of PBMCs | 0.00836 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Axonogenesis | 0.00885 | IGF1R,ADCY3,DICER1,NFIA,PRKCZ,PMP22,PPP2CA |
| | Neuritogenesis | 0.00966 | CSRP1,NFIA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Hematopoiesis in embryo | 0.0114 | ZFPM1,ENG,ARID3A |
| | Differentiation of keratinocytes | 0.0131 | IRF6,LPIN1,LRIG1,RBL2,PRKCH |
| | Myelination of axons | 0.0138 | DICER1,PMP22 |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |
| Tissue Development | Granulopoiesis | 0.00159 | IGF1R,ZFPM1,RALB,SIGLEC8,IL4,CITED2 |
| | Myelopoiesis of leukocytes | 0.00393 | IGF1R,ZFPM1,RALB,SIGLEC8,FOXP1,IL4,CITED2 |
| | Morphogenesis of neurons | 0.00452 | CSRP1,NFIA,HEXA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Growth of epithelial tissue | 0.00596 | ITIH4,ANGPT2,RBL2,IL4,ENG,CITED2,IRF6,IGF1R,NCSTN,LRIG1,RPTOR,DICER1,CTSB,MCC,PRKCH,PRKCZ |
| | Proliferation of connective tissue cells | 0.00708 | RBL2,IL4,ENG,CITED2,IRF6,IGF1R,NCSTN,LRIG1,DICER1,CTSB,PRKCH,PGAM2,ARID3A,GPI |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Proliferation of skeletal muscle cells | 0.00742 | IGF1R,ANGPT2 |
| | Development of PBMCs | 0.00836 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Proliferation of myofibroblasts | 0.00836 | CTSB,IL4 |
| | Axonogenesis | 0.00885 | IGF1R,ADCY3,DICER1,NFIA,PRKCZ,PMP22,PPP2CA |
| | Accumulation of lymphatic system cells | 0.00936 | NCSTN,IL4 |
| | Differentiation of eosinophils | 0.00936 | SIGLEC8,IL4 |
| | Proliferation of epithelial cells | 0.00947 | IRF6,IGF1R,NCSTN,ITIH4,LRIG1,DICER1,RBL2,IL4,MCC,ENG,PRKCH,CITED2 |
| | Neuritogenesis | 0.00966 | CSRP1,NFIA,KIF3B,IGF1R,RALB,TNIK,ADCY3,DICER1,FBXW8,SHANK2,LRP12,PRKCZ,PMP22,PPP2CA |
| | Leukopoiesis | 0.00985 | ZFPM1,SIGLEC8,FOXP1,RBL2,IL4,IL5RA,IKZF3,CITED2,NR0B2,IGF1R,RALB,RPTOR,DICER1,PRKCH,PRKCZ,ARID3A,TLE4 |
| | Hematopoiesis in embryo | 0.0114 | ZFPM1,ENG,ARID3A |
| | Cell proliferation of fibroblasts | 0.0121 | IGF1R,NCSTN,CTSB,IL4,ENG,PGAM2,ARID3A,CITED2,GPI |
| | Differentiation of keratinocytes | 0.0131 | IRF6,LPIN1,LRIG1,RBL2,PRKCH |
| | Proliferation of hepatocytes | 0.0137 | IGF1R,ITIH4,DICER1,IL4,CITED2 |
| | Myelination of axons | 0.0138 | DICER1,PMP22 |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |

| | | | |
|---|---|---|---|
| Cellular Compromise | Degranulation of cells | 0.00183 | ZFPM1,PRG2,RALB,LPIN1,DICER1,IL4,EHF,MS4A2 |
| | Instability of microtubules | 0.00417 | KIF5C,KIF3B |
| | Damage of hepatocytes | 0.00569 | IGF1R,DICER1 |
| | Degranulation of BMMC cells | 0.0126 | IL4,EHF |
| Cardiovascular Disease | Failure of heart looping | 0.00225 | NCSTN,RBL2,ENG |
| | Development of angioma | 0.00352 | ANGPT2,DICER1,IKZF3,KAT6B |
| | Hypercholesterolemia | 0.00593 | ITIH4,LPIN1,RPTOR,NR0B2 |
| | Hemangioblastoma | 0.0104 | DICER1,IKZF3,KAT6B |
| | Congenital anomaly of cardiovascular system | 0.0104 | NCSTN,ANGPT2,DICER1,RBL2,ENG,KAT6B,CITED2,KCNH2 |
| | Hemangioma | 0.0108 | IGF1R,ANGPT2,DICER1,IKZF3,KAT6B |
| Developmental Disorder | Failure of heart looping | 0.00225 | NCSTN,RBL2,ENG |
| | Susceptibility to autism type 1 | 0.00569 | FOXP1,SHANK2 |
| | Congenital anomaly of cardiovascular system | 0.0104 | NCSTN,ANGPT2,DICER1,RBL2,ENG,KAT6B,CITED2,KCNH2 |
| | Congenital malformation of brain | 0.0123 | RALB,KIF5C,RPTOR,DICER1,ATP2C1,EMG1,NFIA,CITED2,KIF3B |
| | Autosomal dominant Emery-Dreifuss muscular dystrophy | 0.0125 | BNIP3L,ENG,CYB561 |
| Dermatological Diseases and Conditions | Chronic idiopathic urticaria | 0.00231 | IL5RA,MS4A2 |
| | Skin papilloma | 0.00523 | ATP2C1,ENG,PRKCH |
| | Abnormal morphology of hair follicle | 0.00595 | IGF1R,DICER1,RBL2 |
| | Abnormal morphology of epidermis | 0.00668 | IGF1R,LRIG1,DICER1,RBL2,CTSB |
| | Parakeratosis | 0.0104 | LRIG1,RBL2 |
| | Juvenile dermatomyositis | 0.0109 | BNIP3L,ENG,CYB561 |
| Organismal Survival | Morbidity or mortality | 0.00265 | ZFPM1,DMAP1,RBL2,CSRP1,BNIP3L,VPS52,MITF,IKZF3,HEXA,KCNH2,RALB,KRT19,ADCY3,DICER1,FBXW8,PCYT1A,ATP2C1,STX1B,EPX,PRKCH,HK2,ARID3A,NCK1,TLE4,PMP22,PPP2CA,TANK,ANGPT2,SLC25A25,SLC7A1,IL4,ENG,NFIA,KIF26A,CLEC12A,CITED2,KIF3B,IGF1R,NCSTN,SLC2A9,RPTOR,CTSB,SHANK2,PPT2 |
| | Organismal death | 0.00368 | ZFPM1,DMAP1,RBL2,CSRP1,BNIP3L,VPS52,MITF,IKZF3,HEXA,KCNH2,RALB,KRT19,ADCY3,DICER1,FBXW8,PCYT1A,ATP2C1,STX1B,EPX,PRKCH,HK2,ARID3A,NCK1,TLE4,PMP22,PPP2CA,TANK,ANGPT2,SLC25A25,SLC7A1,IL4,ENG,NFIA,KIF26A,CITED2,KIF3B,IGF1R,NCSTN,SLC2A9,RPTOR,CTSB,SHANK2,PPT2 |
| Gastrointestinal Disease | Growth of pancreatic endocrine tumor | 0.00287 | CTSB,ENG |
| | Damage of hepatocytes | 0.00569 | IGF1R,DICER1 |
| | Polyp | 0.00593 | IL5RA,ENG,PRKCZ,MS4A2 |
| | Diabetes mellitus | 0.0077 | ITIH4,COL15A1,FOXP1,SLC17A4,IL4,NISCH,IKZF3,CLEC12A,NR0B2,KCNH2,IGF1R,SLC2A9,LRIG1,PCYT1A,CTSB,MED27,FBP1,HK2,BANK1,DLGAP2,PPT2 |
| | Apoptosis of hepatocytes | 0.00904 | ITIH4,DICER1,CTSB,IL4,NR0B2 |
| | Polyposis | 0.0104 | IL5RA,ENG,MS4A2 |
| | Barrett syndrome | 0.0156 | IL4,ENG,ASCC1 |
| Cell-mediated Immune Response | Homing of Th2 cells | 0.00287 | PTGDR2,IL4 |
| Skeletal and Muscular System Development and Function | Muscularization of artery | 0.00287 | RPTOR,IL4 |
| | Proliferation of skeletal muscle cells | 0.00742 | IGF1R,ANGPT2 |
| | Fusion of myotube | 0.00836 | IGF1R,IL4 |
| | Proliferation of myofibroblasts | 0.00836 | CTSB,IL4 |
| | Cell viability of muscle cell lines | 0.0138 | IGF1R,CTSB |
| | Cell viability of muscle cells | 0.015 | IGF1R,ANGPT2,HK2 |
| Embryonic Development | Size of embryo | 0.00348 | ZFPM1,IGF1R,NCSTN,DICER1,RBL2,ATP2C1,ENG,CITED2,KIF3B,PPP2CA |

| | | | |
|---|---|---|---|
| | Cell death of embryonic cell lines | 0.00617 | IGF1R,TANK,YWHAQ,RBL2,CTSB,BNIP3L,DDIT4,HK2,CITED2,PMP22 |
| | Development of plasma cells | 0.00742 | DICER1,IL4 |
| | Differentiation of memory B cells | 0.00836 | FOXP1,IL4 |
| | Hematopoiesis in embryo | 0.0114 | ZFPM1,ENG,ARID3A |
| | Differentiation of keratinocytes | 0.0131 | IRF6,LPIN1,LRIG1,RBL2,PRKCH |
| | Abnormal morphology of germinal center | 0.015 | IL4,IKZF3,BANK1 |
| Inflammatory Disease | Severe asthma | 0.00417 | IL5RA,MS4A2 |
| | Juvenile dermatomyositis | 0.0109 | BNIP3L,ENG,CYB561 |
| | Barrett syndrome | 0.0156 | IL4,ENG,ASCC1 |
| Respiratory Disease | Severe asthma | 0.00417 | IL5RA,MS4A2 |
| | Cell death of lung cells | 0.00595 | IGF1R,PRG2,EPX |
| | Cell death of pneumocytes | 0.0138 | PRG2,EPX |
| Free Radical Scavenging | Production of superoxide | 0.0051 | PRG2,ANGPT2,IL4,PRKCZ,PRG3 |
| | Synthesis of reactive oxygen species | 0.00713 | PRG2,IRF6,ITIH4,ANGPT2,BNIP3L,SHANK2,DDIT4,IL4,FBP1,PRKCZ,HK2,PRG3 |
| Hepatic System Disease | Damage of hepatocytes | 0.00569 | IGF1R,DICER1 |
| | Apoptosis of hepatocytes | 0.00904 | ITIH4,DICER1,CTSB,IL4,NR0B2 |
| Neurological Disease | Susceptibility to autism type 1 | 0.00569 | FOXP1,SHANK2 |
| | Demyelination of neurons | 0.0104 | LPIN1,DICER1 |
| | Neurodegeneration of cerebellum | 0.0109 | DICER1,CTSB,PPT2 |
| | Congenital malformation of brain | 0.0123 | RALB,KIF5C,RPTOR,DICER1,ATP2C1,EMG1,NFIA,CITED2,KIF3B |
| | Familial pervasive developmental disorder | 0.0151 | FOXP1,SHANK2 |
| Psychological Disorders | Susceptibility to autism type 1 | 0.00569 | FOXP1,SHANK2 |
| | Familial pervasive developmental disorder | 0.0151 | FOXP1,SHANK2 |
| Metabolic Disease | Hypercholesterolemia | 0.00593 | ITIH4,LPIN1,RPTOR,NR0B2 |
| | Diabetes mellitus | 0.0077 | ITIH4,COL15A1,FOXP1,SLC17A4,IL4,NISCH,IKZF3,CLEC12A,NR0B2,KCNH2,IGF1R,SLC2A9,LRIG1,PCYT1A,CTSB,MED27,FBP1,HK2,BANK1,DLGAP2,PPT2 |
| | Glucose metabolism disorder | 0.0112 | ITIH4,COL15A1,FOXP1,SLC17A4,IL4,NISCH,IKZF3,CLEC12A,NR0B2,KCNH2,IGF1R,LPIN1,SLC2A9,LRIG1,DICER1,PCYT1A,CTSB,MED27,SMARCD3,FBP1,HK2,BANK1,DLGAP2,PPT2 |
| Renal and Urological Disease | Hydronephrosis | 0.00693 | IGF1R,SLC2A9,IL4,NFIA |
| | Injury of renal glomerulus | 0.0138 | ANGPT2,DICER1 |
| Connective Tissue Development and Function | Proliferation of connective tissue cells | 0.00708 | RBL2,IL4,ENG,CITED2,IRF6,IGF1R,NCSTN,LRIG1,DICER1,CTSB,PRKCH,PGAM2,ARID3A,GPI |
| | Development of PBMCs | 0.00836 | DICER1,IL4 |
| | Proliferation of myofibroblasts | 0.00836 | CTSB,IL4 |
| | Cell proliferation of fibroblasts | 0.0121 | IGF1R,NCSTN,CTSB,IL4,ENG,PGAM2,ARID3A,CITED2,GPI |
| Digestive System Development and Function | Proliferation of liver cells | 0.00961 | IGF1R,ITIH4,DICER1,CTSB,IL4,CITED2 |
| | Proliferation of hepatocytes | 0.0137 | IGF1R,ITIH4,DICER1,IL4,CITED2 |
| Hereditary Disorder | Hereditary myopathy | 0.00857 | LPIN1,PTGDR2,AP5B1,BNIP3L,ENG,SLC25A33,KIF26A,ASCC1,ATPAF2,CYB561,PMP22,KCNH2 |
| | Autosomal dominant Emery-Dreifuss muscular dystrophy | 0.0125 | BNIP3L,ENG,CYB561 |
| | Familial pervasive developmental disorder | 0.0151 | FOXP1,SHANK2 |
| Skeletal and Muscular Disorders | Hereditary myopathy | 0.00857 | LPIN1,PTGDR2,AP5B1,BNIP3L,ENG,SLC25A33,KIF26A,ASCC1,ATPAF2,CYB561,PMP22,KCNH2 |
| | Juvenile dermatomyositis | 0.0109 | BNIP3L,ENG,CYB561 |
| | Autosomal dominant Emery-Dreifuss muscular dystrophy | 0.0125 | BNIP3L,ENG,CYB561 |

| | | | |
|---|---|---|---|
| Reproductive System Disease | Proliferation of ovarian cancer cells | 0.0126 | IGF1R,PPP2CA |
| Cell Signaling | Translocation of Ca2+ | 0.00936 | SLC8B1,ATP2C1 |
| Vitamin and Mineral Metabolism | Translocation of Ca2+ | 0.00936 | SLC8B1,ATP2C1 |
| Hepatic System Development and Function | Proliferation of liver cells | 0.00961 | IGF1R,ITIH4,DICER1,CTSB,IL4,CITED2 |
| | Proliferation of hepatocytes | 0.0137 | IGF1R,ITIH4,DICER1,IL4,CITED2 |
| Antimicrobial Response | Antiviral response | 0.0109 | SERINC5,DICER1,BNIP3L,IL4,DDIT4,RNASE2 |

*Diseases and biological functions which had only one gene involved were removed.

*Table E11* *Druggable targets of genes to which the 179 significant CpGs annotated in analysis of asthma in relation to DNA methylation in childhood.*

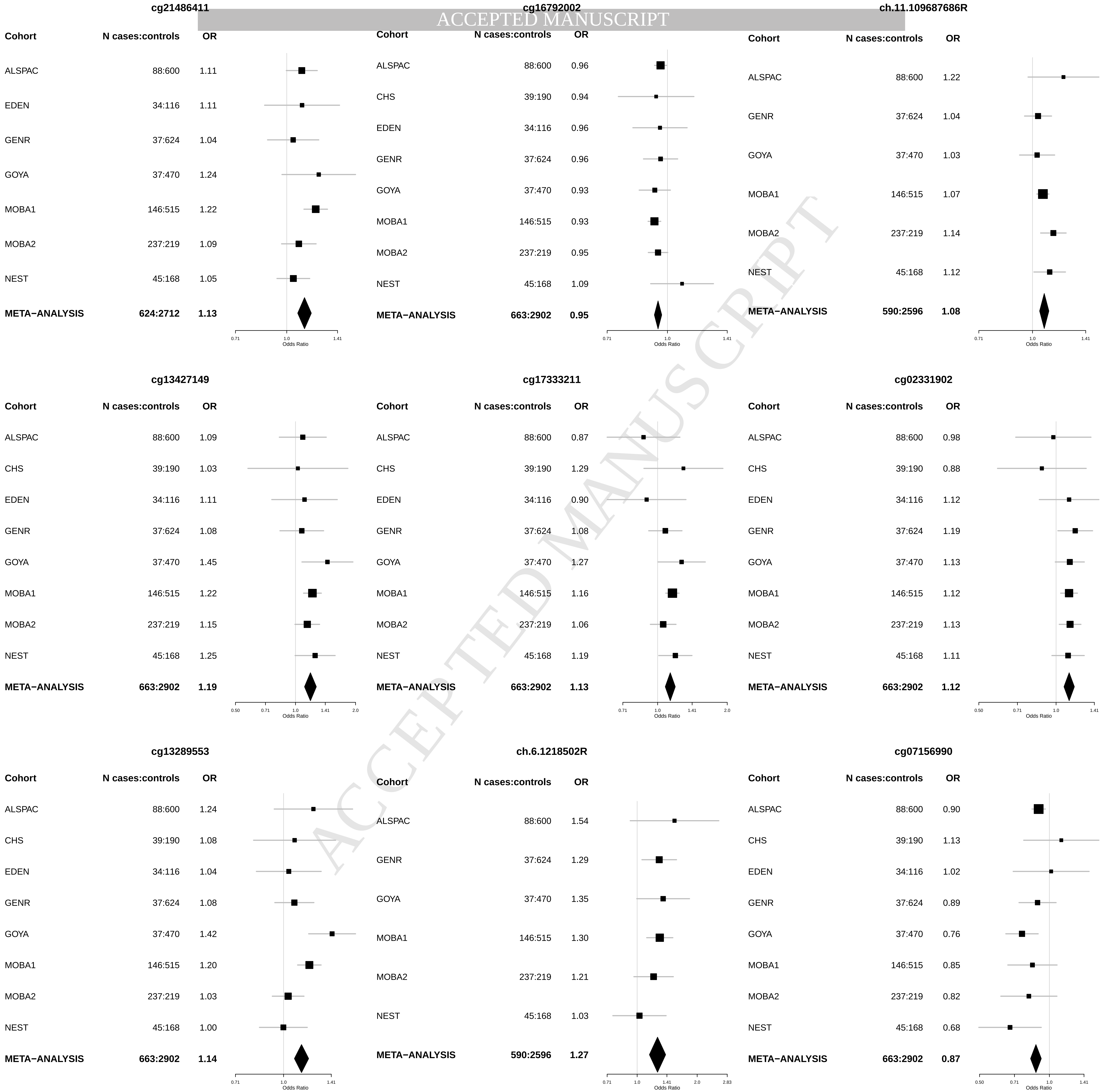
| CpG | chr:pos | Gene* | ChEMBL Target ID | Approved drugs and clinical candidates [ChEMBL ID] | Approved drugs and Clinical candidates [Name] | Mechanism of Action |
|---|---|---|---|---|---|---|
| cg01942646 | chr1:27240694 | NR0B2 | CHEMBL5603 | No | No | |
| cg26752663 | chr2:25142016 | ADCY3 | CHEMBL2097167 | No | No | |
| cg01310029 | chr3:3152374 | IL5RA | CHEMBL3580483 | CHEMBL1742991 | BENRALIZUMAB | Interleukin-5 receptor subunit alpha inhibitor |
| cg10159529 | chr3:3152530 | IL5RA | CHEMBL3580483 | CHEMBL1742991 | BENRALIZUMAB | Interleukin-5 receptor subunit alpha inhibitor |
| cg07386061 | chr3:52492874 | NISCH | CHEMBL3923 | No | No | |
| cg06070625 | chr3:69812798 | MITF | CHEMBL1741165 | No | No | |
| cg09423651 | chr3:136618442 | NCK1 | CHEMBL4846 | No | No | |
| cg08698681 | chr3:171091657 | TNIK | CHEMBL4527 | No | No | |
| cg09597192 | chr6:32141591 | PPT2 | CHEMBL2189137 | No | No | |
| cg24576940 | chr7:150648283 | KCNH2 | CHEMBL240 | CHEMBL473 | DOFETILIDE | HERG blocker |
| | | | | CHEMBL1700 | SOTALOL HYDROCHLORIDE | HERG blocker |
| | | | | CHEMBL1083993 | AMIODARONE HYDROCHLORIDE | HERG blocker |
| | | | | CHEMBL1200564 | IBUTILIDE FUMARATE | HERG blocker |
| | | | | CHEMBL3545040 | AZD7009 | HERG blocker |
| | | | | CHEMBL3545169 | AZD1305 | HERG blocker |
| cg23147443 | chr7:150649655 | KCNH2 | CHEMBL240 | CHEMBL473 | DOFETILIDE | HERG blocker |
| | | | | CHEMBL1700 | SOTALOL HYDROCHLORIDE | HERG blocker |
| | | | | CHEMBL1083993 | AMIODARONE HYDROCHLORIDE | HERG blocker |
| | | | | CHEMBL1200564 | IBUTILIDE FUMARATE | HERG blocker |
| | | | | CHEMBL3545040 | AZD7009 | HERG blocker |
| | | | | CHEMBL3545169 | AZD1305 | HERG blocker |
| cg18666454 | chr7:150651937 | KCNH2 | CHEMBL240 | CHEMBL473 | DOFETILIDE | HERG blocker |
| | | | | CHEMBL1700 | SOTALOL HYDROCHLORIDE | HERG blocker |
| | | | | CHEMBL1083993 | AMIODARONE HYDROCHLORIDE | HERG blocker |
| | | | | CHEMBL1200564 | IBUTILIDE FUMARATE | HERG blocker |
| | | | | CHEMBL3545040 | AZD7009 | HERG blocker |
| | | | | CHEMBL3545169 | AZD1305 | HERG blocker |
| cg03131767 | chr12:123446272 | ABCB9 | CHEMBL1293189 | No | No | |
| cg11266582 | chr15:64275853 | DAPK2 | CHEMBL3123 | No | No | |
| cg20315954 | chr17:15137304 | PMP22 | CHEMBL1293298 | No | No | |
| cg21073212 | chr20:30866501 | KIF3B | CHEMBL6109 | No | No | |

*UCSC Known Gene used to map to drug target database

*Table E12* *Druggable targets of genes to which the 35 DMRs annotated in analysis of school-aged asthma in relation to older child DNA methylation.*

| chr:pos | GeneName* | ChEMBL Target ID | Approved drugs and clinical candidates [ChEMBL ID] | Approved drugs and clinical candidates [Name] | Mechanism of Action |
|---|---|---|---|---|---|
| chr2:149639612-149640260 | KIF5C | CHEMBL2029194 | No | No | |
| chr3:3151795-3152917 | IL5RA | CHEMBL3580483 | CHEMBL1742991 | BENRALIZUMAB | Interleukin-5 receptor subunit alpha inhibitor |
| chr15:64275810-64275854 | DAPK2 | CHEMBL3123 | No | No | |
| chr15:99443213-99443667 | IGF1R | CHEMBL1957 | CHEMBL1201717 | MECASERMIN RINFABATE | Insulin-like growth factor I receptor agonist |
| | | | CHEMBL1201716 | MECASERMIN | Insulin-like growth factor I receptor agonist |
| | | | CHEMBL1091644 | LINSITINIB | Insulin-like growth factor I receptor inhibitor |
| | | | CHEMBL1743019 | FIGITUMUMAB | Insulin-like growth factor I receptor antagonist |
| | | | CHEMBL1743024 | GANITUMAB | Insulin-like growth factor I receptor antagonist |
| | | | CHEMBL283120 | PICROPODOPHYLLOTOXIN | Insulin-like growth factor I receptor inhibitor |
| | | | CHEMBL575448 | BMS-754807 | Insulin-like growth factor I receptor inhibitor |
| | | | CHEMBL1743001 | CIXUTUMUMAB | Insulin-like growth factor I receptor antagonist |
| | | | CHEMBL1743006 | DALOTUZUMAB | Insulin-like growth factor I receptor antagonist |
| | | | CHEMBL1743064 | ROBATUMUMAB | Insulin-like growth factor I receptor antagonist |
| | | | CHEMBL1743079 | TEPROTUMUMAB | Insulin-like growth factor I receptor antagonist |
| | | | CHEMBL2109357 | AVE-1642 | Insulin-like growth factor I receptor antagonist |
| | | | CHEMBL3545025 | INSM-18 | Insulin-like growth factor I receptor inhibitor |
| | | | CHEMBL3545156 | KW-2450 | Insulin-like growth factor I receptor inhibitor |
| | | | CHEMBL551064 | AEW-541 | Insulin-like growth factor I receptor inhibitor |
| | | | CHEMBL3545004 | PL-225B | Insulin-like growth factor I receptor inhibitor |
| | | | CHEMBL3545085 | XL-228 | Insulin-like growth factor I receptor inhibitor |
| chr17:78682785-78683458 | RPTOR | CHEMBL3120040 | No | No | |

* Based on DMRCate annotation to RefGene from Illumina annotation file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ALSPAC 88:600 1.11
EDEN 34:116 1.11
GENR 37:624 1.04
GOYA 37:470 1.24
MOBA1 146:515 1.22
MOBA2 237:219 1.09
NEST 45:168 1.05
META−ANALYSIS 624:2712 1.13
0.71 1.0 1.41
Odds Ratio
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Cohort N cases:controls OR
ALSPAC 88:600 0.96
CHS 39:190 0.94
EDEN 34:116 0.96
GENR 37:624 0.96
GOYA 37:470 0.93
MOBA1 146:515 0.93
MOBA2 237:219 0.95
NEST 45:168 1.09
META−ANALYSIS 663:2902 0.95
0.71 1.0 1.41
Odds Ratio
ch.11.109687686R
Cohort N cases:controls OR
ALSPAC 88:600 1.22
GENR 37:624 1.04
GOYA 37:470 1.03
MOBA1 146:515 1.07
MOBA2 237:219 1.14
NEST 45:168 1.12
META−ANALYSIS 590:2596 1.08
0.71 1.0 1.41
Odds Ratio
cg13427149
Cohort N cases:controls OR
ALSPAC 88:600 1.09
CHS 39:190 1.03
EDEN 34:116 1.11
GENR 37:624 1.08
GOYA 37:470 1.45
MOBA1 146:515 1.22
MOBA2 237:219 1.15
NEST 45:168 1.25
META−ANALYSIS 663:2902 1.19
0.50 0.71 1.0 1.41 2.0
Odds Ratio
cg17333211
Cohort N cases:controls OR
ALSPAC 88:600 0.87
CHS 39:190 1.29
EDEN 34:116 0.90
GENR 37:624 1.08
GOYA 37:470 1.27
MOBA1 146:515 1.16
MOBA2 237:219 1.06
NEST 45:168 1.19
META−ANALYSIS 663:2902 1.13
0.71 1.0 1.41 2.0
Odds Ratio
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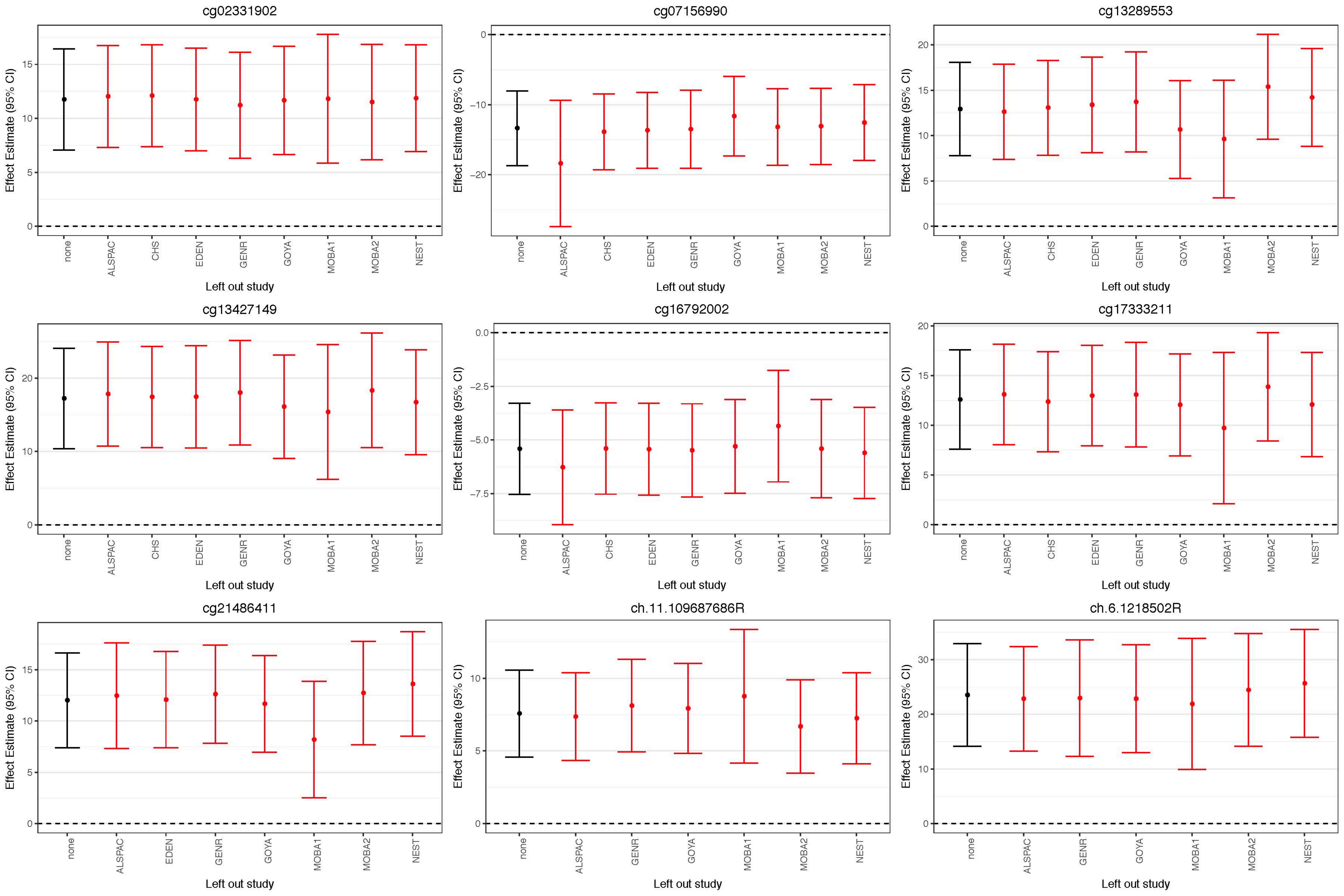
Cohort N cases:controls OR
ALSPAC 88:600 0.98
CHS 39:190 0.88
EDEN 34:116 1.12
GENR 37:624 1.19
GOYA 37:470 1.13
MOBA1 146:515 1.12
MOBA2 237:219 1.13
NEST 45:168 1.11
META−ANALYSIS 663:2902 1.12
0.50 0.71 1.0 1.41
Odds Ratio
cg13289553
Cohort N cases:controls OR
ALSPAC 88:600 1.24
CHS 39:190 1.08
EDEN 34:116 1.04
GENR 37:624 1.08
GOYA 37:470 1.42
MOBA1 146:515 1.20
MOBA2 237:219 1.03
NEST 45:168 1.00
META−ANALYSIS 663:2902 1.14
0.71 1.0 1.41
Odds Ratio
ch.6.1218502R
Cohort N cases:controls OR
ALSPAC 88:600 1.54
GENR 37:624 1.29
GOYA 37:470 1.35
MOBA1 146:515 1.30
MOBA2 237:219 1.21
NEST 45:168 1.03
META−ANALYSIS 590:2596 1.27
0.71 1.0 1.41 2.0 2.83
Odds Ratio
cg07156990
Cohort N cases:controls OR
ALSPAC 88:600 0.90
CHS 39:190 1.13
EDEN 34:116 1.02
GENR 37:624 0.89
GOYA 37:470 0.76
MOBA1 146:515 0.85
MOBA2 237:219 0.82
NEST 45:168 0.68
META−ANALYSIS 663:2902 0.87
0.50 0.71 1.0 1.41
Odds Ratio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Left out study
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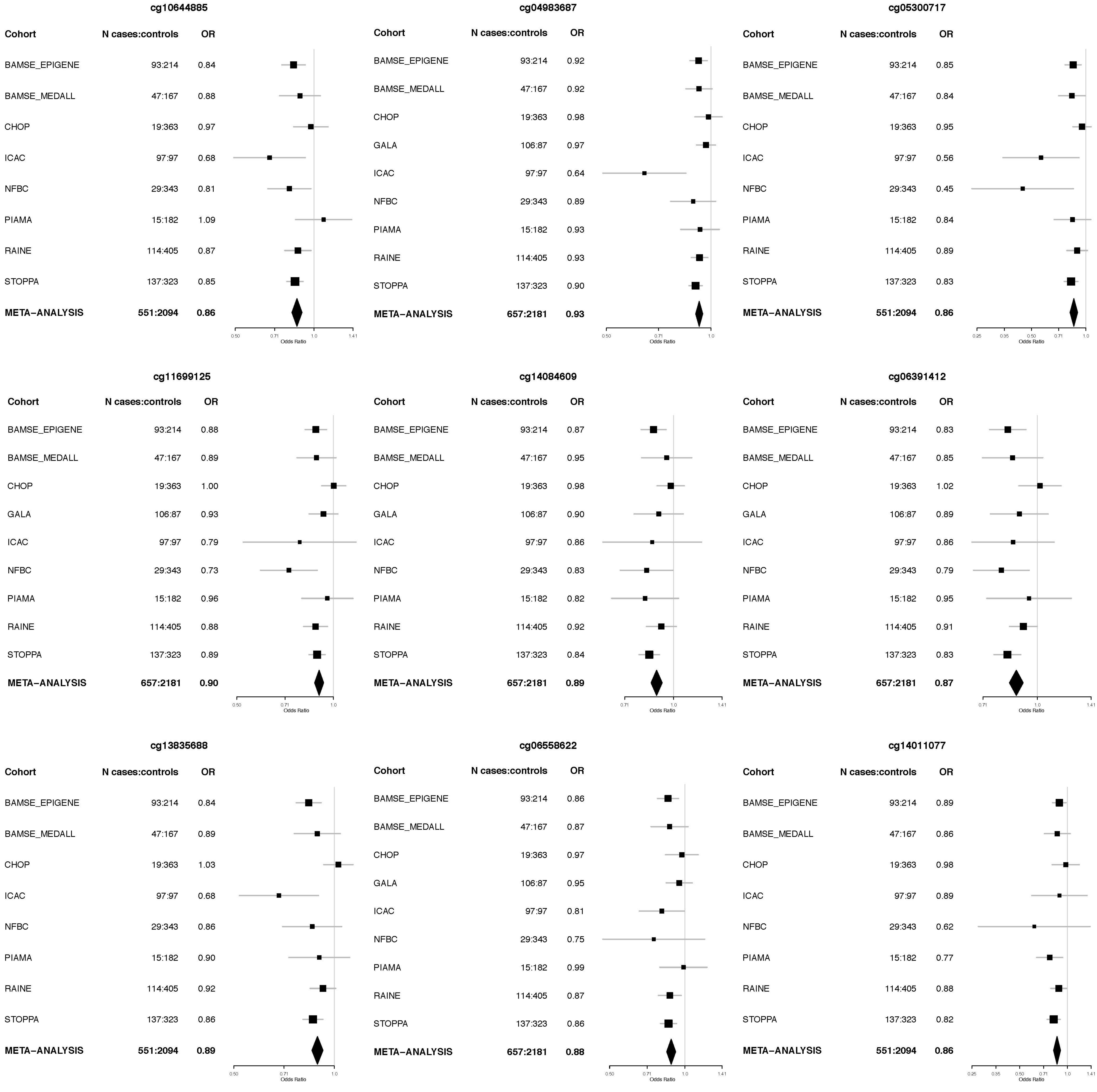
CHS
EDEN
GENR
GOYA
MOBA1
MOBA2
NEST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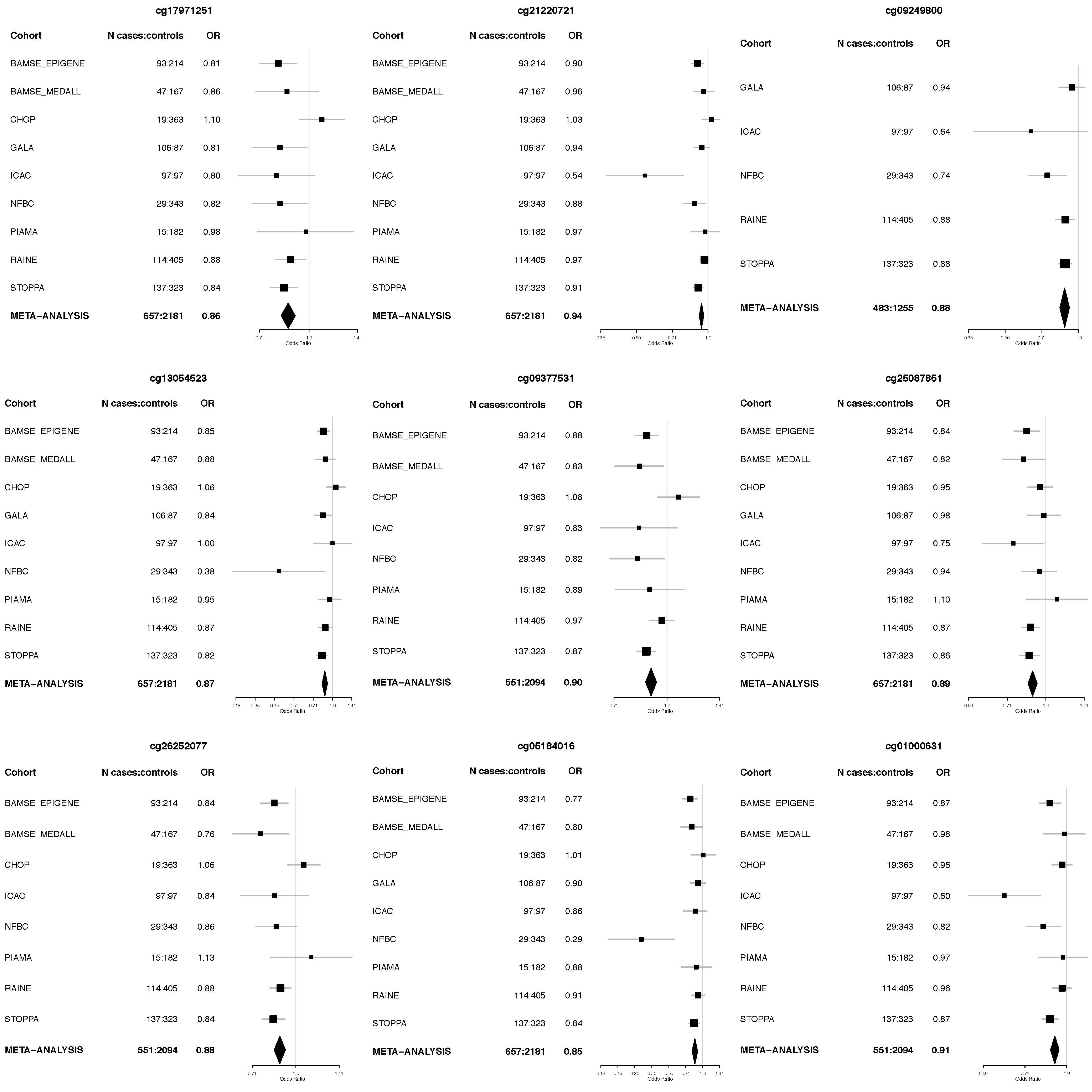
CHOP 19:363 0.97
ICAC 97:97 0.68
NFBC 29:343 0.81
PIAMA 15:182 1.09
RAINE 114:405 0.87
STOPPA 137:323 0.85
META−ANALYSIS 551:2094 0.86
0.50 0.71 1.0 1.41
Odds Ratio
cg04983687
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.92
BAMSE_MEDALL 47:167 0.92
CHOP 19:363 0.98
GALA 106:87 0.97
ICAC 97:97 0.64
NFBC 29:343 0.89
PIAMA 15:182 0.93
RAINE 114:405 0.93
STOPPA 137:323 0.90
META−ANALYSIS 657:2181 0.93
0.50 0.71 1.0
Odds Ratio
cg05300717
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.84
CHOP 19:363 0.95
ICAC 97:97 0.56
NFBC 29:343 0.45
PIAMA 15:182 0.84
RAINE 114:405 0.89
STOPPA 137:323 0.83
META−ANALYSIS 551:2094 0.86
0.25 0.35 0.50 0.71 1.0
Odds Ratio
cg11699125
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.88
BAMSE_MEDALL 47:167 0.89
CHOP 19:363 1.00
GALA 106:87 0.93
ICAC 97:97 0.79
NFBC 29:343 0.73
PIAMA 15:182 0.96
RAINE 114:405 0.88
STOPPA 137:323 0.89
META−ANALYSIS 657:2181 0.90
0.50 0.71 1.0
Odds Ratio
cg14084609
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.87
BAMSE_MEDALL 47:167 0.95
CHOP 19:363 0.98
GALA 106:87 0.90
ICAC 97:97 0.86
NFBC 29:343 0.83
PIAMA 15:182 0.82
RAINE 114:405 0.92
STOPPA 137:323 0.84
META−ANALYSIS 657:2181 0.89
0.71 1.0 1.41
Odds Ratio
cg06391412
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.83
BAMSE_MEDALL 47:167 0.85
CHOP 19:363 1.02
GALA 106:87 0.89
ICAC 97:97 0.86
NFBC 29:343 0.79
PIAMA 15:182 0.95
RAINE 114:405 0.91
STOPPA 137:323 0.83
META−ANALYSIS 657:2181 0.87
0.71 1.0 1.41
Odds Ratio
cg13835688
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.89
CHOP 19:363 1.03
ICAC 97:97 0.68
NFBC 29:343 0.86
PIAMA 15:182 0.90
RAINE 114:405 0.92
STOPPA 137:323 0.86
META−ANALYSIS 551:2094 0.89
0.50 0.71 1.0
Odds Ratio
cg06558622
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.87
CHOP 19:363 0.97
GALA 106:87 0.95
ICAC 97:97 0.81
NFBC 29:343 0.75
PIAMA 15:182 0.99
RAINE 114:405 0.87
STOPPA 137:323 0.86
META−ANALYSIS 657:2181 0.88
0.50 0.71 1.0 1.41
Odds Ratio
cg14011077
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.89
BAMSE_MEDALL 47:167 0.86
CHOP 19:363 0.98
ICAC 97:97 0.89
NFBC 29:343 0.62
PIAMA 15:182 0.77
RAINE 114:405 0.88
STOPPA 137:323 0.82
META−ANALYSIS 551:2094 0.86
0.25 0.35 0.50 0.71 1.0 1.41
Odds Ratio


cg17971251
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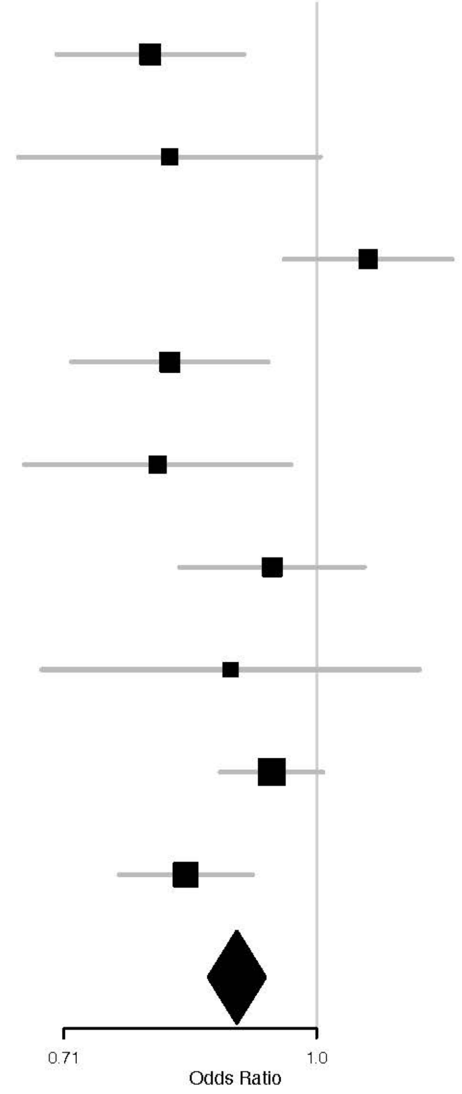
BAMSE_EPIGENE 93:214 0.81
BAMSE_MEDALL 47:167 0.86
CHOP 19:363 1.10
GALA 106:87 0.81
ICAC 97:97 0.80
NFBC 29:343 0.82
PIAMA 15:182 0.98
RAINE 114:405 0.88
STOPPA 137:323 0.84
META−ANALYSIS 657:2181 0.86
Odds Ratio
cg21220721
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.90
BAMSE_MEDALL 47:167 0.96
CHOP 19:363 1.03
GALA 106:87 0.94
ICAC 97:97 0.54
NFBC 29:343 0.88
PIAMA 15:182 0.97
RAINE 114:405 0.97
STOPPA 137:323 0.91
META−ANALYSIS 657:2181 0.94
Odds Ratio
cg09249800
Cohort N cases:controls OR
GALA 106:87 0.94
ICAC 97:97 0.64
NFBC 29:343 0.74
RAINE 114:405 0.88
STOPPA 137:323 0.88
META−ANALYSIS 483:1255 0.88
Odds Ratio
cg13054523
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.88
CHOP 19:363 1.06
GALA 106:87 0.84
ICAC 97:97 1.00
NFBC 29:343 0.38
PIAMA 15:182 0.95
RAINE 114:405 0.87
STOPPA 137:323 0.82
META−ANALYSIS 657:2181 0.87
Odds Ratio
cg09377531
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.88
BAMSE_MEDALL 47:167 0.83
CHOP 19:363 1.08
ICAC 97:97 0.83
NFBC 29:343 0.82
PIAMA 15:182 0.89
RAINE 114:405 0.97
STOPPA 137:323 0.87
META−ANALYSIS 551:2094 0.90
Odds Ratio
cg25087851
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.82
CHOP 19:363 0.95
GALA 106:87 0.98
ICAC 97:97 0.75
NFBC 29:343 0.94
PIAMA 15:182 1.10
RAINE 114:405 0.87
STOPPA 137:323 0.86
META−ANALYSIS 657:2181 0.89
Odds Ratio
cg26252077
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.76
CHOP 19:363 1.06
ICAC 97:97 0.84
NFBC 29:343 0.86
PIAMA 15:182 1.13
RAINE 114:405 0.88
STOPPA 137:323 0.84
META−ANALYSIS 551:2094 0.88
Odds Ratio
cg05184016
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.77
BAMSE_MEDALL 47:167 0.80
CHOP 19:363 1.01
GALA 106:87 0.90
ICAC 97:97 0.86
NFBC 29:343 0.29
PIAMA 15:182 0.88
RAINE 114:405 0.91
STOPPA 137:323 0.84
META−ANALYSIS 657:2181 0.85
Odds Ratio
cg01000631
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.87
BAMSE_MEDALL 47:167 0.98
CHOP 19:363 0.96
ICAC 97:97 0.60
NFBC 29:343 0.82
PIAMA 15:182 0.97
RAINE 114:405 0.96
STOPPA 137:323 0.87
META−ANALYSIS 551:2094 0.91
Odds Ratio

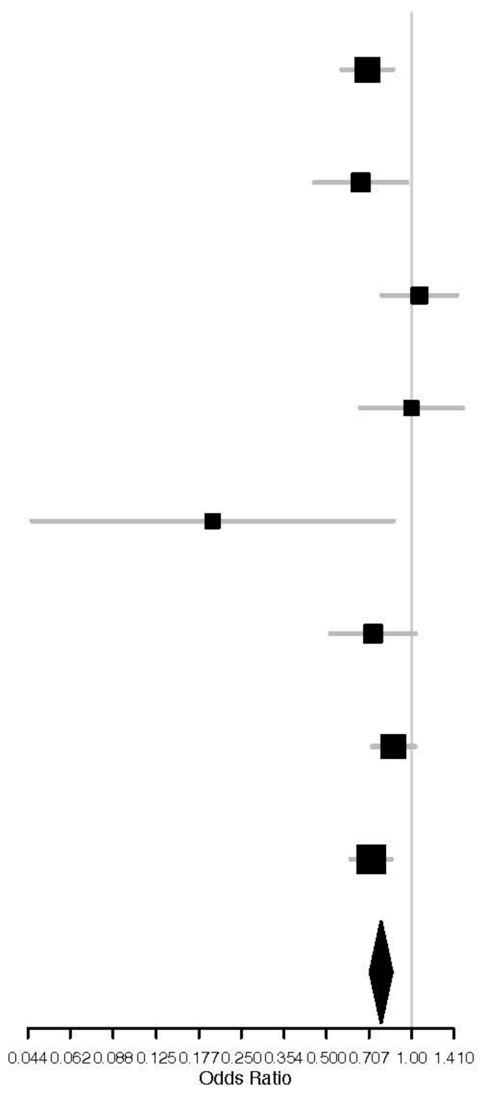
### cg11683482

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.80 |
| BAMSE_MEDALL | 47:167 | 0.82 |
| CHOP | 19:363 | 1.07 |
| GALA | 106:87 | 0.82 |
| ICAC | 97:97 | 0.80 |
| NFBC | 29:343 | 0.94 |
| PIAMA | 15:182 | 0.89 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.84 |
| **META-ANALYSIS** | **657:2181** | **0.90** |



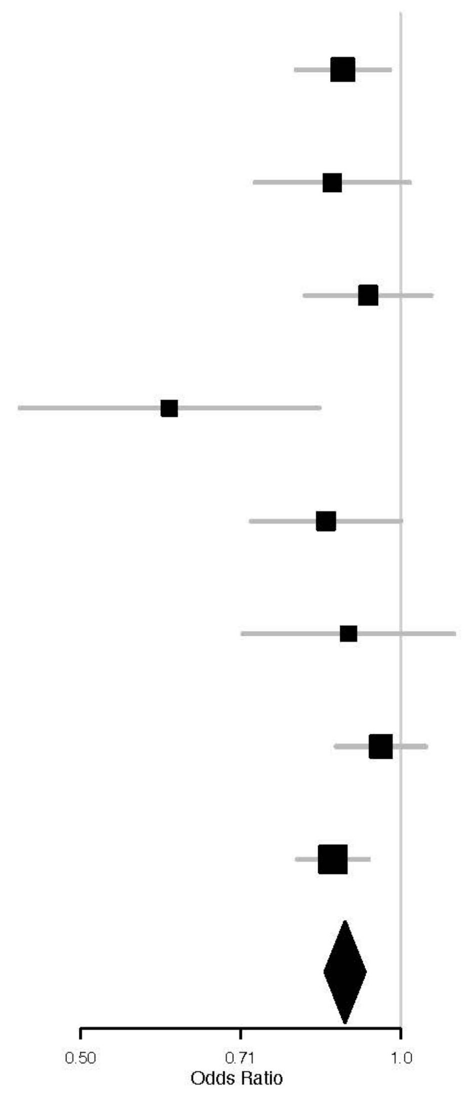

### cg13850063

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.70 |
| BAMSE_MEDALL | 47:167 | 0.66 |
| CHOP | 19:363 | 1.07 |
| ICAC | 97:97 | 1.00 |
| NFBC | 29:343 | 0.20 |
| PIAMA | 15:182 | 0.73 |
| RAINE | 114:405 | 0.86 |
| STOPPA | 137:323 | 0.72 |
| **META-ANALYSIS** | **551:2094** | **0.78** |



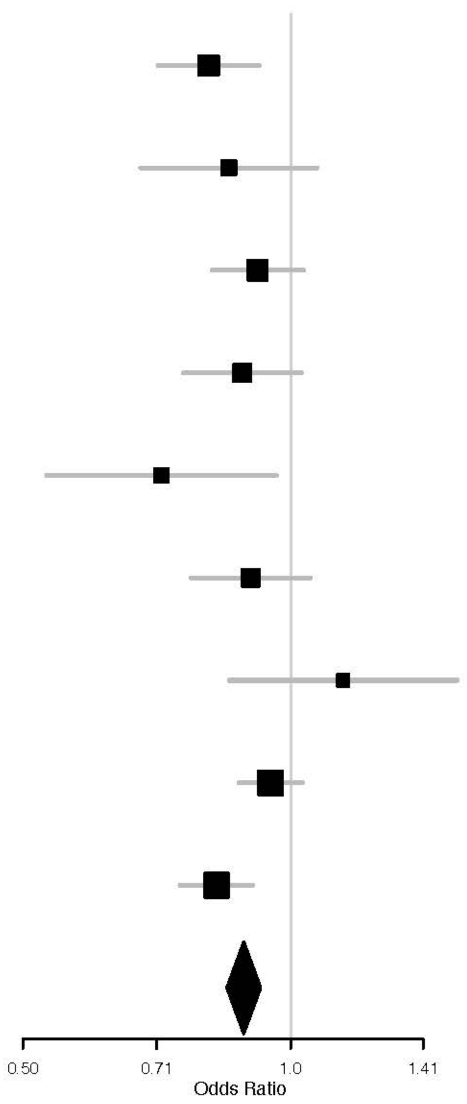

### cg13458609

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.88 |
| BAMSE_MEDALL | 47:167 | 0.86 |
| CHOP | 19:363 | 0.93 |
| ICAC | 97:97 | 0.61 |
| NFBC | 29:343 | 0.85 |
| PIAMA | 15:182 | 0.89 |
| RAINE | 114:405 | 0.96 |
| STOPPA | 137:323 | 0.86 |
| **META-ANALYSIS** | **551:2094** | **0.89** |



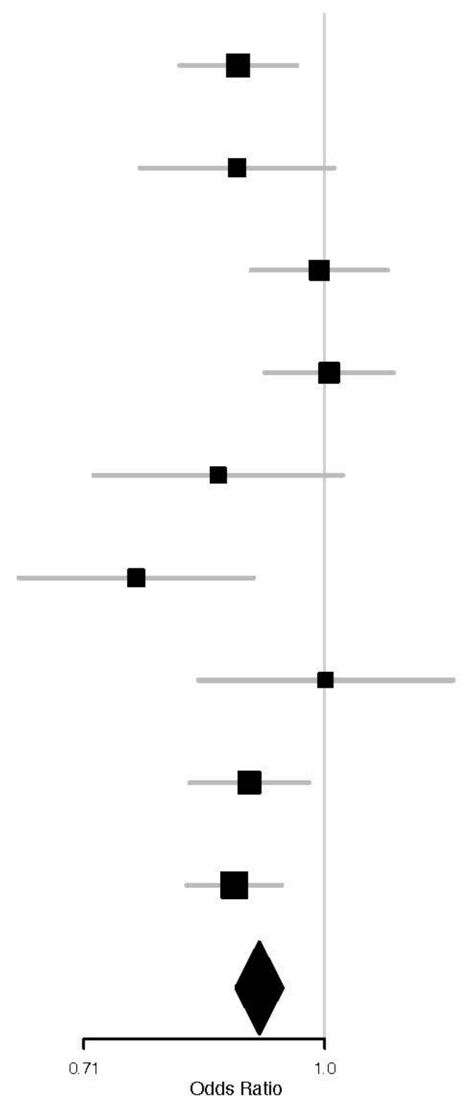

### cg00170714

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.81 |
| BAMSE_MEDALL | 47:167 | 0.85 |
| CHOP | 19:363 | 0.92 |
| GALA | 106:87 | 0.88 |
| ICAC | 97:97 | 0.72 |
| NFBC | 29:343 | 0.90 |
| PIAMA | 15:182 | 1.15 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.83 |
| **META-ANALYSIS** | **657:2181** | **0.89** |



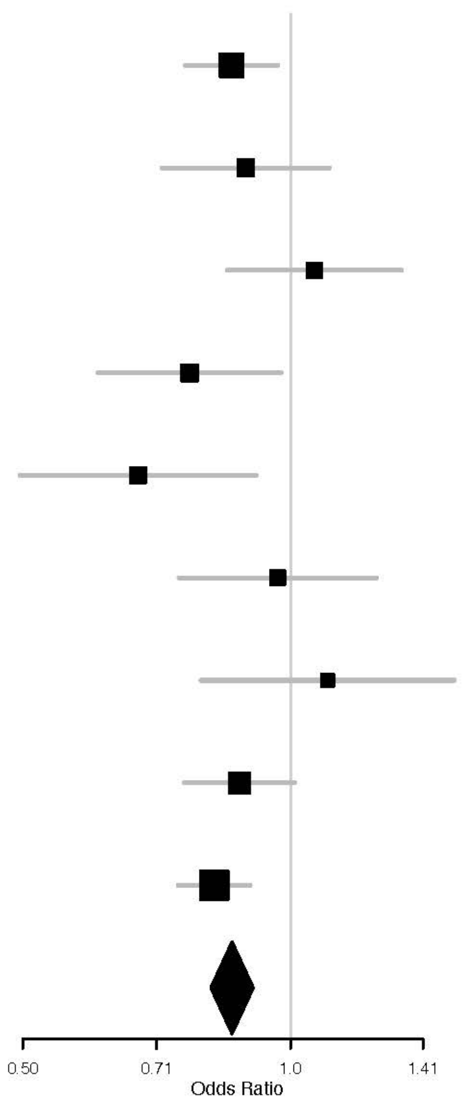

### cg07970948

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.88 |
| BAMSE_MEDALL | 47:167 | 0.88 |
| CHOP | 19:363 | 0.99 |
| GALA | 106:87 | 1.01 |
| ICAC | 97:97 | 0.86 |
| NFBC | 29:343 | 0.76 |
| PIAMA | 15:182 | 1.00 |
| RAINE | 114:405 | 0.90 |
| STOPPA | 137:323 | 0.88 |
| **META-ANALYSIS** | **657:2181** | **0.91** |



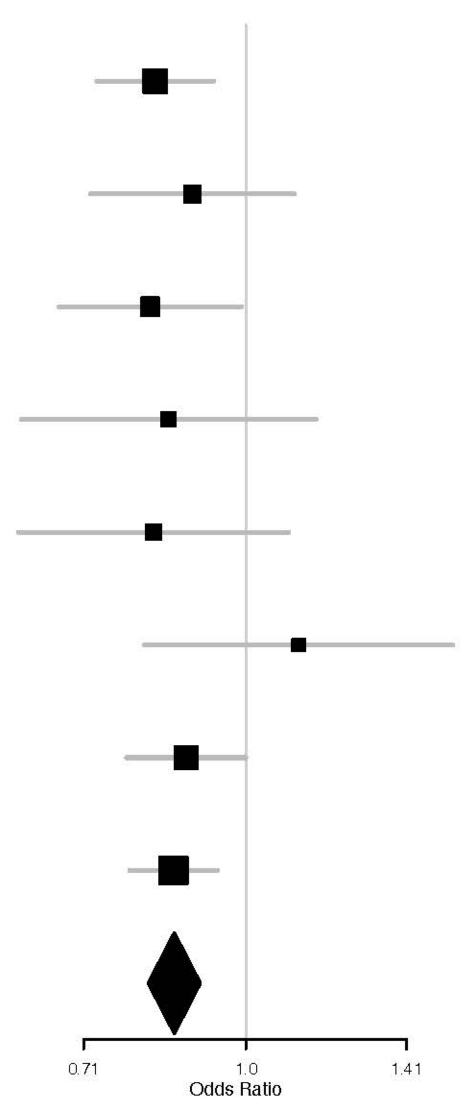

### cg18337287

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.86 |
| BAMSE_MEDALL | 47:167 | 0.89 |
| CHOP | 19:363 | 1.06 |
| GALA | 106:87 | 0.77 |
| ICAC | 97:97 | 0.67 |
| NFBC | 29:343 | 0.97 |
| PIAMA | 15:182 | 1.10 |
| RAINE | 114:405 | 0.88 |
| STOPPA | 137:323 | 0.82 |
| **META-ANALYSIS** | **657:2181** | **0.86** |



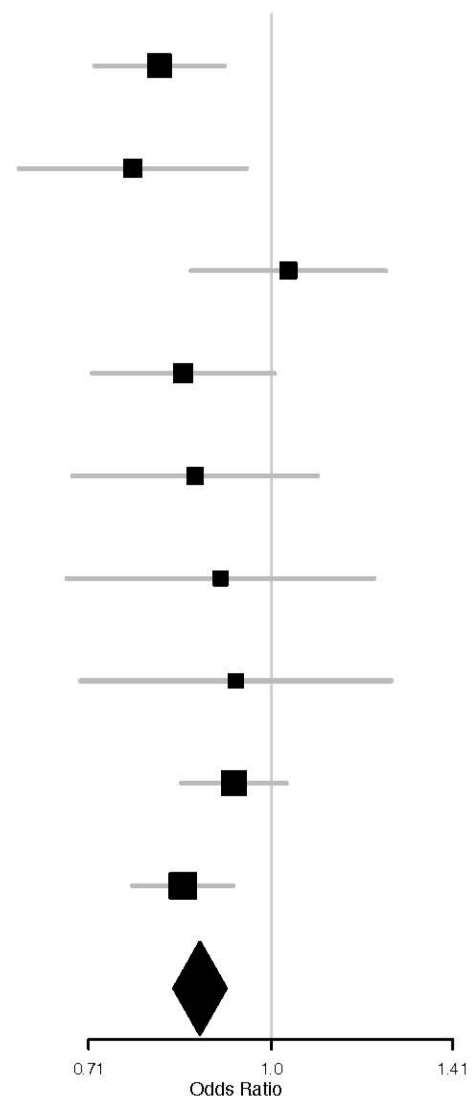

### cg24459209

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.82 |
| BAMSE_MEDALL | 47:167 | 0.89 |
| CHOP | 19:363 | 0.82 |
| ICAC | 97:97 | 0.85 |
| NFBC | 29:343 | 0.82 |
| PIAMA | 15:182 | 1.12 |
| RAINE | 114:405 | 0.88 |
| STOPPA | 137:323 | 0.86 |
| **META-ANALYSIS** | **551:2094** | **0.86** |



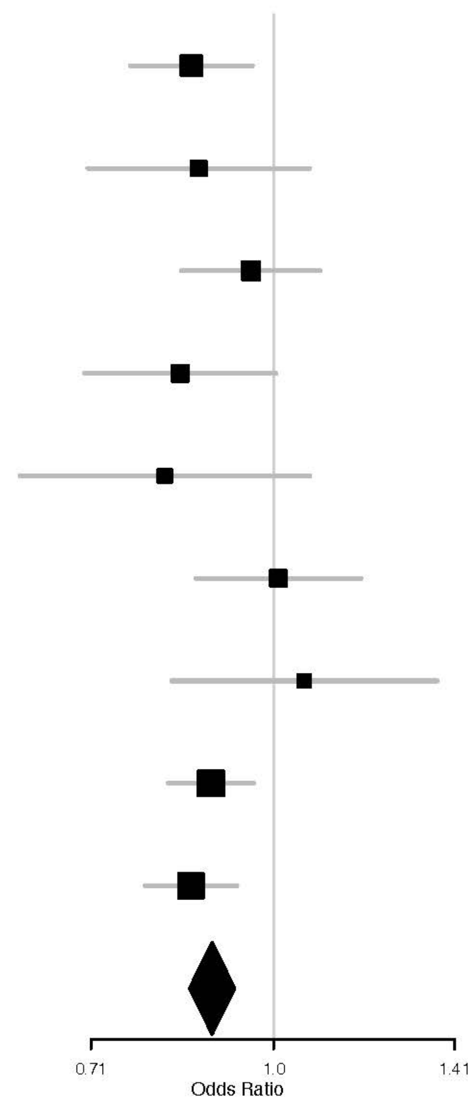

### cg06725287

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.81 |
| BAMSE_MEDALL | 47:167 | 0.77 |
| CHOP | 19:363 | 1.03 |
| GALA | 106:87 | 0.85 |
| ICAC | 97:97 | 0.87 |
| NFBC | 29:343 | 0.91 |
| PIAMA | 15:182 | 0.93 |
| RAINE | 114:405 | 0.93 |
| STOPPA | 137:323 | 0.85 |
| **META-ANALYSIS** | **657:2181** | **0.87** |



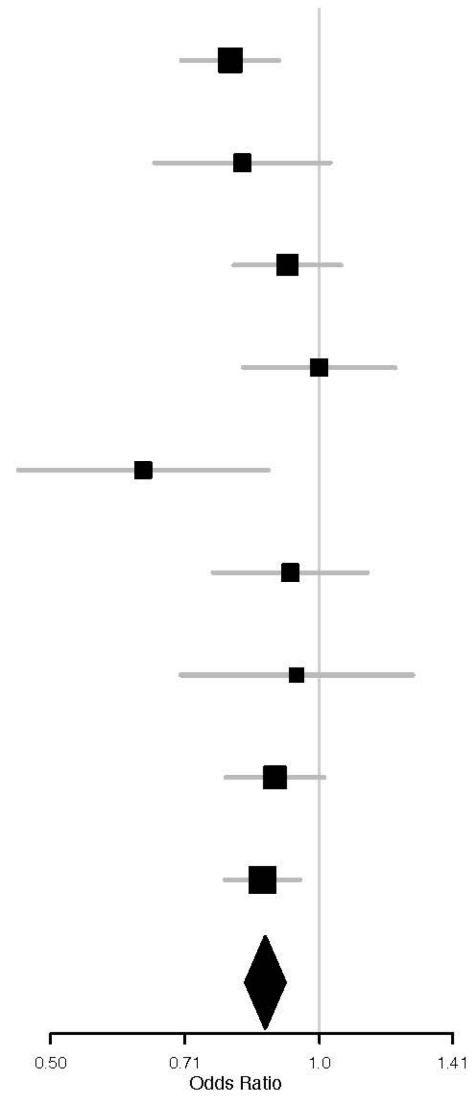

### cg04933530

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.86 |
| BAMSE_MEDALL | 47:167 | 0.87 |
| CHOP | 19:363 | 0.96 |
| GALA | 106:87 | 0.84 |
| ICAC | 97:97 | 0.81 |
| NFBC | 29:343 | 1.01 |
| PIAMA | 15:182 | 1.06 |
| RAINE | 114:405 | 0.89 |
| STOPPA | 137:323 | 0.85 |
| **META-ANALYSIS** | **657:2181** | **0.89** |



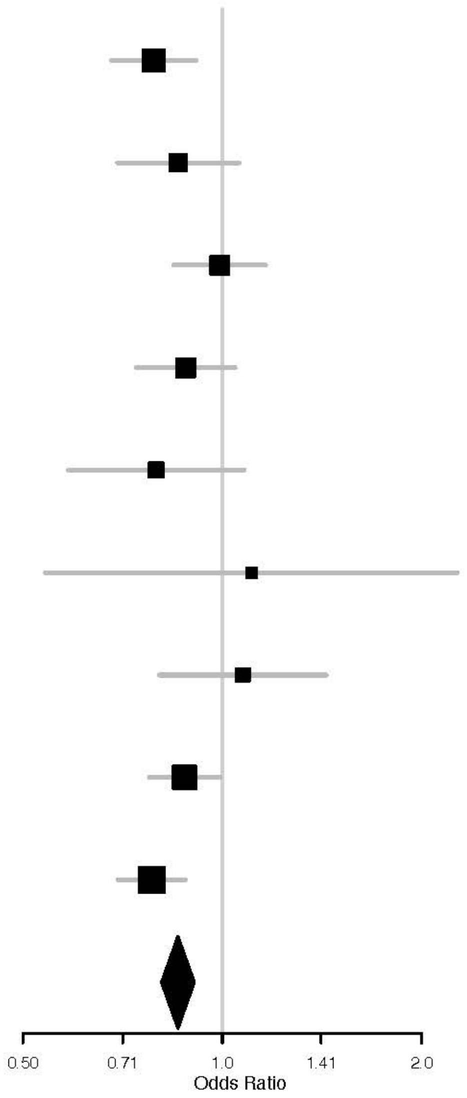
### cg03437605

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.79 |
| BAMSE_MEDALL | 47:167 | 0.82 |
| CHOP | 19:363 | 0.92 |
| GALA | 106:87 | 1.00 |
| ICAC | 97:97 | 0.64 |
| NFBC | 29:343 | 0.93 |
| PIAMA | 15:182 | 0.94 |
| RAINE | 114:405 | 0.89 |
| STOPPA | 137:323 | 0.86 |
| **META−ANALYSIS** | **657:2181** | **0.87** |



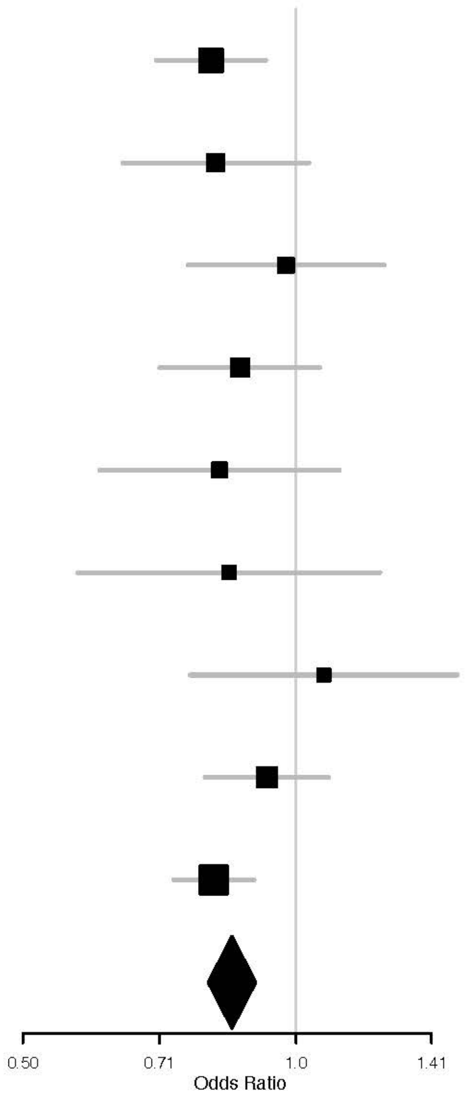

### cg12104982

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.79 |
| BAMSE_MEDALL | 47:167 | 0.86 |
| CHOP | 19:363 | 0.99 |
| GALA | 106:87 | 0.88 |
| ICAC | 97:97 | 0.79 |
| NFBC | 29:343 | 1.11 |
| PIAMA | 15:182 | 1.07 |
| RAINE | 114:405 | 0.88 |
| STOPPA | 137:323 | 0.78 |
| **META−ANALYSIS** | **657:2181** | **0.86** |



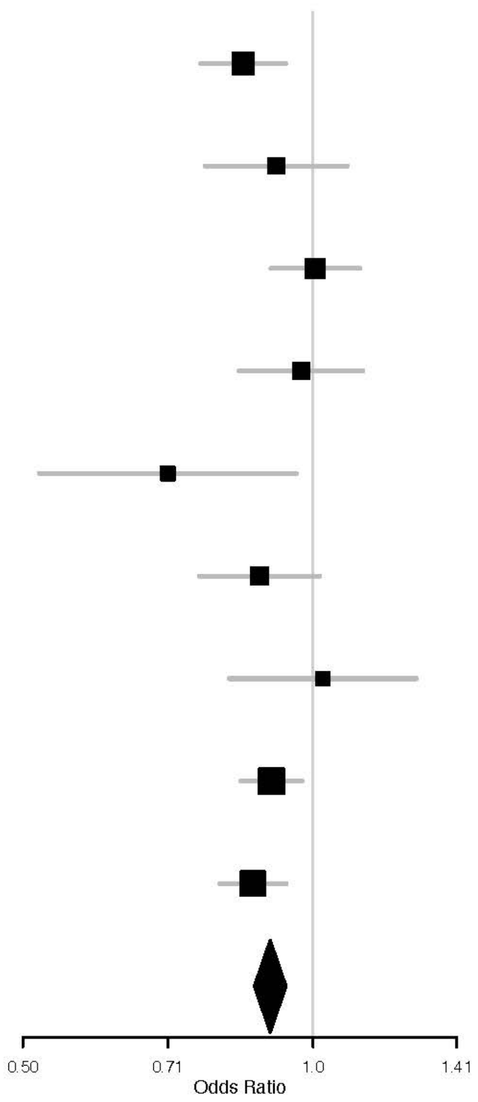

### cg08077807

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.81 |
| BAMSE_MEDALL | 47:167 | 0.82 |
| CHOP | 19:363 | 0.97 |
| GALA | 106:87 | 0.87 |
| ICAC | 97:97 | 0.82 |
| NFBC | 29:343 | 0.84 |
| PIAMA | 15:182 | 1.07 |
| RAINE | 114:405 | 0.93 |
| STOPPA | 137:323 | 0.81 |
| **META−ANALYSIS** | **657:2181** | **0.85** |



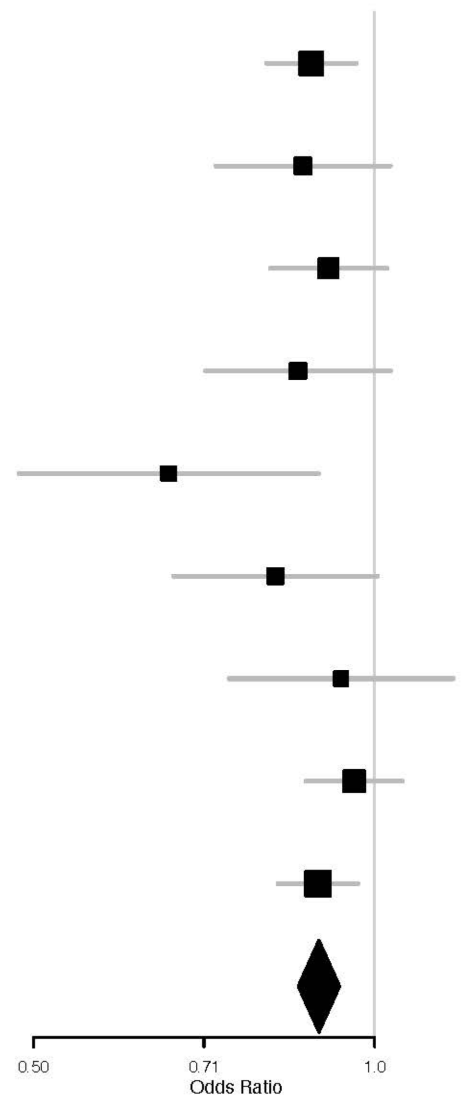

### cg10065736

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.85 |
| BAMSE_MEDALL | 47:167 | 0.92 |
| CHOP | 19:363 | 1.01 |
| GALA | 106:87 | 0.97 |
| ICAC | 97:97 | 0.71 |
| NFBC | 29:343 | 0.88 |
| PIAMA | 15:182 | 1.02 |
| RAINE | 114:405 | 0.91 |
| STOPPA | 137:323 | 0.87 |
| **META−ANALYSIS** | **657:2181** | **0.90** |



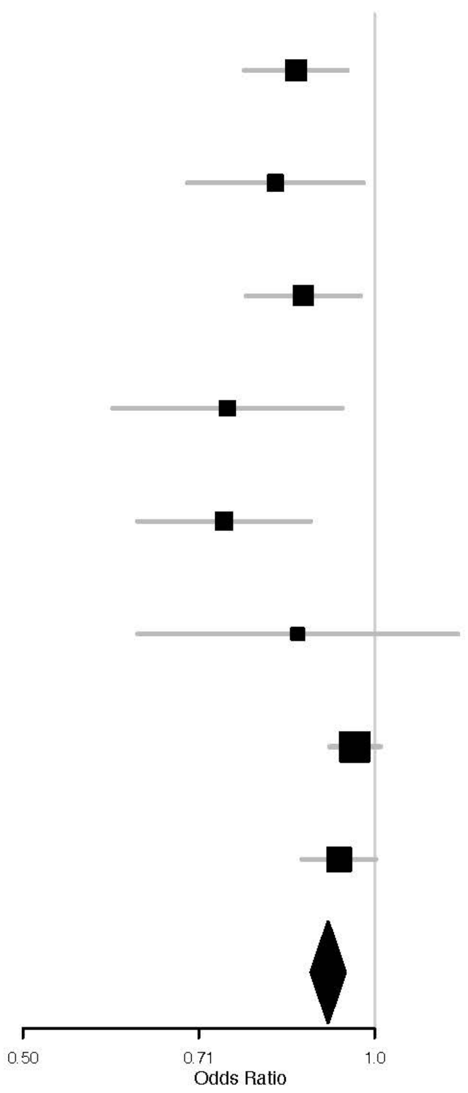

### cg18666454

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.88 |
| BAMSE_MEDALL | 47:167 | 0.86 |
| CHOP | 19:363 | 0.91 |
| GALA | 106:87 | 0.86 |
| ICAC | 97:97 | 0.66 |
| NFBC | 29:343 | 0.82 |
| PIAMA | 15:182 | 0.93 |
| RAINE | 114:405 | 0.96 |
| STOPPA | 137:323 | 0.89 |
| **META−ANALYSIS** | **657:2181** | **0.89** |



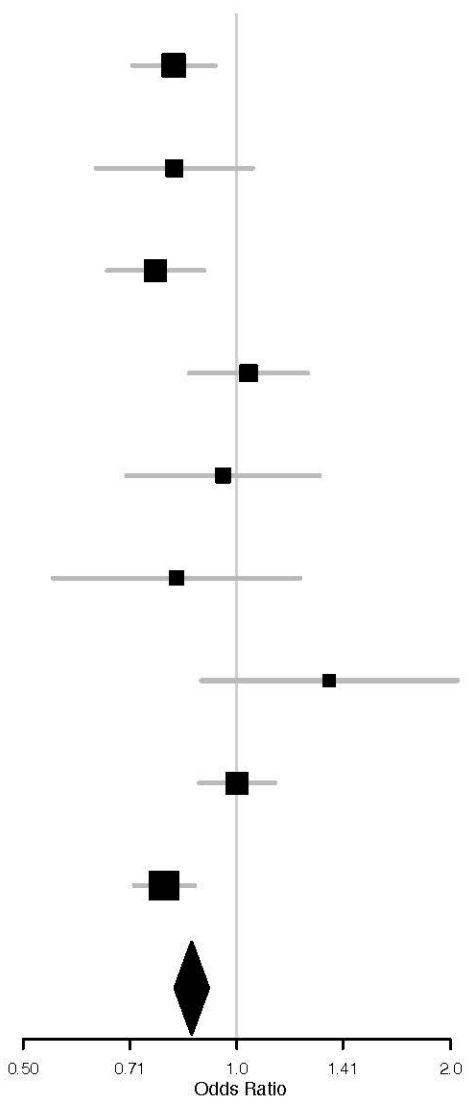

### cg09705784

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.86 |
| BAMSE_MEDALL | 47:167 | 0.82 |
| CHOP | 19:363 | 0.87 |
| ICAC | 97:97 | 0.75 |
| NFBC | 29:343 | 0.74 |
| PIAMA | 15:182 | 0.86 |
| RAINE | 114:405 | 0.96 |
| STOPPA | 137:323 | 0.93 |
| **META−ANALYSIS** | **551:2094** | **0.91** |



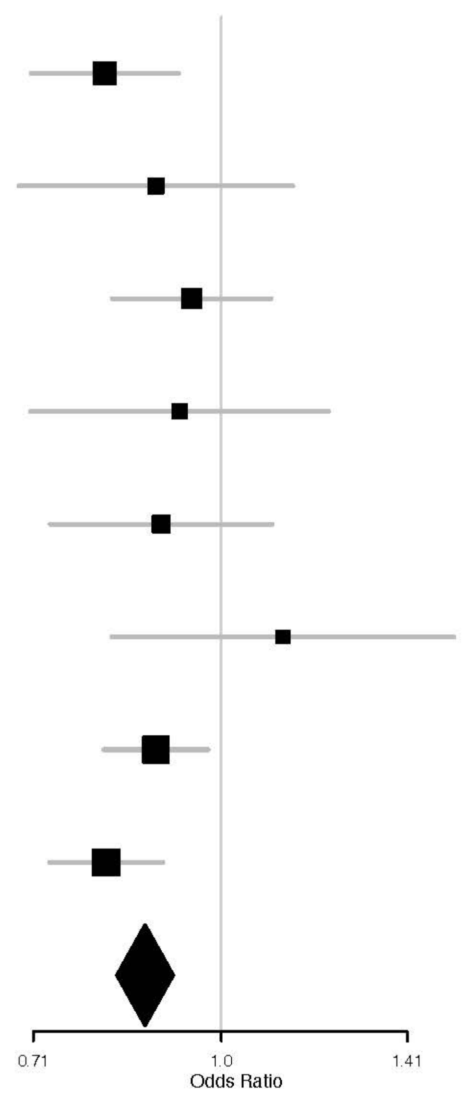

### cg02494549

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.82 |
| BAMSE_MEDALL | 47:167 | 0.82 |
| CHOP | 19:363 | 0.77 |
| GALA | 106:87 | 1.04 |
| ICAC | 97:97 | 0.96 |
| NFBC | 29:343 | 0.82 |
| PIAMA | 15:182 | 1.35 |
| RAINE | 114:405 | 1.00 |
| STOPPA | 137:323 | 0.79 |
| **META−ANALYSIS** | **657:2181** | **0.86** |



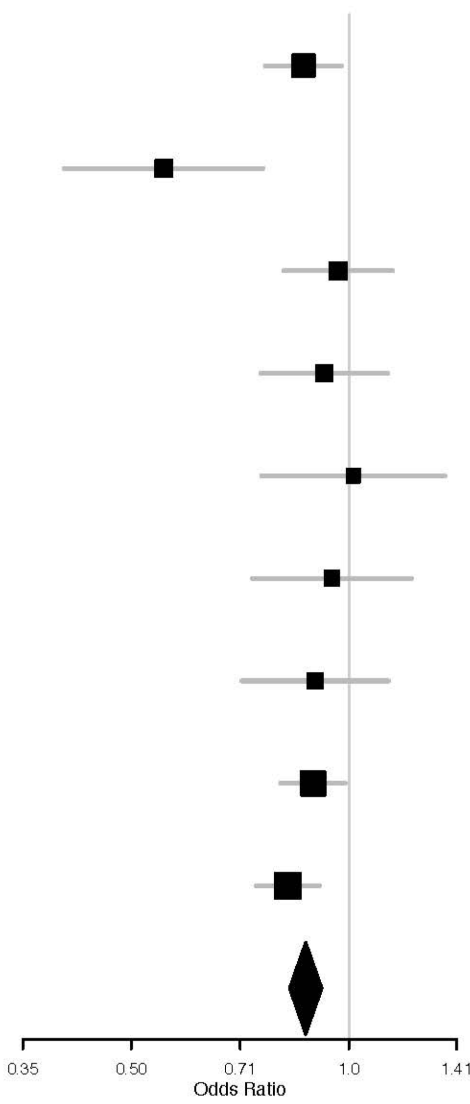

### cg21723861

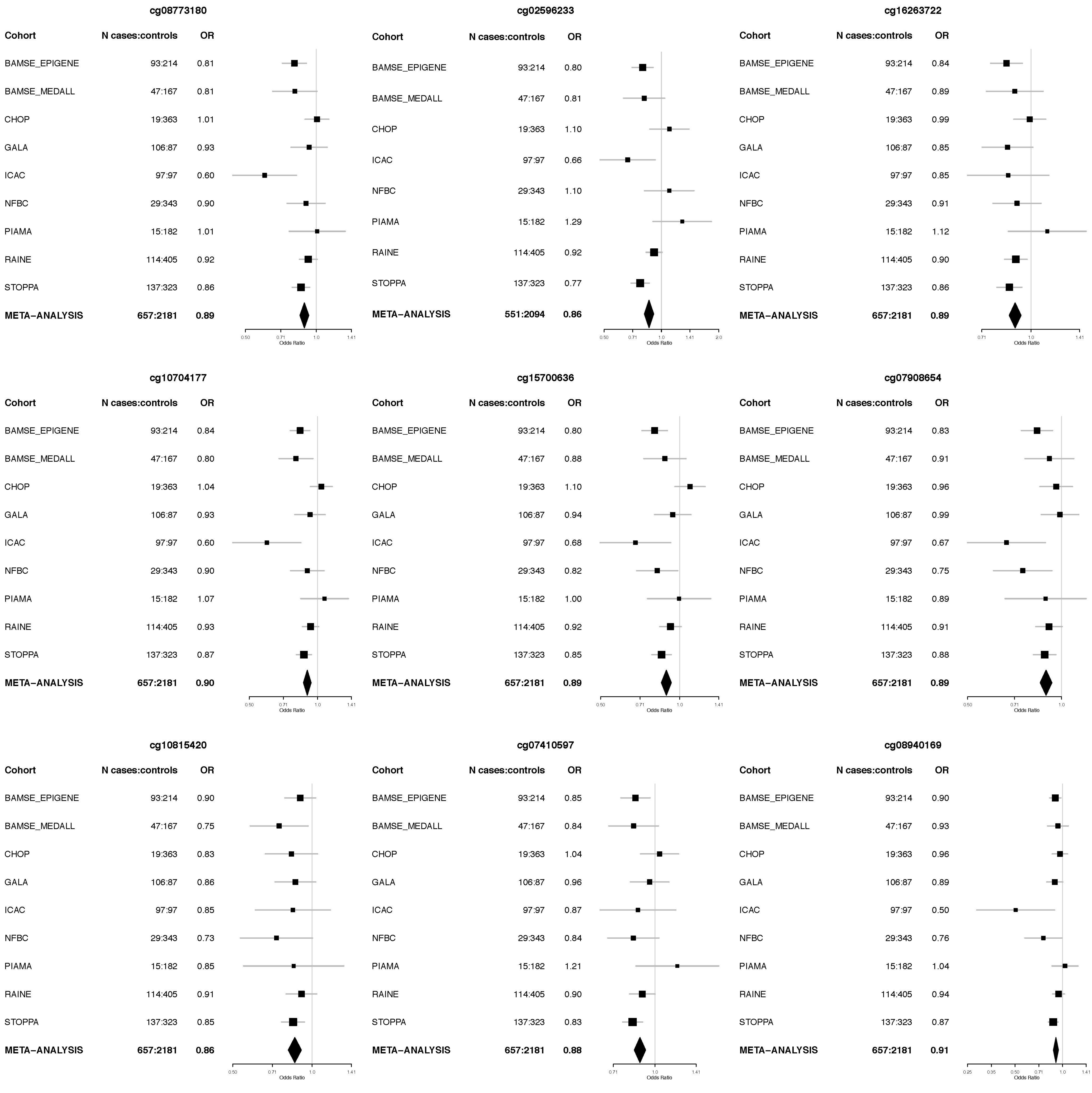
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.81 |
| BAMSE_MEDALL | 47:167 | 0.89 |
| CHOP | 19:363 | 0.95 |
| ICAC | 97:97 | 0.93 |
| NFBC | 29:343 | 0.90 |
| PIAMA | 15:182 | 1.12 |
| RAINE | 114:405 | 0.89 |
| STOPPA | 137:323 | 0.81 |
| **META−ANALYSIS** | **551:2094** | **0.87** |




### cg05875066

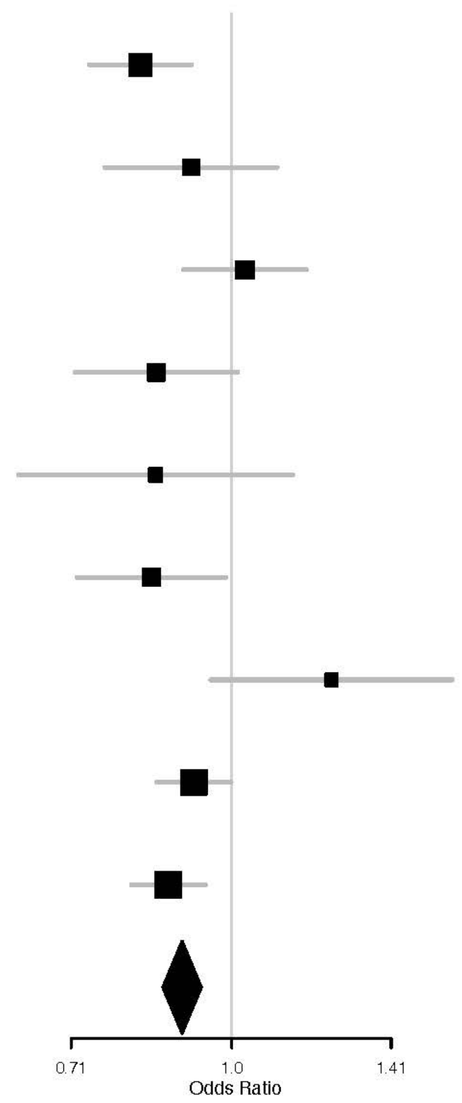
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.86 |
| BAMSE_MEDALL | 47:167 | 0.55 |
| CHOP | 19:363 | 0.97 |
| GALA | 106:87 | 0.92 |
| ICAC | 97:97 | 1.01 |
| NFBC | 29:343 | 0.95 |
| PIAMA | 15:182 | 0.90 |
| RAINE | 114:405 | 0.89 |
| STOPPA | 137:323 | 0.82 |
| **META−ANALYSIS** | **657:2181** | **0.87** |




cg08773180
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.81
BAMSE_MEDALL 47:167 0.81
CHOP 19:363 1.01
GALA 106:87 0.93
ICAC 97:97 0.60
NFBC 29:343 0.90
PIAMA 15:182 1.01
RAINE 114:405 0.92
STOPPA 137:323 0.86
META−ANALYSIS 657:2181 0.89
0.50 0.71 1.0 1.41
Odds Ratio
cg02596233
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.80
BAMSE_MEDALL 47:167 0.81
CHOP 19:363 1.10
ICAC 97:97 0.66
NFBC 29:343 1.10
PIAMA 15:182 1.29
RAINE 114:405 0.92
STOPPA 137:323 0.77
META−ANALYSIS 551:2094 0.86
0.50 0.71 1.0 1.41 2.0
Odds Ratio
cg16263722
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.89
CHOP 19:363 0.99
GALA 106:87 0.85
ICAC 97:97 0.85
NFBC 29:343 0.91
PIAMA 15:182 1.12
RAINE 114:405 0.90
STOPPA 137:323 0.86
META−ANALYSIS 657:2181 0.89
0.71 1.0 1.41
Odds Ratio
cg10704177
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.80
CHOP 19:363 1.04
GALA 106:87 0.93
ICAC 97:97 0.60
NFBC 29:343 0.90
PIAMA 15:182 1.07
RAINE 114:405 0.93
STOPPA 137:323 0.87
META−ANALYSIS 657:2181 0.90
0.50 0.71 1.0 1.41
Odds Ratio
cg15700636
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.80
BAMSE_MEDALL 47:167 0.88
CHOP 19:363 1.10
GALA 106:87 0.94
ICAC 97:97 0.68
NFBC 29:343 0.82
PIAMA 15:182 1.00
RAINE 114:405 0.92
STOPPA 137:323 0.85
META−ANALYSIS 657:2181 0.89
0.50 0.71 1.0 1.41
Odds Ratio
cg07908654
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.83
BAMSE_MEDALL 47:167 0.91
CHOP 19:363 0.96
GALA 106:87 0.99
ICAC 97:97 0.67
NFBC 29:343 0.75
PIAMA 15:182 0.89
RAINE 114:405 0.91
STOPPA 137:323 0.88
META−ANALYSIS 657:2181 0.89
0.50 0.71 1.0
Odds Ratio
cg10815420
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.90
BAMSE_MEDALL 47:167 0.75
CHOP 19:363 0.83
GALA 106:87 0.86
ICAC 97:97 0.85
NFBC 29:343 0.73
PIAMA 15:182 0.85
RAINE 114:405 0.91
STOPPA 137:323 0.85
META−ANALYSIS 657:2181 0.86
0.50 0.71 1.0 1.41
Odds Ratio
cg07410597
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.84
CHOP 19:363 1.04
GALA 106:87 0.96
ICAC 97:97 0.87
NFBC 29:343 0.84
PIAMA 15:182 1.21
RAINE 114:405 0.90
STOPPA 137:323 0.83
META−ANALYSIS 657:2181 0.88
0.71 1.0 1.41
Odds Ratio
cg08940169
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.90
BAMSE_MEDALL 47:167 0.93
CHOP 19:363 0.96
GALA 106:87 0.89
ICAC 97:97 0.50
NFBC 29:343 0.76
PIAMA 15:182 1.04
RAINE 114:405 0.94
STOPPA 137:323 0.87
META−ANALYSIS 657:2181 0.91
0.25 0.35 0.50 0.71 1.0 1.41
Odds Ratio

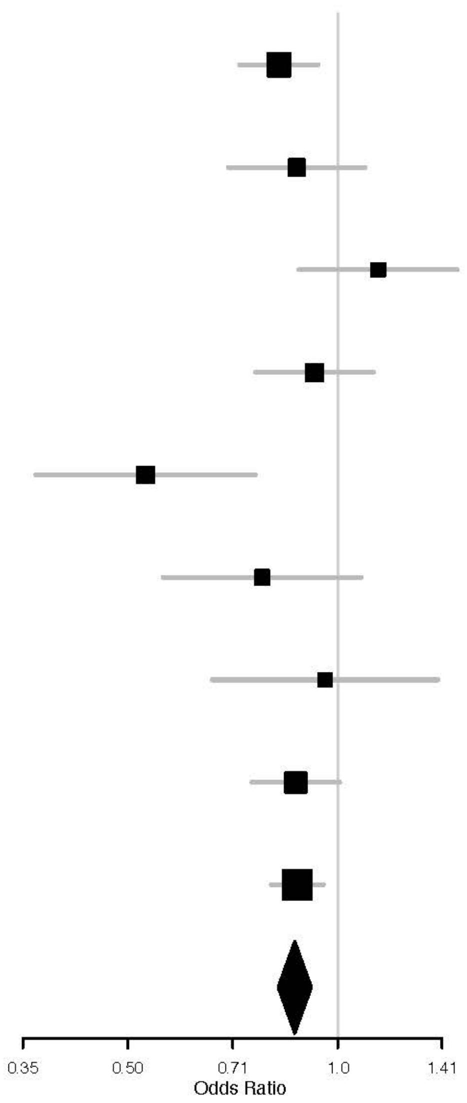
**cg00944309**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.82 |
| BAMSE_MEDALL | 47:167 | 0.92 |
| CHOP | 19:363 | 1.03 |
| GALA | 106:87 | 0.85 |
| ICAC | 97:97 | 0.85 |
| NFBC | 29:343 | 0.84 |
| PIAMA | 15:182 | 1.24 |
| RAINE | 114:405 | 0.92 |
| STOPPA | 137:323 | 0.87 |
| **META–ANALYSIS** | **657:2181** | **0.90** |



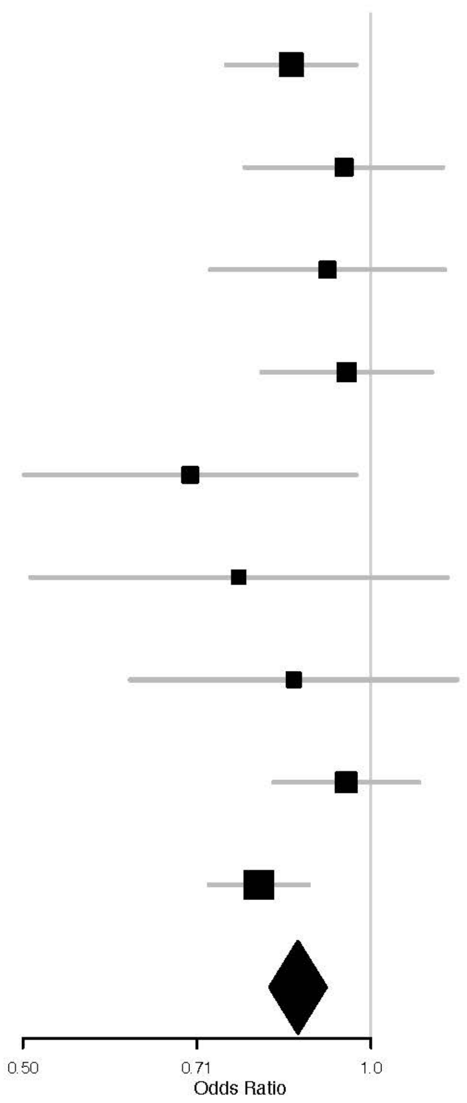

**cg20263733**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.82 |
| BAMSE_MEDALL | 47:167 | 0.87 |
| CHOP | 19:363 | 1.14 |
| GALA | 106:87 | 0.93 |
| ICAC | 97:97 | 0.53 |
| NFBC | 29:343 | 0.78 |
| PIAMA | 15:182 | 0.96 |
| RAINE | 114:405 | 0.87 |
| STOPPA | 137:323 | 0.87 |
| **META–ANALYSIS** | **657:2181** | **0.87** |



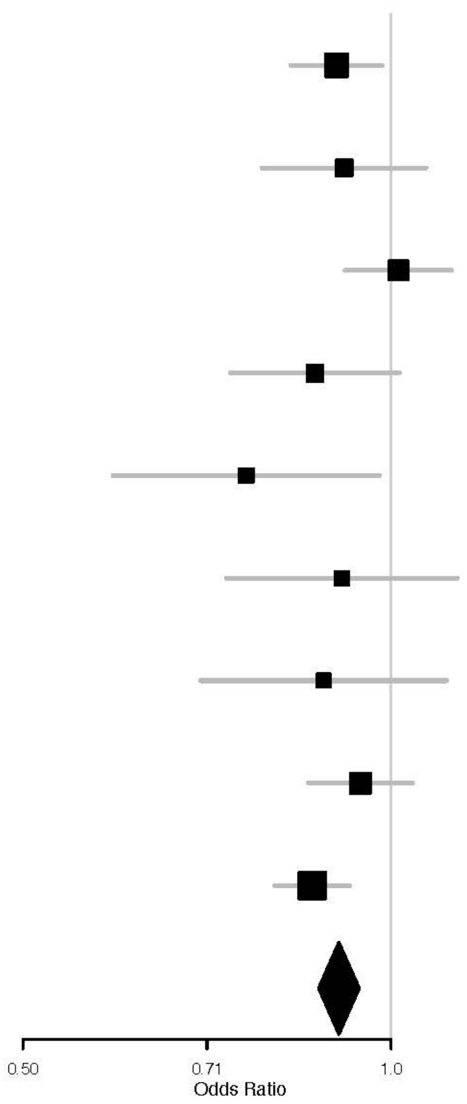

**cg25270424**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.85 |
| BAMSE_MEDALL | 47:167 | 0.95 |
| CHOP | 19:363 | 0.92 |
| GALA | 106:87 | 0.95 |
| ICAC | 97:97 | 0.70 |
| NFBC | 29:343 | 0.77 |
| PIAMA | 15:182 | 0.86 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.80 |
| **META–ANALYSIS** | **657:2181** | **0.86** |



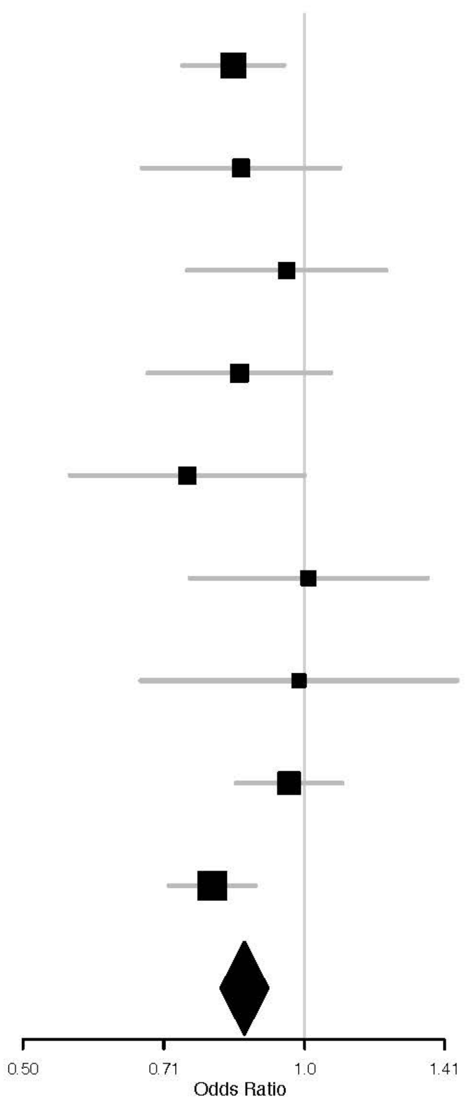

**cg16409452**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.92 |
| CHOP | 19:363 | 1.01 |
| GALA | 106:87 | 0.87 |
| ICAC | 97:97 | 0.76 |
| NFBC | 29:343 | 0.91 |
| PIAMA | 15:182 | 0.88 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.86 |
| **META–ANALYSIS** | **657:2181** | **0.91** |



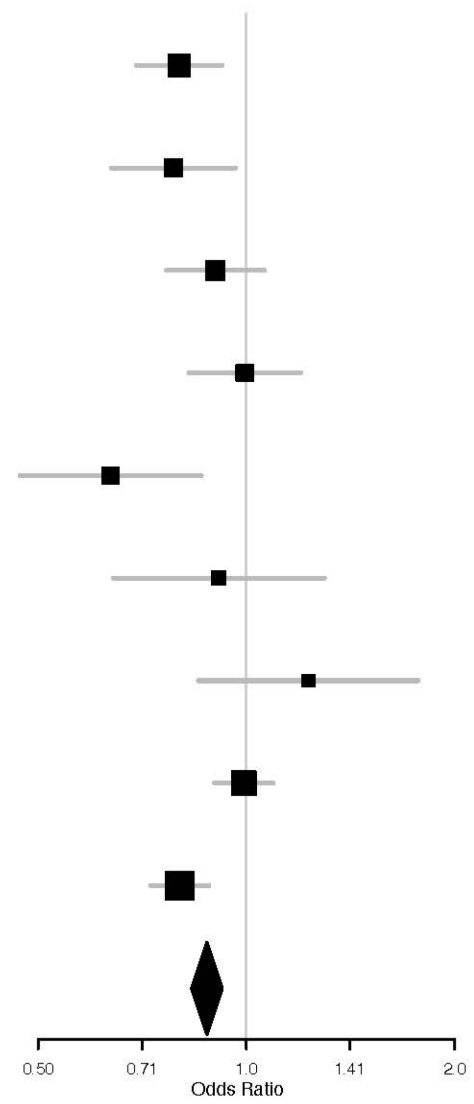

**cg04077085**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.84 |
| BAMSE_MEDALL | 47:167 | 0.86 |
| CHOP | 19:363 | 0.96 |
| GALA | 106:87 | 0.85 |
| ICAC | 97:97 | 0.75 |
| NFBC | 29:343 | 1.01 |
| PIAMA | 15:182 | 0.99 |
| RAINE | 114:405 | 0.96 |
| STOPPA | 137:323 | 0.80 |
| **META–ANALYSIS** | **657:2181** | **0.86** |



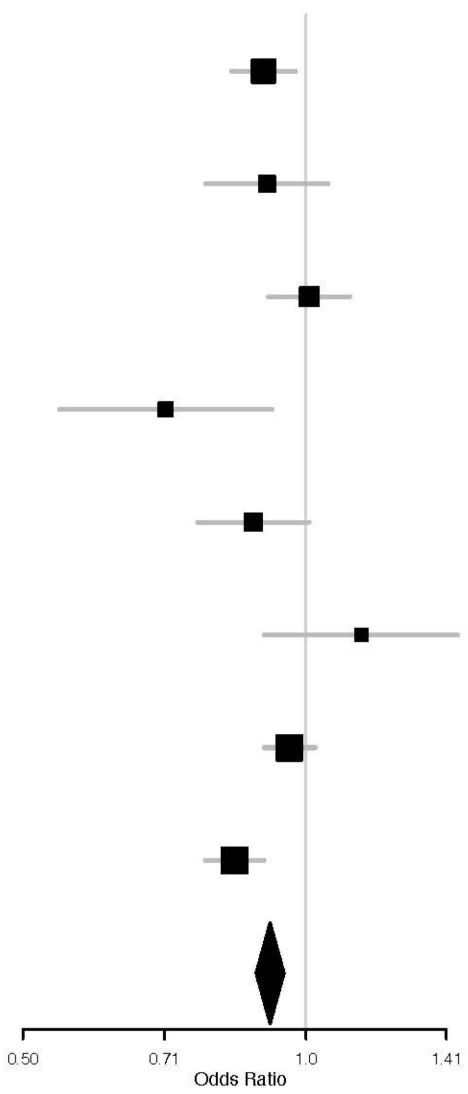

**cg05477517**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.80 |
| BAMSE_MEDALL | 47:167 | 0.78 |
| CHOP | 19:363 | 0.90 |
| GALA | 106:87 | 0.99 |
| ICAC | 97:97 | 0.64 |
| NFBC | 29:343 | 0.91 |
| PIAMA | 15:182 | 1.23 |
| RAINE | 114:405 | 0.99 |
| STOPPA | 137:323 | 0.80 |
| **META–ANALYSIS** | **657:2181** | **0.88** |



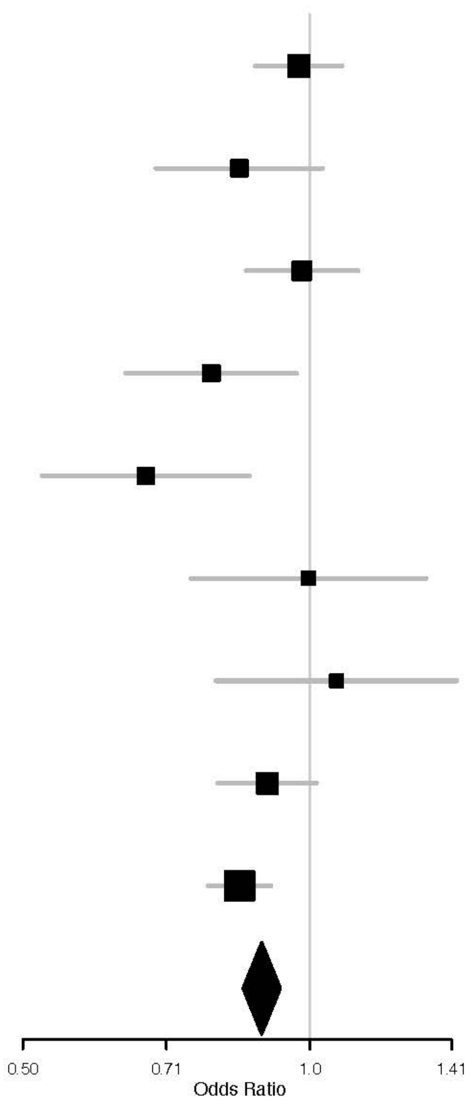

**cg23706836**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.91 |
| CHOP | 19:363 | 1.01 |
| ICAC | 97:97 | 0.71 |
| NFBC | 29:343 | 0.88 |
| PIAMA | 15:182 | 1.14 |
| RAINE | 114:405 | 0.96 |
| STOPPA | 137:323 | 0.84 |
| **META–ANALYSIS** | **551:2094** | **0.92** |



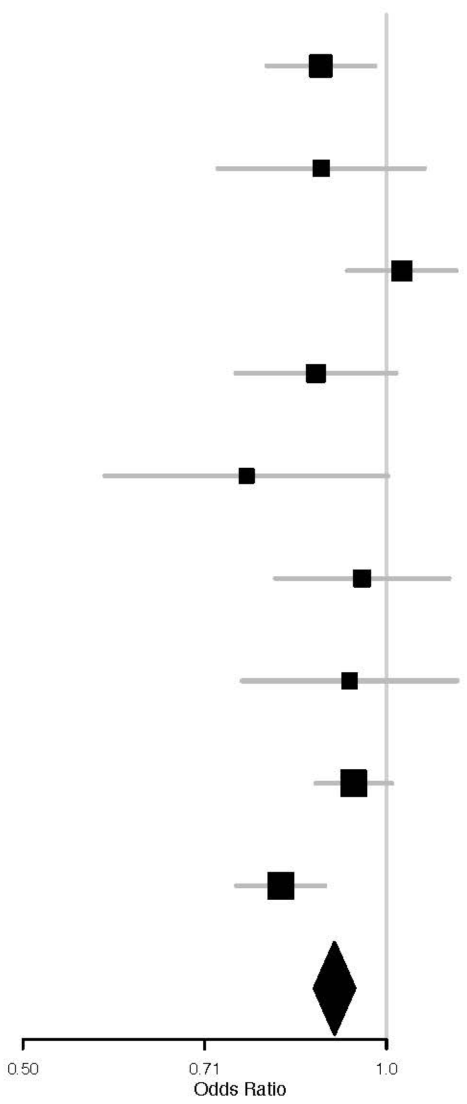

**cg18460809**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.97 |
| BAMSE_MEDALL | 47:167 | 0.84 |
| CHOP | 19:363 | 0.98 |
| GALA | 106:87 | 0.79 |
| ICAC | 97:97 | 0.67 |
| NFBC | 29:343 | 1.00 |
| PIAMA | 15:182 | 1.07 |
| RAINE | 114:405 | 0.90 |
| STOPPA | 137:323 | 0.84 |
| **META–ANALYSIS** | **657:2181** | **0.89** |



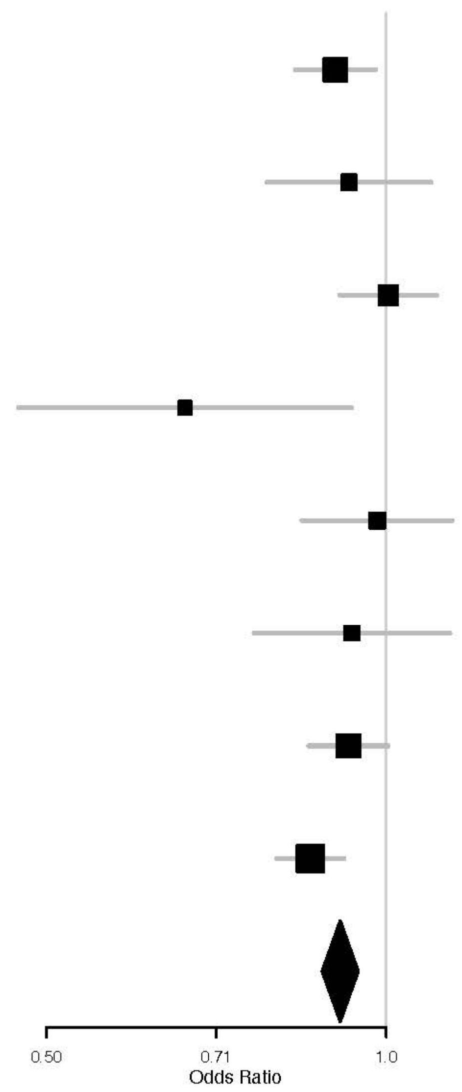

**cg01998785**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.88 |
| BAMSE_MEDALL | 47:167 | 0.88 |
| CHOP | 19:363 | 1.03 |
| GALA | 106:87 | 0.87 |
| ICAC | 97:97 | 0.77 |
| NFBC | 29:343 | 0.95 |
| PIAMA | 15:182 | 0.93 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.82 |
| **META–ANALYSIS** | **657:2181** | **0.91** |



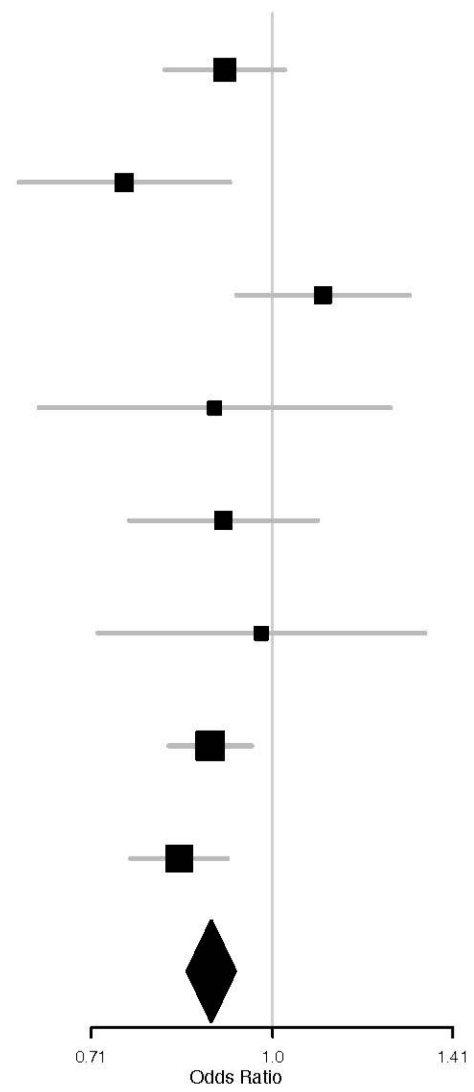
**cg18550847**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.93 |
| CHOP | 19:363 | 1.00 |
| ICAC | 97:97 | 0.66 |
| NFBC | 29:343 | 0.98 |
| PIAMA | 15:182 | 0.93 |
| RAINE | 114:405 | 0.93 |
| STOPPA | 137:323 | 0.86 |
| **META−ANALYSIS** | **551:2094** | **0.91** |



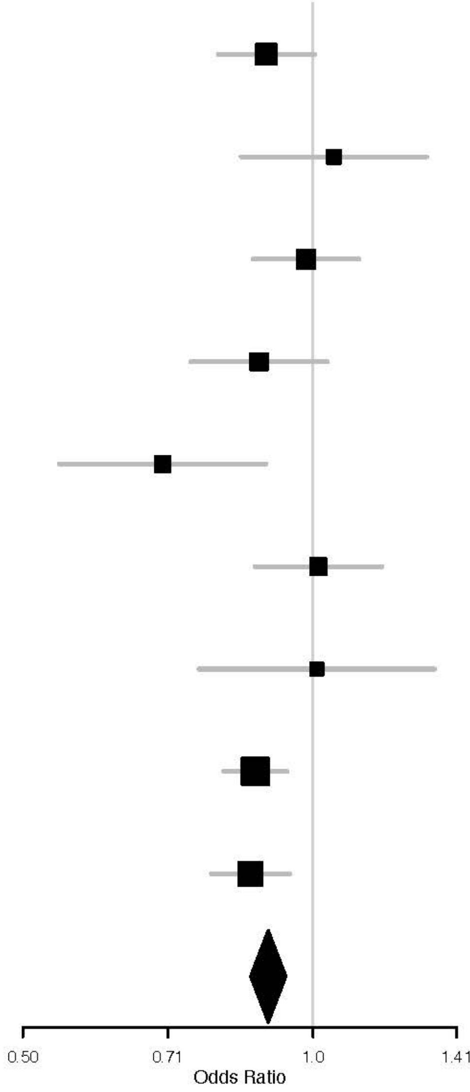

**cg03131767**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.91 |
| BAMSE_MEDALL | 47:167 | 0.75 |
| CHOP | 19:363 | 1.10 |
| ICAC | 97:97 | 0.90 |
| NFBC | 29:343 | 0.91 |
| PIAMA | 15:182 | 0.98 |
| RAINE | 114:405 | 0.89 |
| STOPPA | 137:323 | 0.84 |
| **META−ANALYSIS** | **551:2094** | **0.89** |



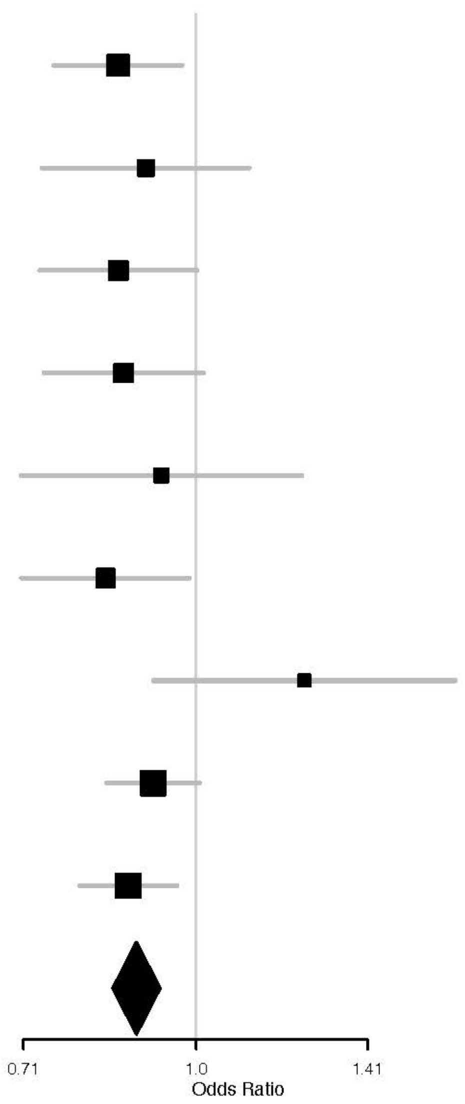

**cg02435538**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.89 |
| BAMSE_MEDALL | 47:167 | 1.05 |
| CHOP | 19:363 | 0.98 |
| GALA | 106:87 | 0.88 |
| ICAC | 97:97 | 0.70 |
| NFBC | 29:343 | 1.01 |
| PIAMA | 15:182 | 1.01 |
| RAINE | 114:405 | 0.87 |
| STOPPA | 137:323 | 0.86 |
| **META−ANALYSIS** | **657:2181** | **0.90** |



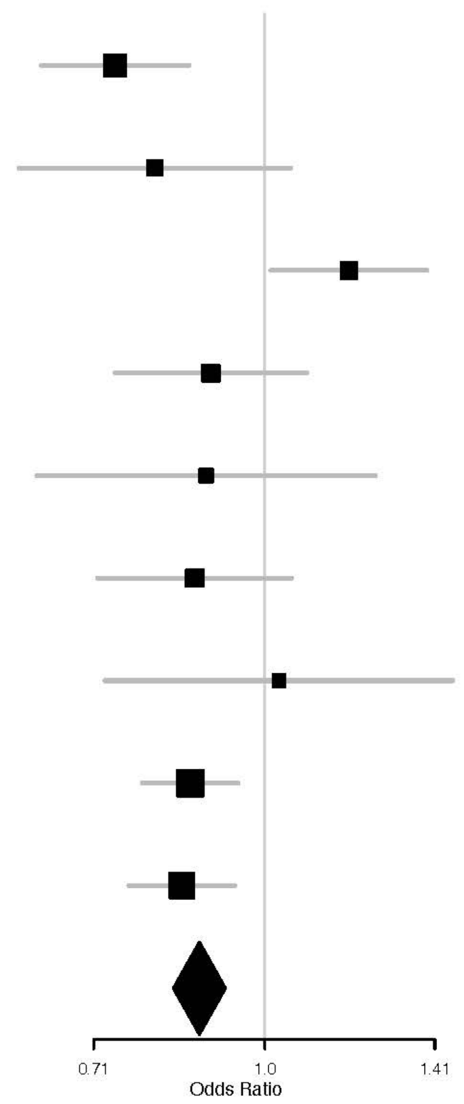

**cg11987455**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.86 |
| BAMSE_MEDALL | 47:167 | 0.90 |
| CHOP | 19:363 | 0.86 |
| GALA | 106:87 | 0.86 |
| ICAC | 97:97 | 0.93 |
| NFBC | 29:343 | 0.83 |
| PIAMA | 15:182 | 1.24 |
| RAINE | 114:405 | 0.92 |
| STOPPA | 137:323 | 0.87 |
| **META−ANALYSIS** | **657:2181** | **0.89** |



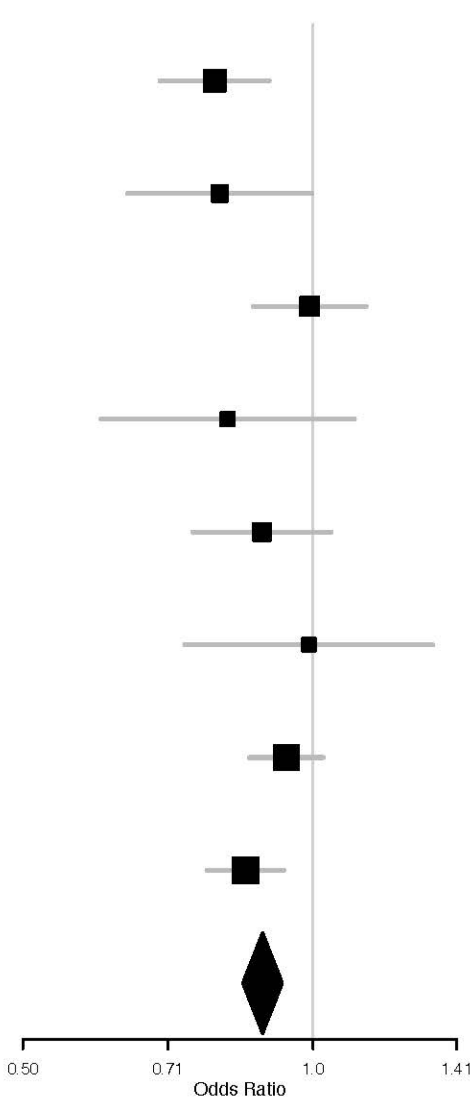

**cg09447105**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.74 |
| BAMSE_MEDALL | 47:167 | 0.80 |
| CHOP | 19:363 | 1.19 |
| GALA | 106:87 | 0.90 |
| ICAC | 97:97 | 0.89 |
| NFBC | 29:343 | 0.87 |
| PIAMA | 15:182 | 1.03 |
| RAINE | 114:405 | 0.86 |
| STOPPA | 137:323 | 0.85 |
| **META−ANALYSIS** | **657:2181** | **0.88** |



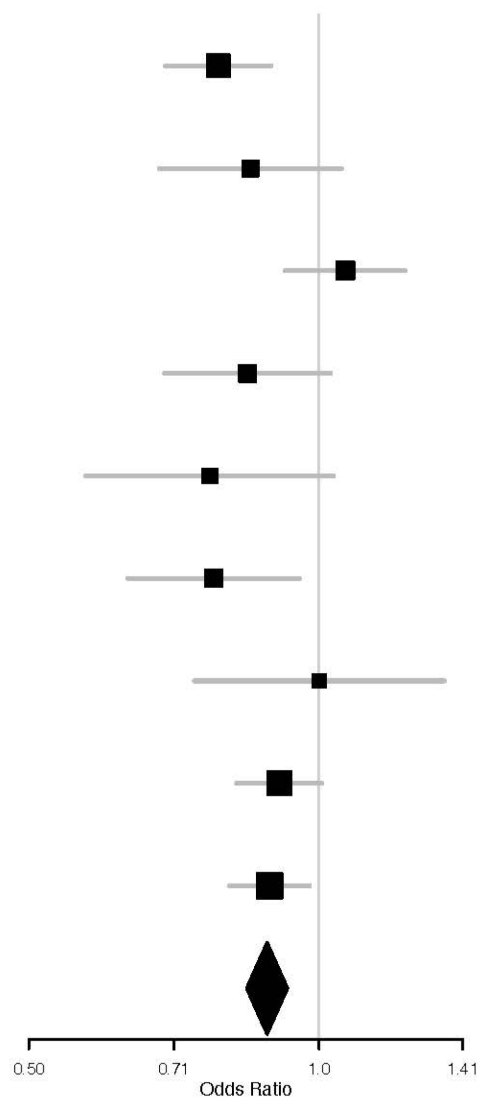

**cg13628444**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.79 |
| BAMSE_MEDALL | 47:167 | 0.80 |
| CHOP | 19:363 | 0.99 |
| ICAC | 97:97 | 0.82 |
| NFBC | 29:343 | 0.89 |
| PIAMA | 15:182 | 0.99 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.85 |
| **META−ANALYSIS** | **551:2094** | **0.89** |



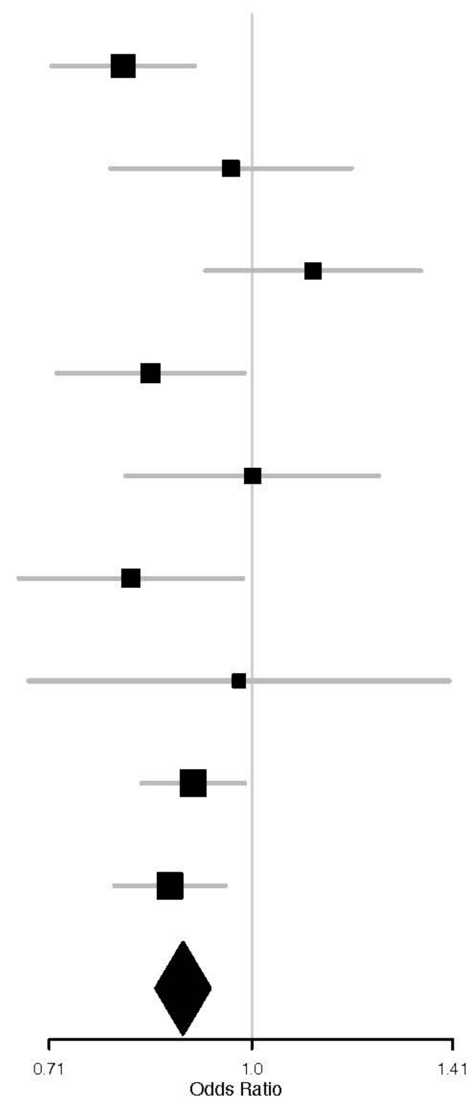

**cg25173129**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.79 |
| BAMSE_MEDALL | 47:167 | 0.85 |
| CHOP | 19:363 | 1.06 |
| GALA | 106:87 | 0.84 |
| ICAC | 97:97 | 0.77 |
| NFBC | 29:343 | 0.78 |
| PIAMA | 15:182 | 1.00 |
| RAINE | 114:405 | 0.91 |
| STOPPA | 137:323 | 0.89 |
| **META−ANALYSIS** | **657:2181** | **0.88** |



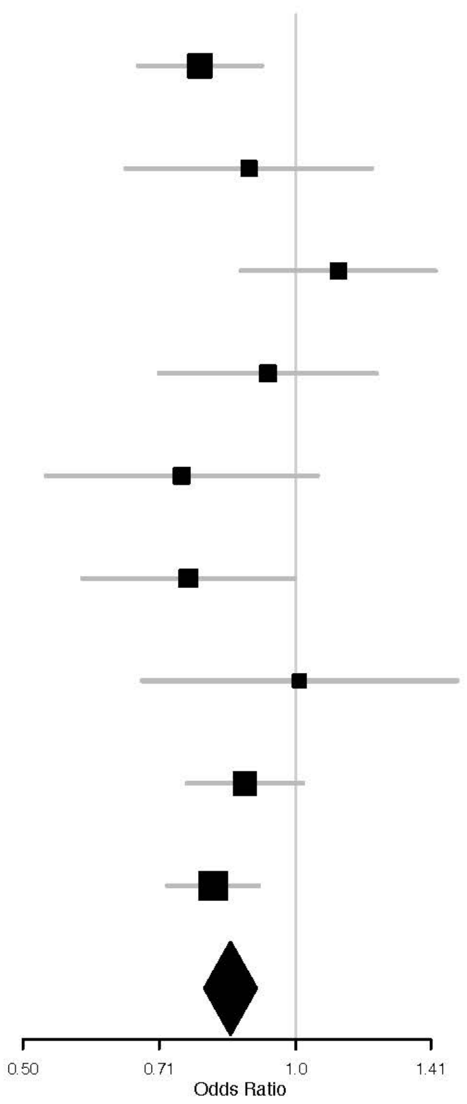

**cg14025883**

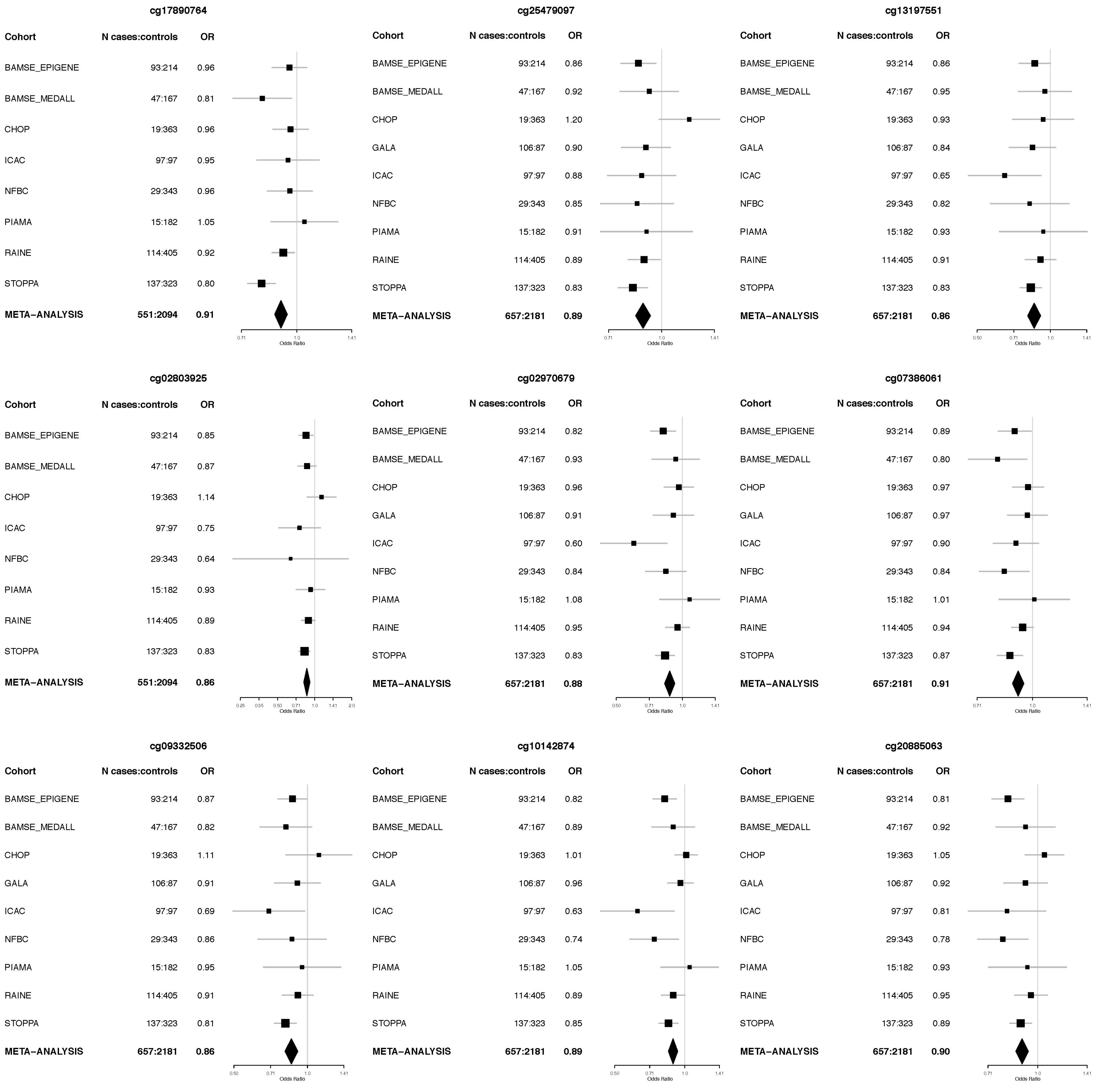
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.80 |
| BAMSE_MEDALL | 47:167 | 0.97 |
| CHOP | 19:363 | 1.11 |
| GALA | 106:87 | 0.84 |
| ICAC | 97:97 | 1.00 |
| NFBC | 29:343 | 0.81 |
| PIAMA | 15:182 | 0.98 |
| RAINE | 114:405 | 0.90 |
| STOPPA | 137:323 | 0.87 |
| **META−ANALYSIS** | **657:2181** | **0.89** |

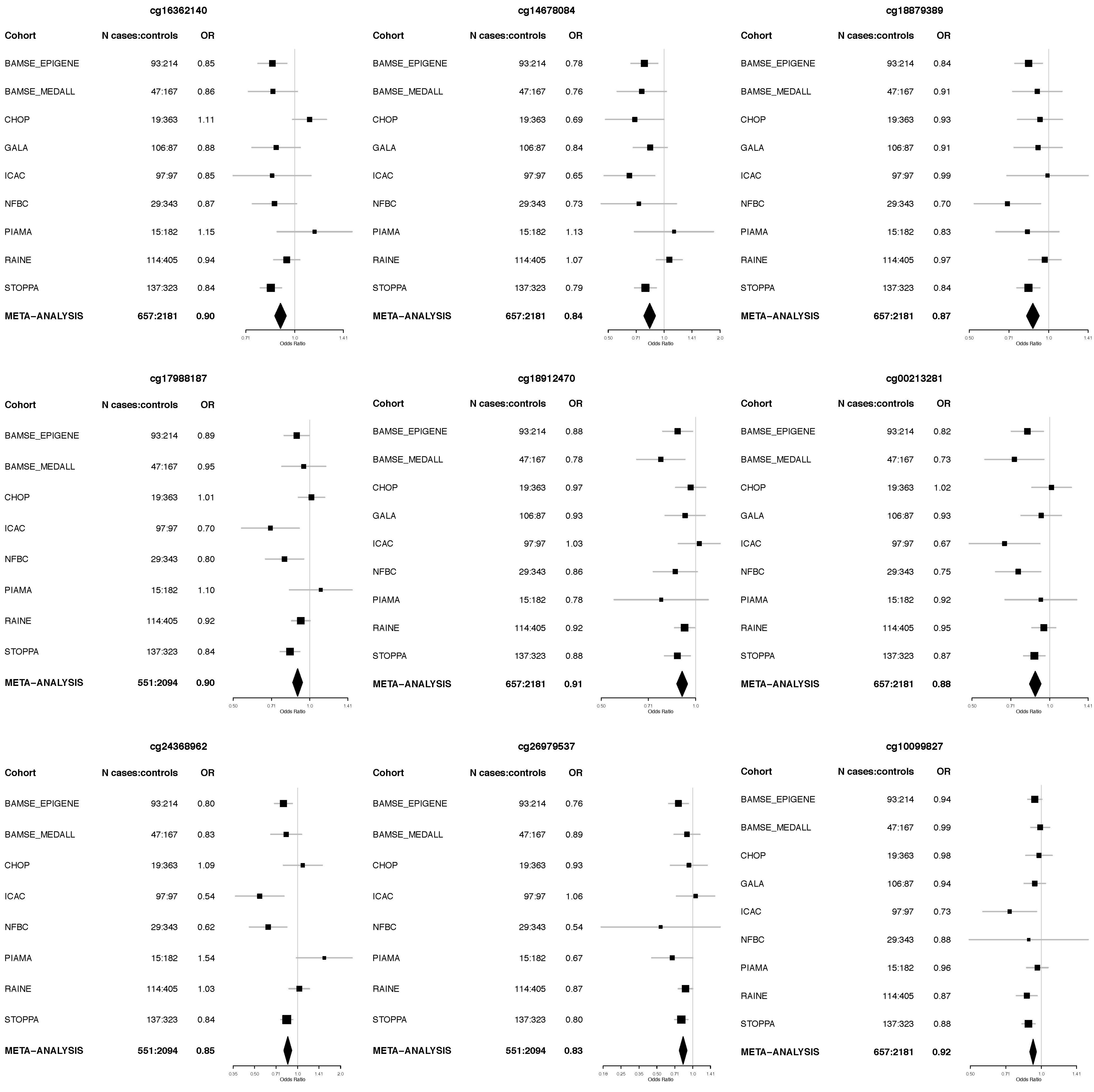



**cg02133716**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.78 |
| BAMSE_MEDALL | 47:167 | 0.89 |
| CHOP | 19:363 | 1.11 |
| GALA | 106:87 | 0.93 |
| ICAC | 97:97 | 0.75 |
| NFBC | 29:343 | 0.76 |
| PIAMA | 15:182 | 1.01 |
| RAINE | 114:405 | 0.88 |
| STOPPA | 137:323 | 0.81 |
| **META−ANALYSIS** | **657:2181** | **0.85** |

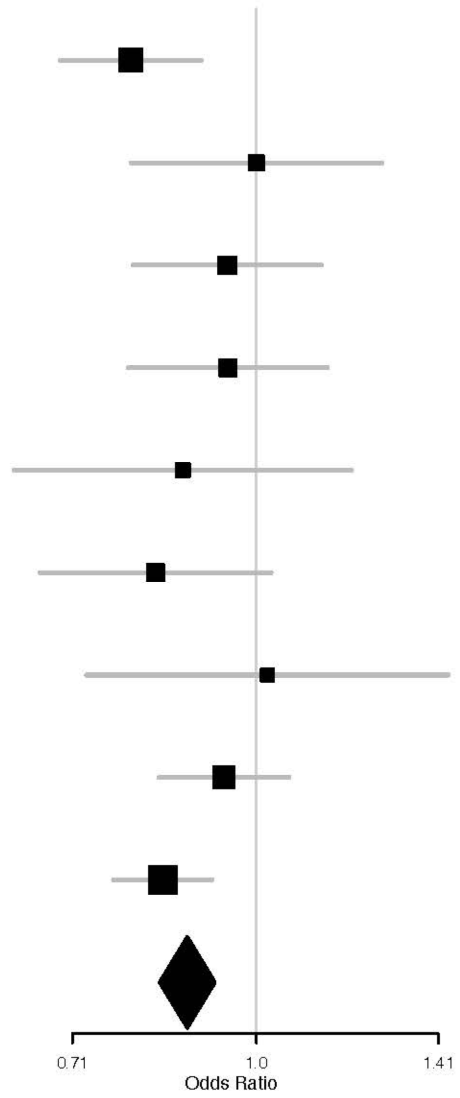



cg17890764
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.96
BAMSE_MEDALL 47:167 0.81
CHOP 19:363 0.96
ICAC 97:97 0.95
NFBC 29:343 0.96
PIAMA 15:182 1.05
RAINE 114:405 0.92
STOPPA 137:323 0.80
META-ANALYSIS 551:2094 0.91
Odds Ratio
cg25479097
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.92
CHOP 19:363 1.20
GALA 106:87 0.90
ICAC 97:97 0.88
NFBC 29:343 0.85
PIAMA 15:182 0.91
RAINE 114:405 0.89
STOPPA 137:323 0.83
META-ANALYSIS 657:2181 0.89
Odds Ratio
cg13197551
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.95
CHOP 19:363 0.93
GALA 106:87 0.84
ICAC 97:97 0.65
NFBC 29:343 0.82
PIAMA 15:182 0.93
RAINE 114:405 0.91
STOPPA 137:323 0.83
META-ANALYSIS 657:2181 0.86
Odds Ratio
cg02803925
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.87
CHOP 19:363 1.14
ICAC 97:97 0.75
NFBC 29:343 0.64
PIAMA 15:182 0.93
RAINE 114:405 0.89
STOPPA 137:323 0.83
META-ANALYSIS 551:2094 0.86
Odds Ratio
cg02970679
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.82
BAMSE_MEDALL 47:167 0.93
CHOP 19:363 0.96
GALA 106:87 0.91
ICAC 97:97 0.60
NFBC 29:343 0.84
PIAMA 15:182 1.08
RAINE 114:405 0.95
STOPPA 137:323 0.83
META-ANALYSIS 657:2181 0.88
Odds Ratio
cg07386061
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.89
BAMSE_MEDALL 47:167 0.80
CHOP 19:363 0.97
GALA 106:87 0.97
ICAC 97:97 0.90
NFBC 29:343 0.84
PIAMA 15:182 1.01
RAINE 114:405 0.94
STOPPA 137:323 0.87
META-ANALYSIS 657:2181 0.91
Odds Ratio
cg09332506
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.87
BAMSE_MEDALL 47:167 0.82
CHOP 19:363 1.11
GALA 106:87 0.91
ICAC 97:97 0.69
NFBC 29:343 0.86
PIAMA 15:182 0.95
RAINE 114:405 0.91
STOPPA 137:323 0.81
META-ANALYSIS 657:2181 0.86
Odds Ratio
cg10142874
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.82
BAMSE_MEDALL 47:167 0.89
CHOP 19:363 1.01
GALA 106:87 0.96
ICAC 97:97 0.63
NFBC 29:343 0.74
PIAMA 15:182 1.05
RAINE 114:405 0.89
STOPPA 137:323 0.85
META-ANALYSIS 657:2181 0.89
Odds Ratio
cg20885063
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.81
BAMSE_MEDALL 47:167 0.92
CHOP 19:363 1.05
GALA 106:87 0.92
ICAC 97:97 0.81
NFBC 29:343 0.78
PIAMA 15:182 0.93
RAINE 114:405 0.95
STOPPA 137:323 0.89
META-ANALYSIS 657:2181 0.90
Odds Ratio


cg16362140
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.86
CHOP 19:363 1.11
GALA 106:87 0.88
ICAC 97:97 0.85
NFBC 29:343 0.87
PIAMA 15:182 1.15
RAINE 114:405 0.94
STOPPA 137:323 0.84
META−ANALYSIS 657:2181 0.90
0.71 1.0 1.41
Odds Ratio
cg14678084
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.78
BAMSE_MEDALL 47:167 0.76
CHOP 19:363 0.69
GALA 106:87 0.84
ICAC 97:97 0.65
NFBC 29:343 0.73
PIAMA 15:182 1.13
RAINE 114:405 1.07
STOPPA 137:323 0.79
META−ANALYSIS 657:2181 0.84
0.50 0.71 1.0 1.41 2.0
Odds Ratio
cg18879389
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.91
CHOP 19:363 0.93
GALA 106:87 0.91
ICAC 97:97 0.99
NFBC 29:343 0.70
PIAMA 15:182 0.83
RAINE 114:405 0.97
STOPPA 137:323 0.84
META−ANALYSIS 657:2181 0.87
0.50 0.71 1.0 1.41
Odds Ratio
cg17988187
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.89
BAMSE_MEDALL 47:167 0.95
CHOP 19:363 1.01
ICAC 97:97 0.70
NFBC 29:343 0.80
PIAMA 15:182 1.10
RAINE 114:405 0.92
STOPPA 137:323 0.84
META−ANALYSIS 551:2094 0.90
0.50 0.71 1.0 1.41
Odds Ratio
cg18912470
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.88
BAMSE_MEDALL 47:167 0.78
CHOP 19:363 0.97
GALA 106:87 0.93
ICAC 97:97 1.03
NFBC 29:343 0.86
PIAMA 15:182 0.78
RAINE 114:405 0.92
STOPPA 137:323 0.88
META−ANALYSIS 657:2181 0.91
0.50 0.71 1.0
Odds Ratio
cg00213281
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.82
BAMSE_MEDALL 47:167 0.73
CHOP 19:363 1.02
GALA 106:87 0.93
ICAC 97:97 0.67
NFBC 29:343 0.75
PIAMA 15:182 0.92
RAINE 114:405 0.95
STOPPA 137:323 0.87
META−ANALYSIS 657:2181 0.88
0.50 0.71 1.0 1.41
Odds Ratio
cg24368962
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.80
BAMSE_MEDALL 47:167 0.83
CHOP 19:363 1.09
ICAC 97:97 0.54
NFBC 29:343 0.62
PIAMA 15:182 1.54
RAINE 114:405 1.03
STOPPA 137:323 0.84
META−ANALYSIS 551:2094 0.85
0.35 0.50 0.71 1.0 1.41 2.0
Odds Ratio
cg26979537
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.76
BAMSE_MEDALL 47:167 0.89
CHOP 19:363 0.93
ICAC 97:97 1.06
NFBC 29:343 0.54
PIAMA 15:182 0.67
RAINE 114:405 0.87
STOPPA 137:323 0.80
META−ANALYSIS 551:2094 0.83
0.18 0.25 0.35 0.50 0.71 1.0 1.41
Odds Ratio
cg10099827
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.94
BAMSE_MEDALL 47:167 0.99
CHOP 19:363 0.98
GALA 106:87 0.94
ICAC 97:97 0.73
NFBC 29:343 0.88
PIAMA 15:182 0.96
RAINE 114:405 0.87
STOPPA 137:323 0.88
META−ANALYSIS 657:2181 0.92
0.50 0.71 1.0 1.41
Odds Ratio

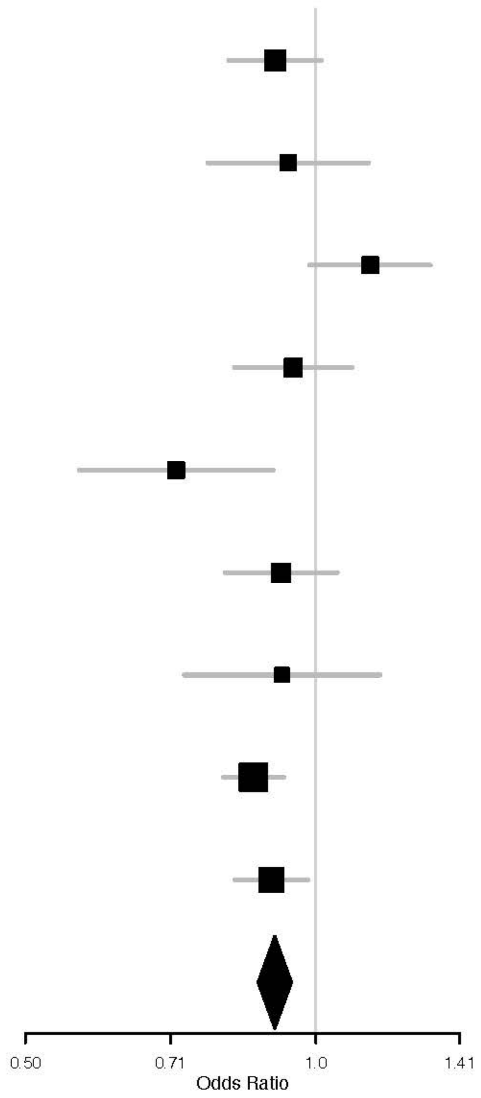
**cg01942646**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.79 |
| BAMSE_MEDALL | 47:167 | 1.00 |
| CHOP | 19:363 | 0.95 |
| GALA | 106:87 | 0.95 |
| ICAC | 97:97 | 0.87 |
| NFBC | 29:343 | 0.83 |
| PIAMA | 15:182 | 1.02 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.84 |
| **META−ANALYSIS** | **657:2181** | **0.88** |



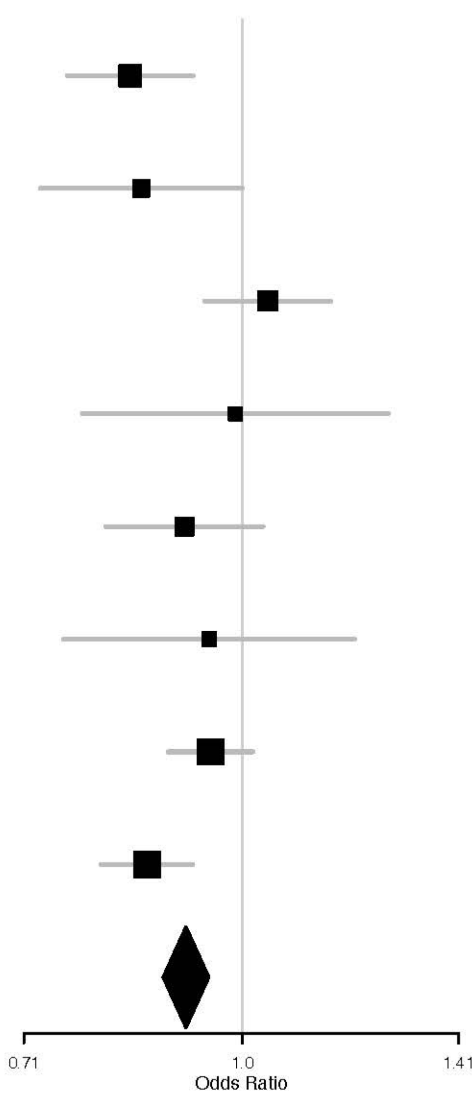

**cg23387863**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.91 |
| BAMSE_MEDALL | 47:167 | 0.94 |
| CHOP | 19:363 | 1.14 |
| GALA | 106:87 | 0.95 |
| ICAC | 97:97 | 0.72 |
| NFBC | 29:343 | 0.92 |
| PIAMA | 15:182 | 0.92 |
| RAINE | 114:405 | 0.86 |
| STOPPA | 137:323 | 0.90 |
| **META−ANALYSIS** | **657:2181** | **0.91** |



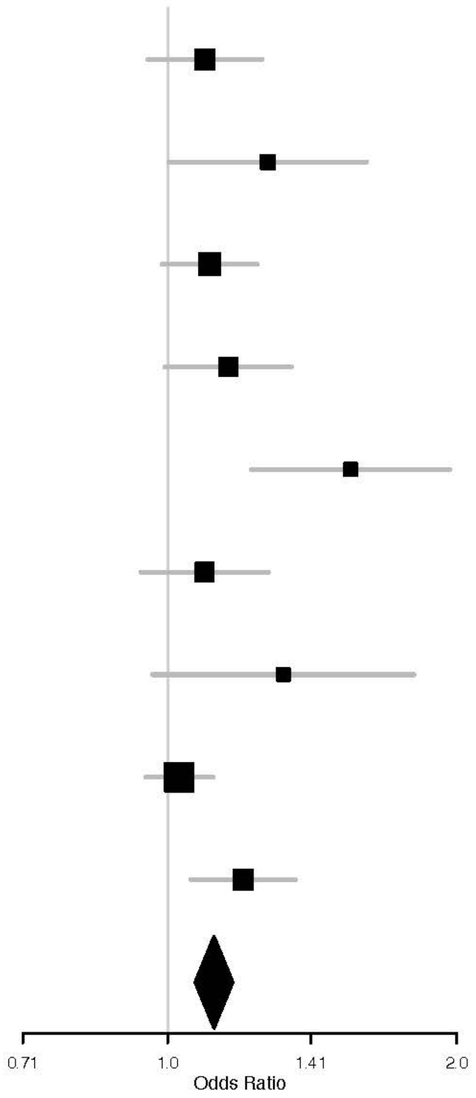

**cg19434937**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.84 |
| BAMSE_MEDALL | 47:167 | 0.85 |
| CHOP | 19:363 | 1.04 |
| ICAC | 97:97 | 0.99 |
| NFBC | 29:343 | 0.91 |
| PIAMA | 15:182 | 0.95 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.86 |
| **META−ANALYSIS** | **551:2094** | **0.91** |



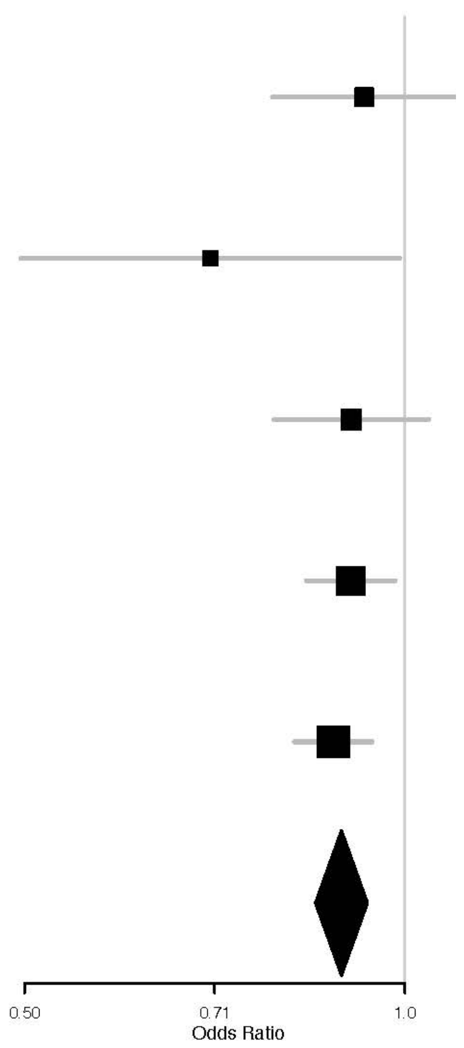

**cg26752663**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 1.09 |
| BAMSE_MEDALL | 47:167 | 1.27 |
| CHOP | 19:363 | 1.11 |
| GALA | 106:87 | 1.16 |
| ICAC | 97:97 | 1.55 |
| NFBC | 29:343 | 1.09 |
| PIAMA | 15:182 | 1.32 |
| RAINE | 114:405 | 1.03 |
| STOPPA | 137:323 | 1.20 |
| **META−ANALYSIS** | **657:2181** | **1.12** |



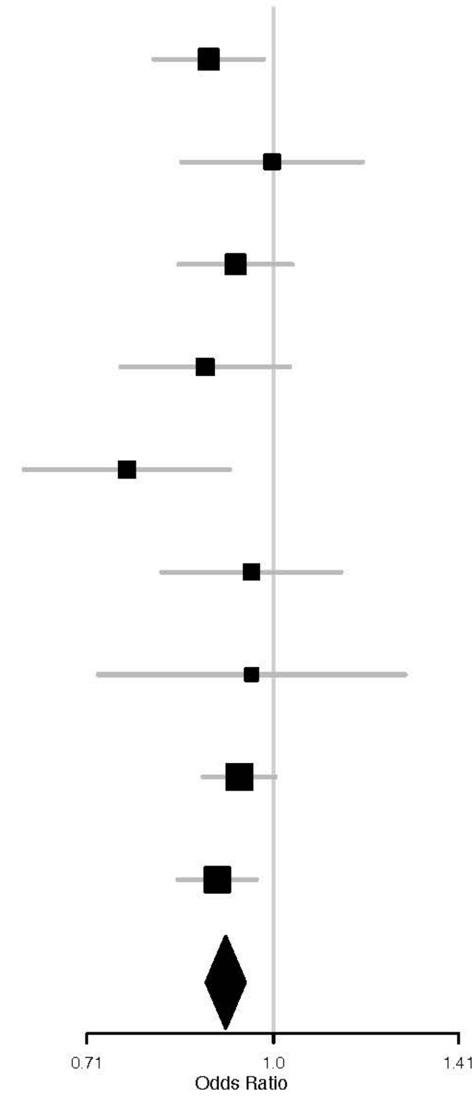

**cg23147443**

| Cohort | N cases:controls | OR |
|---|---|---|
| GALA | 106:87 | 0.93 |
| ICAC | 97:97 | 0.70 |
| NFBC | 29:343 | 0.91 |
| RAINE | 114:405 | 0.91 |
| STOPPA | 137:323 | 0.88 |
| **META−ANALYSIS** | **483:1255** | **0.89** |



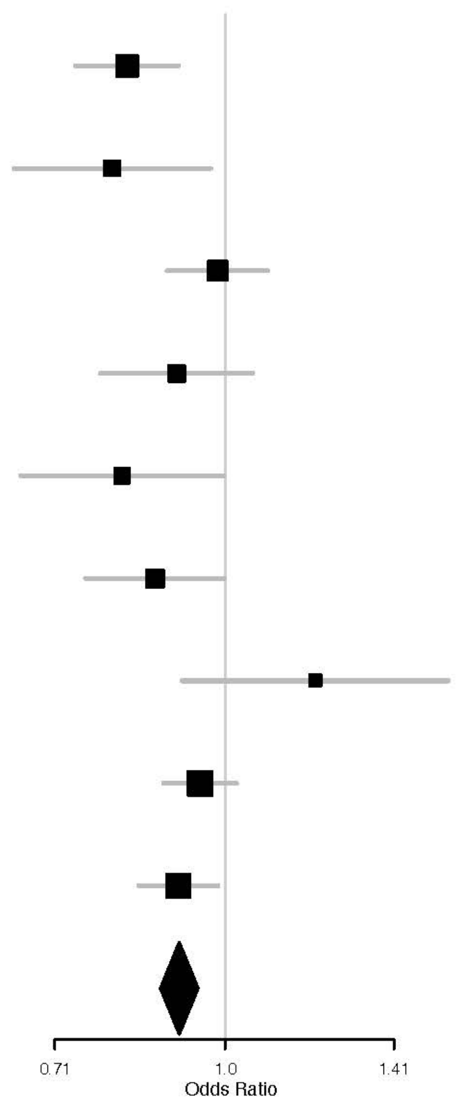

**cg18042632**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.89 |
| BAMSE_MEDALL | 47:167 | 1.00 |
| CHOP | 19:363 | 0.93 |
| GALA | 106:87 | 0.88 |
| ICAC | 97:97 | 0.76 |
| NFBC | 29:343 | 0.96 |
| PIAMA | 15:182 | 0.96 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.90 |
| **META−ANALYSIS** | **657:2181** | **0.92** |



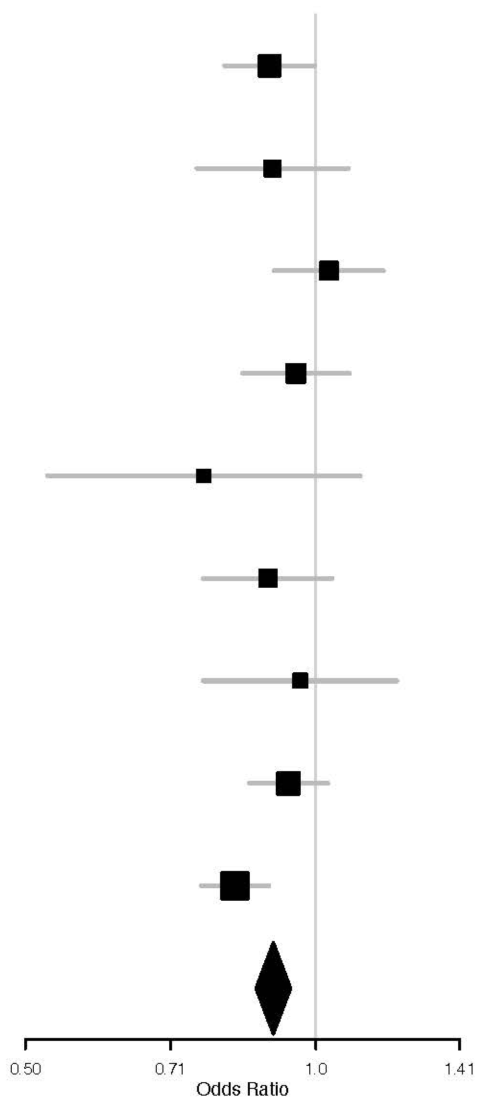

**cg25939647**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.82 |
| BAMSE_MEDALL | 47:167 | 0.79 |
| CHOP | 19:363 | 0.98 |
| GALA | 106:87 | 0.91 |
| ICAC | 97:97 | 0.81 |
| NFBC | 29:343 | 0.87 |
| PIAMA | 15:182 | 1.20 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.91 |
| **META−ANALYSIS** | **657:2181** | **0.91** |



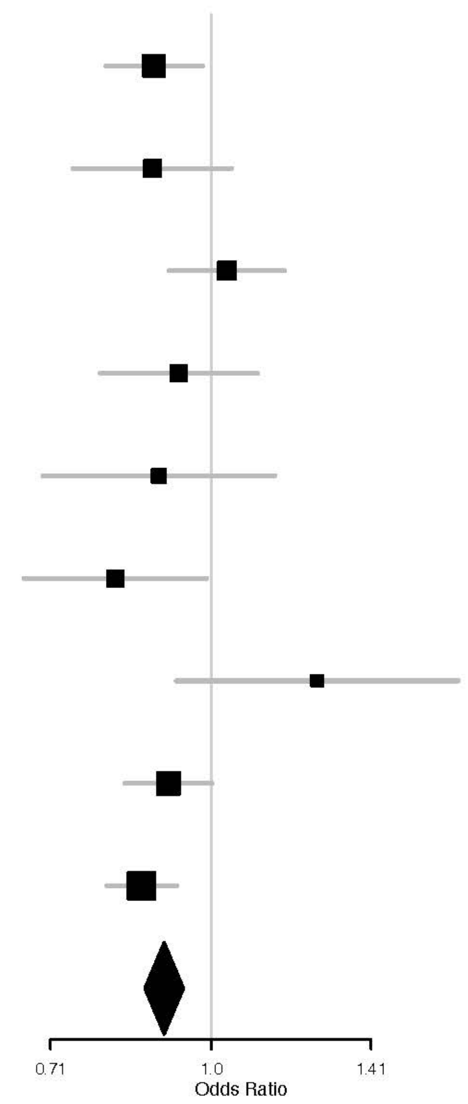

**cg04497992**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.90 |
| CHOP | 19:363 | 1.03 |
| GALA | 106:87 | 0.95 |
| ICAC | 97:97 | 0.77 |
| NFBC | 29:343 | 0.89 |
| PIAMA | 15:182 | 0.96 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.82 |
| **META−ANALYSIS** | **657:2181** | **0.90** |



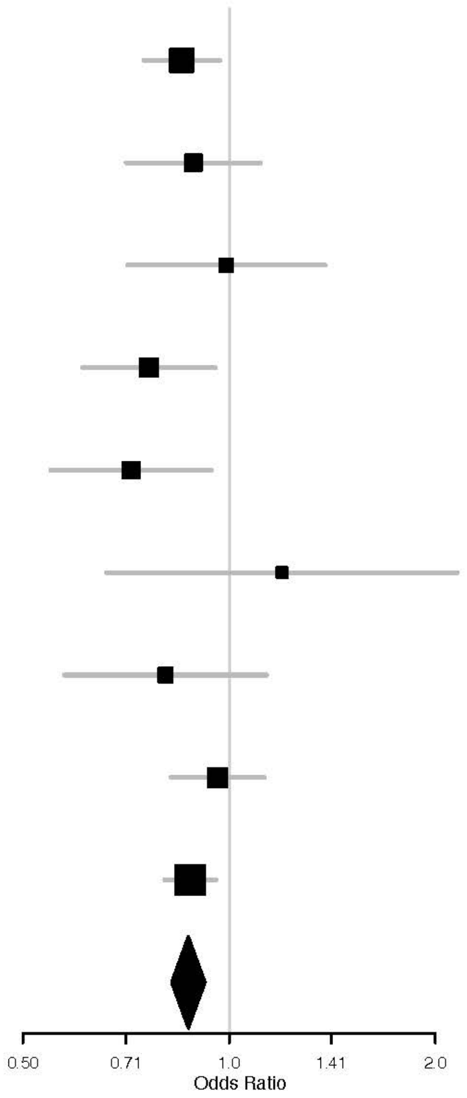

**cg00736681**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.88 |
| BAMSE_MEDALL | 47:167 | 0.88 |
| CHOP | 19:363 | 1.03 |
| GALA | 106:87 | 0.93 |
| ICAC | 97:97 | 0.89 |
| NFBC | 29:343 | 0.81 |
| PIAMA | 15:182 | 1.26 |
| RAINE | 114:405 | 0.91 |
| STOPPA | 137:323 | 0.86 |
| **META−ANALYSIS** | **657:2181** | **0.90** |



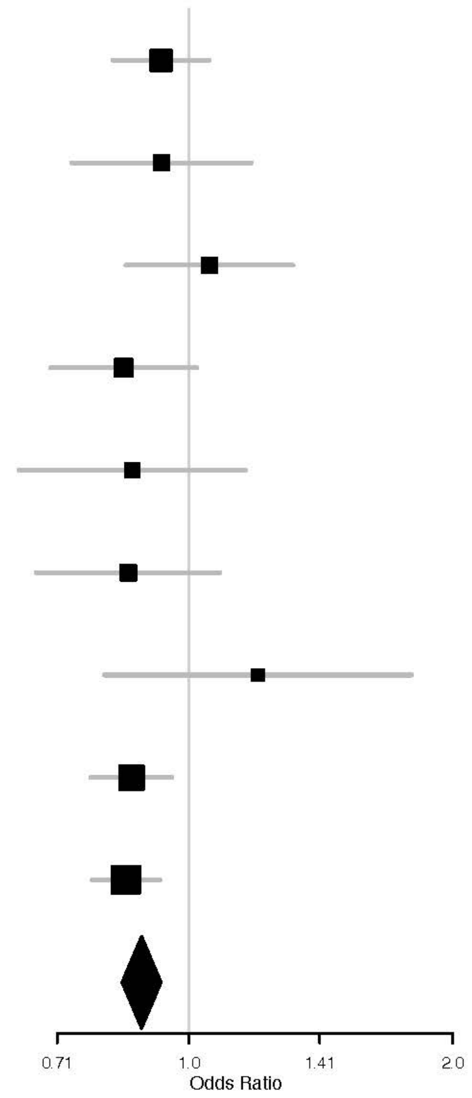
**cg24028828**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.85 |
| BAMSE_MEDALL | 47:167 | 0.89 |
| CHOP | 19:363 | 0.99 |
| GALA | 106:87 | 0.76 |
| ICAC | 97:97 | 0.72 |
| NFBC | 29:343 | 1.19 |
| PIAMA | 15:182 | 0.81 |
| RAINE | 114:405 | 0.96 |
| STOPPA | 137:323 | 0.88 |
| **META-ANALYSIS** | **657:2181** | **0.87** |



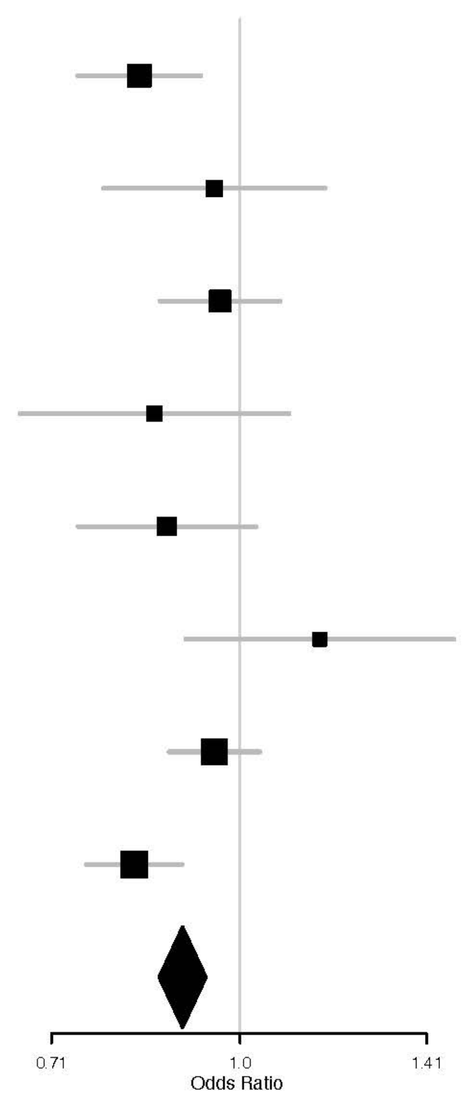

**cg01499988**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.93 |
| BAMSE_MEDALL | 47:167 | 0.93 |
| CHOP | 19:363 | 1.06 |
| GALA | 106:87 | 0.84 |
| ICAC | 97:97 | 0.86 |
| NFBC | 29:343 | 0.85 |
| PIAMA | 15:182 | 1.20 |
| RAINE | 114:405 | 0.86 |
| STOPPA | 137:323 | 0.85 |
| **META-ANALYSIS** | **657:2181** | **0.88** |



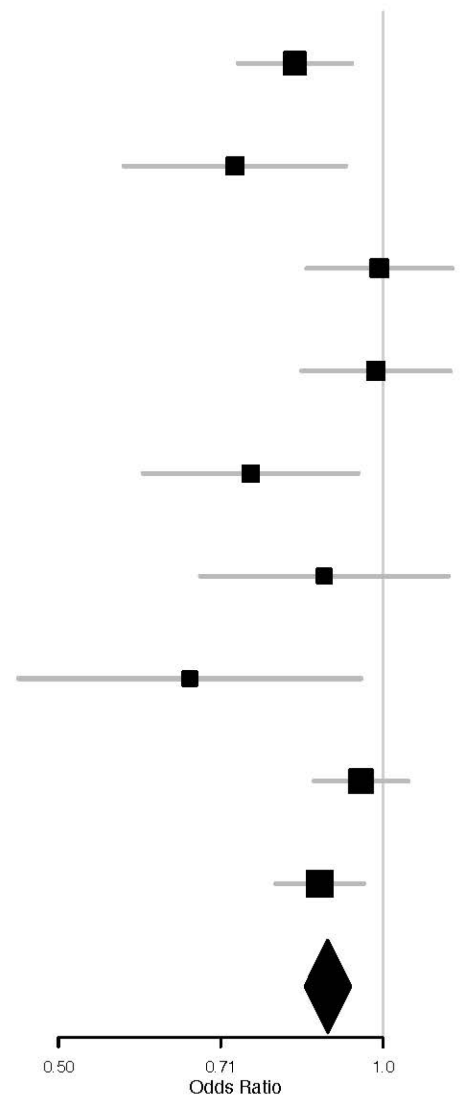

**cg17374802**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.83 |
| BAMSE_MEDALL | 47:167 | 0.95 |
| CHOP | 19:363 | 0.96 |
| ICAC | 97:97 | 0.85 |
| NFBC | 29:343 | 0.87 |
| PIAMA | 15:182 | 1.16 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.82 |
| **META-ANALYSIS** | **551:2094** | **0.90** |



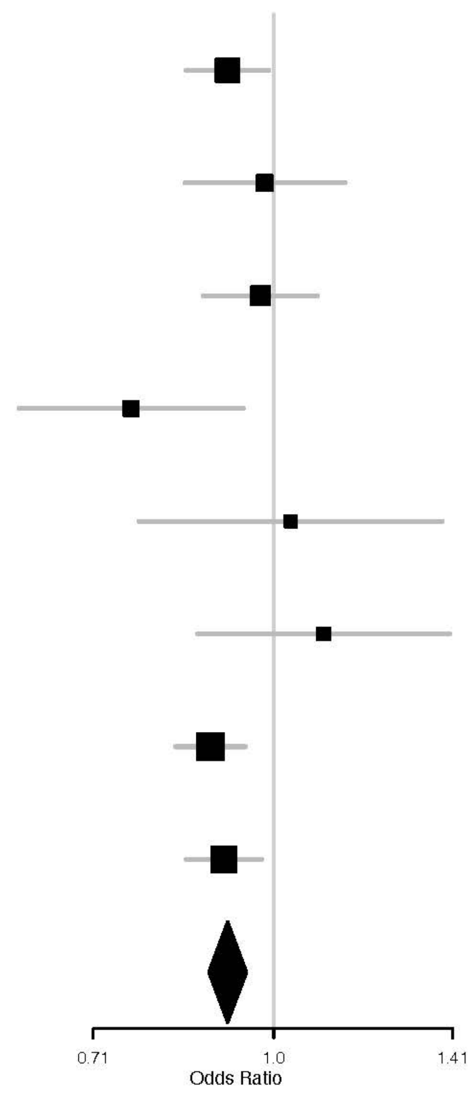

**cg22816343**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.83 |
| BAMSE_MEDALL | 47:167 | 0.73 |
| CHOP | 19:363 | 0.99 |
| GALA | 106:87 | 0.99 |
| ICAC | 97:97 | 0.75 |
| NFBC | 29:343 | 0.88 |
| PIAMA | 15:182 | 0.66 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.87 |
| **META-ANALYSIS** | **657:2181** | **0.89** |



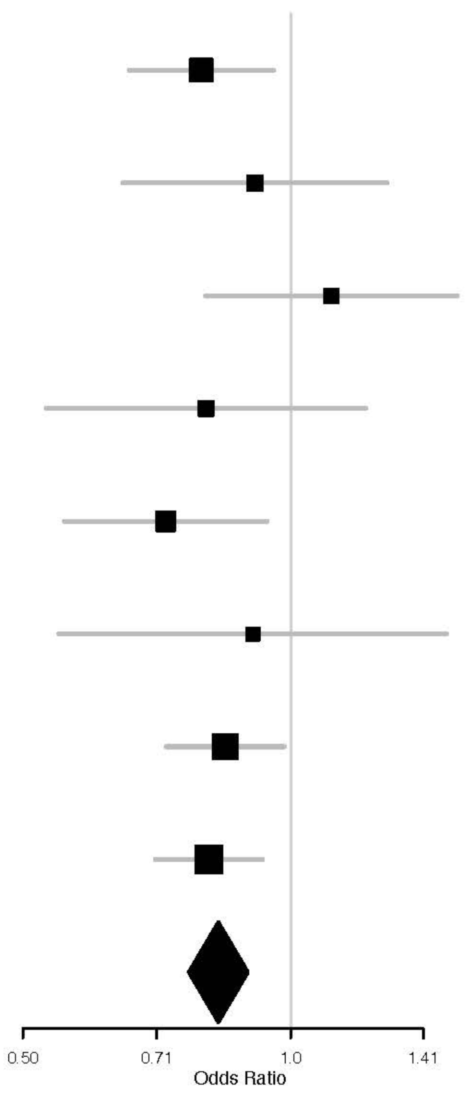

**cg03014680**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.92 |
| BAMSE_MEDALL | 47:167 | 0.98 |
| CHOP | 19:363 | 0.97 |
| ICAC | 97:97 | 0.76 |
| NFBC | 29:343 | 1.03 |
| PIAMA | 15:182 | 1.10 |
| RAINE | 114:405 | 0.89 |
| STOPPA | 137:323 | 0.91 |
| **META-ANALYSIS** | **551:2094** | **0.92** |



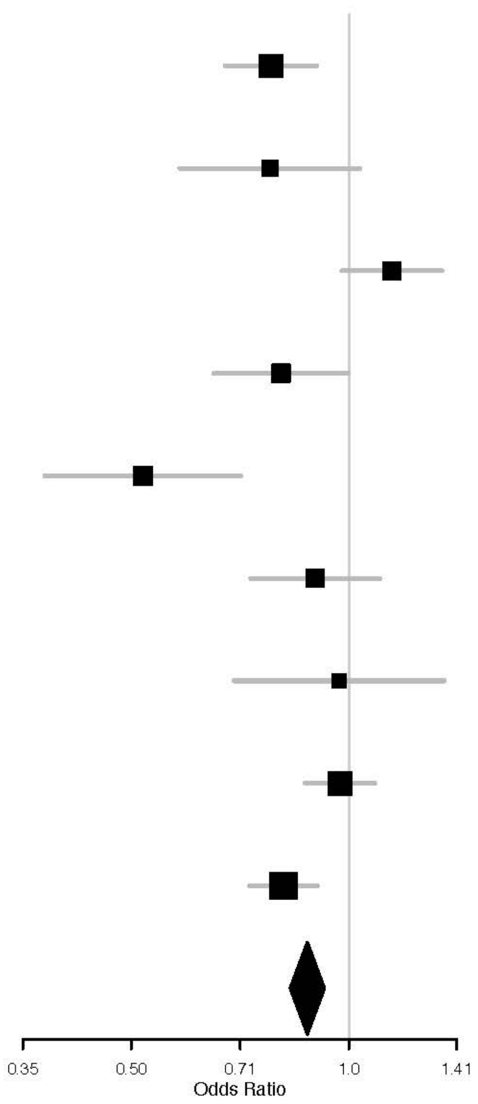

**cg06426027**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.79 |
| BAMSE_MEDALL | 47:167 | 0.91 |
| CHOP | 19:363 | 1.11 |
| ICAC | 97:97 | 0.80 |
| NFBC | 29:343 | 0.72 |
| PIAMA | 15:182 | 0.91 |
| RAINE | 114:405 | 0.84 |
| STOPPA | 137:323 | 0.81 |
| **META-ANALYSIS** | **551:2094** | **0.83** |



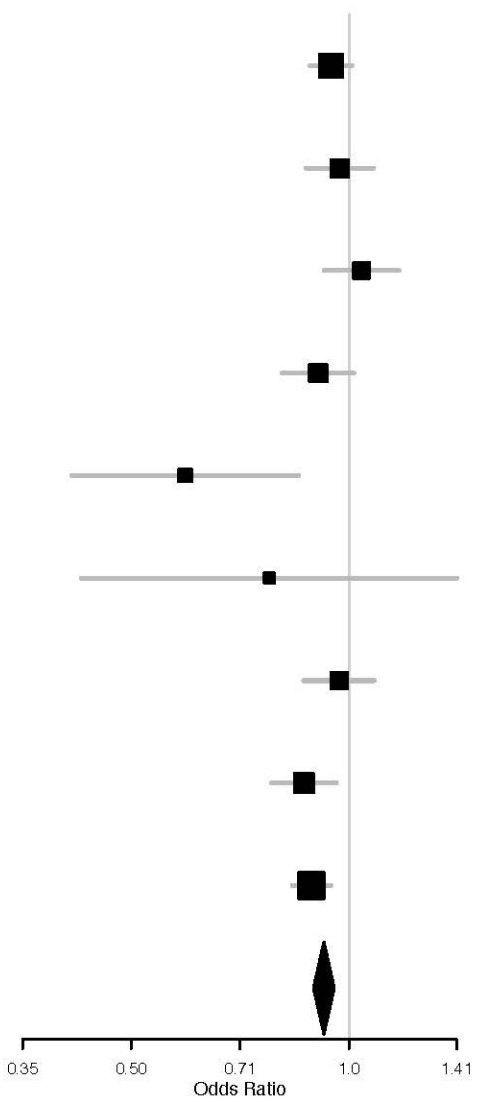

**cg04217850**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.78 |
| BAMSE_MEDALL | 47:167 | 0.78 |
| CHOP | 19:363 | 1.15 |
| GALA | 106:87 | 0.81 |
| ICAC | 97:97 | 0.52 |
| NFBC | 29:343 | 0.90 |
| PIAMA | 15:182 | 0.97 |
| RAINE | 114:405 | 0.97 |
| STOPPA | 137:323 | 0.81 |
| **META-ANALYSIS** | **657:2181** | **0.88** |



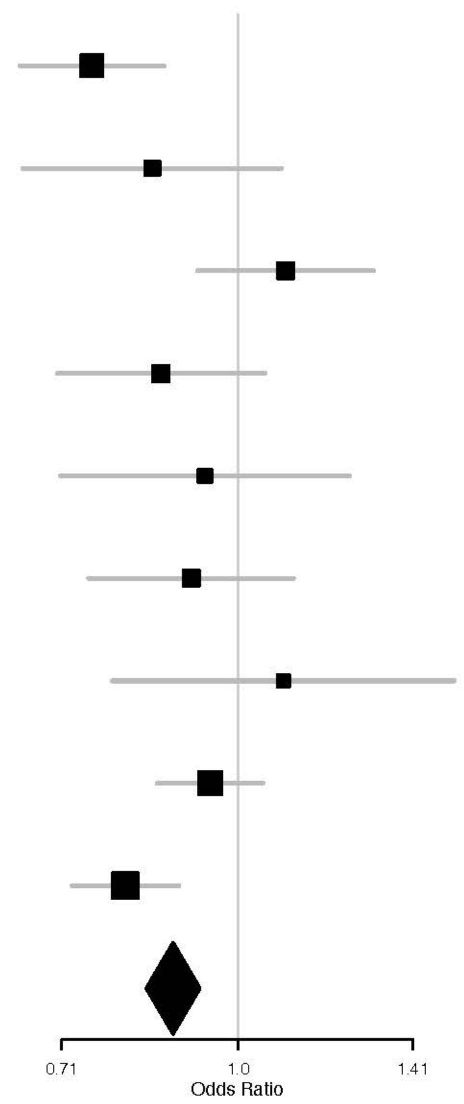

**cg08640475**

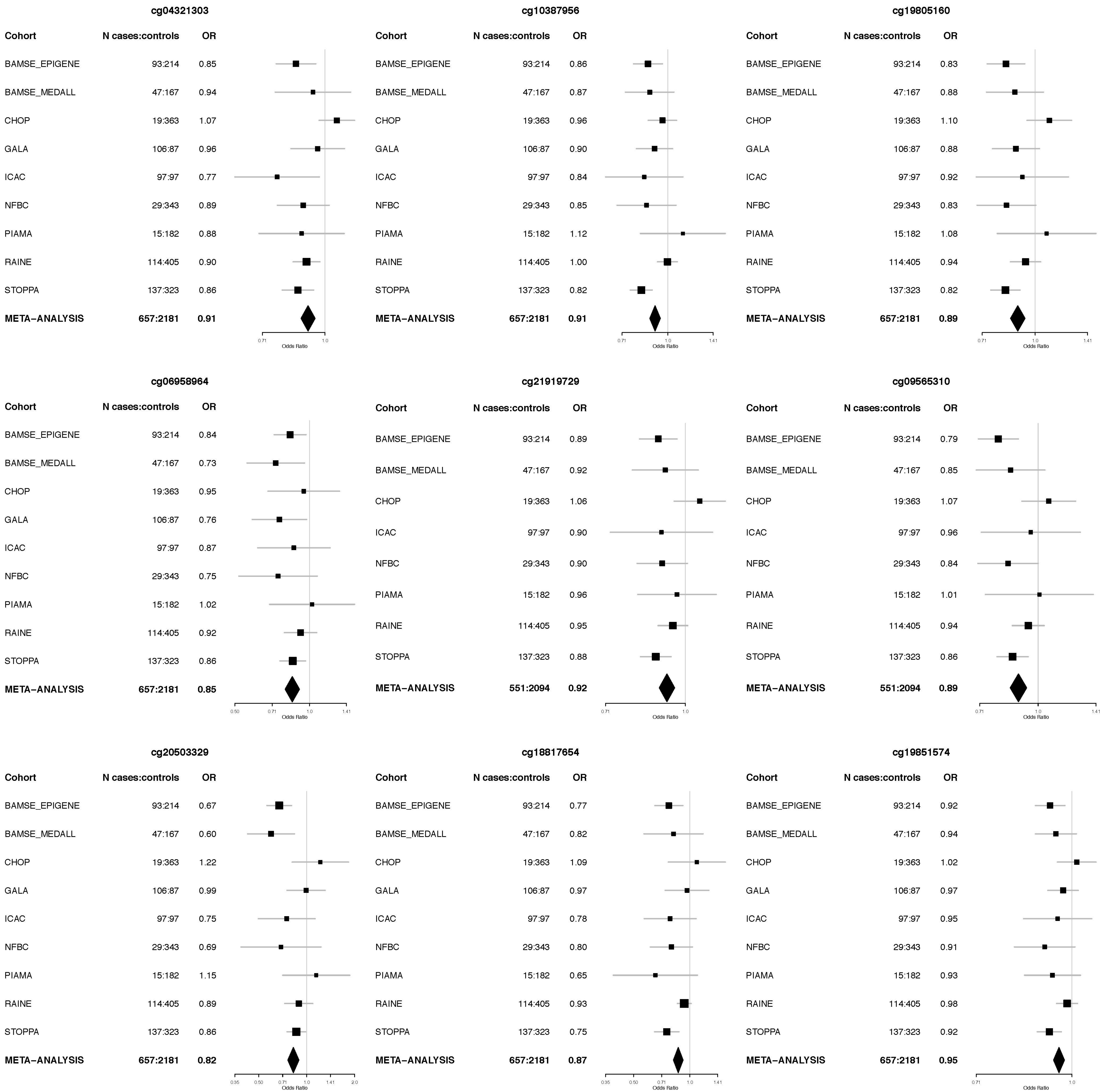
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.94 |
| BAMSE_MEDALL | 47:167 | 0.97 |
| CHOP | 19:363 | 1.04 |
| GALA | 106:87 | 0.91 |
| ICAC | 97:97 | 0.59 |
| NFBC | 29:343 | 0.78 |
| PIAMA | 15:182 | 0.97 |
| RAINE | 114:405 | 0.87 |
| STOPPA | 137:323 | 0.89 |
| **META-ANALYSIS** | **657:2181** | **0.92** |




**cg02359181**

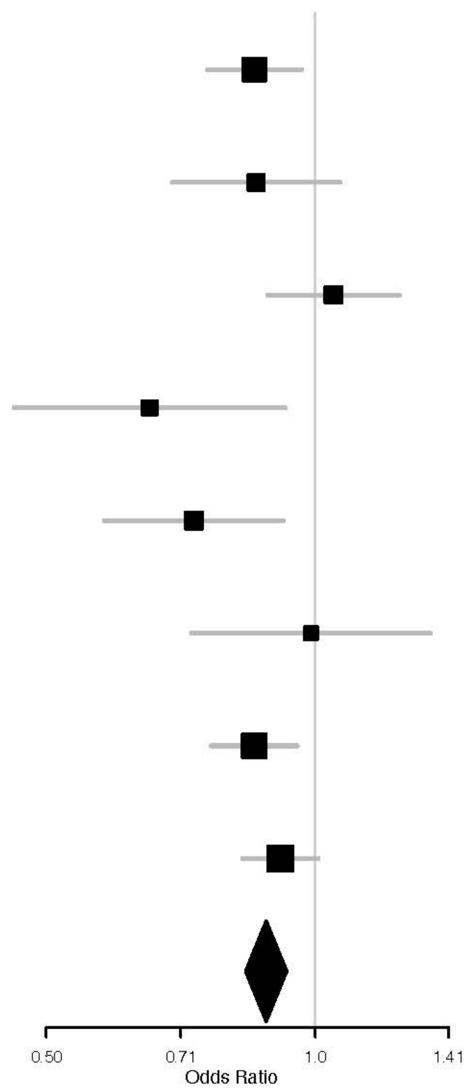
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.75 |
| BAMSE_MEDALL | 47:167 | 0.85 |
| CHOP | 19:363 | 1.10 |
| GALA | 106:87 | 0.86 |
| ICAC | 97:97 | 0.94 |
| NFBC | 29:343 | 0.91 |
| PIAMA | 15:182 | 1.09 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.80 |
| **META-ANALYSIS** | **657:2181** | **0.88** |




cg04321303
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.94
CHOP 19:363 1.07
GALA 106:87 0.96
ICAC 97:97 0.77
NFBC 29:343 0.89
PIAMA 15:182 0.88
RAINE 114:405 0.90
STOPPA 137:323 0.86
META−ANALYSIS 657:2181 0.91
0.71 1.0
Odds Ratio
cg10387956
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.87
CHOP 19:363 0.96
GALA 106:87 0.90
ICAC 97:97 0.84
NFBC 29:343 0.85
PIAMA 15:182 1.12
RAINE 114:405 1.00
STOPPA 137:323 0.82
META−ANALYSIS 657:2181 0.91
0.71 1.0 1.41
Odds Ratio
cg19805160
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.83
BAMSE_MEDALL 47:167 0.88
CHOP 19:363 1.10
GALA 106:87 0.88
ICAC 97:97 0.92
NFBC 29:343 0.83
PIAMA 15:182 1.08
RAINE 114:405 0.94
STOPPA 137:323 0.82
META−ANALYSIS 657:2181 0.89
0.71 1.0 1.41
Odds Ratio
cg06958964
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.73
CHOP 19:363 0.95
GALA 106:87 0.76
ICAC 97:97 0.87
NFBC 29:343 0.75
PIAMA 15:182 1.02
RAINE 114:405 0.92
STOPPA 137:323 0.86
META−ANALYSIS 657:2181 0.85
0.50 0.71 1.0 1.41
Odds Ratio
cg21919729
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.89
BAMSE_MEDALL 47:167 0.92
CHOP 19:363 1.06
ICAC 97:97 0.90
NFBC 29:343 0.90
PIAMA 15:182 0.96
RAINE 114:405 0.95
STOPPA 137:323 0.88
META−ANALYSIS 551:2094 0.92
0.71 1.0
Odds Ratio
cg09565310
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.79
BAMSE_MEDALL 47:167 0.85
CHOP 19:363 1.07
ICAC 97:97 0.96
NFBC 29:343 0.84
PIAMA 15:182 1.01
RAINE 114:405 0.94
STOPPA 137:323 0.86
META−ANALYSIS 551:2094 0.89
0.71 1.0 1.41
Odds Ratio
cg20503329
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.67
BAMSE_MEDALL 47:167 0.60
CHOP 19:363 1.22
GALA 106:87 0.99
ICAC 97:97 0.75
NFBC 29:343 0.69
PIAMA 15:182 1.15
RAINE 114:405 0.89
STOPPA 137:323 0.86
META−ANALYSIS 657:2181 0.82
0.35 0.50 0.71 1.0 1.41 2.0
Odds Ratio
cg18817654
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.77
BAMSE_MEDALL 47:167 0.82
CHOP 19:363 1.09
GALA 106:87 0.97
ICAC 97:97 0.78
NFBC 29:343 0.80
PIAMA 15:182 0.65
RAINE 114:405 0.93
STOPPA 137:323 0.75
META−ANALYSIS 657:2181 0.87
0.35 0.50 0.71 1.0 1.41
Odds Ratio
cg19851574
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.92
BAMSE_MEDALL 47:167 0.94
CHOP 19:363 1.02
GALA 106:87 0.97
ICAC 97:97 0.95
NFBC 29:343 0.91
PIAMA 15:182 0.93
RAINE 114:405 0.98
STOPPA 137:323 0.92
META−ANALYSIS 657:2181 0.95
0.71 1.0
Odds Ratio

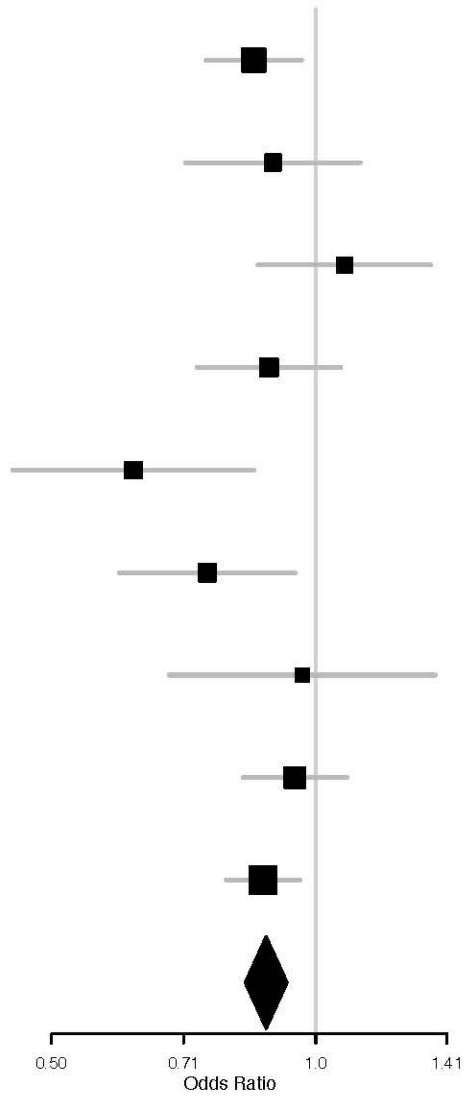
**cg20315954**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.86 |
| BAMSE_MEDALL | 47:167 | 0.86 |
| CHOP | 19:363 | 1.05 |
| ICAC | 97:97 | 0.65 |
| NFBC | 29:343 | 0.73 |
| PIAMA | 15:182 | 0.99 |
| RAINE | 114:405 | 0.85 |
| STOPPA | 137:323 | 0.91 |
| **META−ANALYSIS** | **551:2094** | **0.88** |



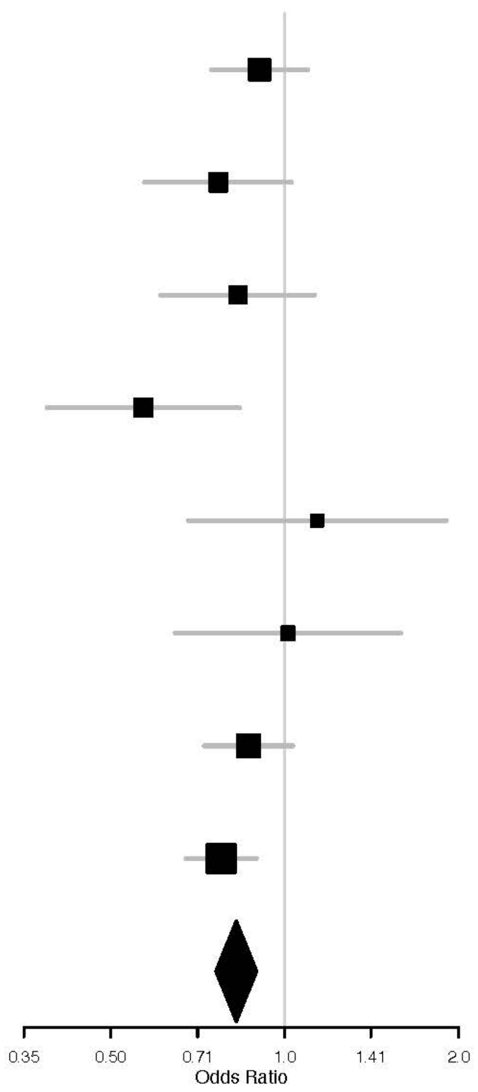

**cg13233042**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.85 |
| BAMSE_MEDALL | 47:167 | 0.89 |
| CHOP | 19:363 | 1.08 |
| GALA | 106:87 | 0.88 |
| ICAC | 97:97 | 0.62 |
| NFBC | 29:343 | 0.75 |
| PIAMA | 15:182 | 0.97 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.87 |
| **META−ANALYSIS** | **657:2181** | **0.88** |



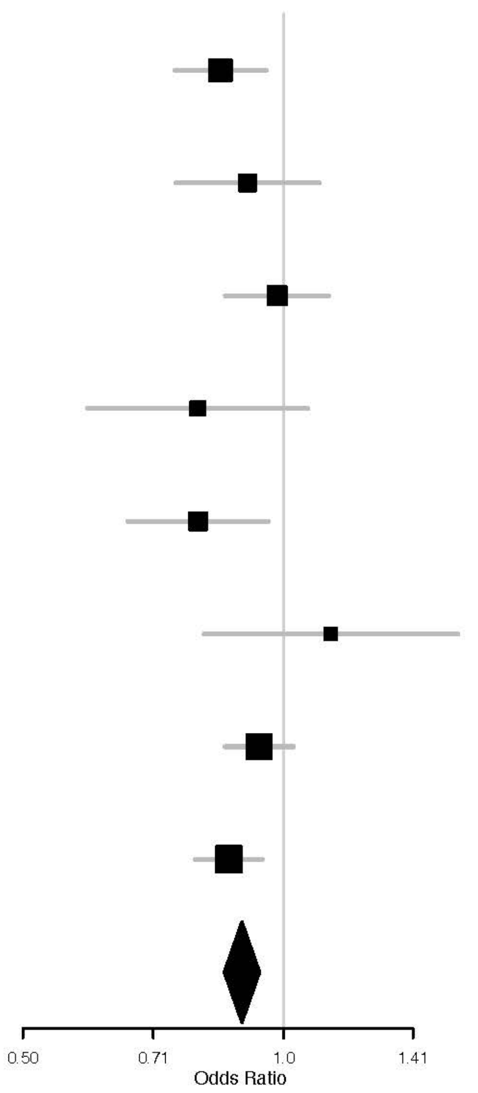

**cg27533472**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.77 |
| CHOP | 19:363 | 0.83 |
| ICAC | 97:97 | 0.57 |
| NFBC | 29:343 | 1.14 |
| PIAMA | 15:182 | 1.01 |
| RAINE | 114:405 | 0.87 |
| STOPPA | 137:323 | 0.78 |
| **META−ANALYSIS** | **551:2094** | **0.82** |



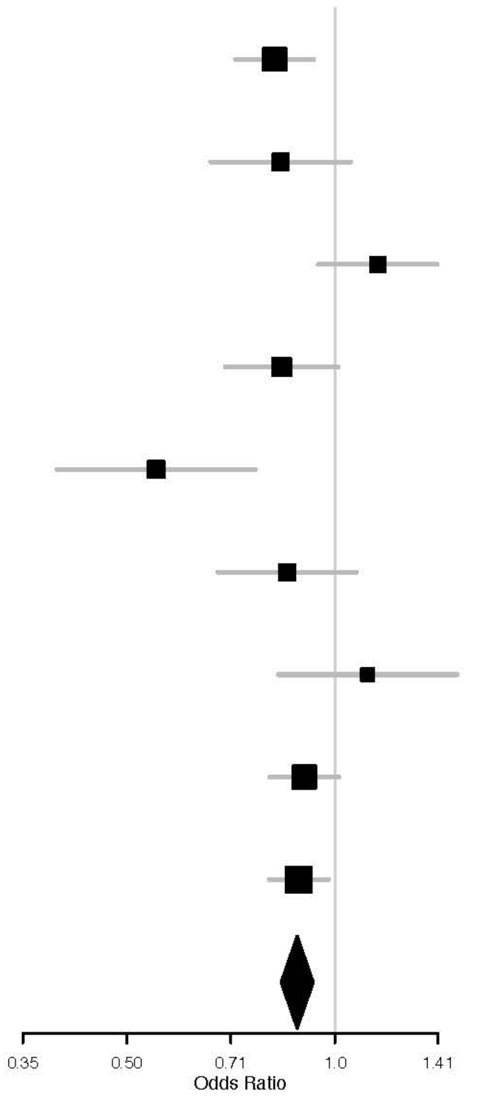

**cg01310029**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.85 |
| BAMSE_MEDALL | 47:167 | 0.91 |
| CHOP | 19:363 | 0.98 |
| ICAC | 97:97 | 0.80 |
| NFBC | 29:343 | 0.80 |
| PIAMA | 15:182 | 1.13 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.86 |
| **META−ANALYSIS** | **551:2094** | **0.89** |



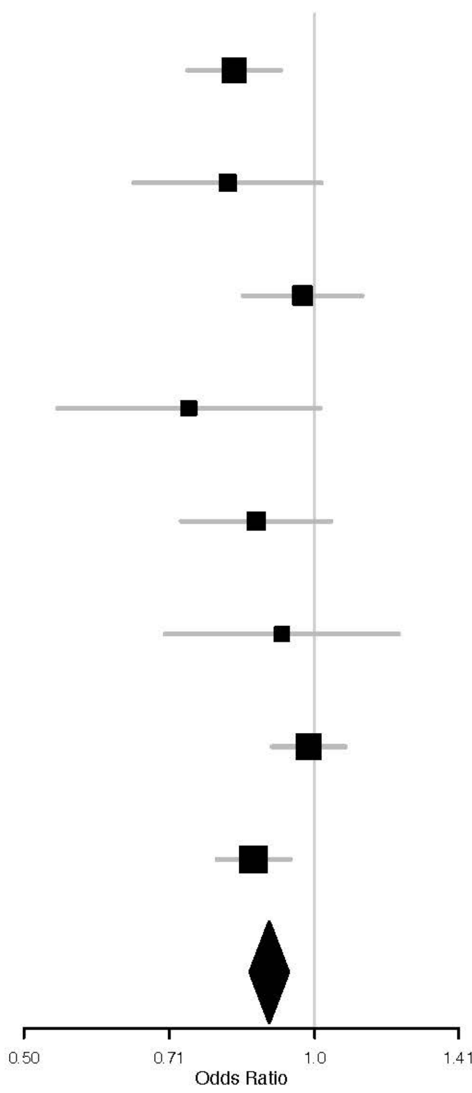

**cg09597192**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.82 |
| BAMSE_MEDALL | 47:167 | 0.84 |
| CHOP | 19:363 | 1.15 |
| GALA | 106:87 | 0.84 |
| ICAC | 97:97 | 0.55 |
| NFBC | 29:343 | 0.85 |
| PIAMA | 15:182 | 1.12 |
| RAINE | 114:405 | 0.90 |
| STOPPA | 137:323 | 0.89 |
| **META−ANALYSIS** | **657:2181** | **0.88** |



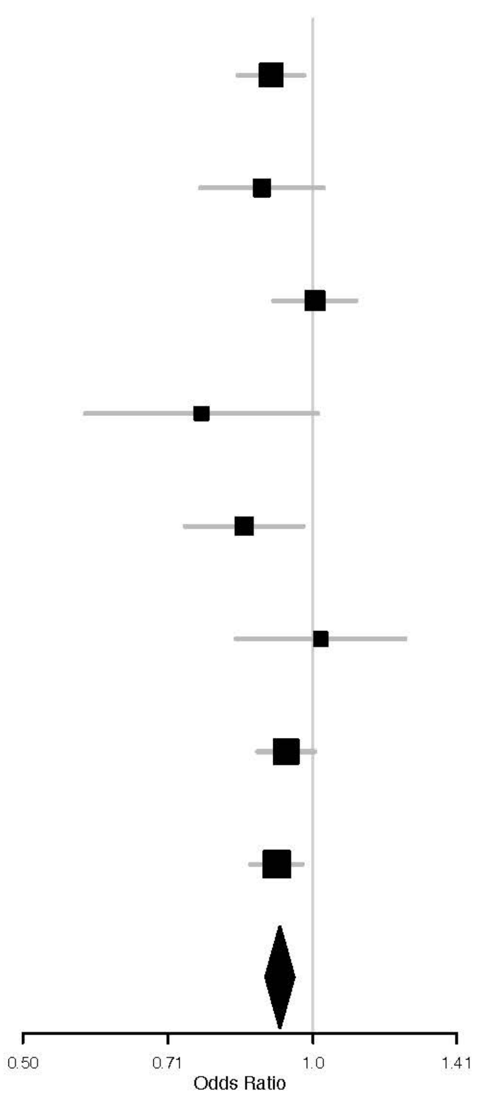

**cg10159529**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.83 |
| BAMSE_MEDALL | 47:167 | 0.81 |
| CHOP | 19:363 | 0.97 |
| ICAC | 97:97 | 0.74 |
| NFBC | 29:343 | 0.87 |
| PIAMA | 15:182 | 0.92 |
| RAINE | 114:405 | 0.99 |
| STOPPA | 137:323 | 0.86 |
| **META−ANALYSIS** | **551:2094** | **0.90** |



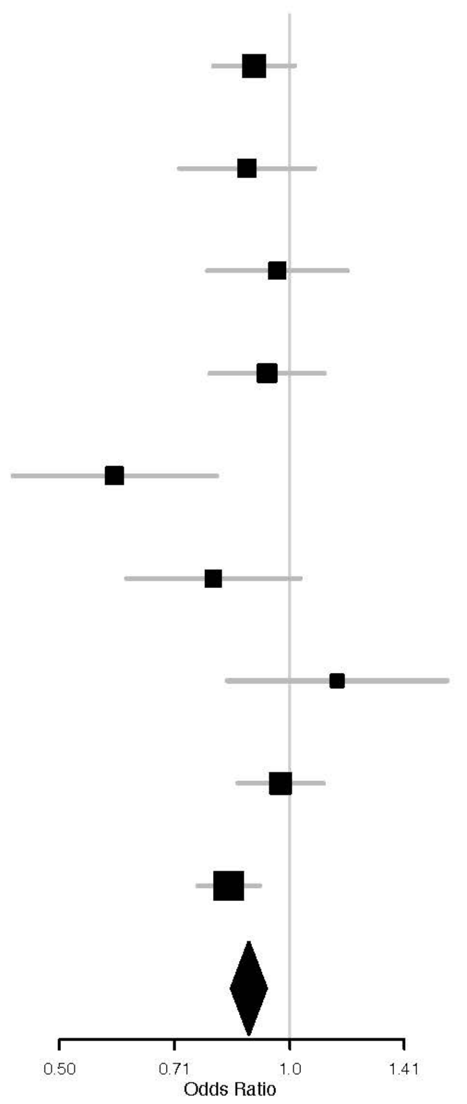

**cg12077754**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.89 |
| CHOP | 19:363 | 1.00 |
| ICAC | 97:97 | 0.77 |
| NFBC | 29:343 | 0.85 |
| PIAMA | 15:182 | 1.02 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.92 |
| **META−ANALYSIS** | **551:2094** | **0.92** |



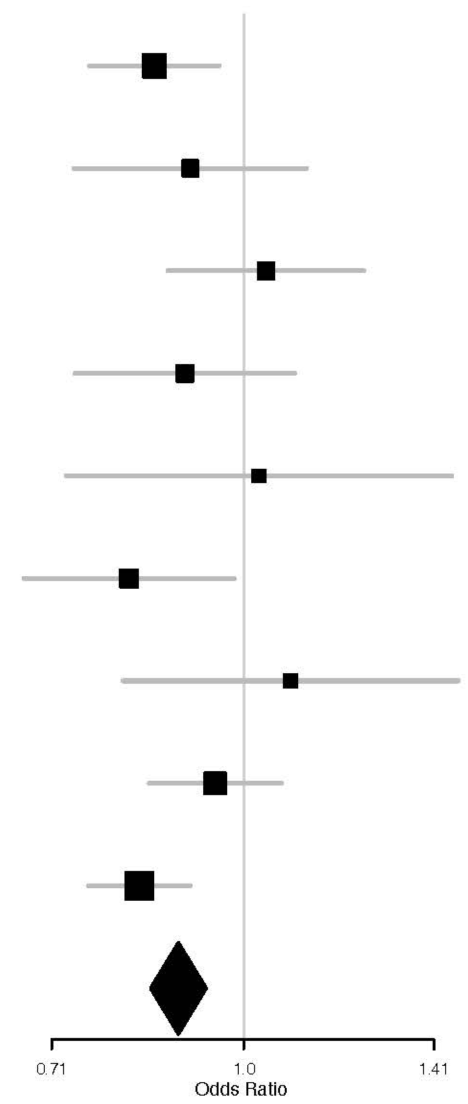

**cg13482814**

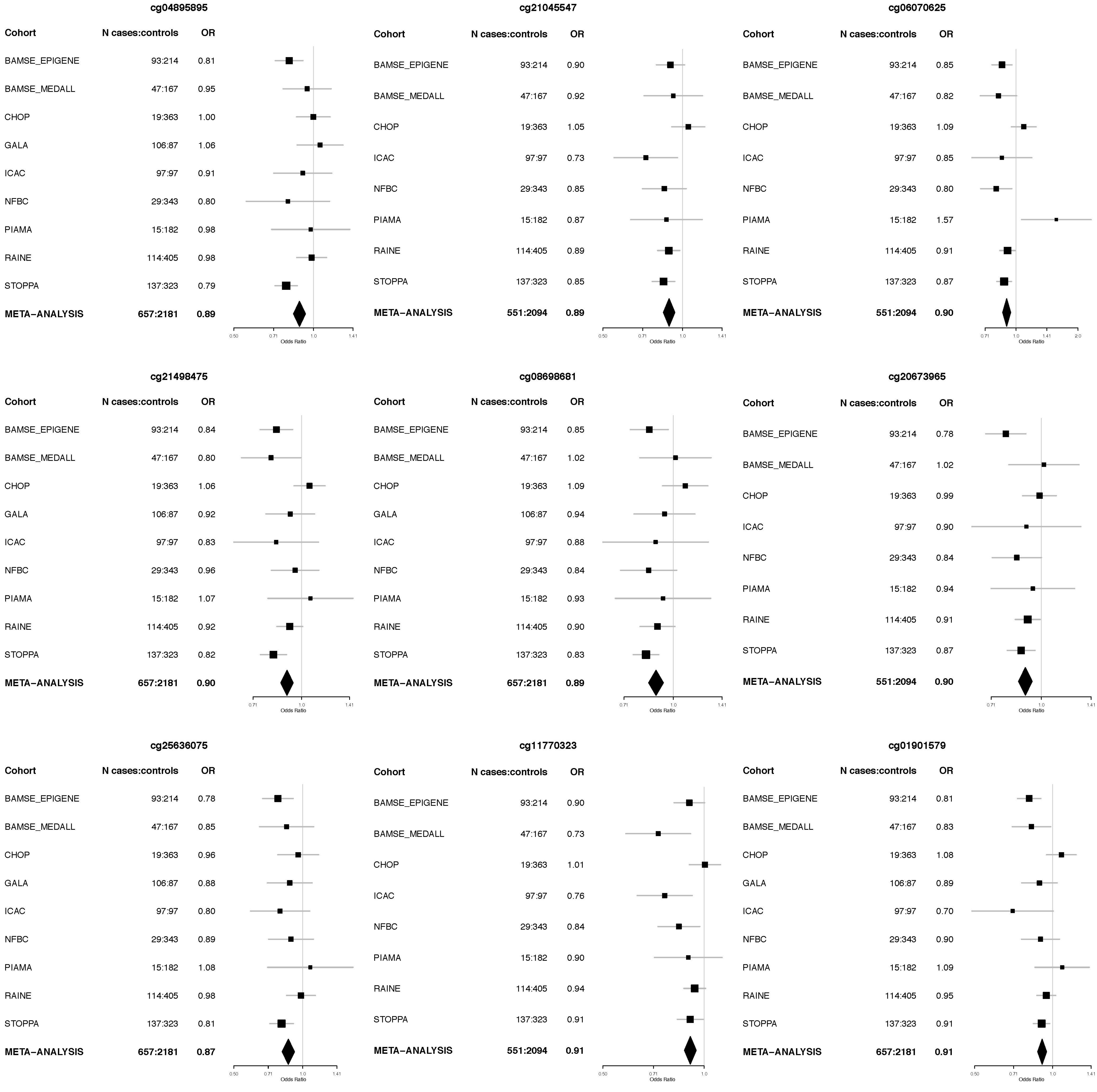
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.88 |
| CHOP | 19:363 | 0.96 |
| GALA | 106:87 | 0.93 |
| ICAC | 97:97 | 0.59 |
| NFBC | 29:343 | 0.79 |
| PIAMA | 15:182 | 1.15 |
| RAINE | 114:405 | 0.97 |
| STOPPA | 137:323 | 0.83 |
| **META−ANALYSIS** | **657:2181** | **0.88** |




**cg18368116**

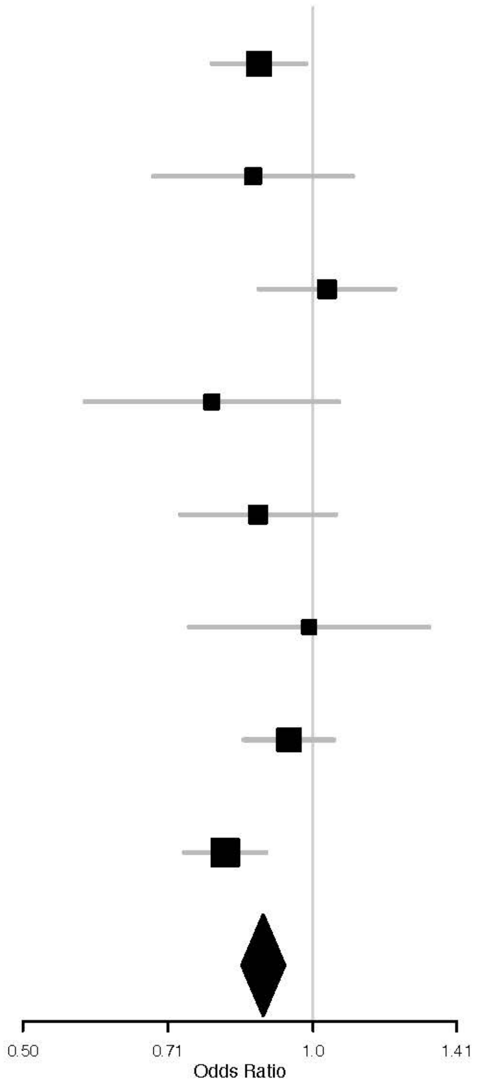
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.85 |
| BAMSE_MEDALL | 47:167 | 0.91 |
| CHOP | 19:363 | 1.04 |
| GALA | 106:87 | 0.90 |
| ICAC | 97:97 | 1.03 |
| NFBC | 29:343 | 0.81 |
| PIAMA | 15:182 | 1.09 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.83 |
| **META−ANALYSIS** | **657:2181** | **0.89** |




cg04895895
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.81
BAMSE_MEDALL 47:167 0.95
CHOP 19:363 1.00
GALA 106:87 1.06
ICAC 97:97 0.91
NFBC 29:343 0.80
PIAMA 15:182 0.98
RAINE 114:405 0.98
STOPPA 137:323 0.79
META−ANALYSIS 657:2181 0.89
0.50 0.71 1.0 1.41
Odds Ratio
cg21045547
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.90
BAMSE_MEDALL 47:167 0.92
CHOP 19:363 1.05
ICAC 97:97 0.73
NFBC 29:343 0.85
PIAMA 15:182 0.87
RAINE 114:405 0.89
STOPPA 137:323 0.85
META−ANALYSIS 551:2094 0.89
0.50 0.71 1.0 1.41
Odds Ratio
cg06070625
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.82
CHOP 19:363 1.09
ICAC 97:97 0.85
NFBC 29:343 0.80
PIAMA 15:182 1.57
RAINE 114:405 0.91
STOPPA 137:323 0.87
META−ANALYSIS 551:2094 0.90
0.71 1.0 1.41 2.0
Odds Ratio
cg21498475
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.80
CHOP 19:363 1.06
GALA 106:87 0.92
ICAC 97:97 0.83
NFBC 29:343 0.96
PIAMA 15:182 1.07
RAINE 114:405 0.92
STOPPA 137:323 0.82
META−ANALYSIS 657:2181 0.90
0.71 1.0 1.41
Odds Ratio
cg08698681
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 1.02
CHOP 19:363 1.09
GALA 106:87 0.94
ICAC 97:97 0.88
NFBC 29:343 0.84
PIAMA 15:182 0.93
RAINE 114:405 0.90
STOPPA 137:323 0.83
META−ANALYSIS 657:2181 0.89
0.71 1.0 1.41
Odds Ratio
cg20673965
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.78
BAMSE_MEDALL 47:167 1.02
CHOP 19:363 0.99
ICAC 97:97 0.90
NFBC 29:343 0.84
PIAMA 15:182 0.94
RAINE 114:405 0.91
STOPPA 137:323 0.87
META−ANALYSIS 551:2094 0.90
0.71 1.0 1.41
Odds Ratio
cg25636075
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.78
BAMSE_MEDALL 47:167 0.85
CHOP 19:363 0.96
GALA 106:87 0.88
ICAC 97:97 0.80
NFBC 29:343 0.89
PIAMA 15:182 1.08
RAINE 114:405 0.98
STOPPA 137:323 0.81
META−ANALYSIS 657:2181 0.87
0.50 0.71 1.0 1.41
Odds Ratio
cg11770323
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.90
BAMSE_MEDALL 47:167 0.73
CHOP 19:363 1.01
ICAC 97:97 0.76
NFBC 29:343 0.84
PIAMA 15:182 0.90
RAINE 114:405 0.94
STOPPA 137:323 0.91
META−ANALYSIS 551:2094 0.91
0.50 0.71 1.0
Odds Ratio
cg01901579
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.81
BAMSE_MEDALL 47:167 0.83
CHOP 19:363 1.08
GALA 106:87 0.89
ICAC 97:97 0.70
NFBC 29:343 0.90
PIAMA 15:182 1.09
RAINE 114:405 0.95
STOPPA 137:323 0.91
META−ANALYSIS 657:2181 0.91
0.50 0.71 1.0 1.41
Odds Ratio

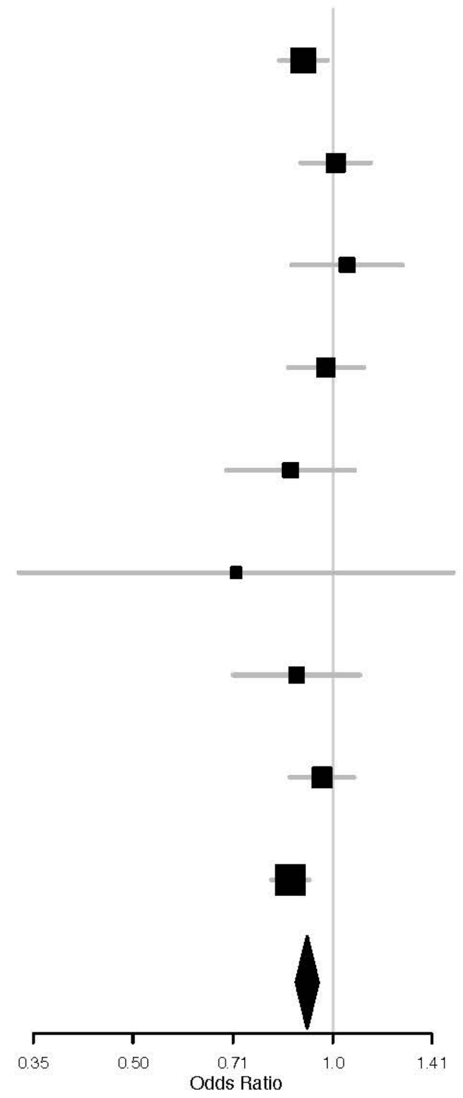
**cg06315149**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.88 |
| BAMSE_MEDALL | 47:167 | 0.87 |
| CHOP | 19:363 | 1.03 |
| ICAC | 97:97 | 0.79 |
| NFBC | 29:343 | 0.88 |
| PIAMA | 15:182 | 0.99 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.81 |
| **META−ANALYSIS** | **551:2094** | **0.89** |



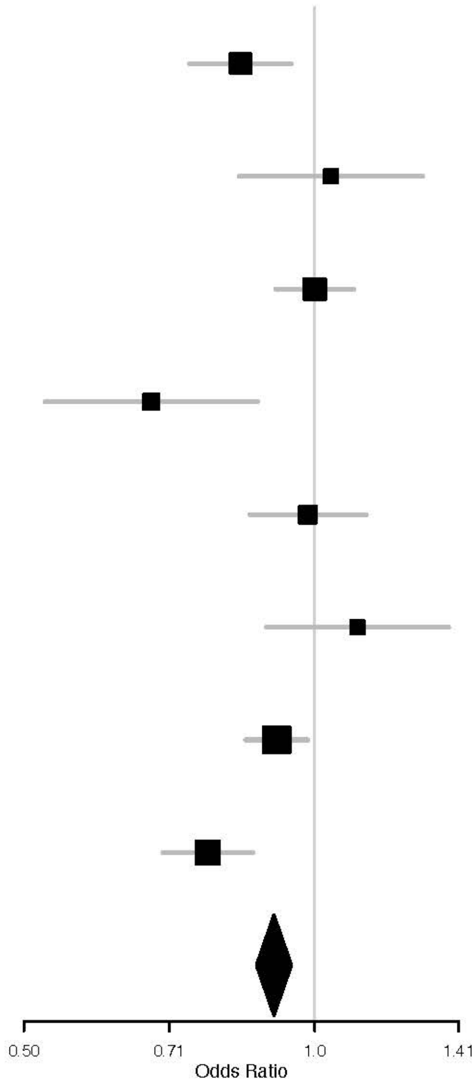

**cg03329755**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 1.01 |
| CHOP | 19:363 | 1.05 |
| GALA | 106:87 | 0.98 |
| ICAC | 97:97 | 0.86 |
| NFBC | 29:343 | 0.71 |
| PIAMA | 15:182 | 0.88 |
| RAINE | 114:405 | 0.96 |
| STOPPA | 137:323 | 0.86 |
| **META−ANALYSIS** | **657:2181** | **0.91** |



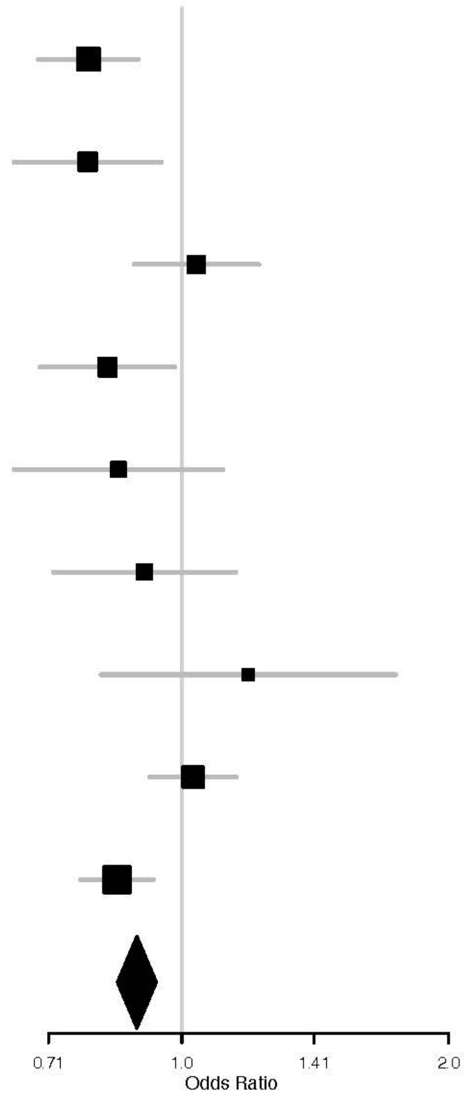

**cg26033504**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.84 |
| BAMSE_MEDALL | 47:167 | 1.04 |
| CHOP | 19:363 | 1.00 |
| ICAC | 97:97 | 0.68 |
| NFBC | 29:343 | 0.98 |
| PIAMA | 15:182 | 1.11 |
| RAINE | 114:405 | 0.91 |
| STOPPA | 137:323 | 0.78 |
| **META−ANALYSIS** | **551:2094** | **0.91** |



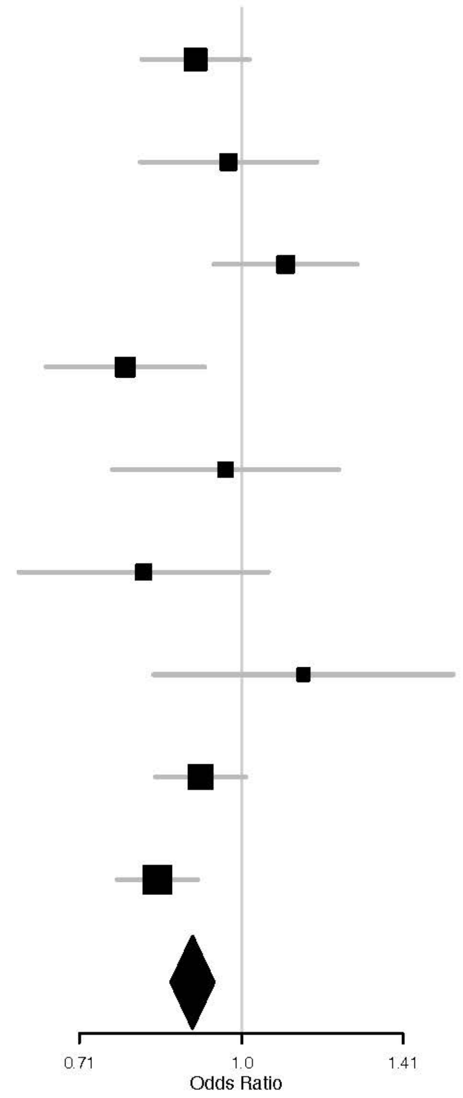

**cg14611258**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.78 |
| BAMSE_MEDALL | 47:167 | 0.78 |
| CHOP | 19:363 | 1.04 |
| GALA | 106:87 | 0.82 |
| ICAC | 97:97 | 0.85 |
| NFBC | 29:343 | 0.91 |
| PIAMA | 15:182 | 1.19 |
| RAINE | 114:405 | 1.03 |
| STOPPA | 137:323 | 0.84 |
| **META−ANALYSIS** | **657:2181** | **0.89** |



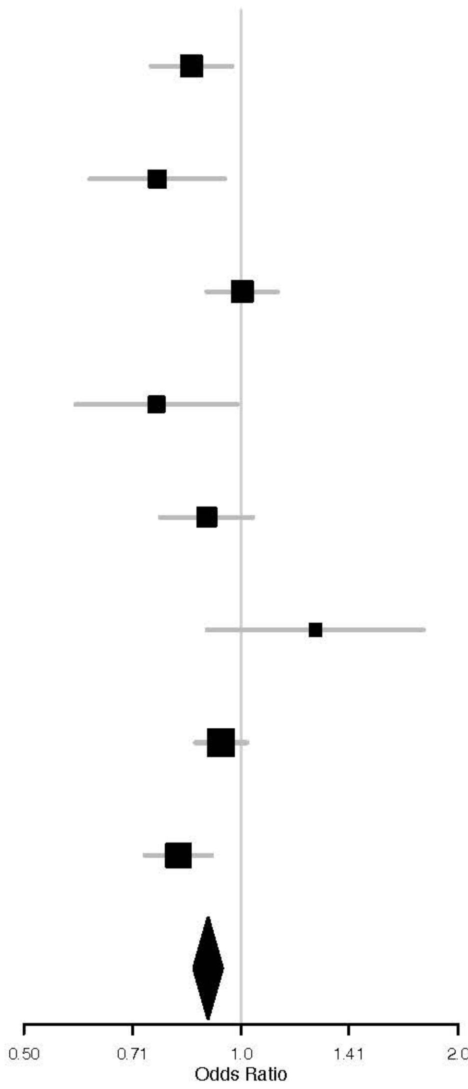

**cg18783781**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.91 |
| BAMSE_MEDALL | 47:167 | 0.97 |
| CHOP | 19:363 | 1.10 |
| GALA | 106:87 | 0.78 |
| ICAC | 97:97 | 0.97 |
| NFBC | 29:343 | 0.81 |
| PIAMA | 15:182 | 1.14 |
| RAINE | 114:405 | 0.92 |
| STOPPA | 137:323 | 0.84 |
| **META−ANALYSIS** | **657:2181** | **0.90** |



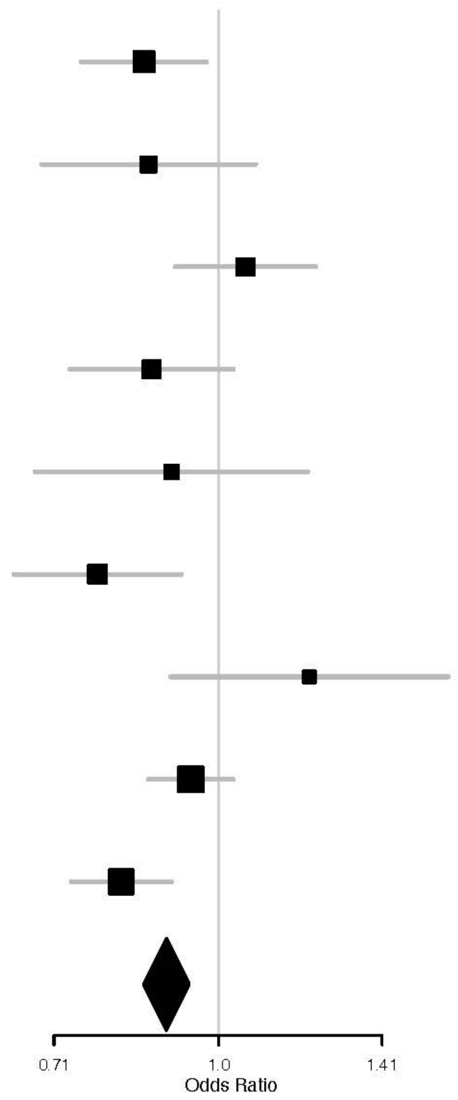

**cg25224369**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.85 |
| BAMSE_MEDALL | 47:167 | 0.77 |
| CHOP | 19:363 | 1.00 |
| ICAC | 97:97 | 0.76 |
| NFBC | 29:343 | 0.90 |
| PIAMA | 15:182 | 1.27 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.82 |
| **META−ANALYSIS** | **551:2094** | **0.90** |



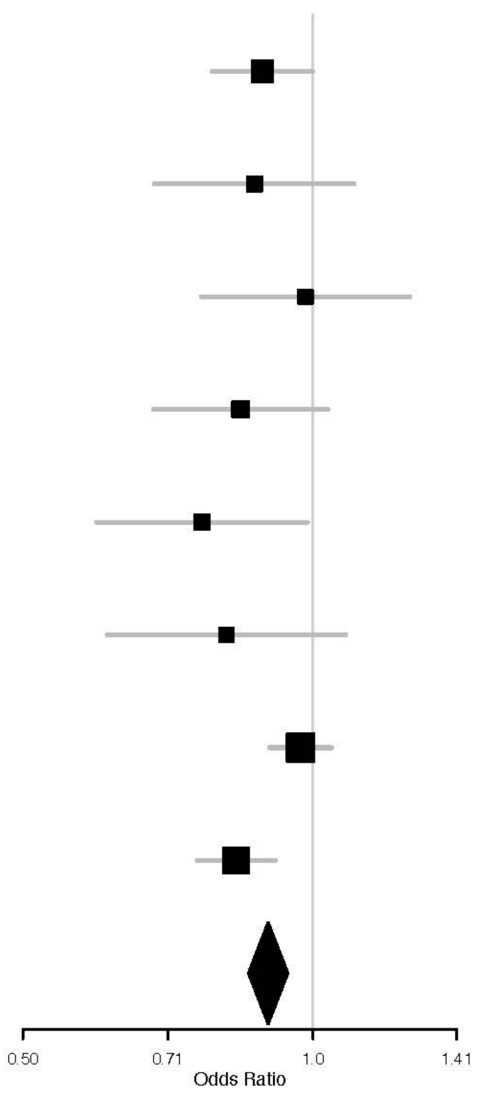

**cg02473287**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.85 |
| BAMSE_MEDALL | 47:167 | 0.86 |
| CHOP | 19:363 | 1.06 |
| GALA | 106:87 | 0.87 |
| ICAC | 97:97 | 0.91 |
| NFBC | 29:343 | 0.78 |
| PIAMA | 15:182 | 1.21 |
| RAINE | 114:405 | 0.94 |
| STOPPA | 137:323 | 0.81 |
| **META−ANALYSIS** | **657:2181** | **0.90** |



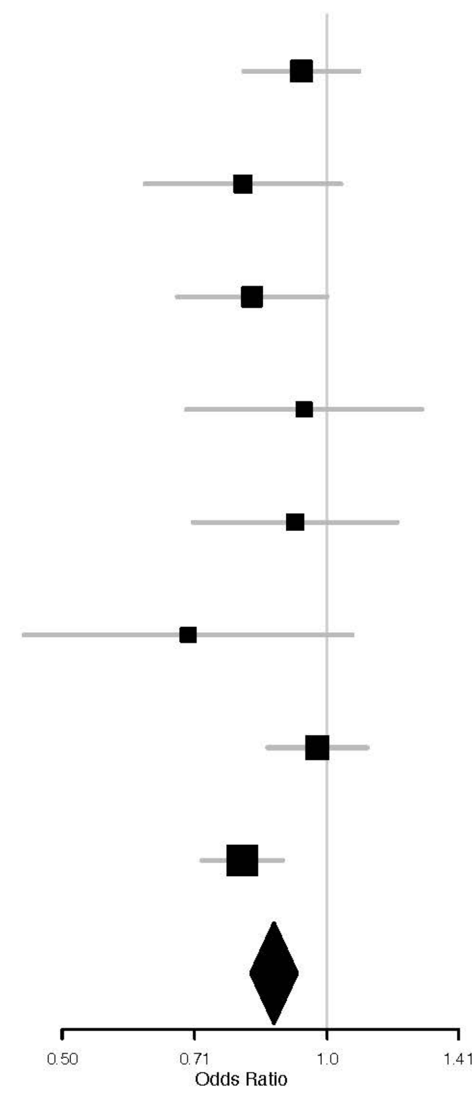

**cg00327263**

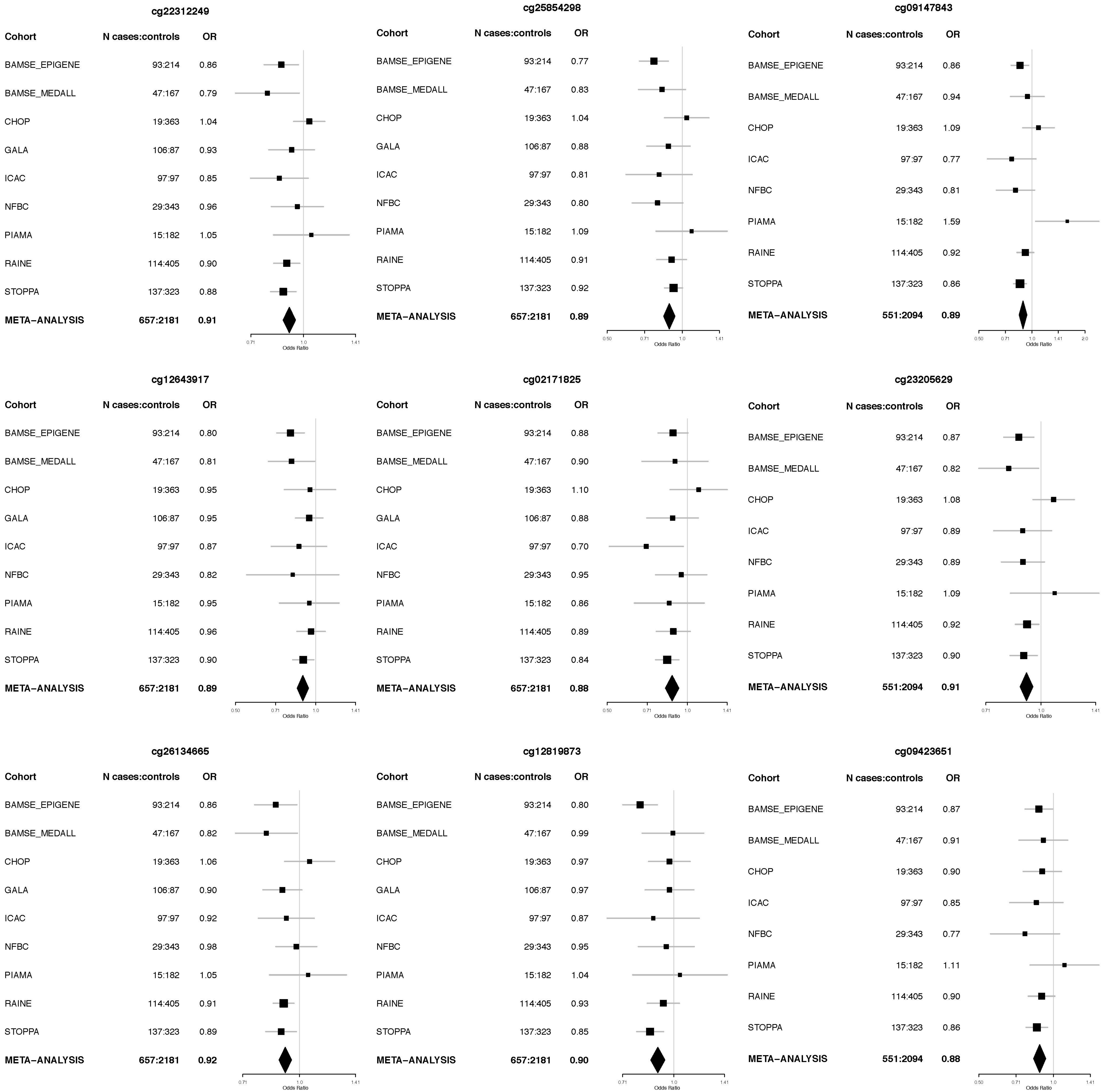
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.89 |
| BAMSE_MEDALL | 47:167 | 0.87 |
| CHOP | 19:363 | 0.98 |
| ICAC | 97:97 | 0.84 |
| NFBC | 29:343 | 0.77 |
| PIAMA | 15:182 | 0.81 |
| RAINE | 114:405 | 0.97 |
| STOPPA | 137:323 | 0.83 |
| **META−ANALYSIS** | **551:2094** | **0.90** |

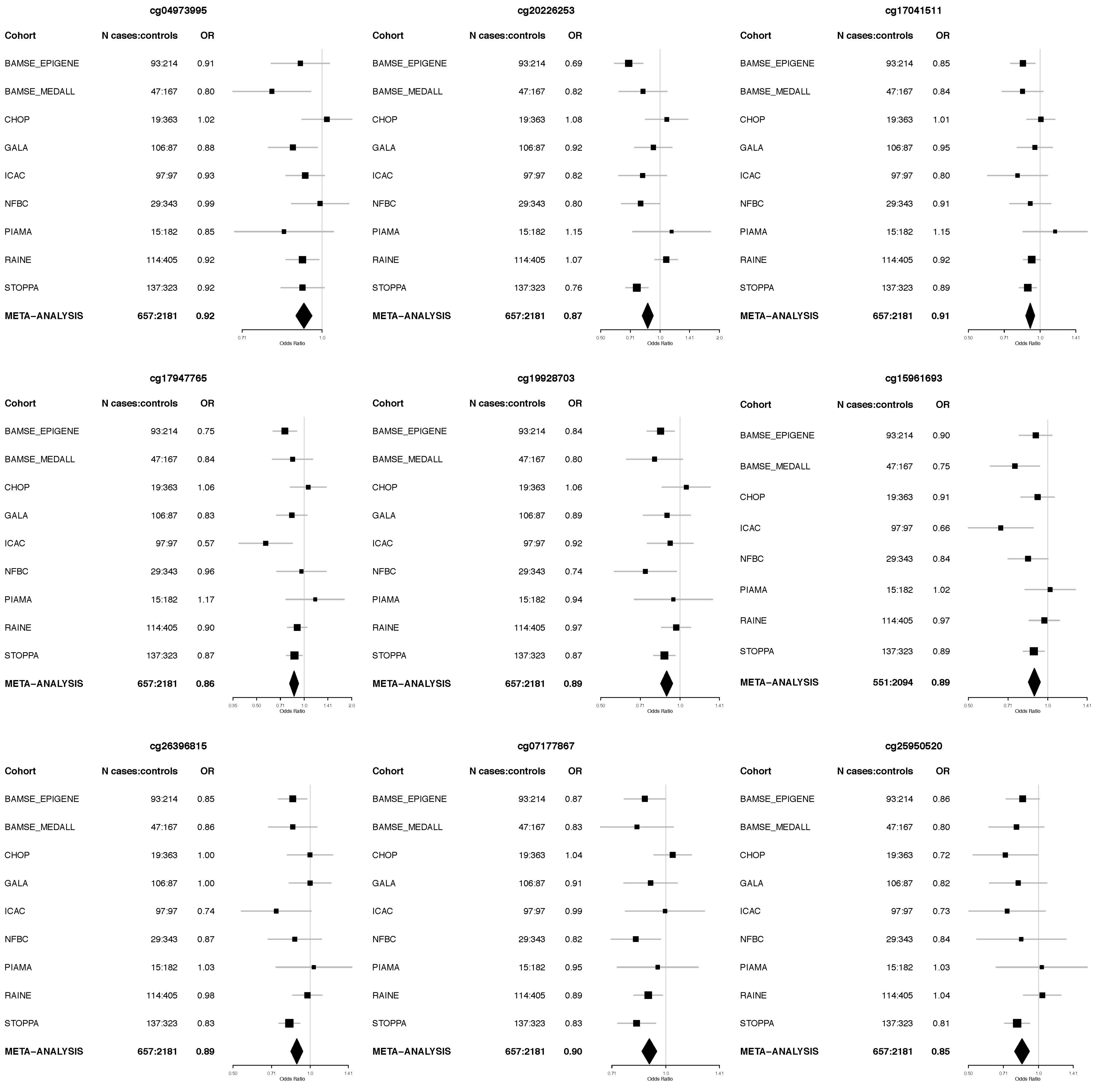


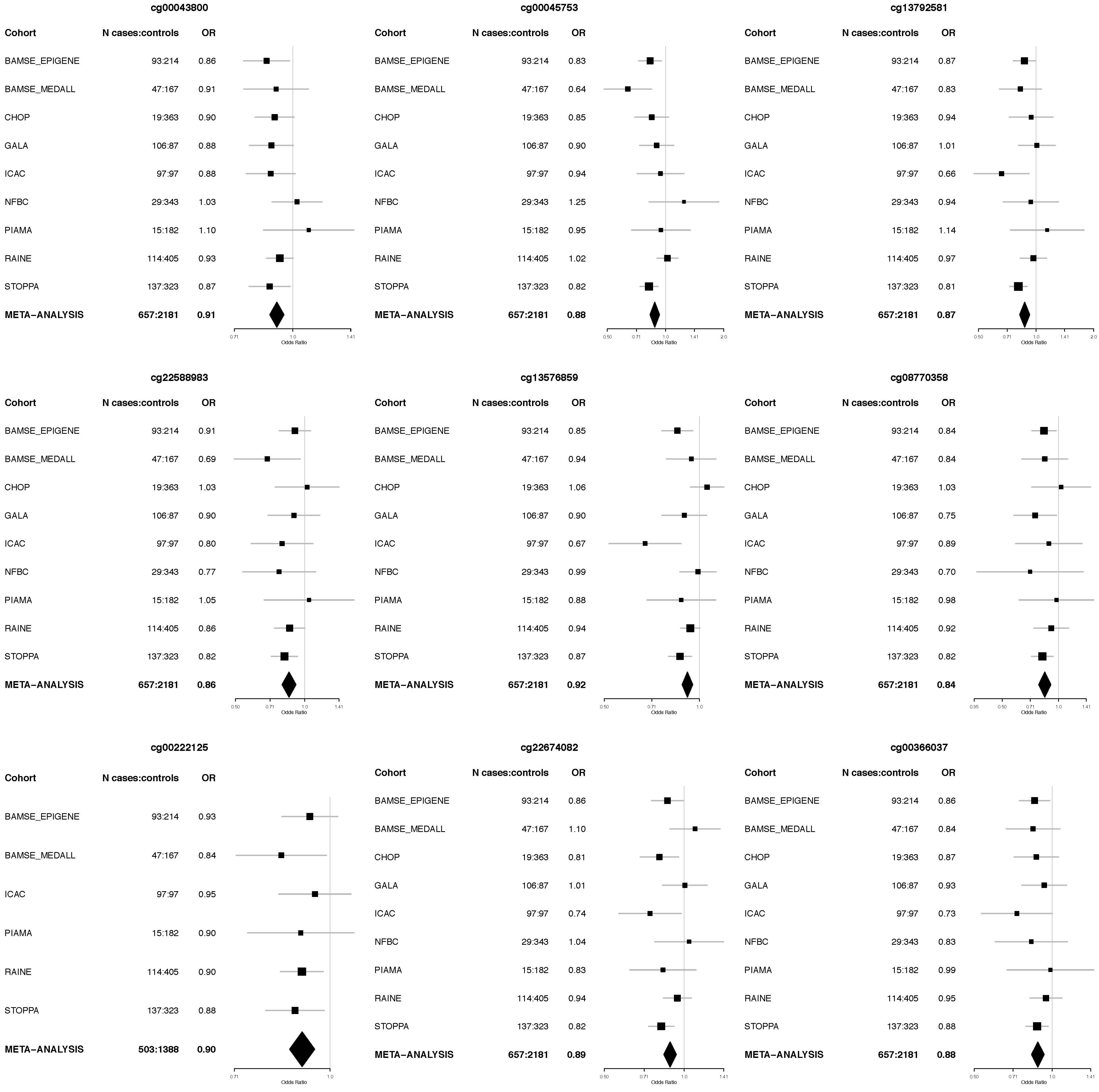

**cg24818699**

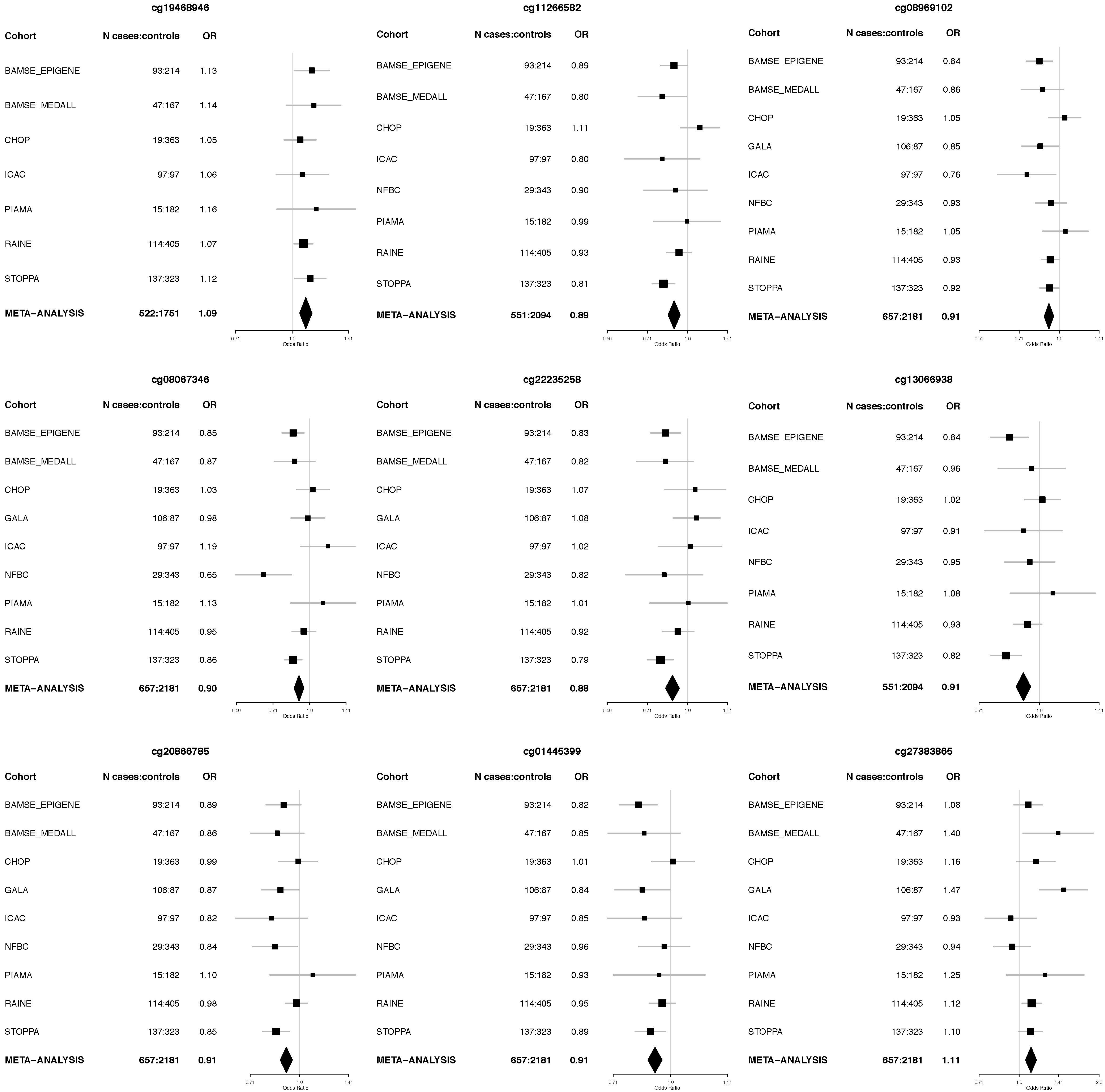
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.93 |
| BAMSE_MEDALL | 47:167 | 0.80 |
| CHOP | 19:363 | 0.82 |
| ICAC | 97:97 | 0.94 |
| NFBC | 29:343 | 0.92 |
| PIAMA | 15:182 | 0.70 |
| RAINE | 114:405 | 0.97 |
| STOPPA | 137:323 | 0.80 |
| **META−ANALYSIS** | **551:2094** | **0.87** |




cg22312249
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.79
CHOP 19:363 1.04
GALA 106:87 0.93
ICAC 97:97 0.85
NFBC 29:343 0.96
PIAMA 15:182 1.05
RAINE 114:405 0.90
STOPPA 137:323 0.88
META−ANALYSIS 657:2181 0.91
Odds Ratio
cg25854298
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.77
BAMSE_MEDALL 47:167 0.83
CHOP 19:363 1.04
GALA 106:87 0.88
ICAC 97:97 0.81
NFBC 29:343 0.80
PIAMA 15:182 1.09
RAINE 114:405 0.91
STOPPA 137:323 0.92
META−ANALYSIS 657:2181 0.89
Odds Ratio
cg09147843
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.94
CHOP 19:363 1.09
ICAC 97:97 0.77
NFBC 29:343 0.81
PIAMA 15:182 1.59
RAINE 114:405 0.92
STOPPA 137:323 0.86
META−ANALYSIS 551:2094 0.89
Odds Ratio
cg12643917
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.80
BAMSE_MEDALL 47:167 0.81
CHOP 19:363 0.95
GALA 106:87 0.95
ICAC 97:97 0.87
NFBC 29:343 0.82
PIAMA 15:182 0.95
RAINE 114:405 0.96
STOPPA 137:323 0.90
META−ANALYSIS 657:2181 0.89
Odds Ratio
cg02171825
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.88
BAMSE_MEDALL 47:167 0.90
CHOP 19:363 1.10
GALA 106:87 0.88
ICAC 97:97 0.70
NFBC 29:343 0.95
PIAMA 15:182 0.86
RAINE 114:405 0.89
STOPPA 137:323 0.84
META−ANALYSIS 657:2181 0.88
Odds Ratio
cg23205629
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.87
BAMSE_MEDALL 47:167 0.82
CHOP 19:363 1.08
ICAC 97:97 0.89
NFBC 29:343 0.89
PIAMA 15:182 1.09
RAINE 114:405 0.92
STOPPA 137:323 0.90
META−ANALYSIS 551:2094 0.91
Odds Ratio
cg26134665
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.82
CHOP 19:363 1.06
GALA 106:87 0.90
ICAC 97:97 0.92
NFBC 29:343 0.98
PIAMA 15:182 1.05
RAINE 114:405 0.91
STOPPA 137:323 0.89
META−ANALYSIS 657:2181 0.92
Odds Ratio
cg12819873
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.80
BAMSE_MEDALL 47:167 0.99
CHOP 19:363 0.97
GALA 106:87 0.97
ICAC 97:97 0.87
NFBC 29:343 0.95
PIAMA 15:182 1.04
RAINE 114:405 0.93
STOPPA 137:323 0.85
META−ANALYSIS 657:2181 0.90
Odds Ratio
cg09423651
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.87
BAMSE_MEDALL 47:167 0.91
CHOP 19:363 0.90
ICAC 97:97 0.85
NFBC 29:343 0.77
PIAMA 15:182 1.11
RAINE 114:405 0.90
STOPPA 137:323 0.86
META−ANALYSIS 551:2094 0.88
Odds Ratio

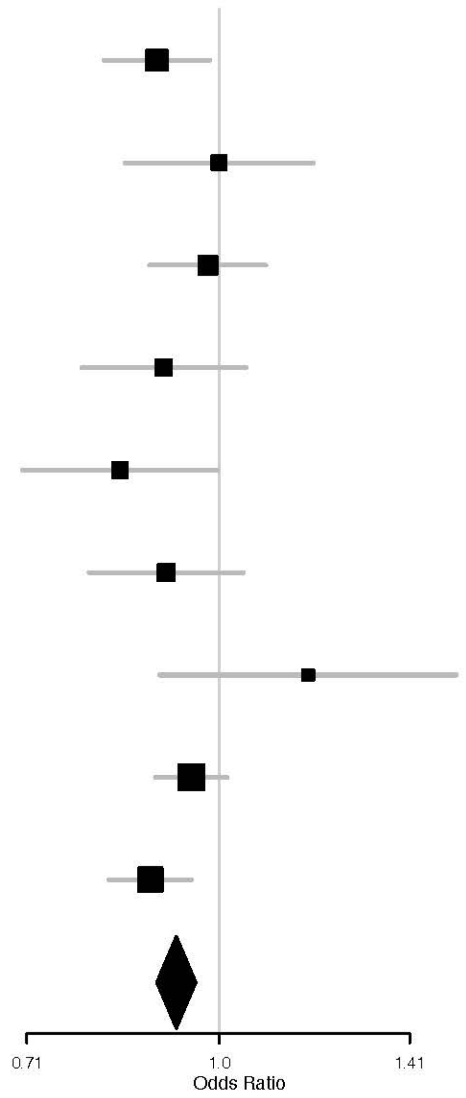

cg04973995
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.91
BAMSE_MEDALL 47:167 0.80
CHOP 19:363 1.02
GALA 106:87 0.88
ICAC 97:97 0.93
NFBC 29:343 0.99
PIAMA 15:182 0.85
RAINE 114:405 0.92
STOPPA 137:323 0.92
META−ANALYSIS 657:2181 0.92
0.71
1.0
Odds Ratio
cg20226253
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.69
BAMSE_MEDALL 47:167 0.82
CHOP 19:363 1.08
GALA 106:87 0.92
ICAC 97:97 0.82
NFBC 29:343 0.80
PIAMA 15:182 1.15
RAINE 114:405 1.07
STOPPA 137:323 0.76
META−ANALYSIS 657:2181 0.87
0.50
0.71
1.0
1.41
2.0
Odds Ratio
cg17041511
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.84
CHOP 19:363 1.01
GALA 106:87 0.95
ICAC 97:97 0.80
NFBC 29:343 0.91
PIAMA 15:182 1.15
RAINE 114:405 0.92
STOPPA 137:323 0.89
META−ANALYSIS 657:2181 0.91
0.50
0.71
1.0
1.41
Odds Ratio
cg17947765
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.75
BAMSE_MEDALL 47:167 0.84
CHOP 19:363 1.06
GALA 106:87 0.83
ICAC 97:97 0.57
NFBC 29:343 0.96
PIAMA 15:182 1.17
RAINE 114:405 0.90
STOPPA 137:323 0.87
META−ANALYSIS 657:2181 0.86
0.35
0.50
0.71
1.0
1.41
2.0
Odds Ratio
cg19928703
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.80
CHOP 19:363 1.06
GALA 106:87 0.89
ICAC 97:97 0.92
NFBC 29:343 0.74
PIAMA 15:182 0.94
RAINE 114:405 0.97
STOPPA 137:323 0.87
META−ANALYSIS 657:2181 0.89
0.50
0.71
1.0
1.41
Odds Ratio
cg15961693
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.90
BAMSE_MEDALL 47:167 0.75
CHOP 19:363 0.91
ICAC 97:97 0.66
NFBC 29:343 0.84
PIAMA 15:182 1.02
RAINE 114:405 0.97
STOPPA 137:323 0.89
META−ANALYSIS 551:2094 0.89
0.50
0.71
1.0
1.41
Odds Ratio
cg26396815
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.86
CHOP 19:363 1.00
GALA 106:87 1.00
ICAC 97:97 0.74
NFBC 29:343 0.87
PIAMA 15:182 1.03
RAINE 114:405 0.98
STOPPA 137:323 0.83
META−ANALYSIS 657:2181 0.89
0.50
0.71
1.0
1.41
Odds Ratio
cg07177867
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.87
BAMSE_MEDALL 47:167 0.83
CHOP 19:363 1.04
GALA 106:87 0.91
ICAC 97:97 0.99
NFBC 29:343 0.82
PIAMA 15:182 0.95
RAINE 114:405 0.89
STOPPA 137:323 0.83
META−ANALYSIS 657:2181 0.90
0.71
1.0
1.41
Odds Ratio
cg25950520
Cohort
N cases:controls
OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.80
CHOP 19:363 0.72
GALA 106:87 0.82
ICAC 97:97 0.73
NFBC 29:343 0.84
PIAMA 15:182 1.03
RAINE 114:405 1.04
STOPPA 137:323 0.81
META−ANALYSIS 657:2181 0.85
0.50
0.71
1.0
1.41
Odds Ratio


cg00043800
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.91
CHOP 19:363 0.90
GALA 106:87 0.88
ICAC 97:97 0.88
NFBC 29:343 1.03
PIAMA 15:182 1.10
RAINE 114:405 0.93
STOPPA 137:323 0.87
META−ANALYSIS 657:2181 0.91
0.71 1.0 1.41
Odds Ratio
cg00045753
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.83
BAMSE_MEDALL 47:167 0.64
CHOP 19:363 0.85
GALA 106:87 0.90
ICAC 97:97 0.94
NFBC 29:343 1.25
PIAMA 15:182 0.95
RAINE 114:405 1.02
STOPPA 137:323 0.82
META−ANALYSIS 657:2181 0.88
0.50 0.71 1.0 1.41 2.0
Odds Ratio
cg13792581
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.87
BAMSE_MEDALL 47:167 0.83
CHOP 19:363 0.94
GALA 106:87 1.01
ICAC 97:97 0.66
NFBC 29:343 0.94
PIAMA 15:182 1.14
RAINE 114:405 0.97
STOPPA 137:323 0.81
META−ANALYSIS 657:2181 0.87
0.50 0.71 1.0 1.41 2.0
Odds Ratio
cg22588983
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.91
BAMSE_MEDALL 47:167 0.69
CHOP 19:363 1.03
GALA 106:87 0.90
ICAC 97:97 0.80
NFBC 29:343 0.77
PIAMA 15:182 1.05
RAINE 114:405 0.86
STOPPA 137:323 0.82
META−ANALYSIS 657:2181 0.86
0.50 0.71 1.0 1.41
Odds Ratio
cg13576859
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.94
CHOP 19:363 1.06
GALA 106:87 0.90
ICAC 97:97 0.67
NFBC 29:343 0.99
PIAMA 15:182 0.88
RAINE 114:405 0.94
STOPPA 137:323 0.87
META−ANALYSIS 657:2181 0.92
0.50 0.71 1.0
Odds Ratio
cg08770358
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.84
CHOP 19:363 1.03
GALA 106:87 0.75
ICAC 97:97 0.89
NFBC 29:343 0.70
PIAMA 15:182 0.98
RAINE 114:405 0.92
STOPPA 137:323 0.82
META−ANALYSIS 657:2181 0.84
0.35 0.50 0.71 1.0 1.41
Odds Ratio
cg00222125
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.93
BAMSE_MEDALL 47:167 0.84
ICAC 97:97 0.95
PIAMA 15:182 0.90
RAINE 114:405 0.90
STOPPA 137:323 0.88
META−ANALYSIS 503:1388 0.90
0.71 1.0
Odds Ratio
cg22674082
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 1.10
CHOP 19:363 0.81
GALA 106:87 1.01
ICAC 97:97 0.74
NFBC 29:343 1.04
PIAMA 15:182 0.83
RAINE 114:405 0.94
STOPPA 137:323 0.82
META−ANALYSIS 657:2181 0.89
0.50 0.71 1.0 1.41
Odds Ratio
cg00366037
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.86
BAMSE_MEDALL 47:167 0.84
CHOP 19:363 0.87
GALA 106:87 0.93
ICAC 97:97 0.73
NFBC 29:343 0.83
PIAMA 15:182 0.99
RAINE 114:405 0.95
STOPPA 137:323 0.88
META−ANALYSIS 657:2181 0.88
0.50 0.71 1.0 1.41
Odds Ratio


cg19468946
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 1.13
BAMSE_MEDALL 47:167 1.14
CHOP 19:363 1.05
ICAC 97:97 1.06
PIAMA 15:182 1.16
RAINE 114:405 1.07
STOPPA 137:323 1.12
META−ANALYSIS 522:1751 1.09
0.71 1.0 1.41
Odds Ratio
cg11266582
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.89
BAMSE_MEDALL 47:167 0.80
CHOP 19:363 1.11
ICAC 97:97 0.80
NFBC 29:343 0.90
PIAMA 15:182 0.99
RAINE 114:405 0.93
STOPPA 137:323 0.81
META−ANALYSIS 551:2094 0.89
0.50 0.71 1.0 1.41
Odds Ratio
cg08969102
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.86
CHOP 19:363 1.05
GALA 106:87 0.85
ICAC 97:97 0.76
NFBC 29:343 0.93
PIAMA 15:182 1.05
RAINE 114:405 0.93
STOPPA 137:323 0.92
META−ANALYSIS 657:2181 0.91
0.50 0.71 1.0 1.41
Odds Ratio
cg08067346
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.85
BAMSE_MEDALL 47:167 0.87
CHOP 19:363 1.03
GALA 106:87 0.98
ICAC 97:97 1.19
NFBC 29:343 0.65
PIAMA 15:182 1.13
RAINE 114:405 0.95
STOPPA 137:323 0.86
META−ANALYSIS 657:2181 0.90
0.50 0.71 1.0 1.41
Odds Ratio
cg22235258
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.83
BAMSE_MEDALL 47:167 0.82
CHOP 19:363 1.07
GALA 106:87 1.08
ICAC 97:97 1.02
NFBC 29:343 0.82
PIAMA 15:182 1.01
RAINE 114:405 0.92
STOPPA 137:323 0.79
META−ANALYSIS 657:2181 0.88
0.50 0.71 1.0 1.41
Odds Ratio
cg13066938
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.84
BAMSE_MEDALL 47:167 0.96
CHOP 19:363 1.02
ICAC 97:97 0.91
NFBC 29:343 0.95
PIAMA 15:182 1.08
RAINE 114:405 0.93
STOPPA 137:323 0.82
META−ANALYSIS 551:2094 0.91
0.71 1.0 1.41
Odds Ratio
cg20866785
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.89
BAMSE_MEDALL 47:167 0.86
CHOP 19:363 0.99
GALA 106:87 0.87
ICAC 97:97 0.82
NFBC 29:343 0.84
PIAMA 15:182 1.10
RAINE 114:405 0.98
STOPPA 137:323 0.85
META−ANALYSIS 657:2181 0.91
0.71 1.0 1.41
Odds Ratio
cg01445399
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 0.82
BAMSE_MEDALL 47:167 0.85
CHOP 19:363 1.01
GALA 106:87 0.84
ICAC 97:97 0.85
NFBC 29:343 0.96
PIAMA 15:182 0.93
RAINE 114:405 0.95
STOPPA 137:323 0.89
META−ANALYSIS 657:2181 0.91
0.71 1.0 1.41
Odds Ratio
cg27383865
Cohort N cases:controls OR
BAMSE_EPIGENE 93:214 1.08
BAMSE_MEDALL 47:167 1.40
CHOP 19:363 1.16
GALA 106:87 1.47
ICAC 97:97 0.93
NFBC 29:343 0.94
PIAMA 15:182 1.25
RAINE 114:405 1.12
STOPPA 137:323 1.10
META−ANALYSIS 657:2181 1.11
0.71 1.0 1.41 2.0
Odds Ratio

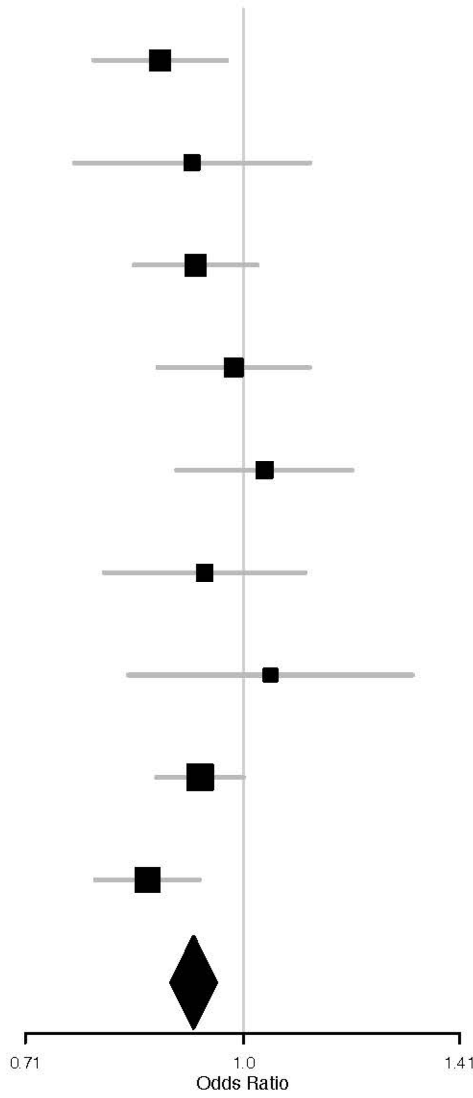
**cg14978242**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.89 |
| BAMSE_MEDALL | 47:167 | 1.00 |
| CHOP | 19:363 | 0.98 |
| GALA | 106:87 | 0.90 |
| ICAC | 97:97 | 0.84 |
| NFBC | 29:343 | 0.91 |
| PIAMA | 15:182 | 1.17 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.88 |
| **META-ANALYSIS** | **657:2181** | **0.93** |



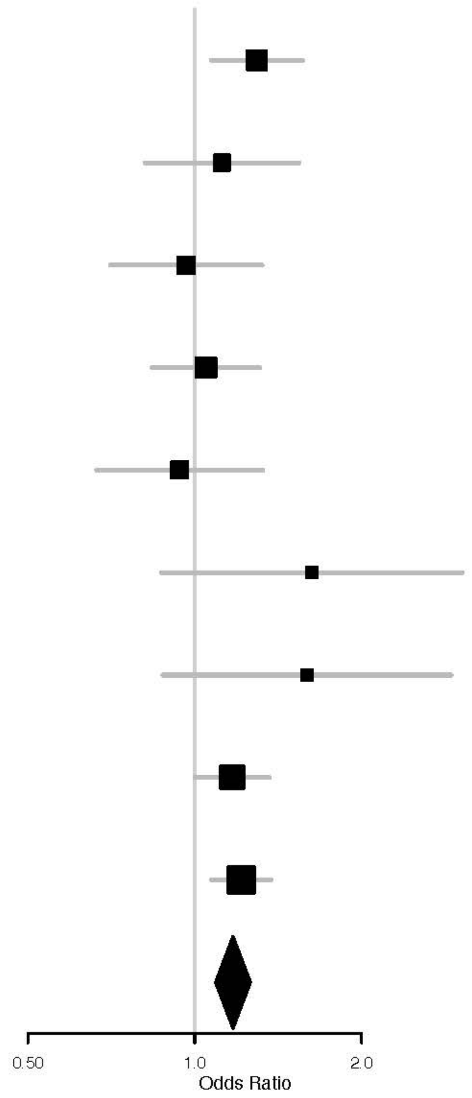

**cg21073212**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.88 |
| BAMSE_MEDALL | 47:167 | 0.92 |
| CHOP | 19:363 | 0.93 |
| GALA | 106:87 | 0.98 |
| ICAC | 97:97 | 1.03 |
| NFBC | 29:343 | 0.94 |
| PIAMA | 15:182 | 1.04 |
| RAINE | 114:405 | 0.93 |
| STOPPA | 137:323 | 0.86 |
| **META-ANALYSIS** | **657:2181** | **0.92** |



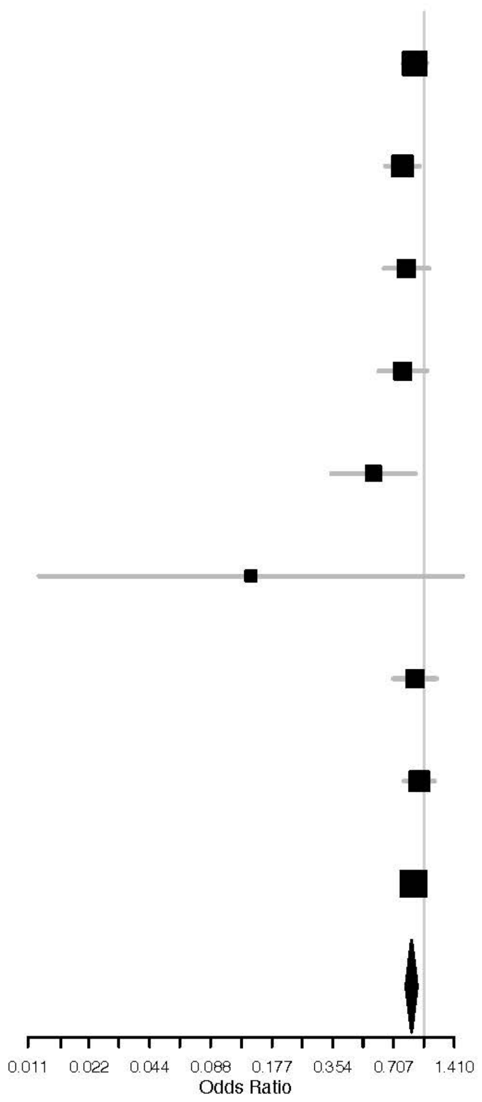

**cg15219163**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 1.29 |
| BAMSE_MEDALL | 47:167 | 1.12 |
| CHOP | 19:363 | 0.97 |
| GALA | 106:87 | 1.05 |
| ICAC | 97:97 | 0.94 |
| NFBC | 29:343 | 1.63 |
| PIAMA | 15:182 | 1.59 |
| RAINE | 114:405 | 1.17 |
| STOPPA | 137:323 | 1.21 |
| **META-ANALYSIS** | **657:2181** | **1.17** |



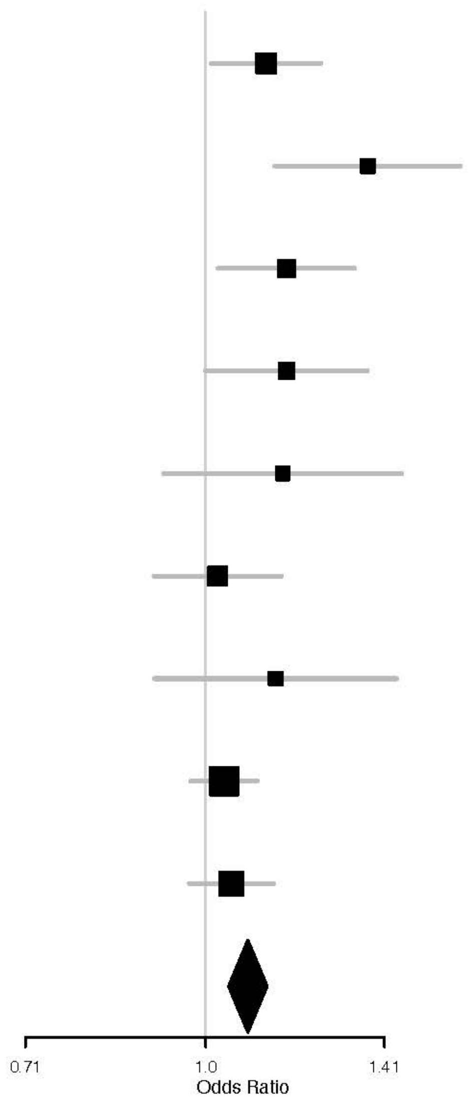

**cg24576940**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.78 |
| CHOP | 19:363 | 0.82 |
| GALA | 106:87 | 0.79 |
| ICAC | 97:97 | 0.56 |
| NFBC | 29:343 | 0.14 |
| PIAMA | 15:182 | 0.90 |
| RAINE | 114:405 | 0.95 |
| STOPPA | 137:323 | 0.89 |
| **META-ANALYSIS** | **657:2181** | **0.87** |



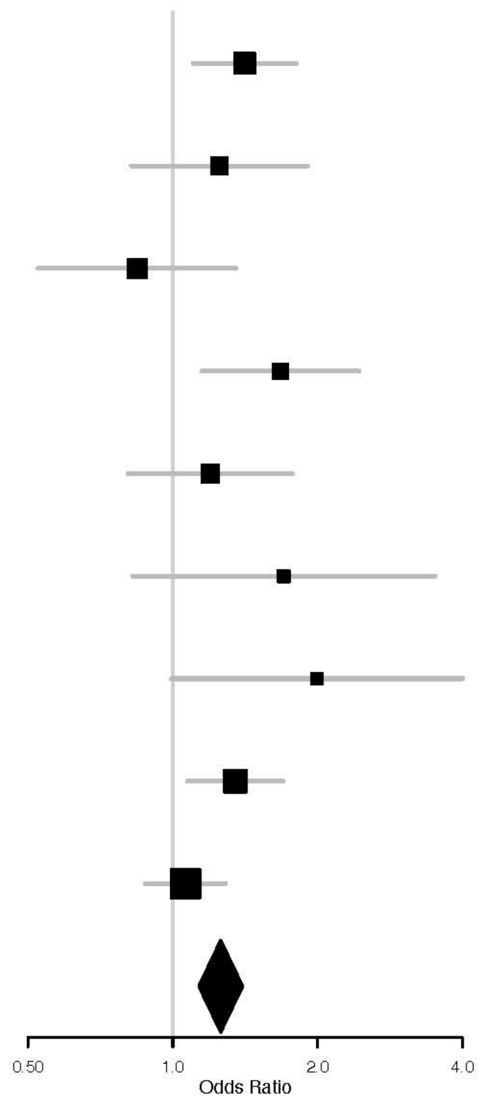

**cg15304012**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 1.12 |
| BAMSE_MEDALL | 47:167 | 1.37 |
| CHOP | 19:363 | 1.17 |
| GALA | 106:87 | 1.17 |
| ICAC | 97:97 | 1.16 |
| NFBC | 29:343 | 1.02 |
| PIAMA | 15:182 | 1.14 |
| RAINE | 114:405 | 1.04 |
| STOPPA | 137:323 | 1.05 |
| **META-ANALYSIS** | **657:2181** | **1.08** |



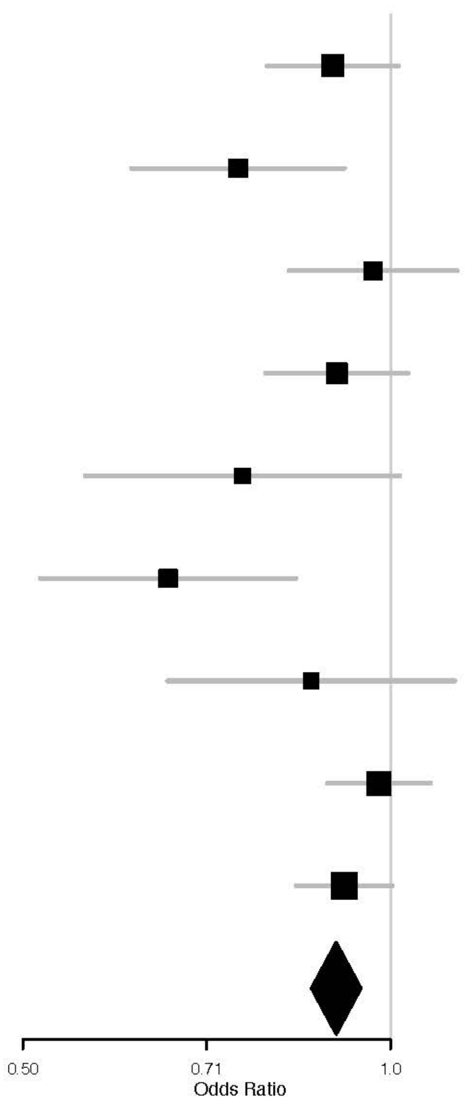

**cg13007207**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 1.41 |
| BAMSE_MEDALL | 47:167 | 1.25 |
| CHOP | 19:363 | 0.84 |
| GALA | 106:87 | 1.67 |
| ICAC | 97:97 | 1.20 |
| NFBC | 29:343 | 1.70 |
| PIAMA | 15:182 | 2.00 |
| RAINE | 114:405 | 1.35 |
| STOPPA | 137:323 | 1.06 |
| **META-ANALYSIS** | **657:2181** | **1.26** |



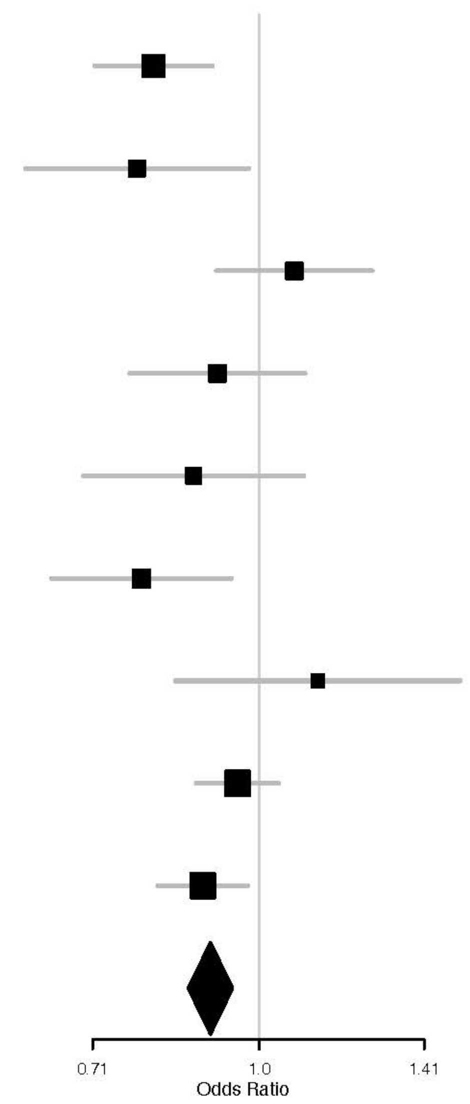

**cg26774971**

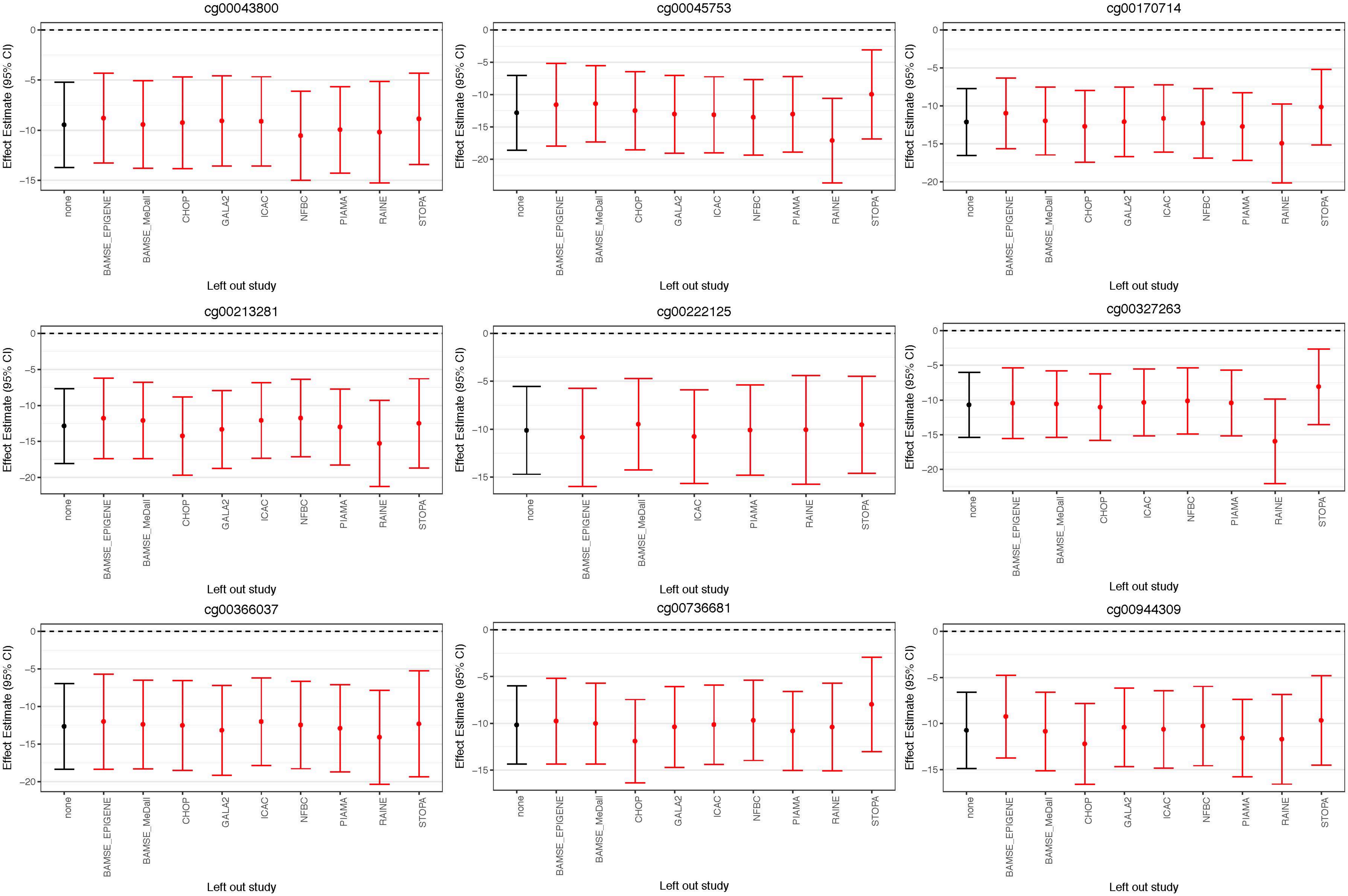
| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.90 |
| BAMSE_MEDALL | 47:167 | 0.75 |
| CHOP | 19:363 | 0.97 |
| GALA | 106:87 | 0.90 |
| ICAC | 97:97 | 0.76 |
| NFBC | 29:343 | 0.66 |
| PIAMA | 15:182 | 0.86 |
| RAINE | 114:405 | 0.98 |
| STOPPA | 137:323 | 0.92 |
| **META-ANALYSIS** | **657:2181** | **0.90** |




**cg21627181**

| Cohort | N cases:controls | OR |
|---|---|---|
| BAMSE_EPIGENE | 93:214 | 0.80 |
| BAMSE_MEDALL | 47:167 | 0.78 |
| CHOP | 19:363 | 1.08 |
| GALA | 106:87 | 0.92 |
| ICAC | 97:97 | 0.87 |
| NFBC | 29:343 | 0.78 |
| PIAMA | 15:182 | 1.13 |
| RAINE | 114:405 | 0.96 |
| STOPPA | 137:323 | 0.89 |
| **META-ANALYSIS** | **657:2181** | **0.90** |




cg00043800
Effect Estimate (95% CI)
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BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg00045753
Effect Estimate (95% CI)
0
−5
−10
−15
−20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg00170714
Effect Estimate (95% CI)
0
−5
−10
−15
−20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg00213281
Effect Estimate (95% CI)
0
−5
−10
−15
−20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg00222125
Effect Estimate (95% CI)
0
−5
−10
−15
none
BAMSE_EPIGENE
BAMSE_MeDall
ICAC
PIAMA
RAINE
STOPA
Left out study
cg00327263
Effect Estimate (95% CI)
0
−5
−10
−15
−20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg00366037
Effect Estimate (95% CI)
0
−5
−10
−15
−20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg00736681
Effect Estimate (95% CI)
0
−5
−10
−15
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg00944309
Effect Estimate (95% CI)
0
−5
−10
−15
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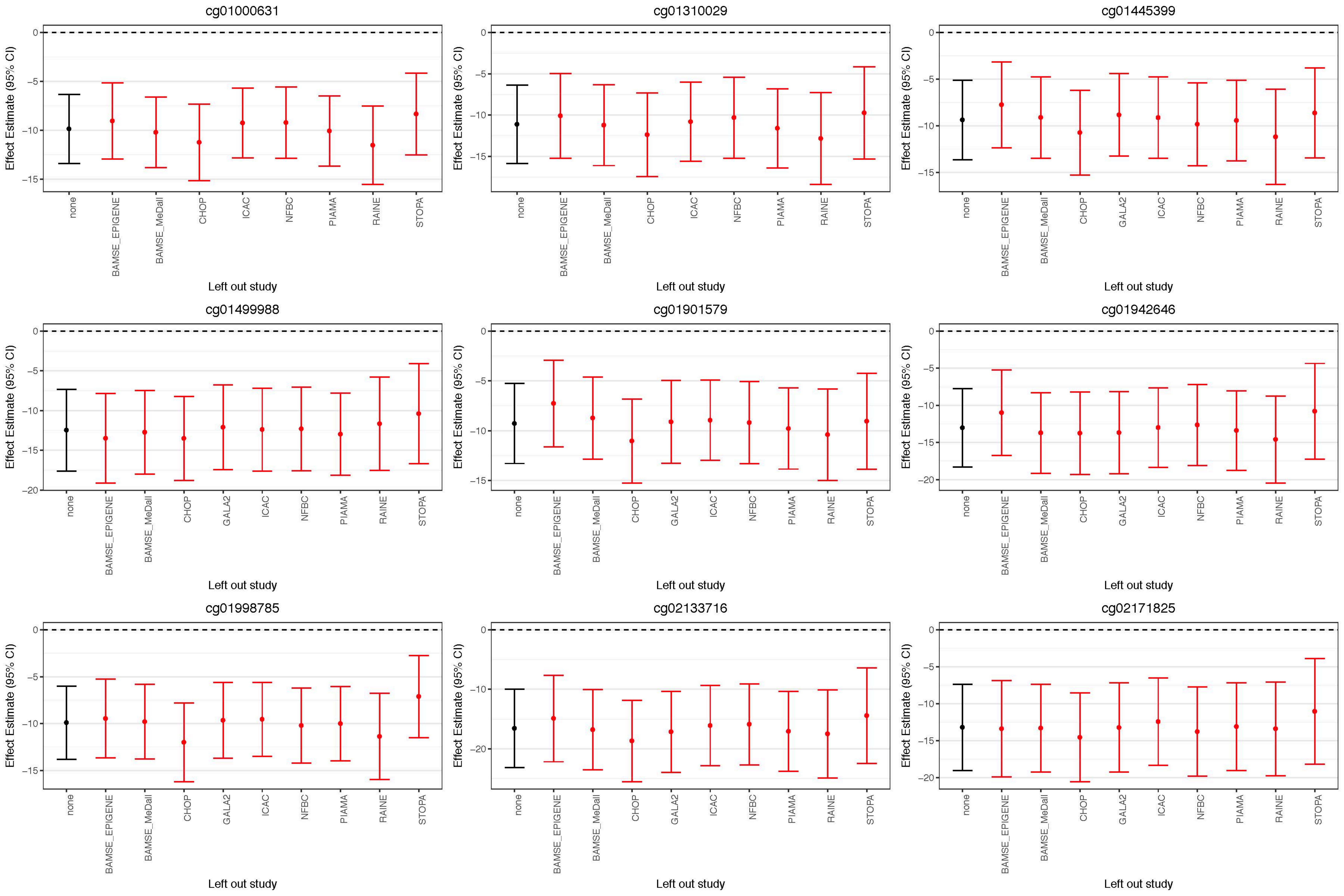
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study



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cg01310029
cg01445399
cg01499988
cg01901579
cg01942646
cg01998785
cg02133716
cg02171825
Effect Estimate (95% CI)
Left out study
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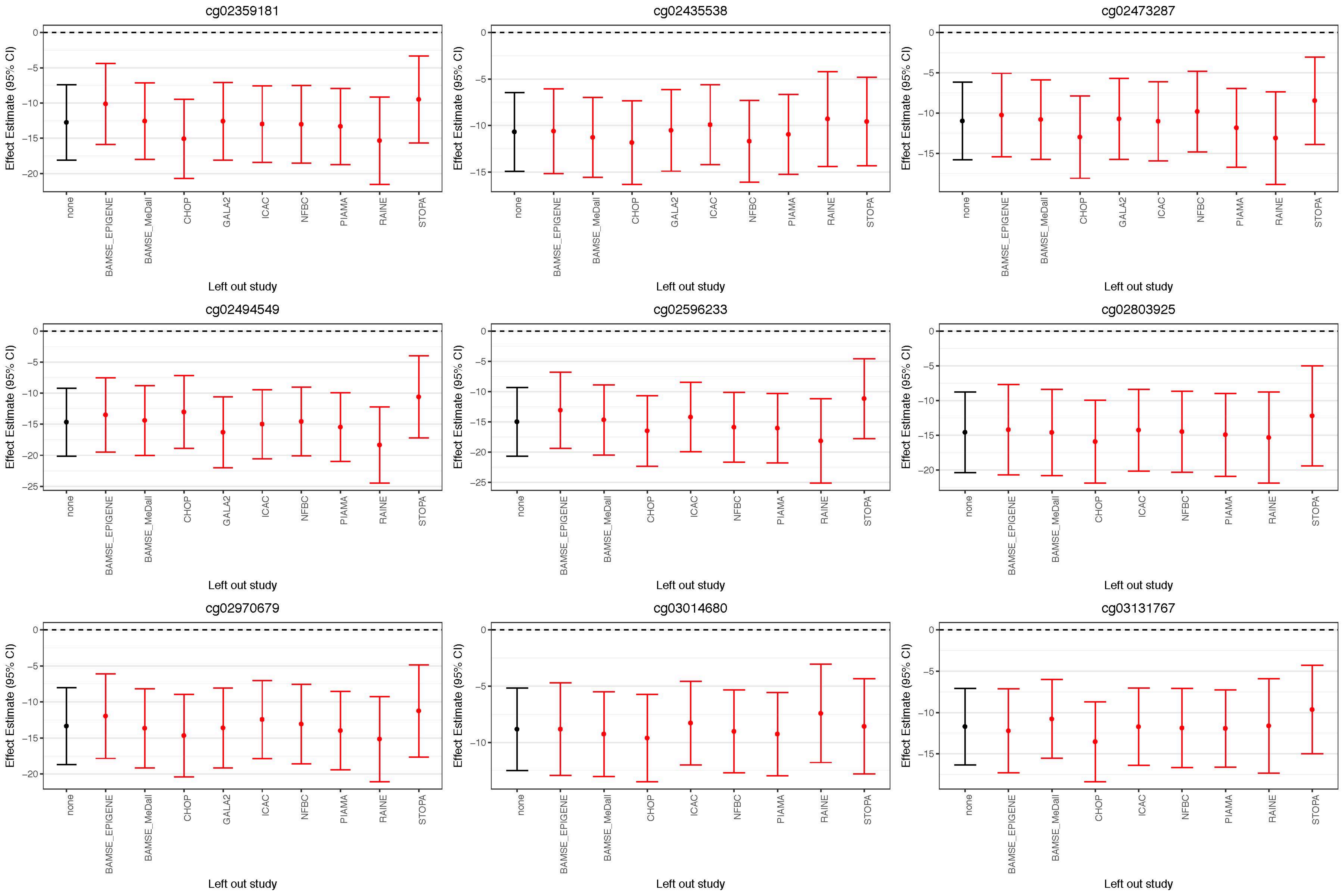
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA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Effect Estimate (95% CI)
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CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg02435538
Effect Estimate (95% CI)
0
-5
-10
-15
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg02473287
Effect Estimate (95% CI)
0
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-15
none
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CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg02494549
Effect Estimate (95% CI)
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-10
-15
-20
-25
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BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg02596233
Effect Estimate (95% CI)
0
-5
-10
-15
-20
-25
none
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BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg02803925
Effect Estimate (95% CI)
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-10
-15
-20
none
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BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg02970679
Effect Estimate (95% CI)
0
-5
-10
-15
-20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg03014680
Effect Estimate (95% CI)
0
-5
-10
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg03131767
Effect Estimate (95% CI)
0
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-10
-15
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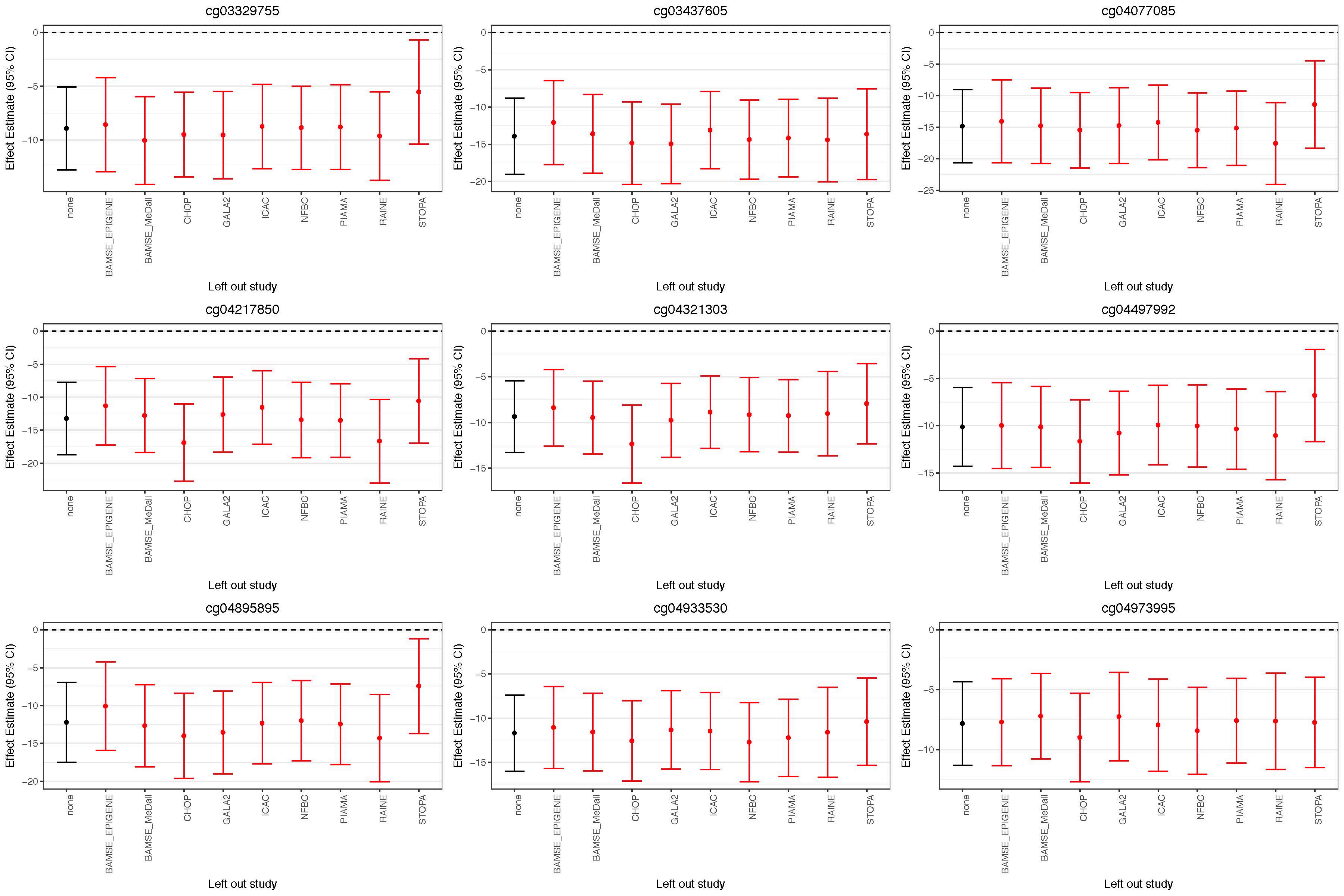
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study



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cg04077085
cg04217850
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cg04497992
cg04895895
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cg04973995
Effect Estimate (95% CI)
Left out study
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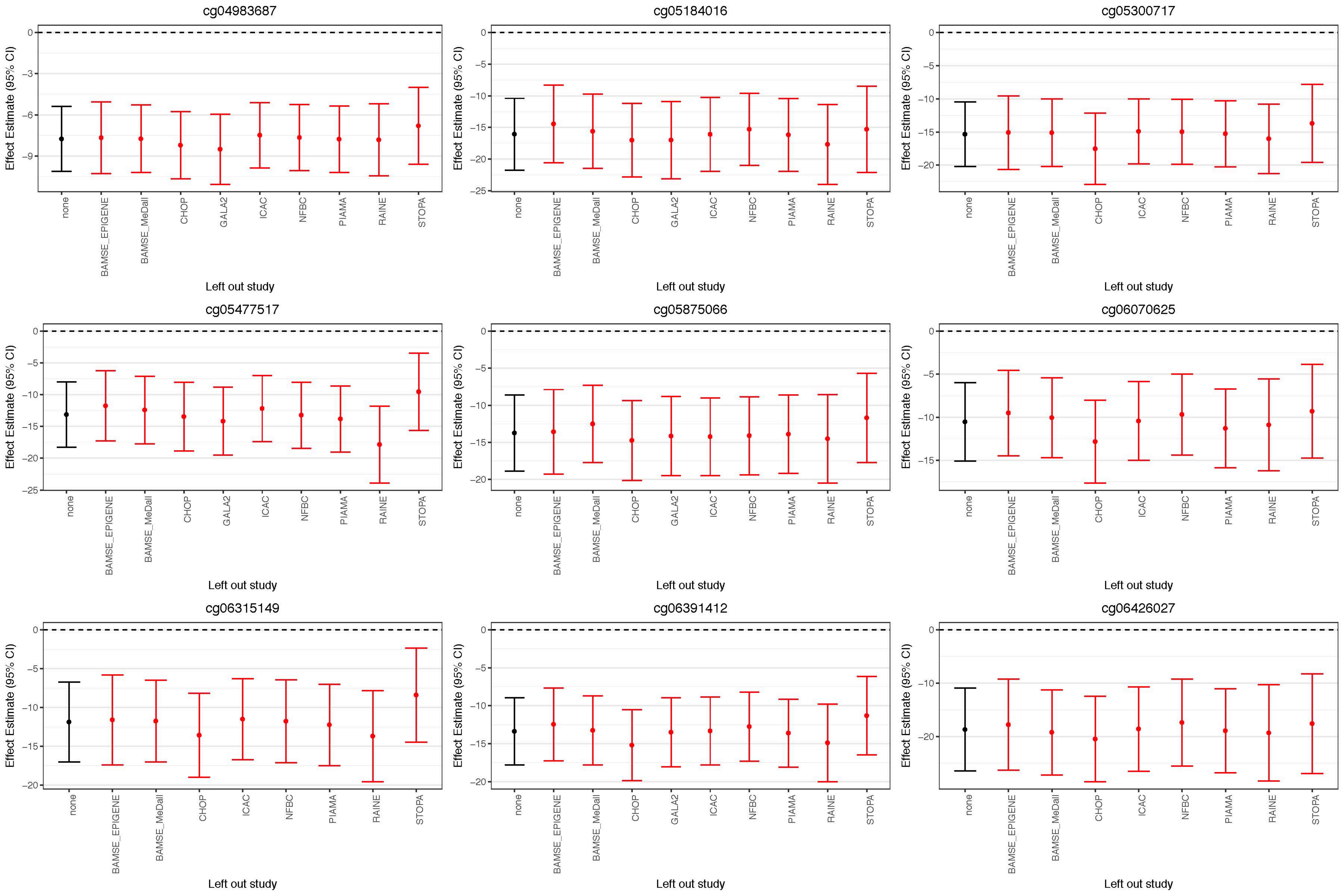
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA


cg04983687
Effect Estimate (95% CI)
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BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg05184016
Effect Estimate (95% CI)
0
-5
-10
-15
-20
-25
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg05300717
Effect Estimate (95% CI)
0
-5
-10
-15
-20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg05477517
Effect Estimate (95% CI)
0
-5
-10
-15
-20
-25
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg05875066
Effect Estimate (95% CI)
0
-5
-10
-15
-20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg06070625
Effect Estimate (95% CI)
0
-5
-10
-15
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg06315149
Effect Estimate (95% CI)
0
-5
-10
-15
-20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg06391412
Effect Estimate (95% CI)
0
-5
-10
-15
-20
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg06426027
Effect Estimate (95% CI)
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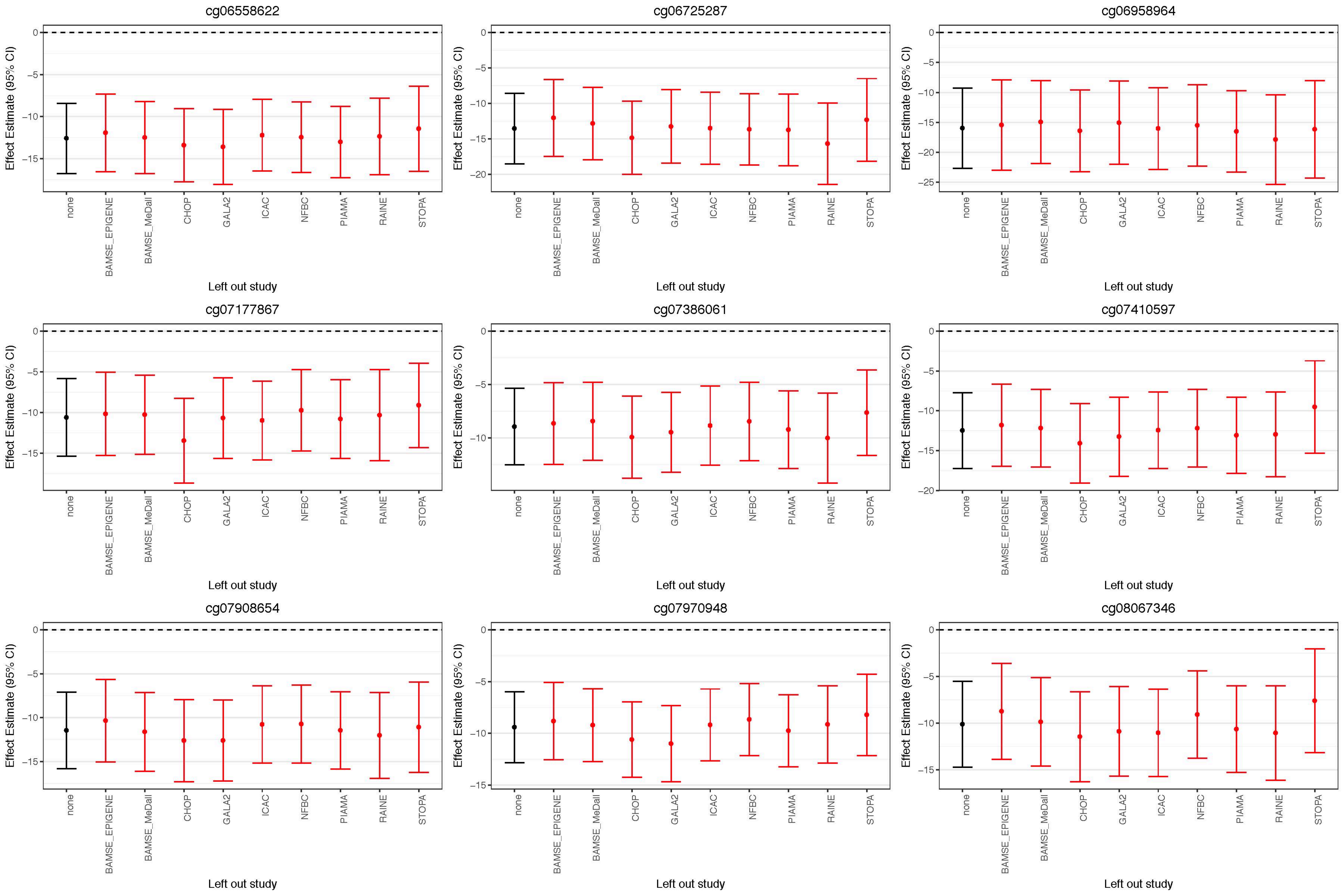
PIAMA
RAINE
STOPA
Left out study



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cg06958964
cg07177867
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Effect Estimate (95% CI)
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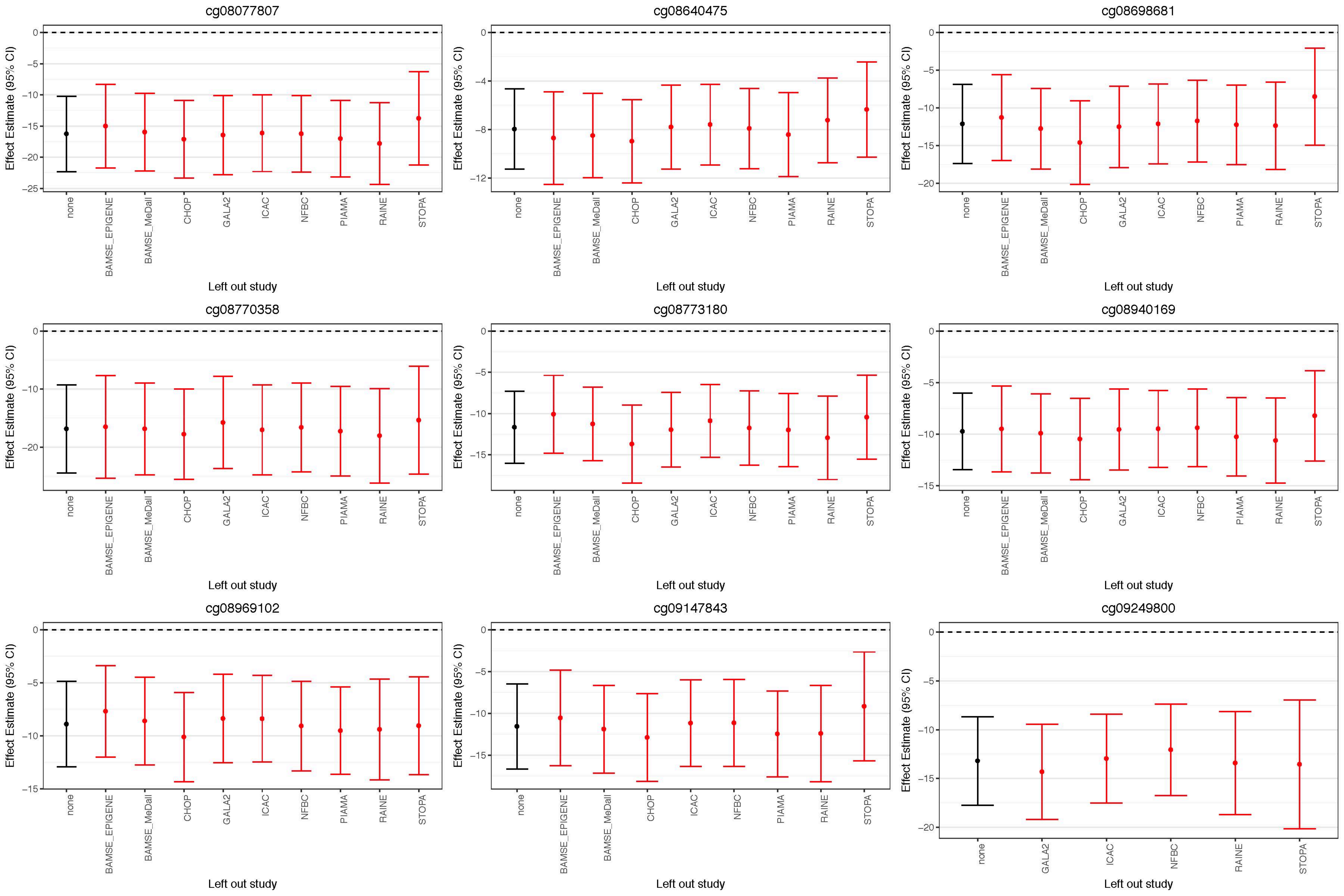
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Effect Estimate (95% CI)
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PIAMA
RAINE
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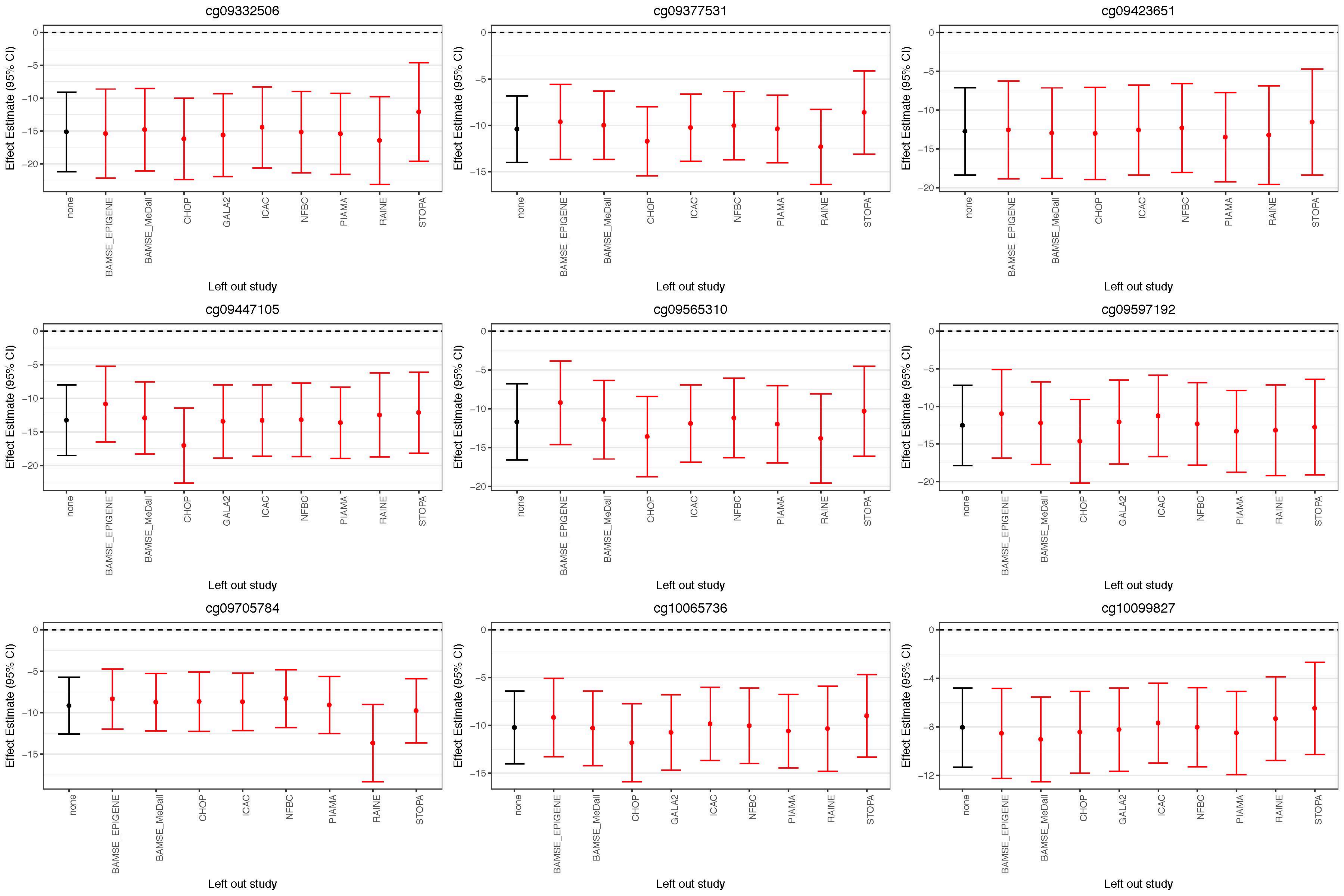
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Effect Estimate (95% CI)
Left out study
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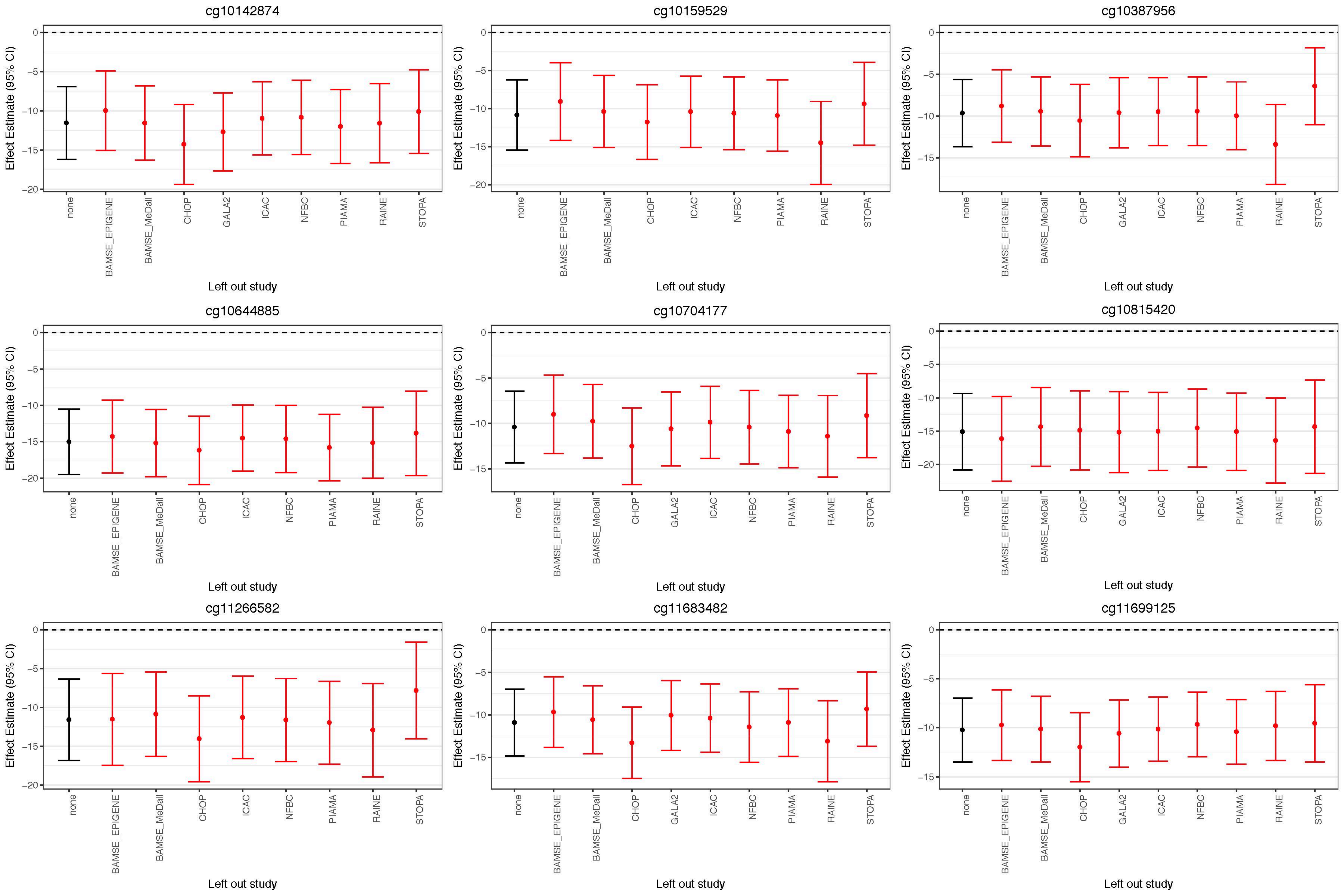
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NFBC
PIAMA
RAINE
STOPA
Left out study
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Effect Estimate (95% CI)
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−10
−15
−20
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ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg10387956
Effect Estimate (95% CI)
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−5
−10
−15
none
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GALA2
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NFBC
PIAMA
RAINE
STOPA
Left out study
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Effect Estimate (95% CI)
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Effect Estimate (95% CI)
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−15
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ICAC
NFBC
PIAMA
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STOPA
Left out study
cg10815420
Effect Estimate (95% CI)
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ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg11266582
Effect Estimate (95% CI)
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−10
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−20
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Left out study
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Effect Estimate (95% CI)
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NFBC
PIAMA
RAINE
STOPA
Left out study
cg11699125
Effect Estimate (95% CI)
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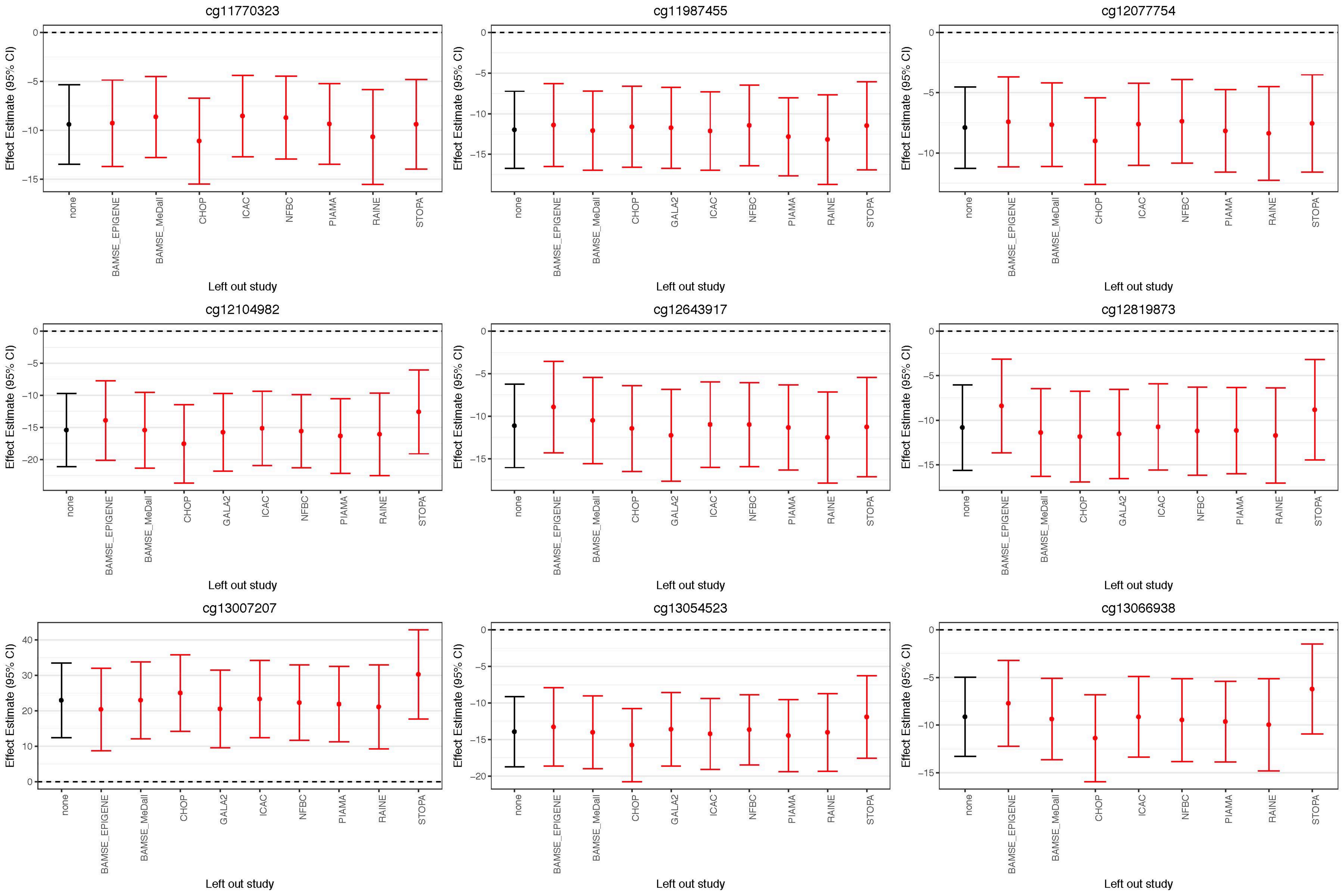
STOPA
Left out study



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Effect Estimate (95% CI)
Left out study
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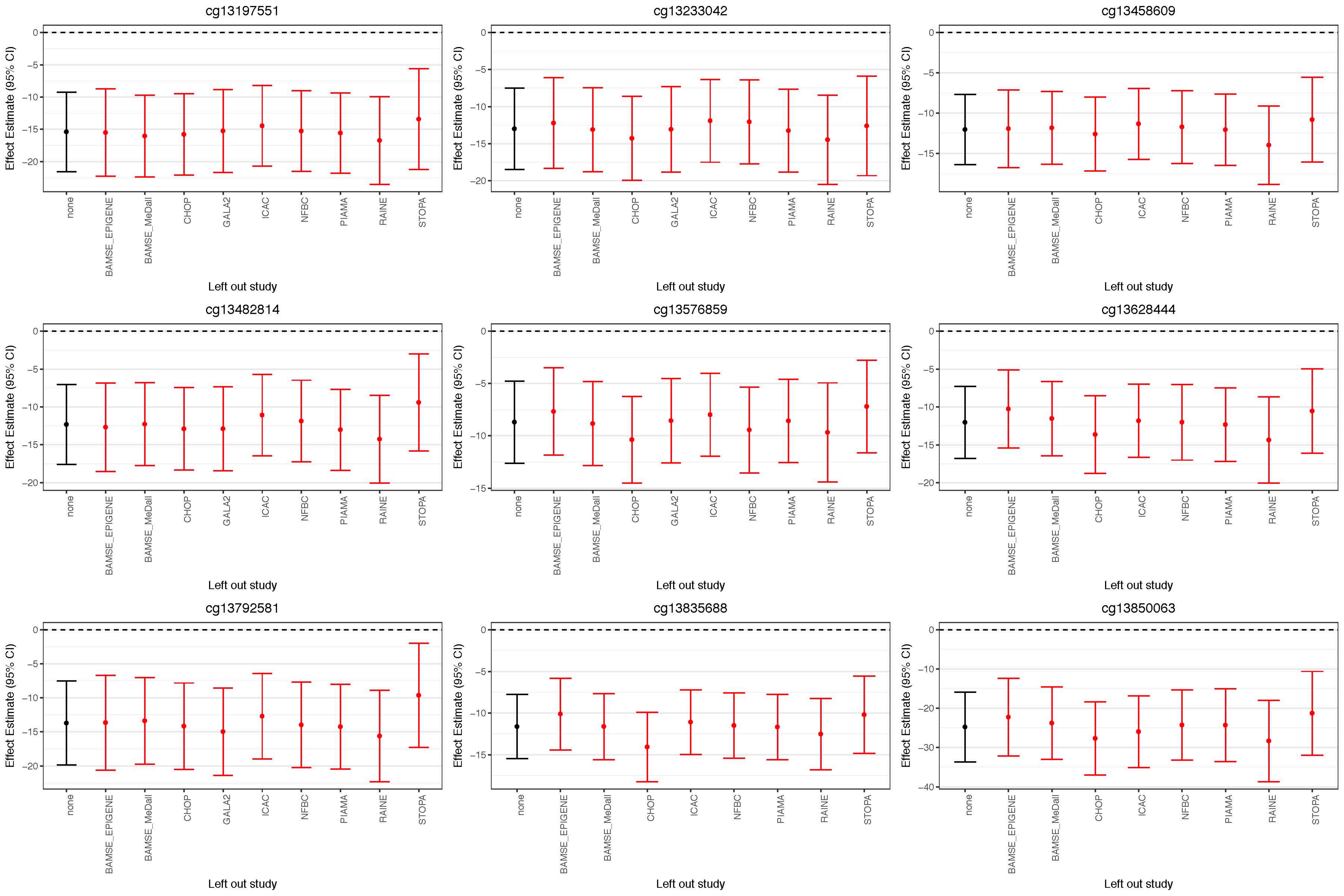
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Effect Estimate (95% CI)
Left out study
none
BAMSE_EPIGENE
BAMSE_MeDall
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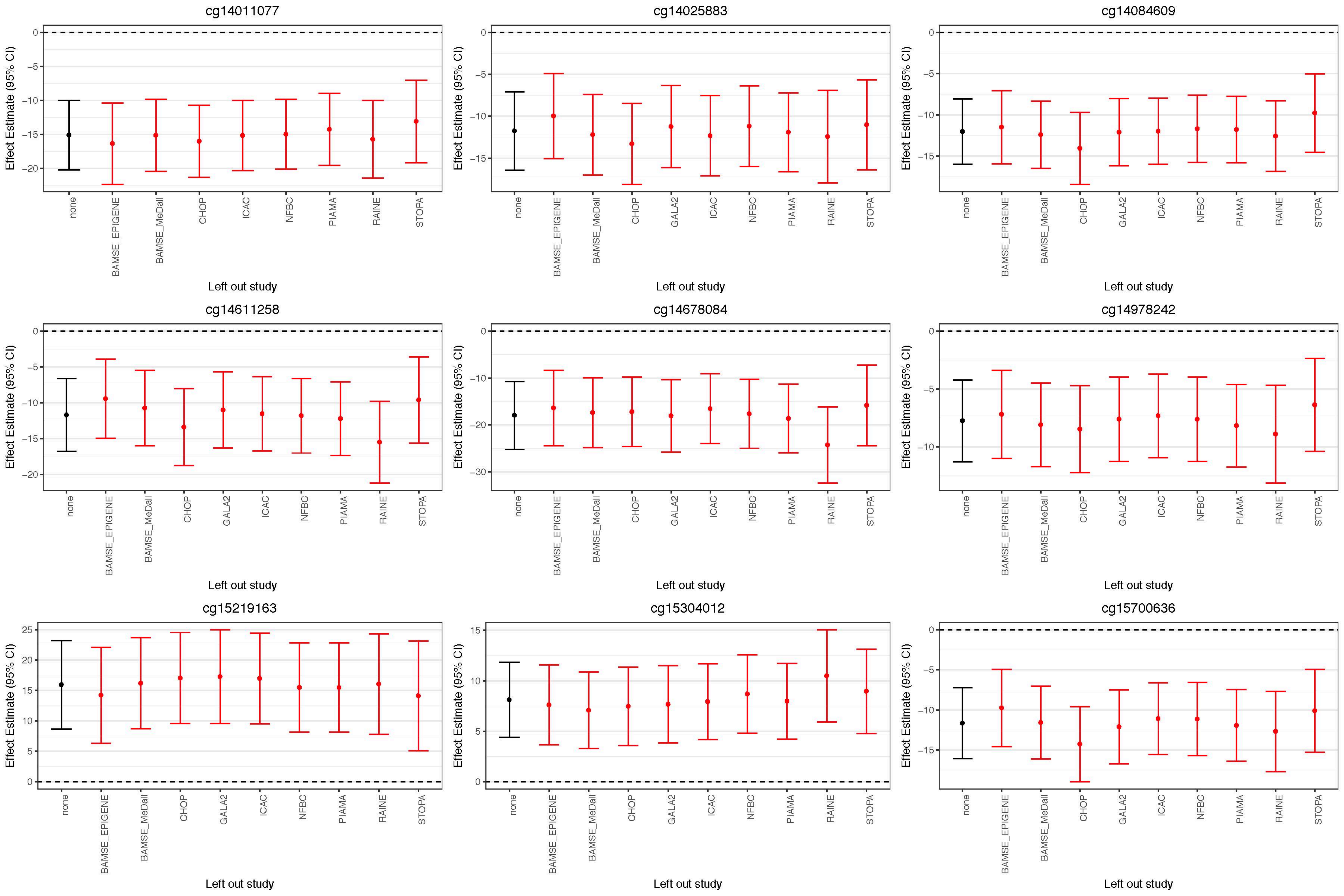
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Effect Estimate (95% CI)
Left out study
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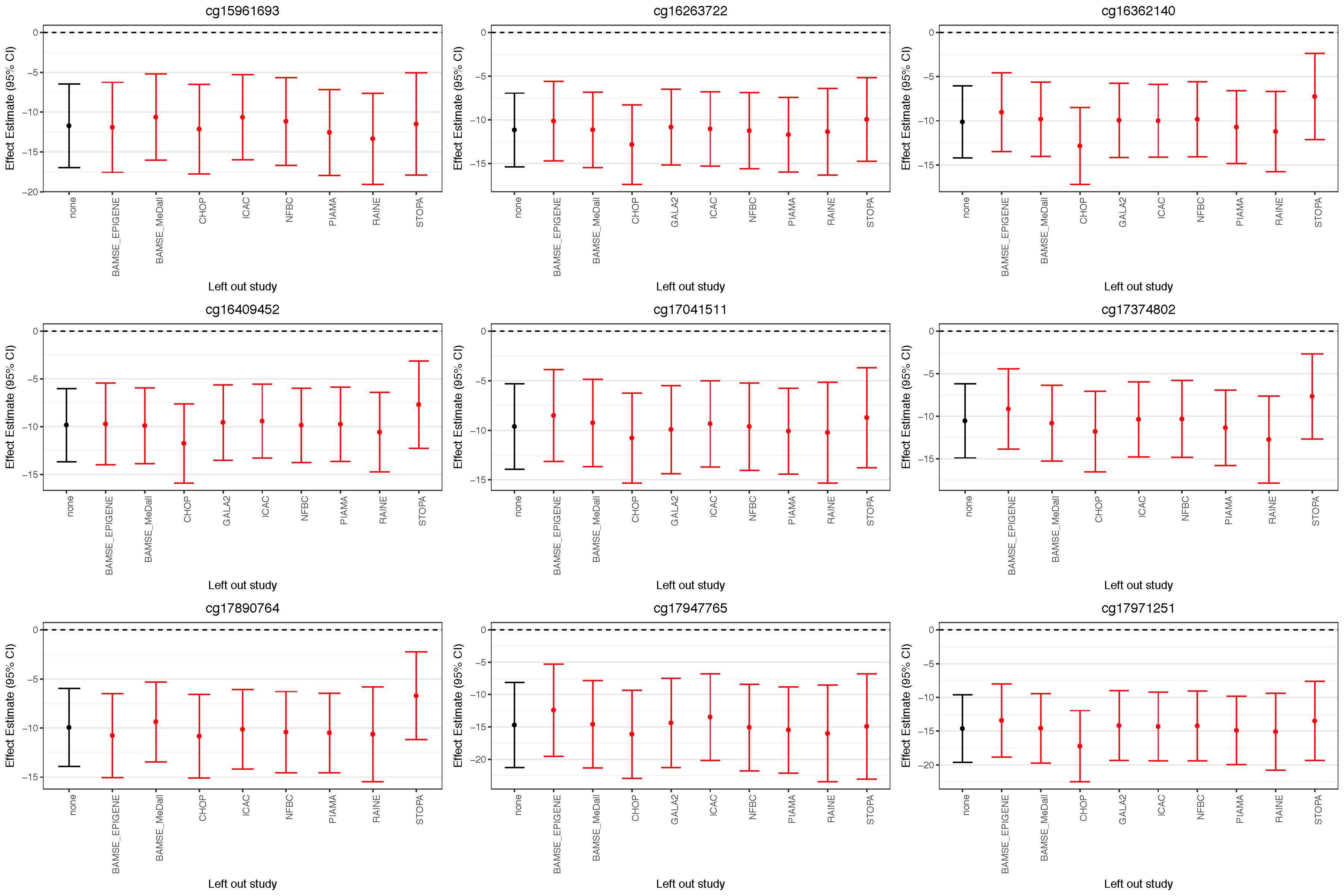
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA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cg17374802
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Effect Estimate (95% CI)
Left out study
none
BAMSE_EPIGENE
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CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
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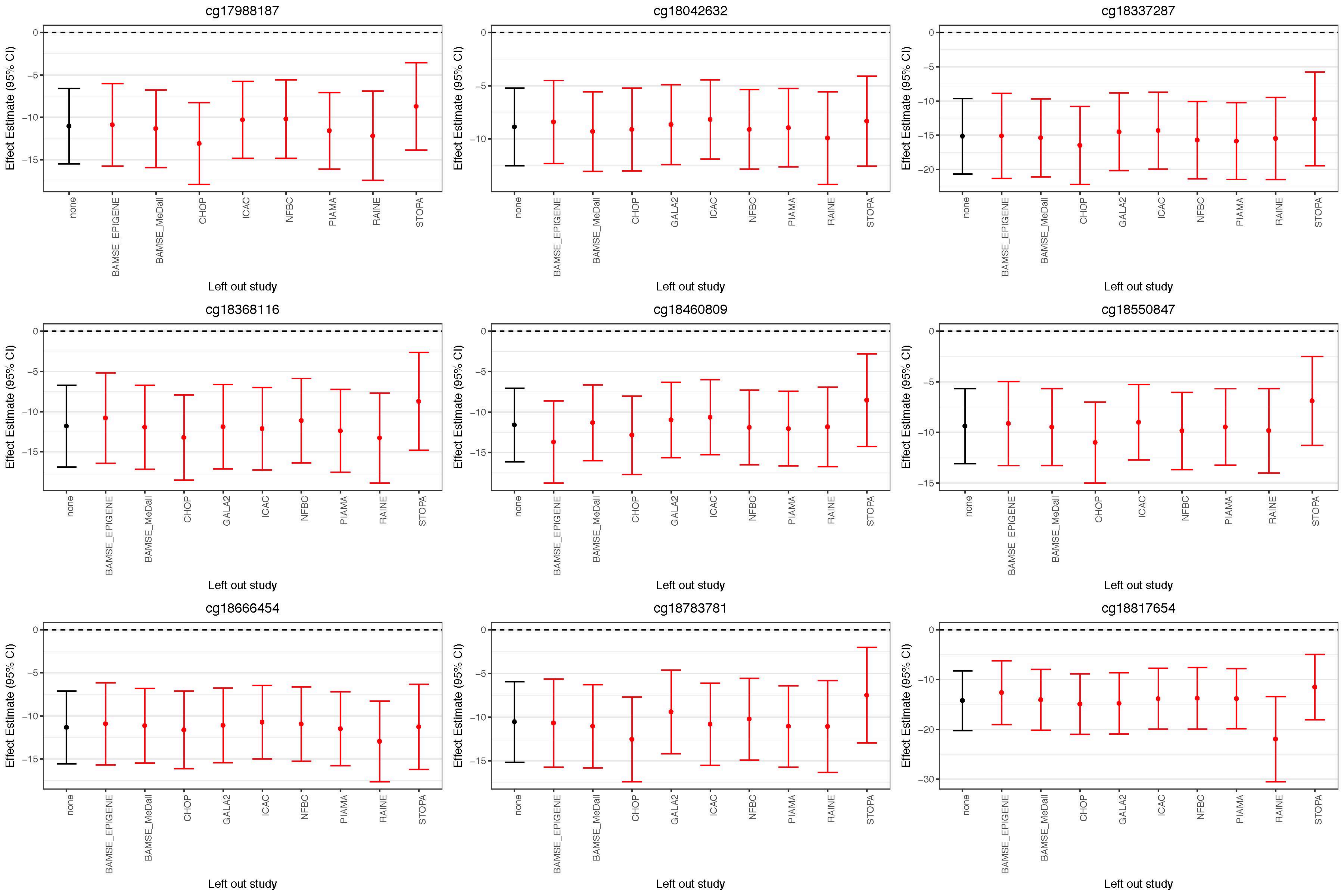

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Effect Estimate (95% CI)
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RAINE
STOPA
Left out study
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Effect Estimate (95% CI)
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−10
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CHOP
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NFBC
PIAMA
RAINE
STOPA
Left out study
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Effect Estimate (95% CI)
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NFBC
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RAINE
STOPA
Left out study
cg18368116
Effect Estimate (95% CI)
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CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg18460809
Effect Estimate (95% CI)
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−10
−15
none
BAMSE_EPIGENE
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg18550847
Effect Estimate (95% CI)
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BAMSE_MeDall
CHOP
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg18666454
Effect Estimate (95% CI)
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−10
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none
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BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg18783781
Effect Estimate (95% CI)
0
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−10
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none
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CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg18817654
Effect Estimate (95% CI)
0
−10
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BAMSE_MeDall
CHOP
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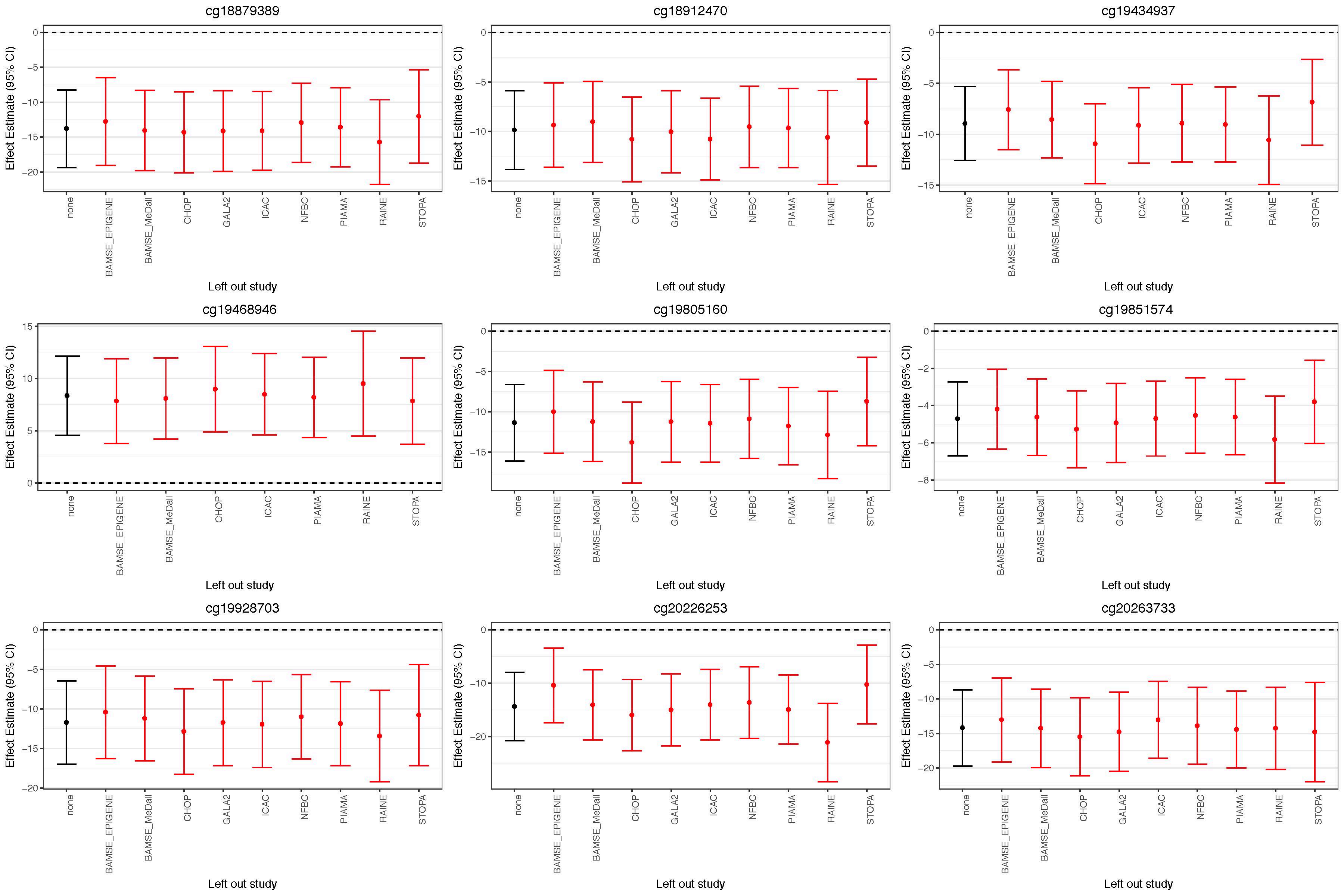
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study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Effect Estimate (95% CI)
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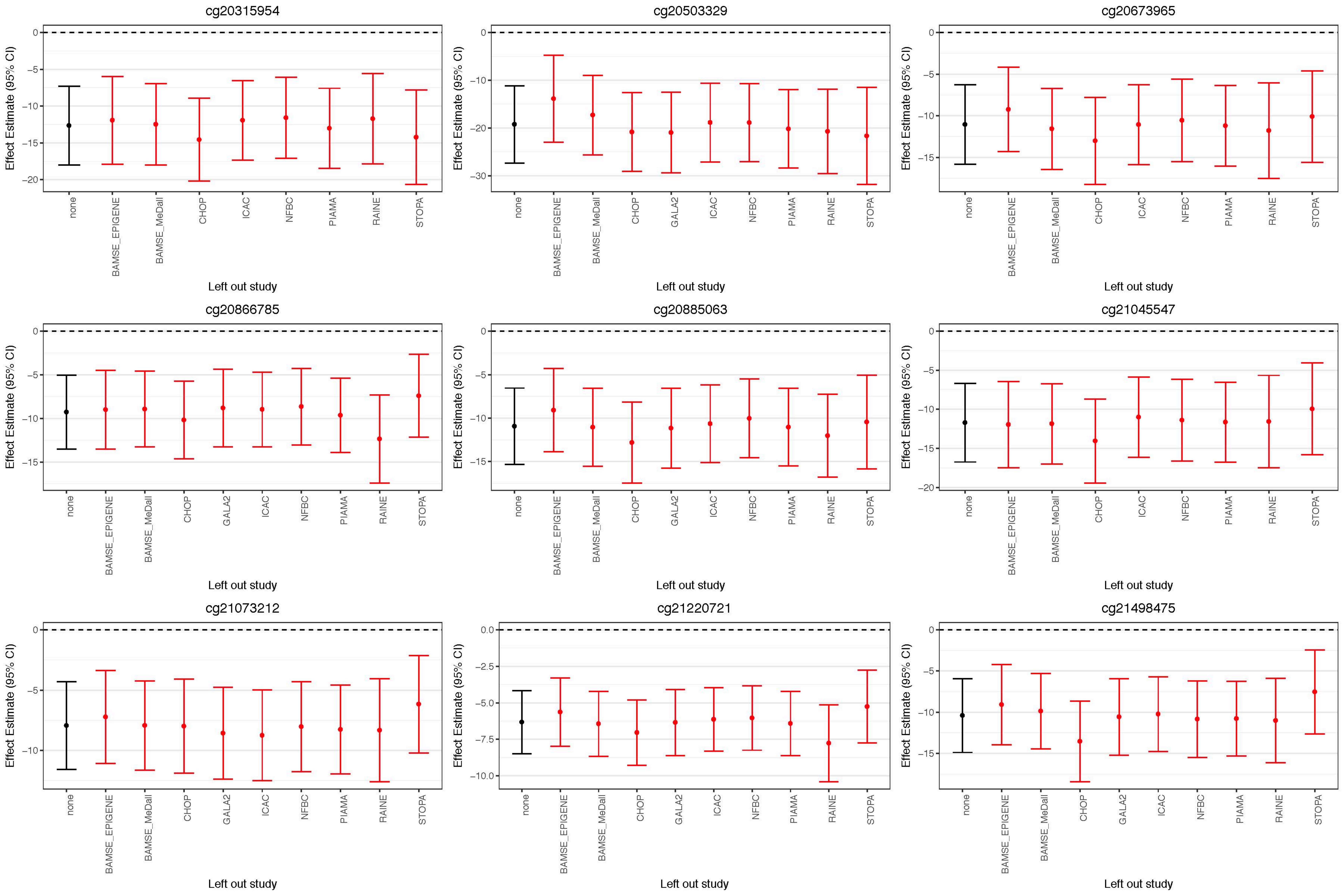
BAMSE_MeDall
CHOP
GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA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Effect Estimate (95% CI)
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BAMSE_EPIGENE
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CHOP
GALA2
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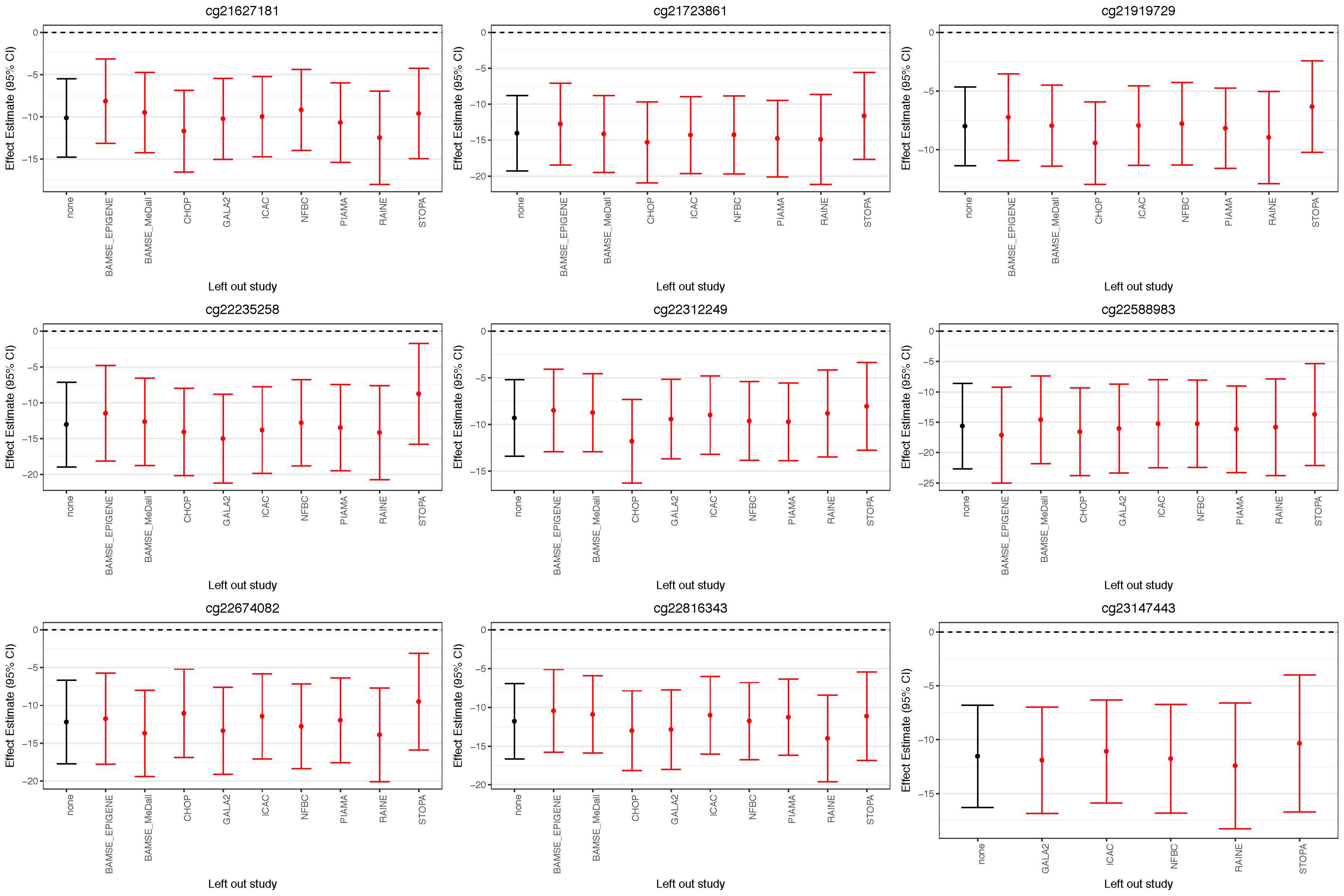
RAINE
STOPA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PIAMA
RAINE
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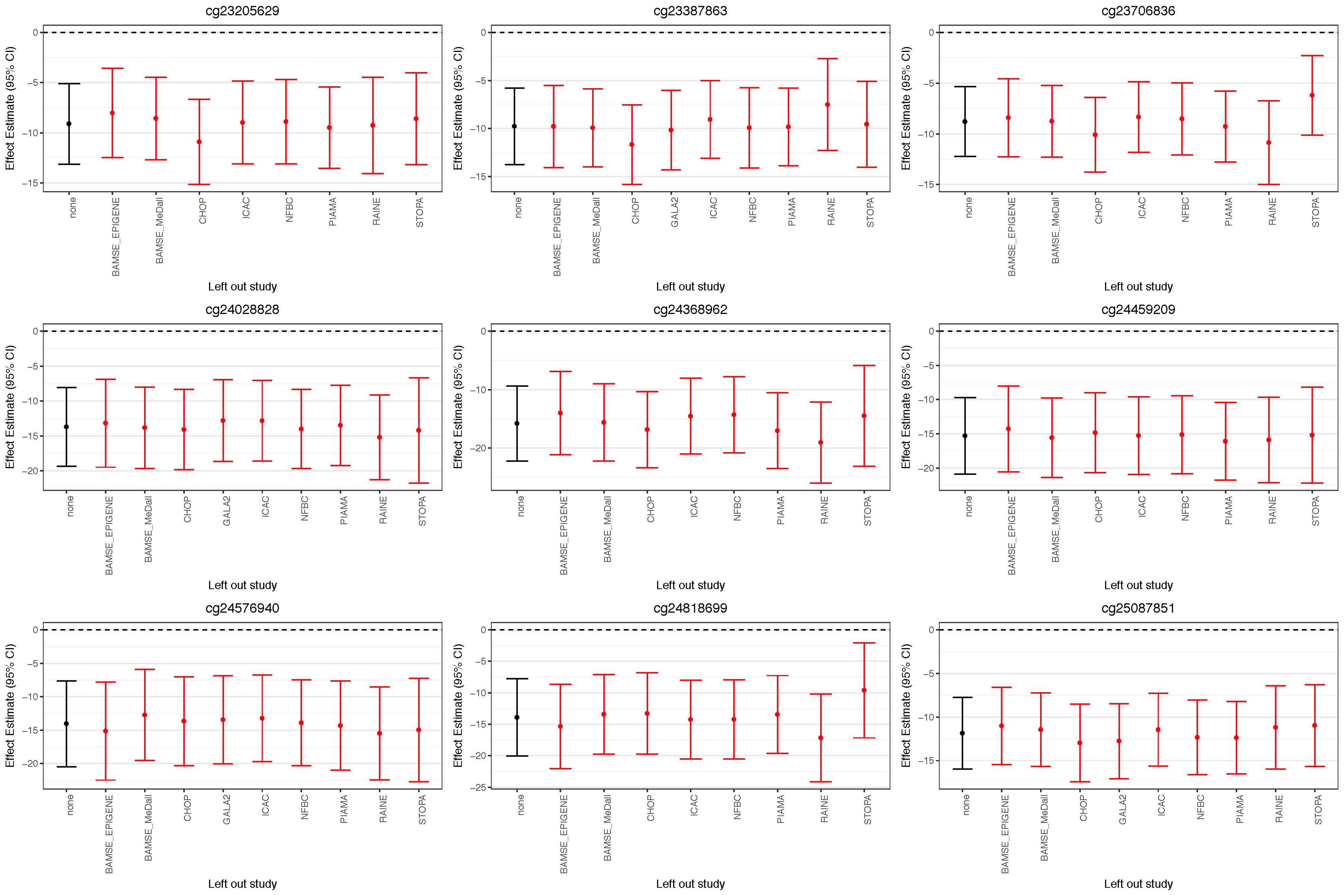
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RAINE
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Left out study
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Effect Estimate (95% CI)
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GALA2
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NFBC
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RAINE
STOPA
Left out study
cg23706836
Effect Estimate (95% CI)
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NFBC
PIAMA
RAINE
STOPA
Left out study
cg24028828
Effect Estimate (95% CI)
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-10
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BAMSE_MeDall
CHOP
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ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg24368962
Effect Estimate (95% CI)
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ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg24459209
Effect Estimate (95% CI)
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ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
cg24576940
Effect Estimate (95% CI)
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GALA2
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NFBC
PIAMA
RAINE
STOPA
Left out study
cg24818699
Effect Estimate (95% CI)
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ICAC
NFBC
PIAMA
RAINE
STOPA
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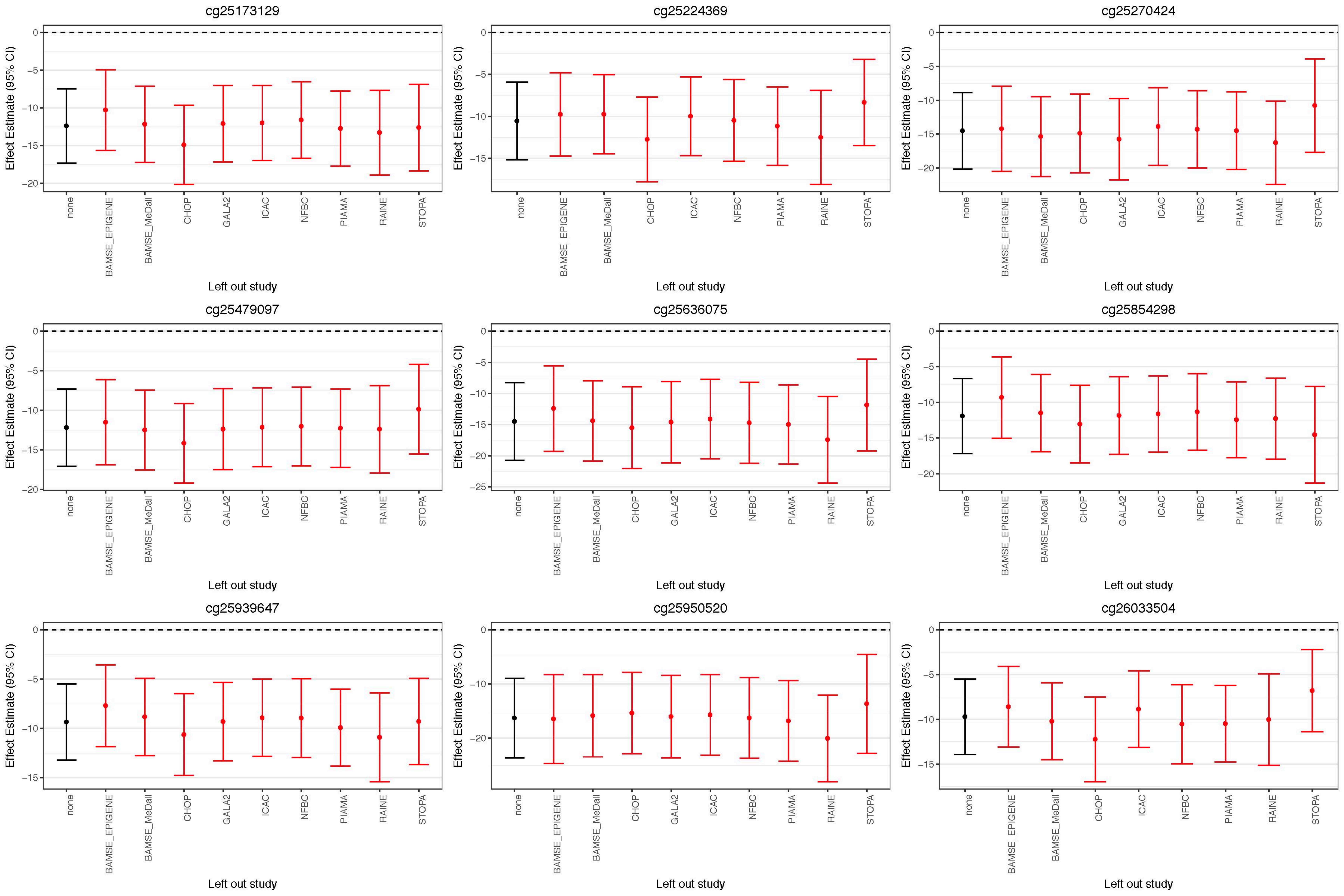
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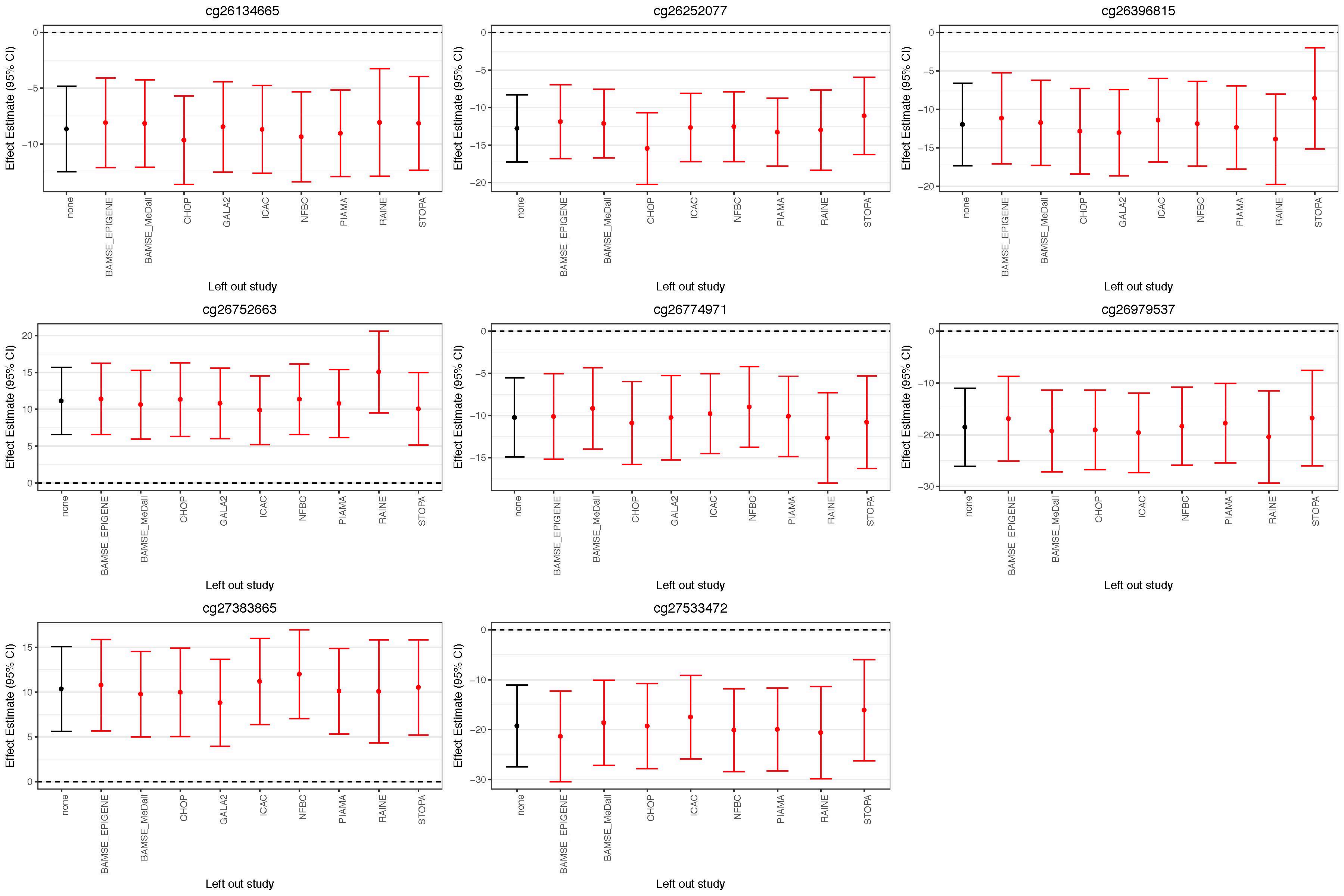
STOPA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Effect Estimate (95% CI)
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STOPA
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NFBC
PIAMA
RAINE
STOPA
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RAINE
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GALA2
ICAC
NFBC
PIAMA
RAINE
STOPA
Left out study
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Effect Estimate (95% CI)
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PIAMA
RAINE
STOPA
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NFBC
PIAMA
RAINE
STOPA
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STOPA
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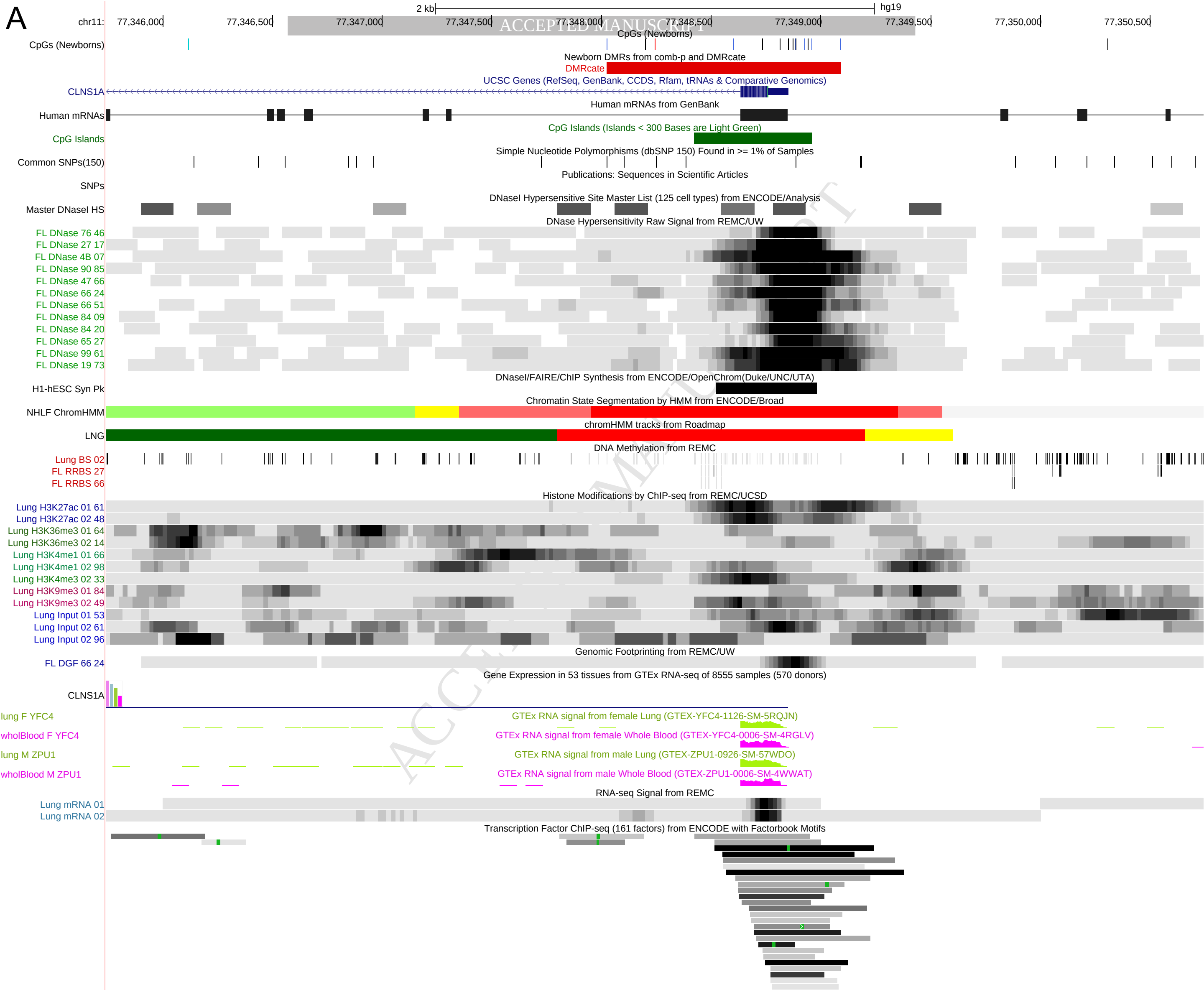
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CpGs (Newborns)
Newborn DMRs from comb-p and DMRcate
DMRcate
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
CLNS1A
Human mRNAs from GenBank
Human mRNAs
CpG Islands (Islands < 300 Bases are Light Green)
CpG Islands
Simple Nucleotide Polymorphisms (dbSNP 150) Found in >= 1% of Samples
Common SNPs(150)
Publications: Sequences in Scientific Articles
SNPs
DNaseI Hypersensitive Site Master List (125 cell types) from ENCODE/Analysis
Master DNaseI HS
DNase Hypersensitivity Raw Signal from REMC/UW
FL DNase 76 46
FL DNase 27 17
FL DNase 4B 07
FL DNase 90 85
FL DNase 47 66
FL DNase 66 24
FL DNase 66 51
FL DNase 84 09
FL DNase 84 20
FL DNase 65 27
FL DNase 99 61
FL DNase 19 73
DNaseI/FAIRE/ChIP Synthesis from ENCODE/OpenChrom(Duke/UNC/UTA)
H1-hESC Syn Pk
Chromatin State Segmentation by HMM from ENCODE/Broad
NHLF ChromHMM
chromHMM tracks from Roadmap
LNG
DNA Methylation from REMC
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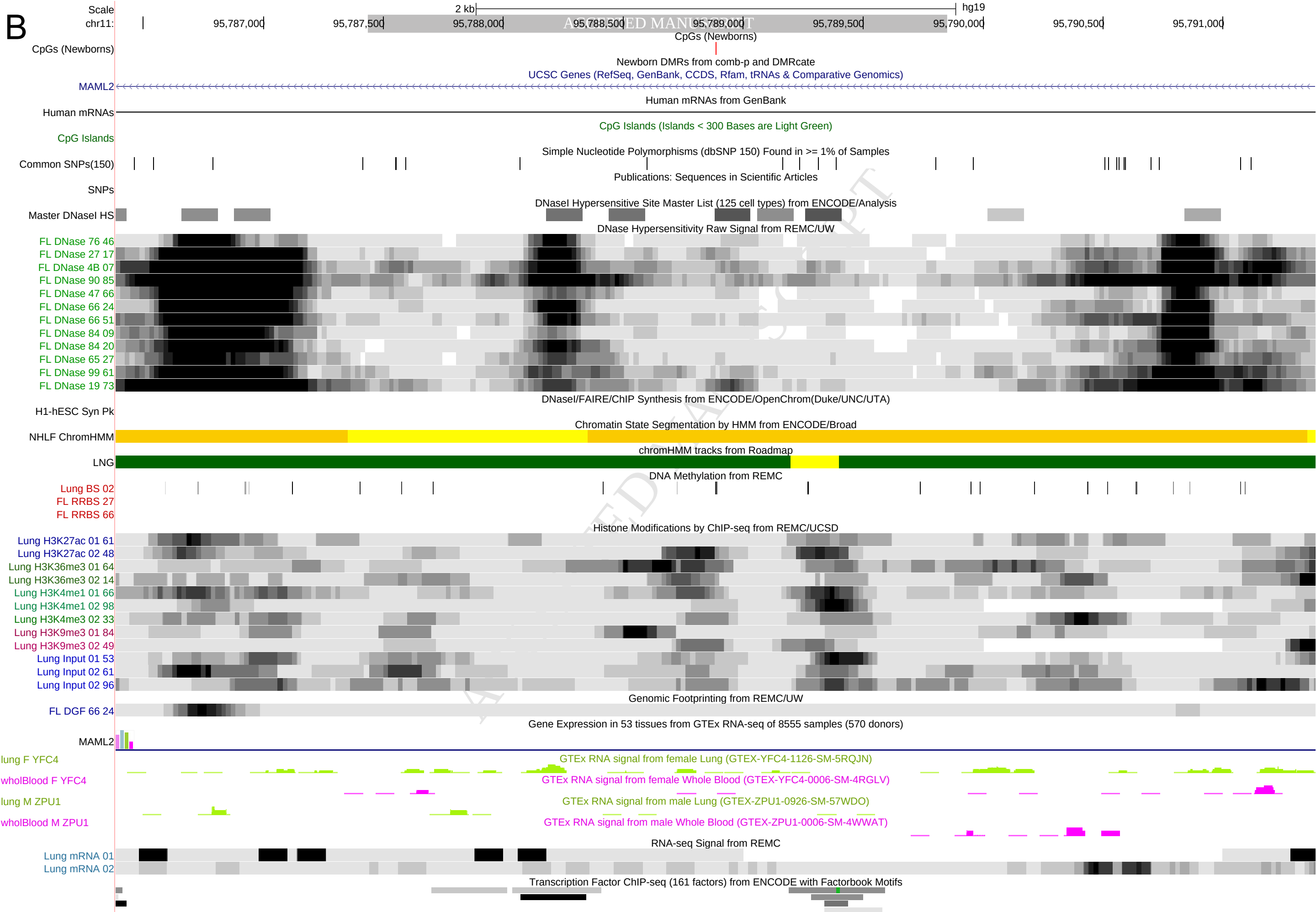
Lung H3K4me1 02 98
Lung H3K4me3 02 33
Lung H3K9me3 01 84
Lung H3K9me3 02 49
Lung Input 01 53
Lung Input 02 61
Lung Input 02 96
Genomic Footprinting from REMC/UW
FL DGF 66 24
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors)
CLNS1A
lung F YFC4
GTEx RNA signal from female Lung (GTEX-YFC4-1126-SM-5RQJN)
wholBlood F YFC4
GTEx RNA signal from female Whole Blood (GTEX-YFC4-0006-SM-4RGLV)
lung M ZPU1
GTEx RNA signal from male Lung (GTEX-ZPU1-0926-SM-57WDO)
wholBlood M ZPU1
GTEx RNA signal from male Whole Blood (GTEX-ZPU1-0006-SM-4WWAT)
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs

B



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CpGs (Newborns)
CpGs (Newborns)
Newborn DMRs from comb-p and DMRcate
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
MAML2
Human mRNAs from GenBank
Human mRNAs
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CpG Islands
Simple Nucleotide Polymorphisms (dbSNP 150) Found in >= 1% of Samples
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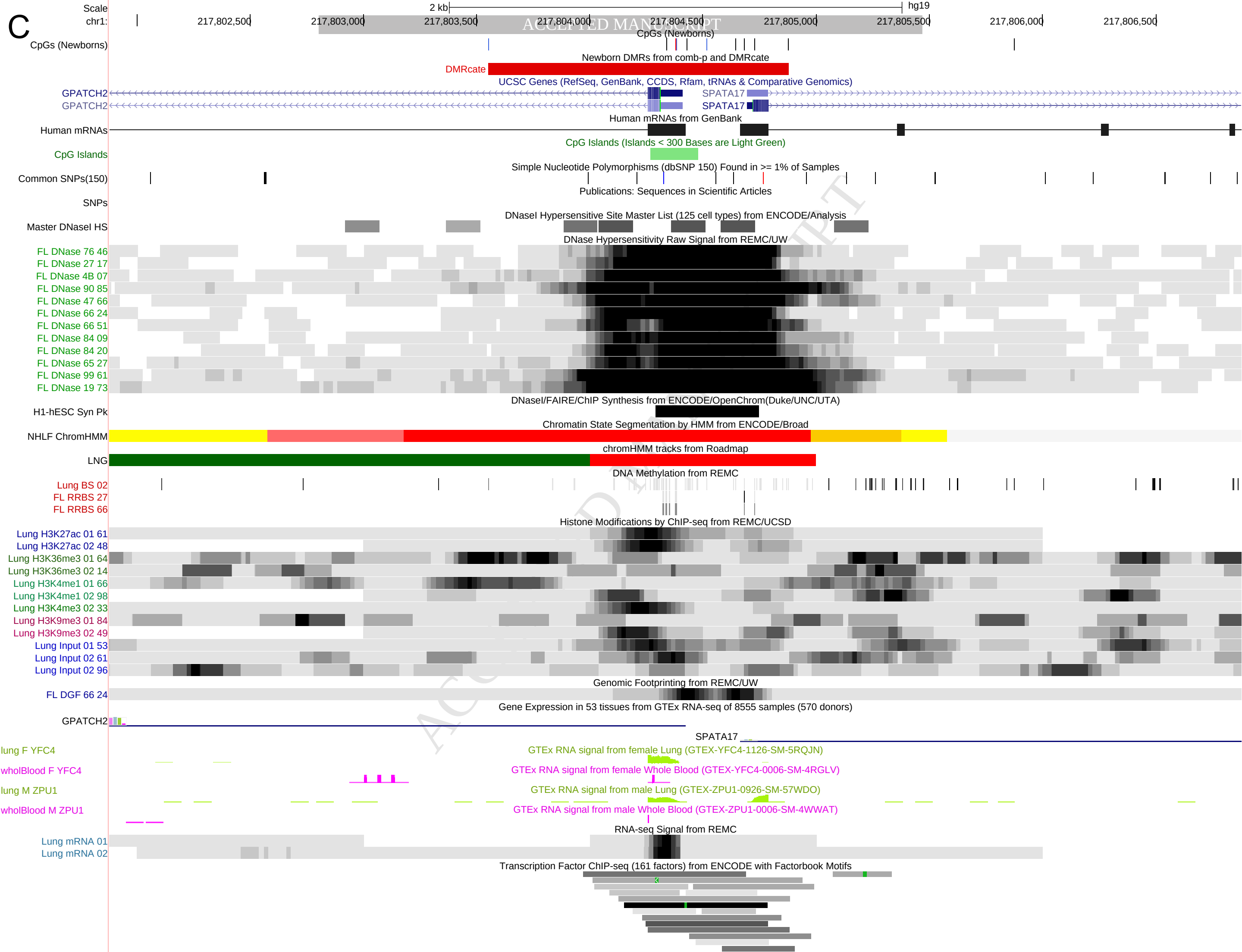
FL DNase 27 17
FL DNase 4B 07
FL DNase 90 85
FL DNase 47 66
FL DNase 66 24
FL DNase 66 51
FL DNase 84 09
FL DNase 84 20
FL DNase 65 27
FL DNase 99 61
FL DNase 19 73
DNaseI/FAIRE/ChIP Synthesis from ENCODE/OpenChrom(Duke/UNC/UTA)
H1-hESC Syn Pk
Chromatin State Segmentation by HMM from ENCODE/Broad
NHLF ChromHMM
chromHMM tracks from Roadmap
LNG
DNA Methylation from REMC
Lung BS 02
FL RRBS 27
FL RRBS 66
Histone Modifications by ChIP-seq from REMC/UCSD
Lung H3K27ac 01 61
Lung H3K27ac 02 48
Lung H3K36me3 01 64
Lung H3K36me3 02 14
Lung H3K4me1 01 66
Lung H3K4me1 02 98
Lung H3K4me3 02 33
Lung H3K9me3 01 84
Lung H3K9me3 02 49
Lung Input 01 53
Lung Input 02 61
Lung Input 02 96
Genomic Footprinting from REMC/UW
FL DGF 66 24
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors)
MAML2
lung F YFC4
GTEx RNA signal from female Lung (GTEX-YFC4-1126-SM-5RQJN)
wholBlood F YFC4
GTEx RNA signal from female Whole Blood (GTEX-YFC4-0006-SM-4RGLV)
lung M ZPU1
GTEx RNA signal from male Lung (GTEX-ZPU1-0926-SM-57WDO)
wholBlood M ZPU1
GTEx RNA signal from male Whole Blood (GTEX-ZPU1-0006-SM-4WWAT)
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs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CpGs (Newborns)
CpGs (Newborns)
Newborn DMRs from comb-p and DMRcate
DMRcate
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
GPATCH2
GPATCH2
SPATA17
SPATA17
Human mRNAs from GenBank
Human mRNAs
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DNase Hypersensitivity Raw Signal from REMC/UW
FL DNase 76 46
FL DNase 27 17
FL DNase 4B 07
FL DNase 90 85
FL DNase 47 66
FL DNase 66 24
FL DNase 66 51
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FL DNase 99 61
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DNaseI/FAIRE/ChIP Synthesis from ENCODE/OpenChrom(Duke/UNC/UTA)
H1-hESC Syn Pk
Chromatin State Segmentation by HMM from ENCODE/Broad
NHLF ChromHMM
chromHMM tracks from Roadmap
LNG
DNA Methylation from REMC
Lung BS 02
FL RRBS 27
FL RRBS 66
Histone Modifications by ChIP-seq from REMC/UCSD
Lung H3K27ac 01 61
Lung H3K27ac 02 48
Lung H3K36me3 01 64
Lung H3K36me3 02 14
Lung H3K4me1 01 66
Lung H3K4me1 02 98
Lung H3K4me3 02 33
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Lung Input 01 53
Lung Input 02 61
Lung Input 02 96
Genomic Footprinting from REMC/UW
FL DGF 66 24
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors)
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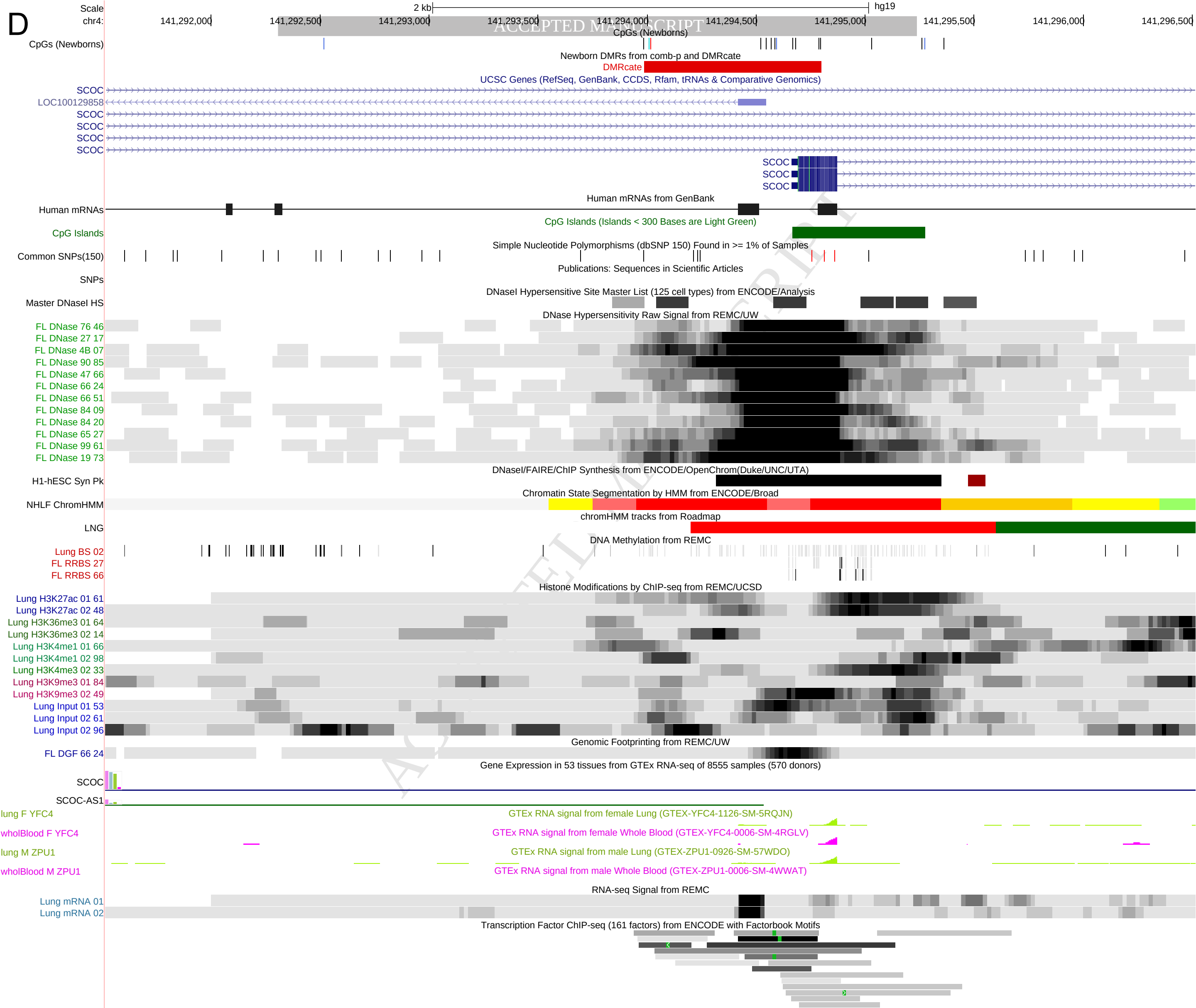
lung F YFC4
GTEx RNA signal from female Lung (GTEX-YFC4-1126-SM-5RQJN)
wholBlood F YFC4
GTEx RNA signal from female Whole Blood (GTEX-YFC4-0006-SM-4RGLV)
lung M ZPU1
GTEx RNA signal from male Lung (GTEX-ZPU1-0926-SM-57WDO)
wholBlood M ZPU1
GTEx RNA signal from male Whole Blood (GTEX-ZPU1-0006-SM-4WWAT)
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs

D



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FL DNase 99 61
FL DNase 19 73
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Lung Input 01 53
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Genomic Footprinting from REMC/UW
FL DGF 66 24
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors)
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lung F YFC4
GTEx RNA signal from female Lung (GTEX-YFC4-1126-SM-5RQJN)
wholBlood F YFC4
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RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs

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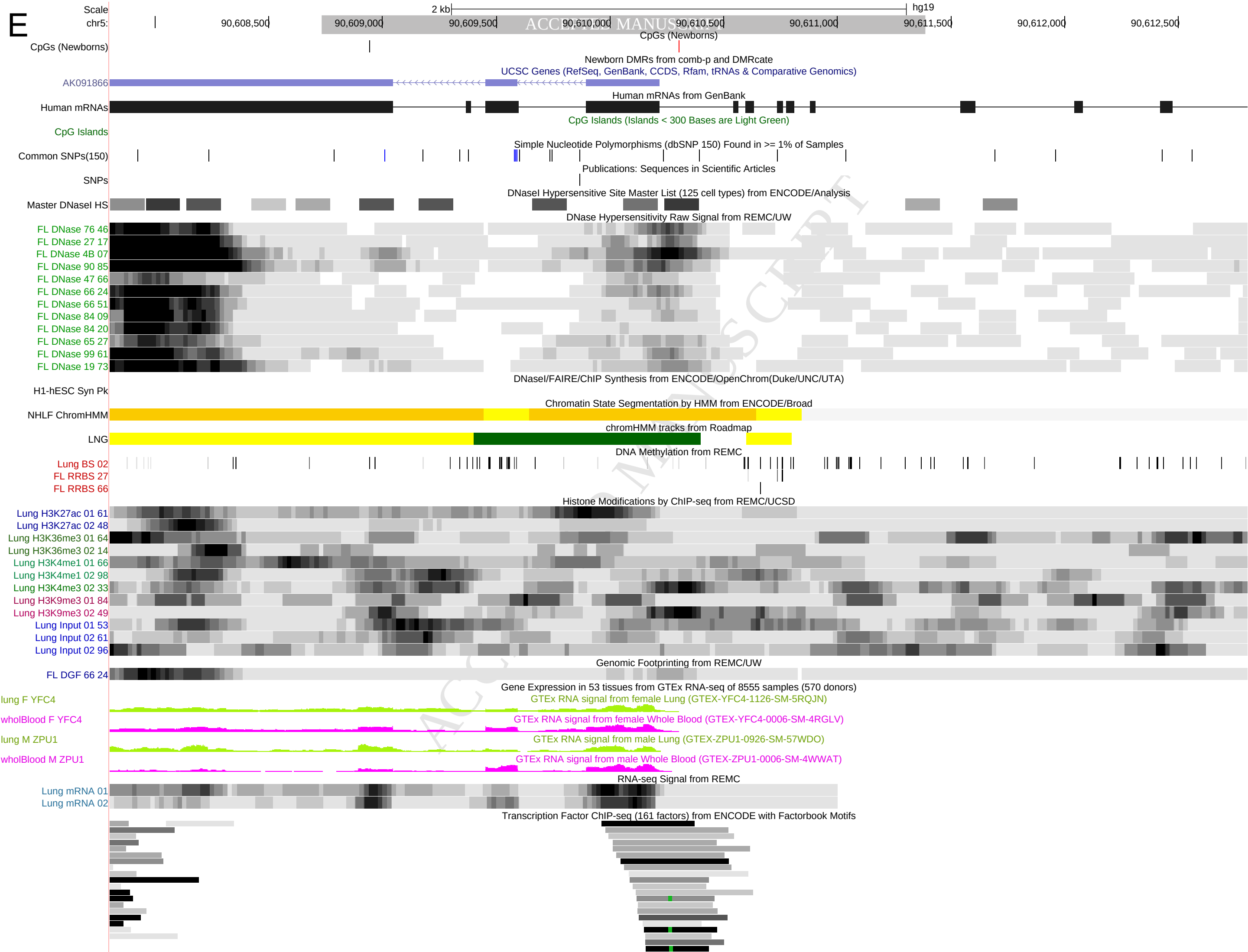

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RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs

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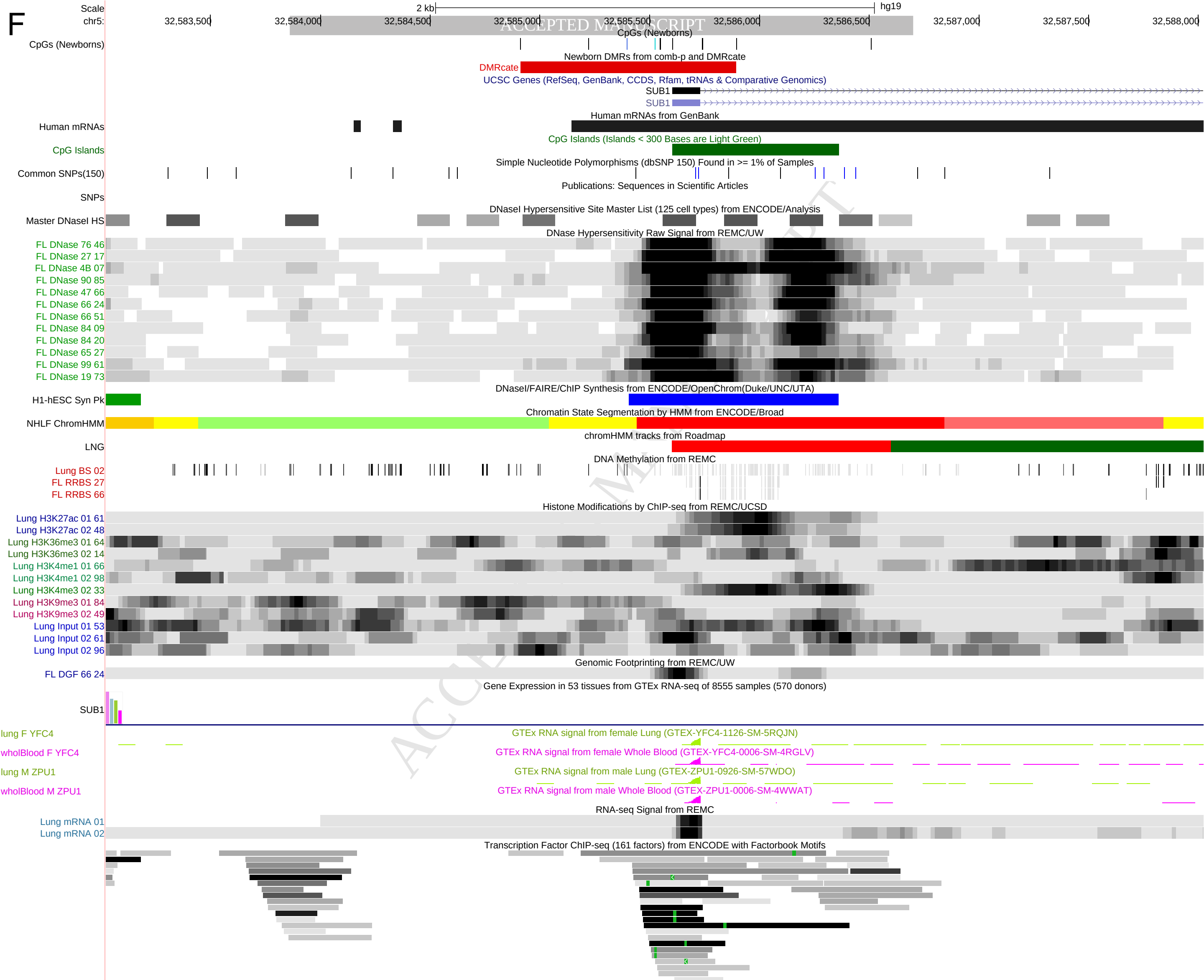

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Newborn DMRs from comb-p and DMRcate
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UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
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SUB1
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Human mRNAs from GenBank
CpG Islands
CpG Islands (Islands < 300 Bases are Light Green)
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lung F YFC4
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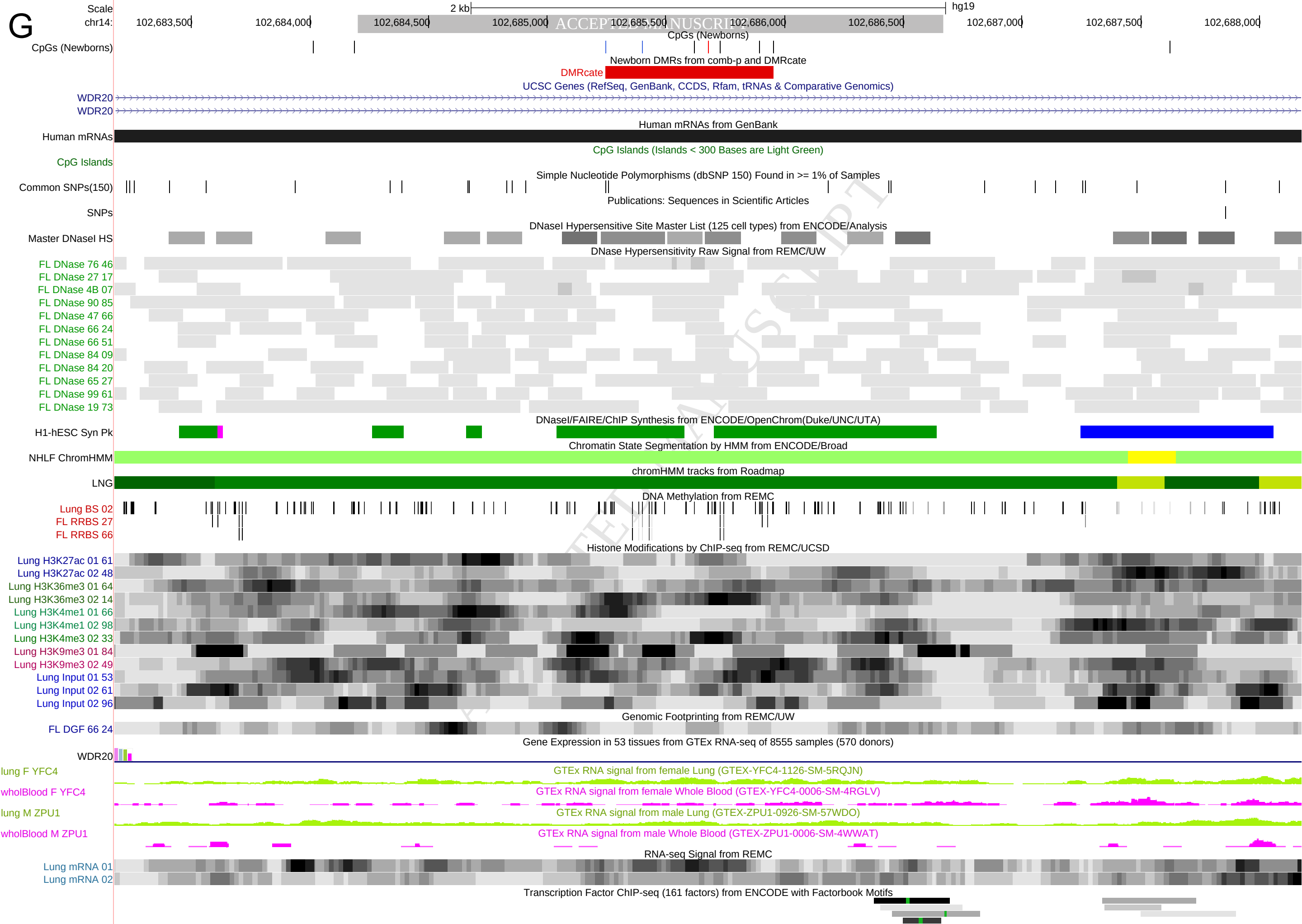
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs



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Newborn DMRs from comb-p and DMRcate
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UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
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FL DGF 66 24
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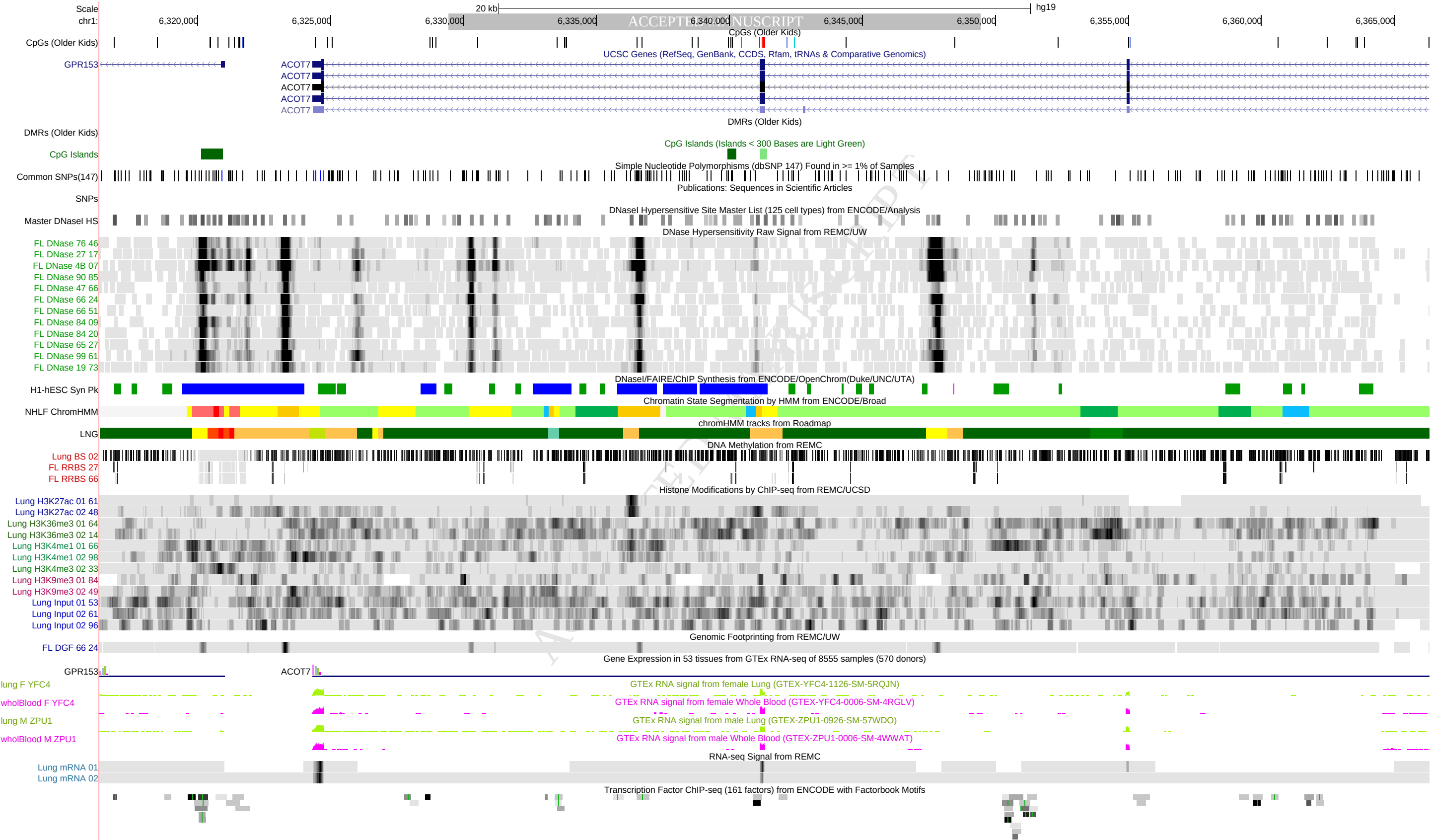
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs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DMRs (Older Kids)
CpG Islands (Islands < 300 Bases are Light Green)
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Simple Nucleotide Polymorphisms (dbSNP 147) Found in >= 1% of Samples
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NHLF ChromHMM
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Genomic Footprinting from REMC/UW
FL DGF 66 24
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors)
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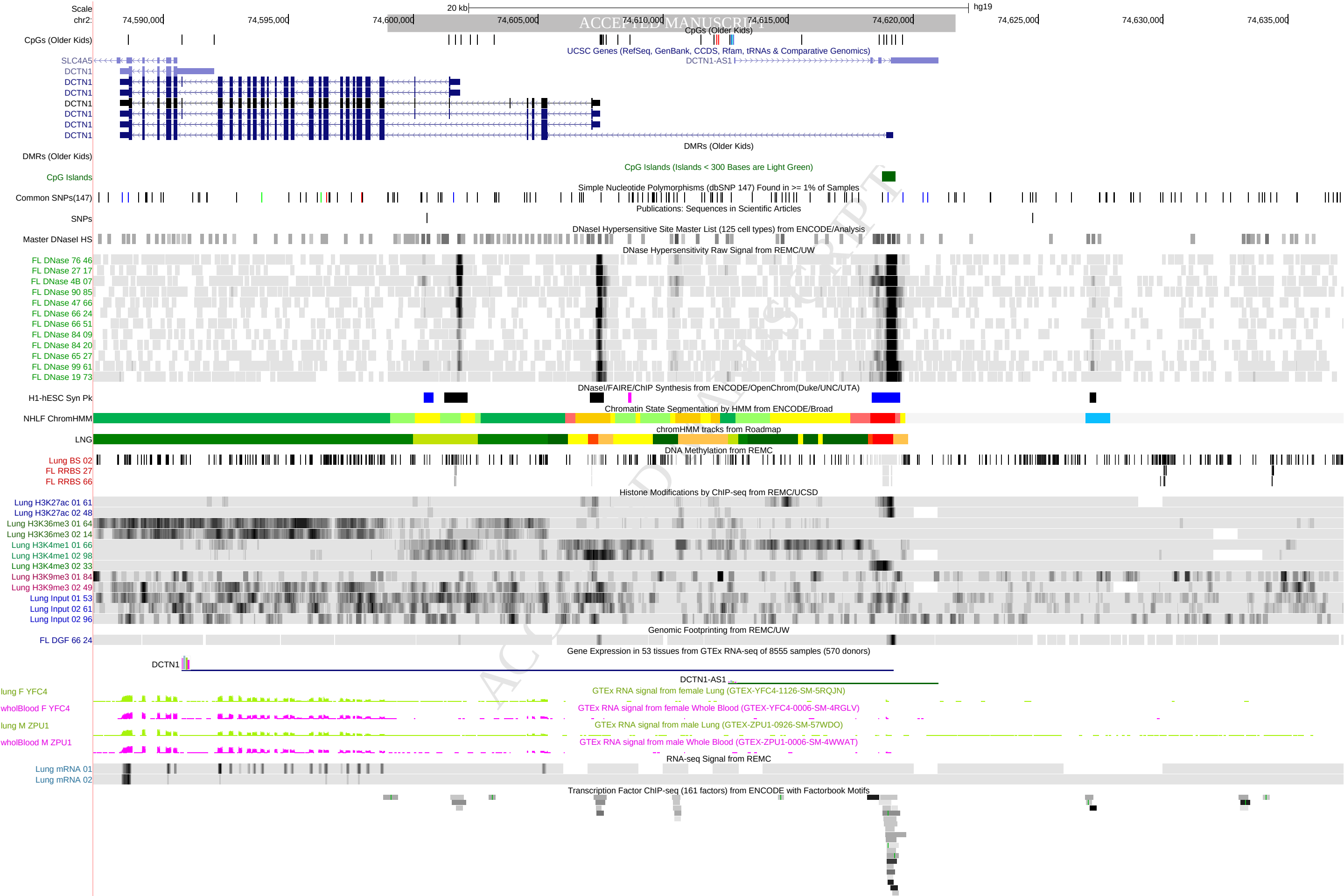
GTEx RNA signal from female Whole Blood (GTEX-YFC4-0006-SM-4RGLV)
wholBlood F YFC4
GTEx RNA signal from male Lung (GTEX-ZPU1-0926-SM-57WDO)
lung M ZPU1
GTEx RNA signal from male Whole Blood (GTEX-ZPU1-0006-SM-4WWAT)
wholBlood M ZPU1
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs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CpGs (Older Kids)
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
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DMRs (Older Kids)
CpG Islands
CpG Islands (Islands < 300 Bases are Light Green)
Simple Nucleotide Polymorphisms (dbSNP 147) Found in >= 1% of Samples
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Publications: Sequences in Scientific Articles
SNPs
DNaseI Hypersensitive Site Master List (125 cell types) from ENCODE/Analysis
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DNase Hypersensitivity Raw Signal from REMC/UW
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FL DGF 66 24
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RNA-seq Signal from REMC
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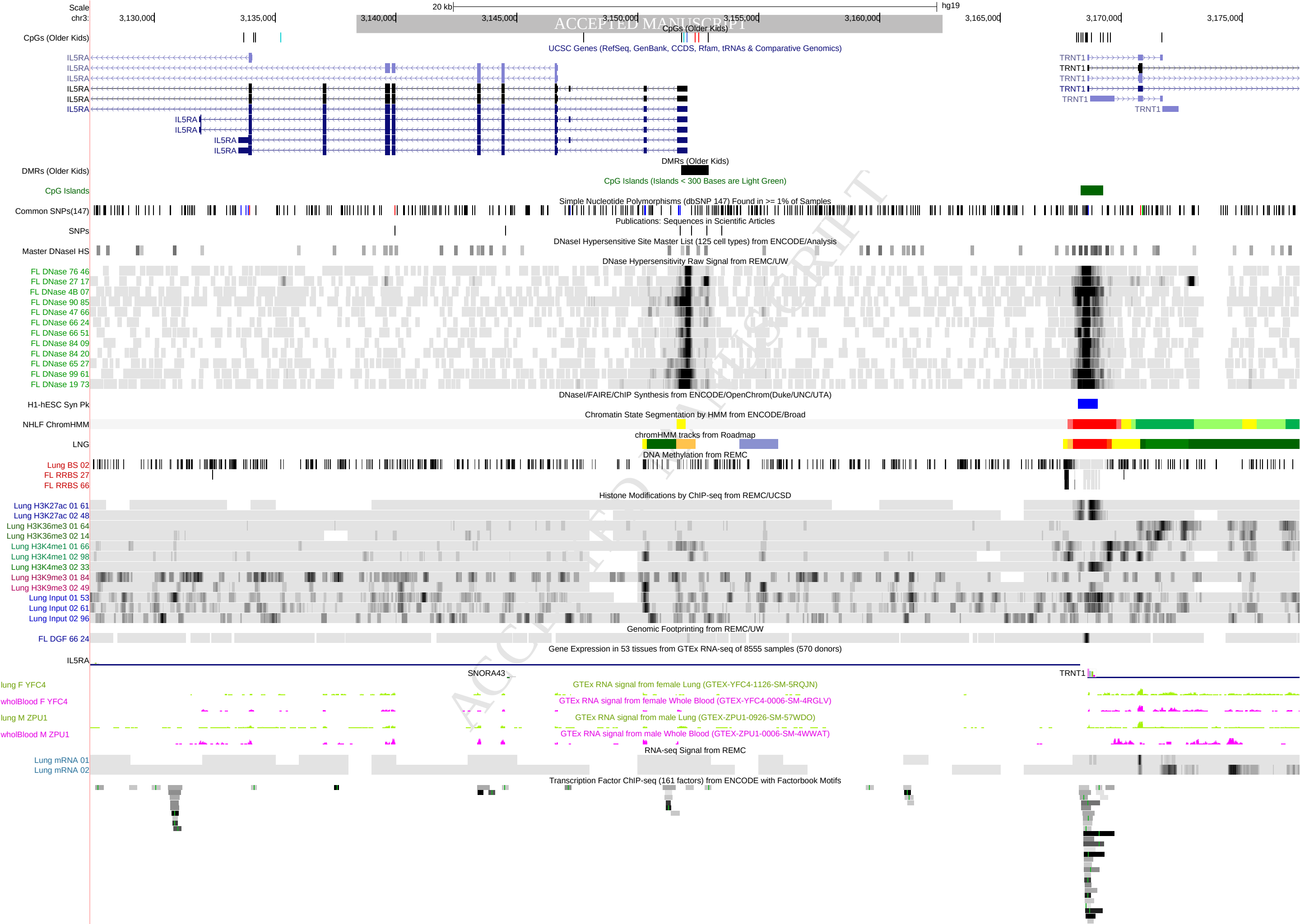
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs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CpGs (Older Kids)
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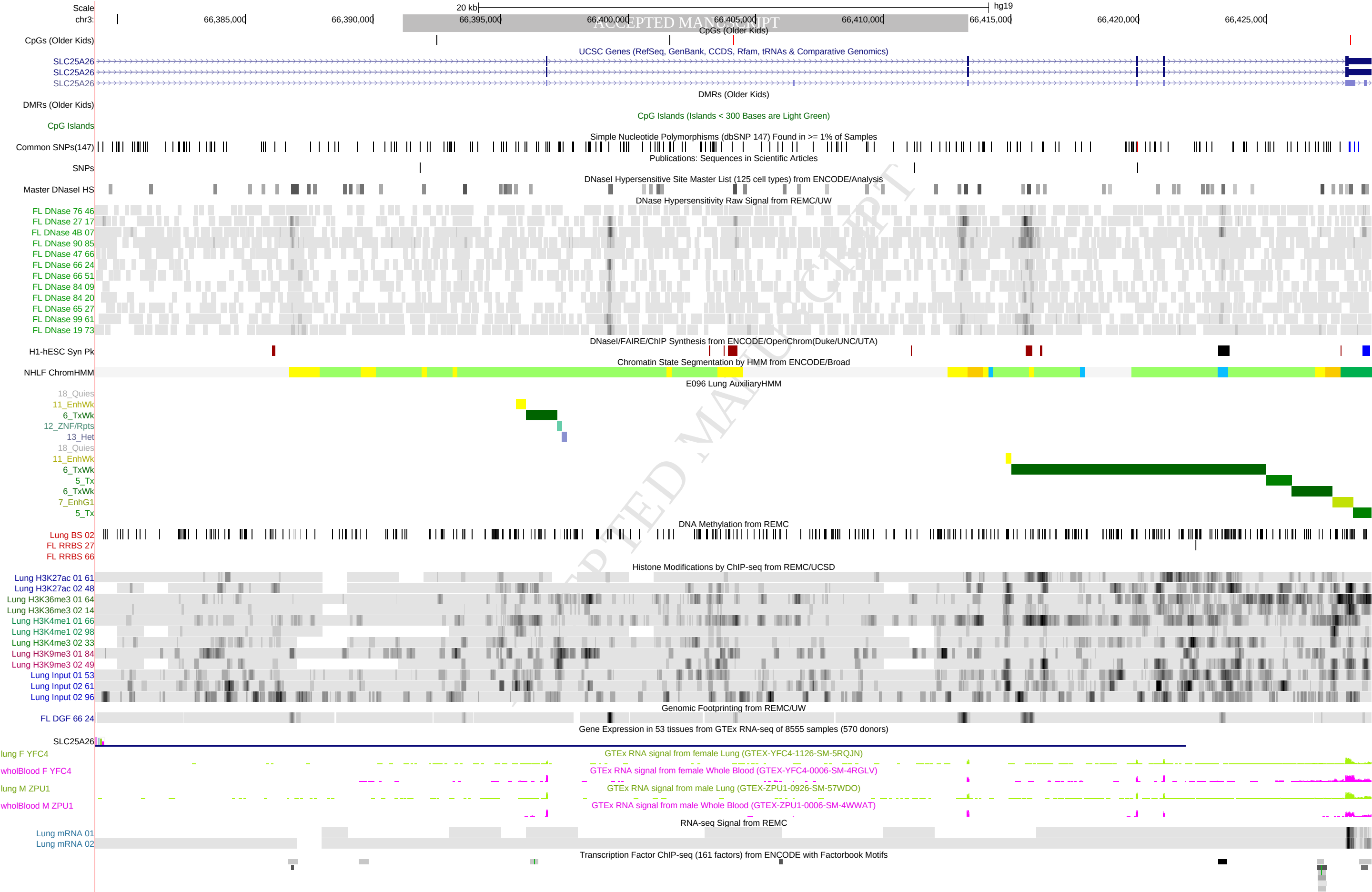
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SLC25A26
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NHLF ChromHMM
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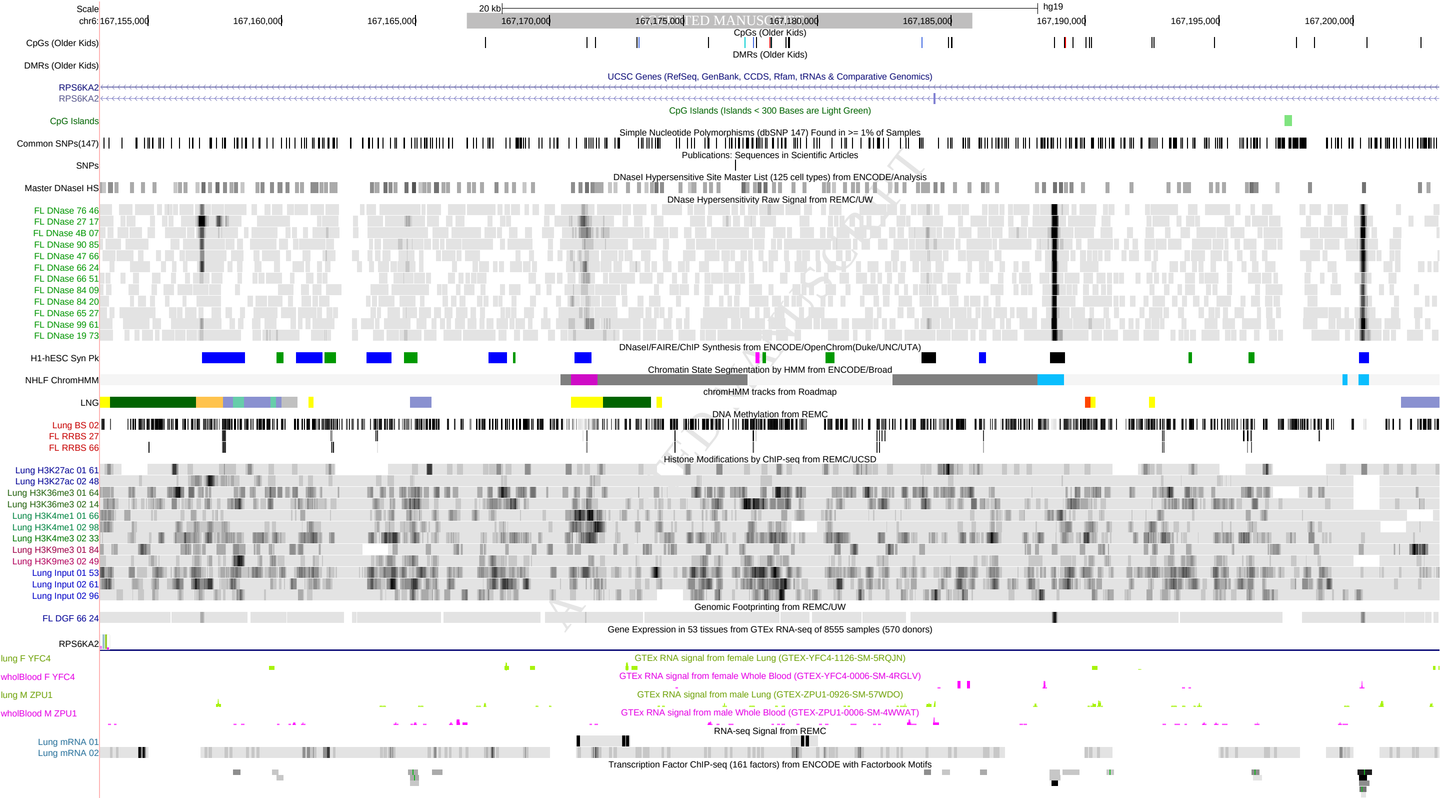
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CpGs (Older Kids)
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RPS6KA2
RPS6KA2
CpG Islands (Islands < 300 Bases are Light Green)
CpG Islands
Simple Nucleotide Polymorphisms (dbSNP 147) Found in >= 1% of Samples
Common SNPs(147)
Publications: Sequences in Scientific Articles
SNPs
DNaseI Hypersensitive Site Master List (125 cell types) from ENCODE/Analysis
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DNase Hypersensitivity Raw Signal from REMC/UW
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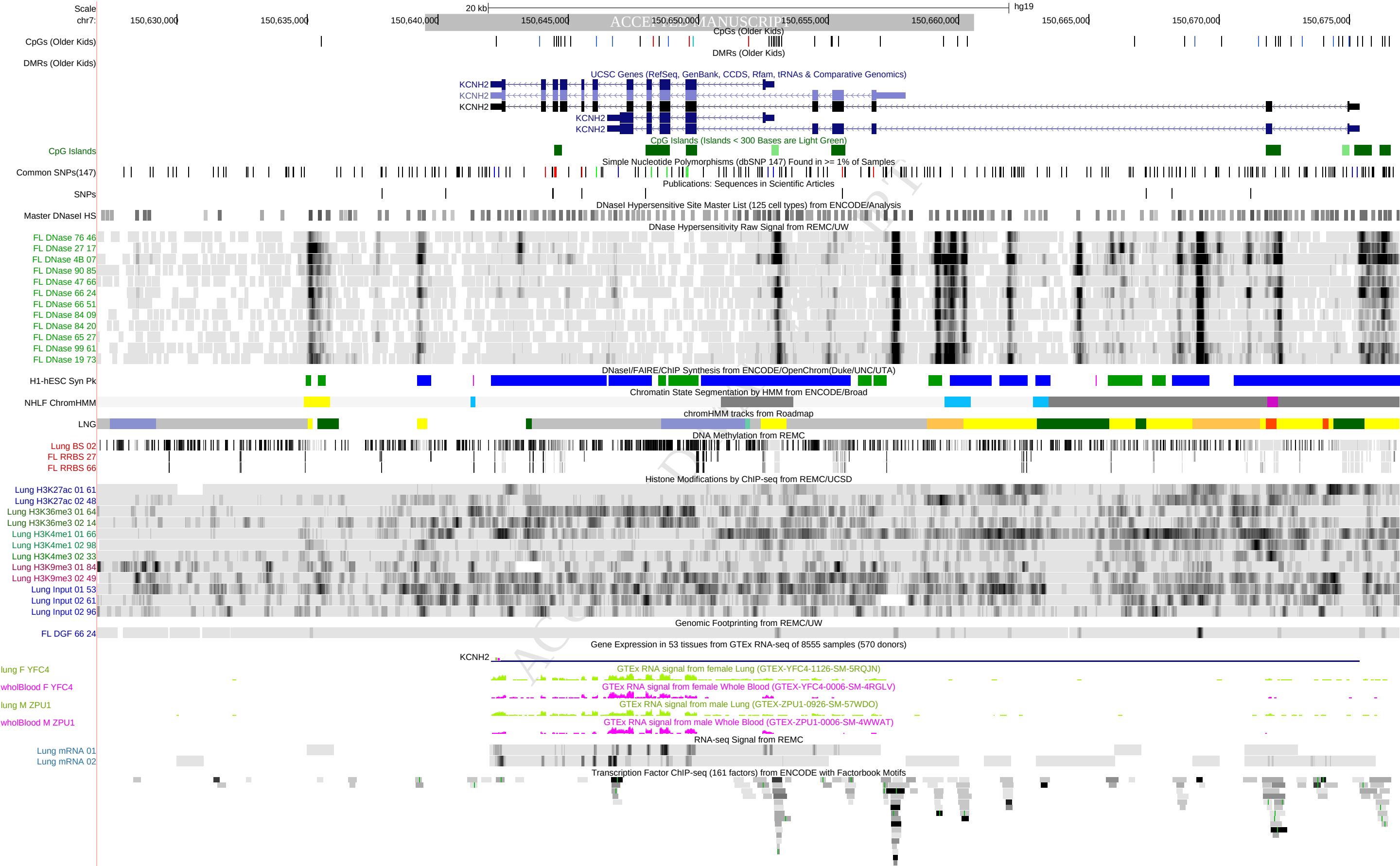
FL DNase 65 27
FL DNase 99 61
FL DNase 19 73
DNaseI/FAIRE/ChIP Synthesis from ENCODE/OpenChrom(Duke/UNC/UTA)
H1-hESC Syn Pk
Chromatin State Segmentation by HMM from ENCODE/Broad
NHLF ChromHMM
chromHMM tracks from Roadmap
LNG
DNA Methylation from REMC
Lung BS 02
FL RRBS 27
FL RRBS 66
Histone Modifications by ChIP-seq from REMC/UCSD
Lung H3K27ac 01 61
Lung H3K27ac 02 48
Lung H3K36me3 01 64
Lung H3K36me3 02 14
Lung H3K4me1 01 66
Lung H3K4me1 02 98
Lung H3K4me3 02 33
Lung H3K9me3 01 84
Lung H3K9me3 02 49
Lung Input 01 53
Lung Input 02 61
Lung Input 02 96
Genomic Footprinting from REMC/UW
FL DGF 66 24
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors)
RPS6KA2
GTEx RNA signal from female Lung (GTEX-YFC4-1126-SM-5RQJN)
lung F YFC4
GTEx RNA signal from female Whole Blood (GTEX-YFC4-0006-SM-4RGLV)
wholBlood F YFC4
GTEx RNA signal from male Lung (GTEX-ZPU1-0926-SM-57WDO)
lung M ZPU1
GTEx RNA signal from male Whole Blood (GTEX-ZPU1-0006-SM-4WWAT)
wholBlood M ZPU1
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs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UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
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CpG Islands (Islands < 300 Bases are Light Green)
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Lung H3K9me3 02 49
Lung Input 01 53
Lung Input 02 61
Lung Input 02 96
Genomic Footprinting from REMC/UW
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KCNH2
lung F YFC4
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lung M ZPU1
GTEx RNA signal from male Lung (GTEX-ZPU1-0926-SM-57WDO)
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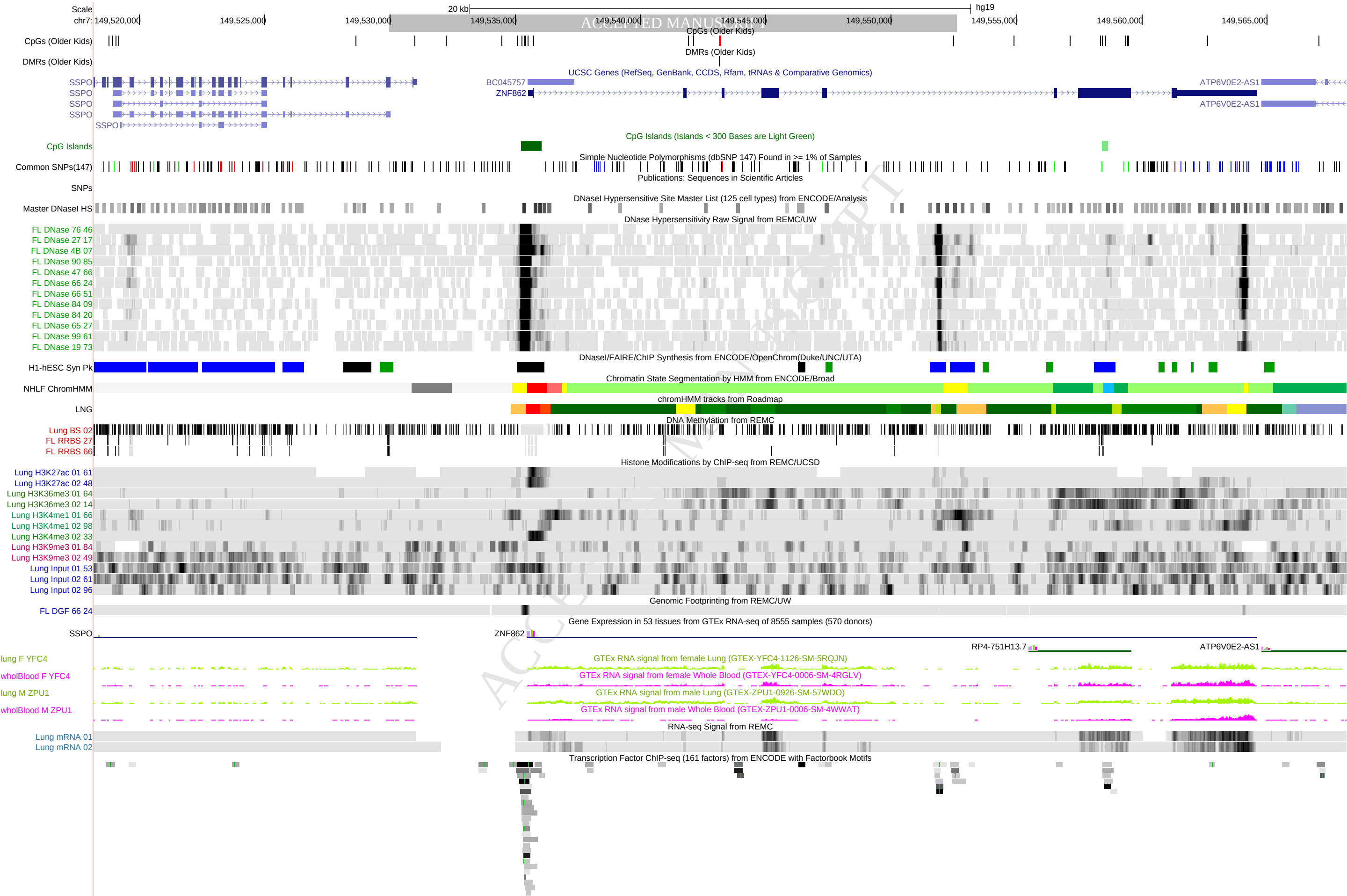
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DMRs (Older Kids)
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CpG Islands (Islands < 300 Bases are Light Green)
CpG Islands
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SSPO
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RP4-751H13.7
ATP6V0E2-AS1
lung F YFC4
GTEx RNA signal from female Lung (GTEX-YFC4-1126-SM-5RQJN)
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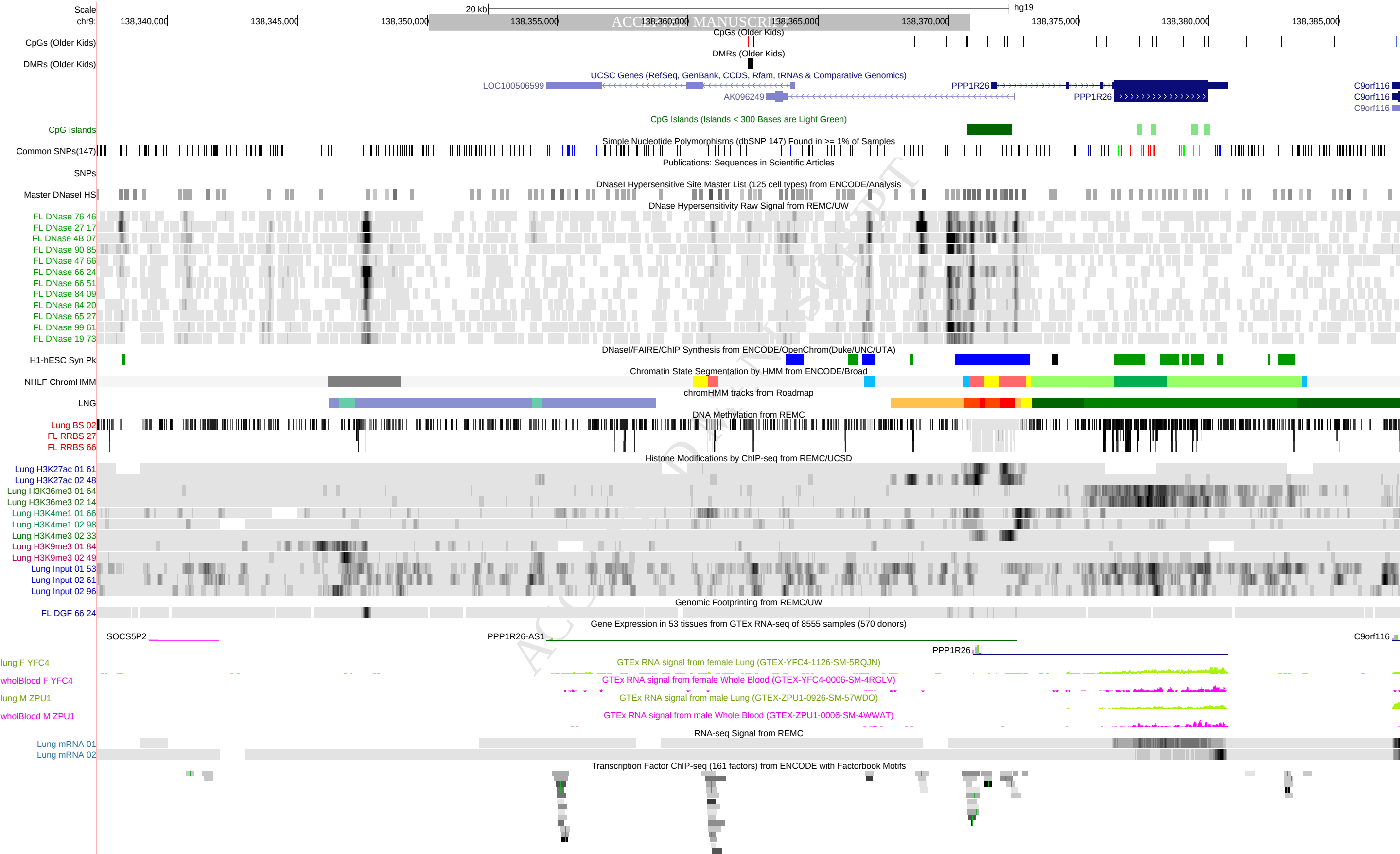
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CpG Islands
CpG Islands (Islands < 300 Bases are Light Green)
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FL DNase 84 20
FL DNase 65 27
FL DNase 99 61
FL DNase 19 73
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Lung Input 02 96
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FL DGF 66 24
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors)
SOCS5P2
PPP1R26-AS1
PPP1R26
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lung F YFC4
GTEx RNA signal from female Lung (GTEX-YFC4-1126-SM-5RQJN)
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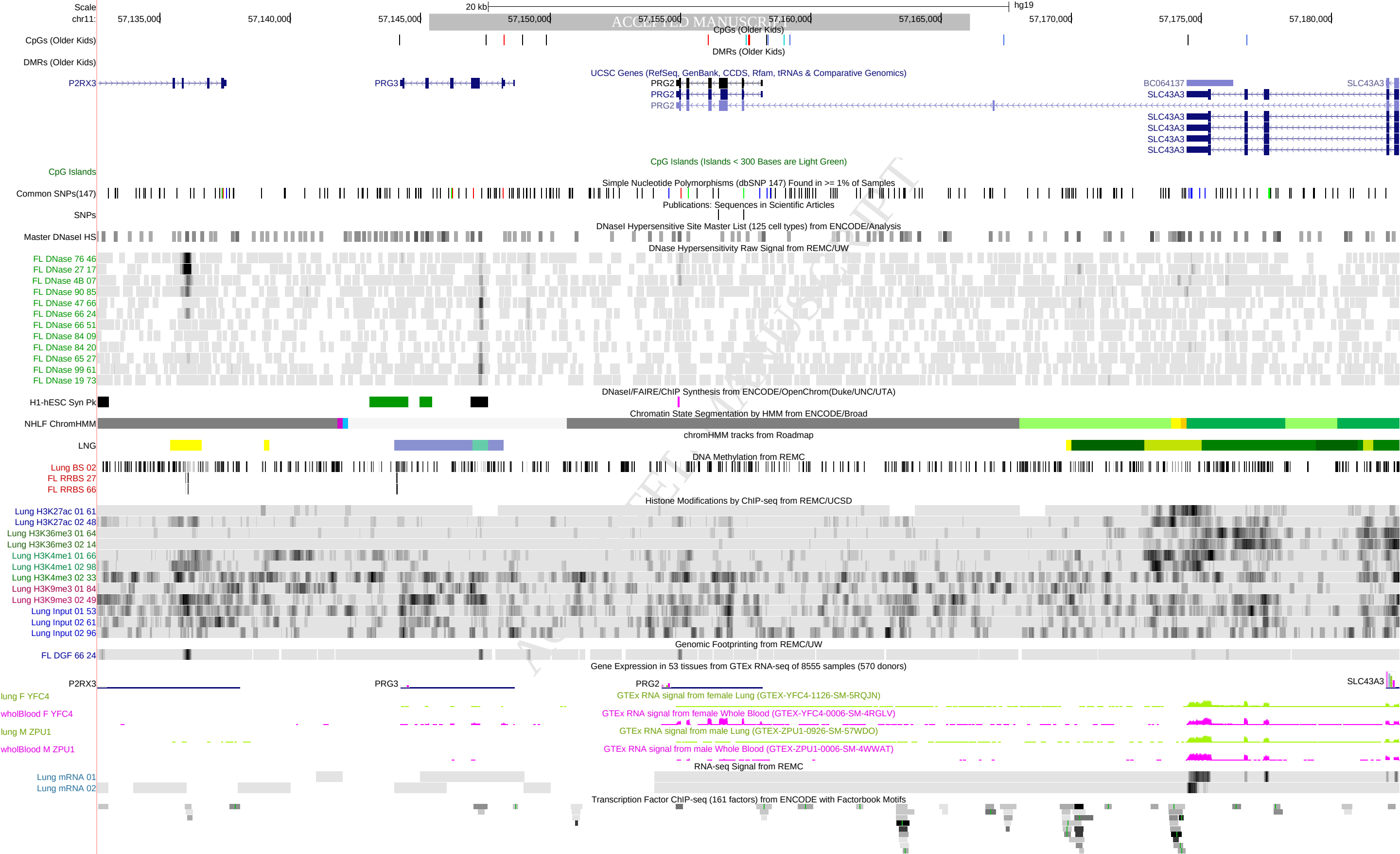
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CpGs (Older Kids)
DMRs (Older Kids)
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
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CpG Islands (Islands < 300 Bases are Light Green)
CpG Islands
Simple Nucleotide Polymorphisms (dbSNP 147) Found in >= 1% of Samples
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FL DNase 19 73
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NHLF ChromHMM
chromHMM tracks from Roadmap
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DNA Methylation from REMC
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PRG3
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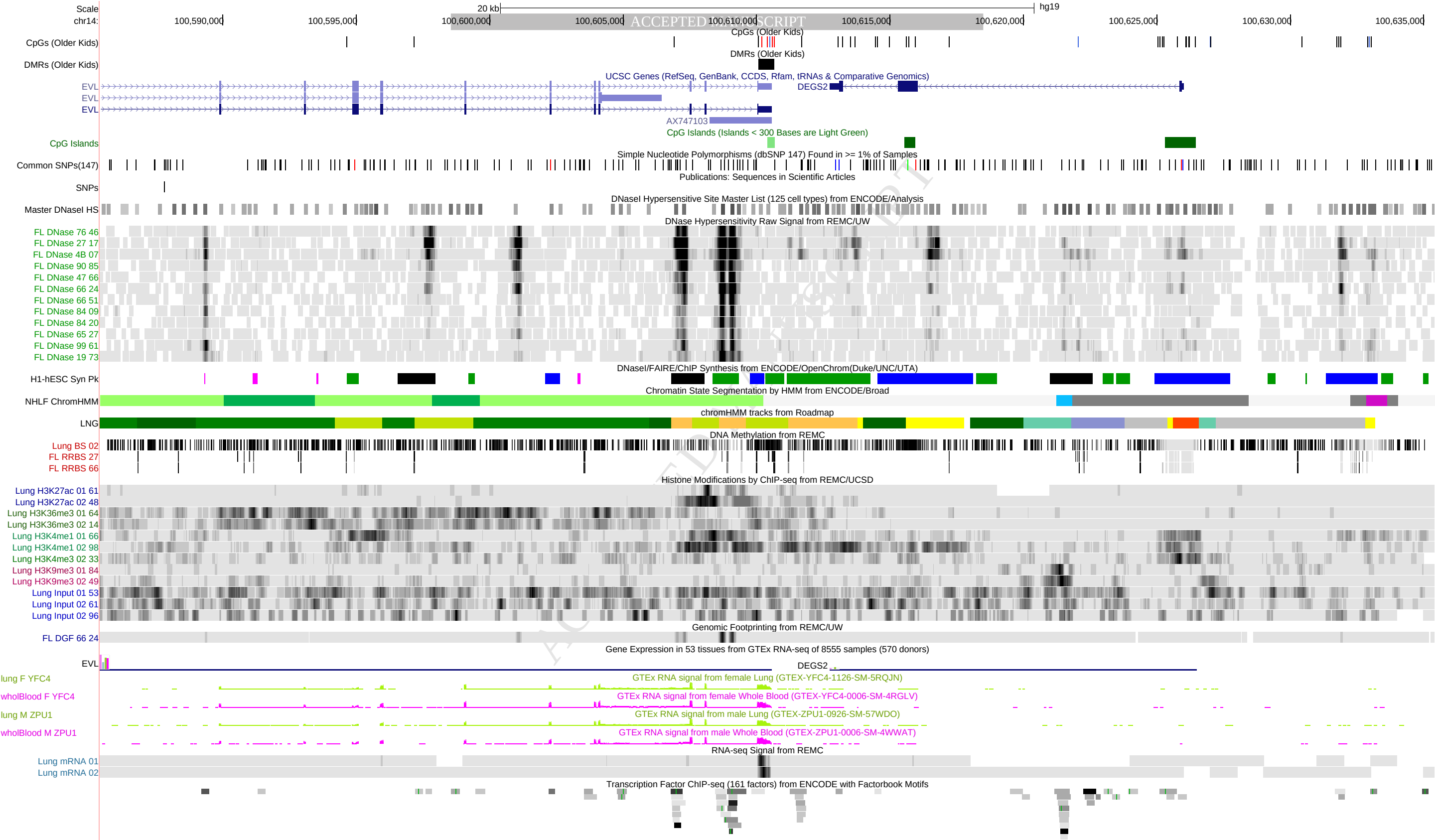
wholBlood F YFC4
GTEx RNA signal from male Lung (GTEX-ZPU1-0926-SM-57WDO)
lung M ZPU1
GTEx RNA signal from male Whole Blood (GTEX-ZPU1-0006-SM-4WWAT)
wholBlood M ZPU1
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs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ACCEPTED MANUSCRIPT
CpGs (Older Kids)
DMRs (Older Kids)
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)
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CpG Islands (Islands < 300 Bases are Light Green)
CpG Islands
Simple Nucleotide Polymorphisms (dbSNP 147) Found in >= 1% of Samples
Common SNPs(147)
Publications: Sequences in Scientific Articles
SNPs
DNaseI Hypersensitive Site Master List (125 cell types) from ENCODE/Analysis
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DNase Hypersensitivity Raw Signal from REMC/UW
FL DNase 76 46
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DNaseI/FAIRE/ChIP Synthesis from ENCODE/OpenChrom(Duke/UNC/UTA)
H1-hESC Syn Pk
Chromatin State Segmentation by HMM from ENCODE/Broad
NHLF ChromHMM
chromHMM tracks from Roadmap
LNG
DNA Methylation from REMC
Lung BS 02
FL RRBS 27
FL RRBS 66
Histone Modifications by ChIP-seq from REMC/UCSD
Lung H3K27ac 01 61
Lung H3K27ac 02 48
Lung H3K36me3 01 64
Lung H3K36me3 02 14
Lung H3K4me1 01 66
Lung H3K4me1 02 98
Lung H3K4me3 02 33
Lung H3K9me3 01 84
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Lung Input 01 53
Lung Input 02 61
Lung Input 02 96
Genomic Footprinting from REMC/UW
FL DGF 66 24
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (570 donors)
EVL
DEGS2
GTEx RNA signal from female Lung (GTEX-YFC4-1126-SM-5RQJN)
lung F YFC4
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wholBlood F YFC4
GTEx RNA signal from male Lung (GTEX-ZPU1-0926-SM-57WDO)
lung M ZPU1
GTEx RNA signal from male Whole Blood (GTEX-ZPU1-0006-SM-4WWAT)
wholBlood M ZPU1
RNA-seq Signal from REMC
Lung mRNA 01
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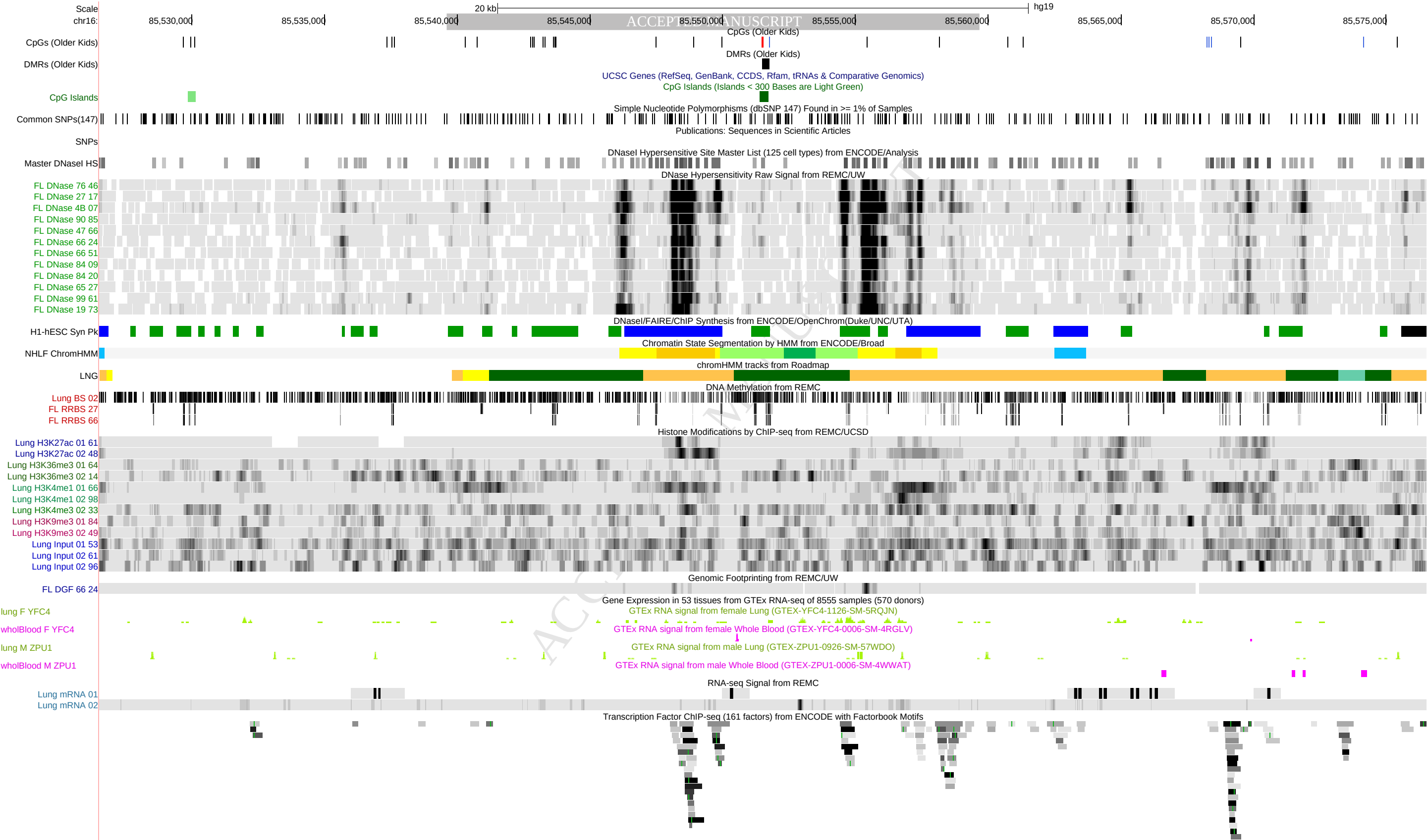
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs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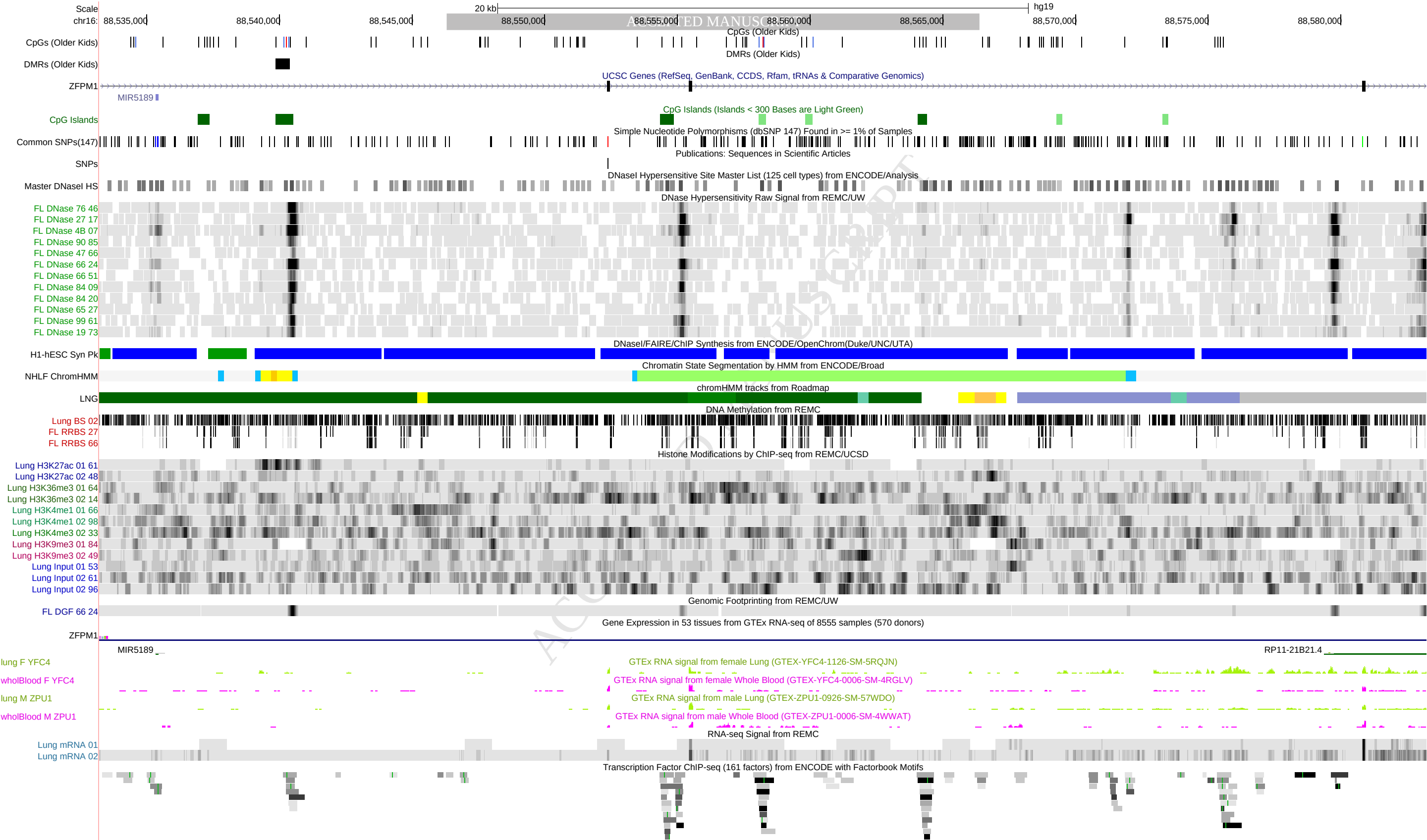
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ZFPM1
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wholBlood M ZPU1
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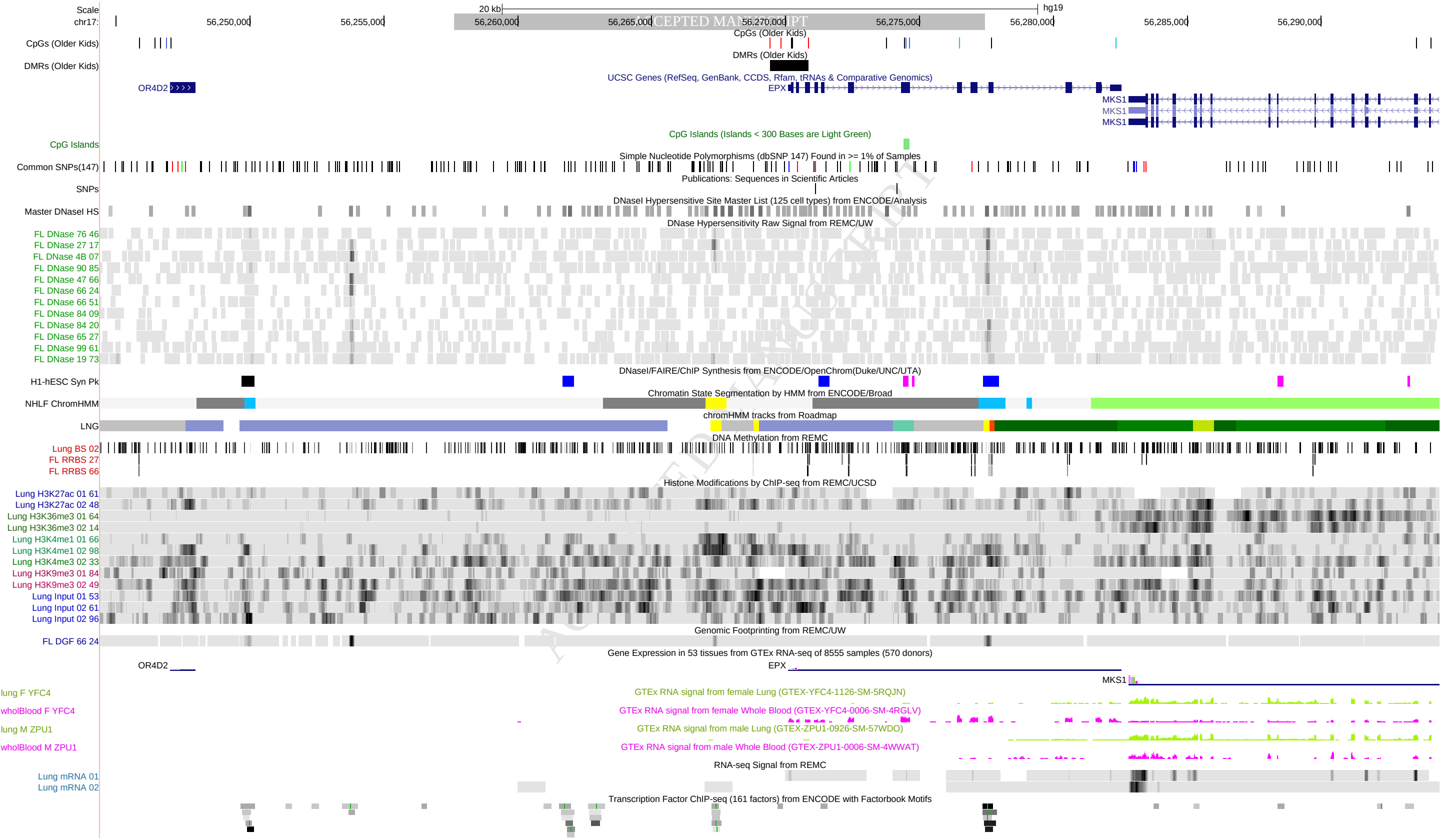
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wholBlood M ZPU1
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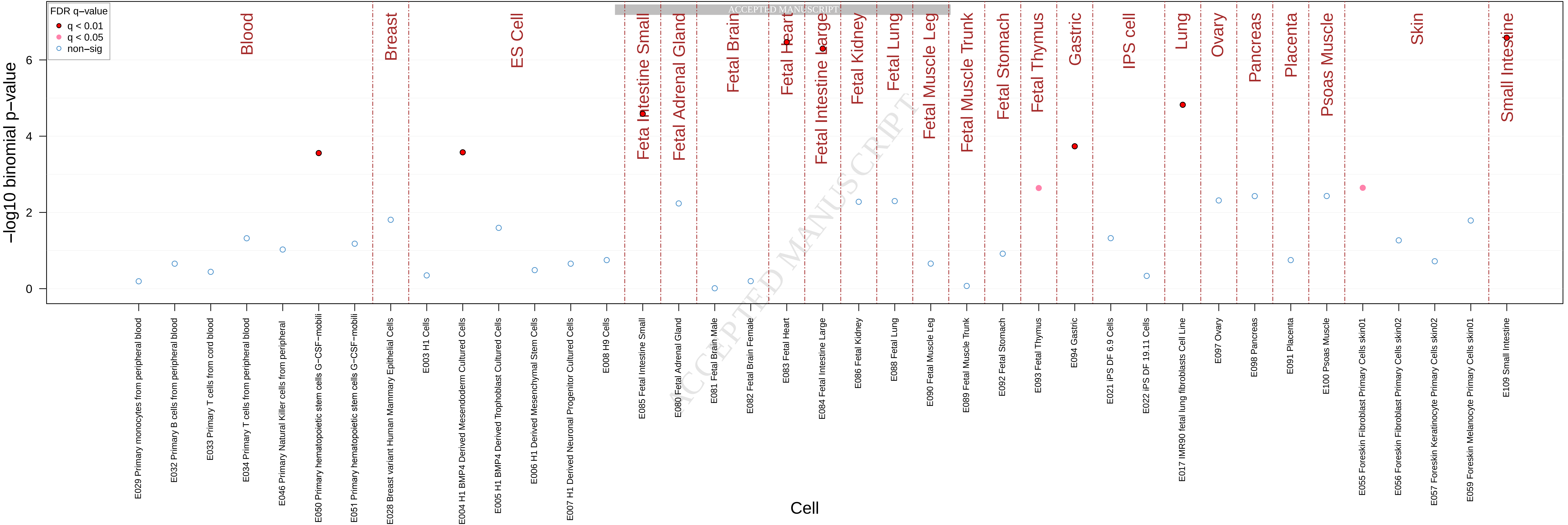
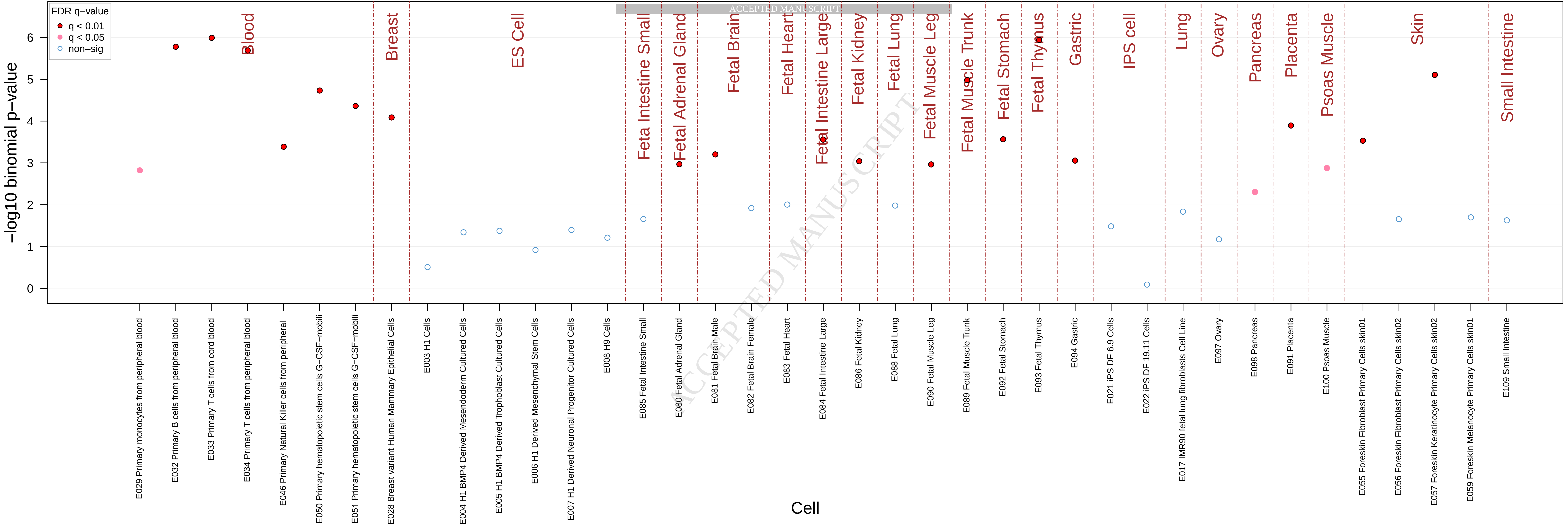
RNA-seq Signal from REMC
Lung mRNA 01
Lung mRNA 02
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs



FDR q−value
q < 0.01
q < 0.05
non−sig
−log10 binomial p−value
0
2
4
6
Blood
Breast
ES Cell
Feta Intestine Small
Fetal Adrenal Gland
Fetal Brain
Fetal Heart
Fetal Intestine Large
Fetal Kidney
Fetal Lung
Fetal Muscle Leg
Fetal Muscle Trunk
Fetal Stomach
Fetal Thymus
Gastric
IPS cell
Lung
Ovary
Pancreas
Placenta
Psoas Muscle
Skin
Small Intestine
E029 Primary monocytes from peripheral blood
E032 Primary B cells from peripheral blood
E033 Primary T cells from cord blood
E034 Primary T cells from peripheral blood
E046 Primary Natural Killer cells from peripheral
E050 Primary hematopoietic stem cells G−CSF−mobili
E051 Primary hematopoietic stem cells G−CSF−mobili
E028 Breast variant Human Mammary Epithelial Cells
E003 H1 Cells
E004 H1 BMP4 Derived Mesendoderm Cultured Cells
E005 H1 BMP4 Derived Trophoblast Cultured Cells
E006 H1 Derived Mesenchymal Stem Cells
E007 H1 Derived Neuronal Progenitor Cultured Cells
E008 H9 Cells
E085 Fetal Intestine Small
E080 Fetal Adrenal Gland
E081 Fetal Brain Male
E082 Fetal Brain Female
E083 Fetal Heart
E084 Fetal Intestine Large
E086 Fetal Kidney
E088 Fetal Lung
E090 Fetal Muscle Leg
E089 Fetal Muscle Trunk
E092 Fetal Stomach
E093 Fetal Thymus
E094 Gastric
E021 iPS DF 6.9 Cells
E022 iPS DF 19.11 Cells
E017 IMR90 fetal lung fibroblasts Cell Line
E097 Ovary
E098 Pancreas
E091 Placenta
E100 Psoas Muscle
E055 Foreskin Fibroblast Primary Cells skin01
E056 Foreskin Fibroblast Primary Cells skin02
E057 Foreskin Keratinocyte Primary Cells skin02
E059 Foreskin Melanocyte Primary Cells skin01
E109 Small Intestine
Cell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−log10 binomial p−value
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Breast
ES Cell
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Fetal Brain
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E057 Foreskin Keratinocyte Primary Cells skin02
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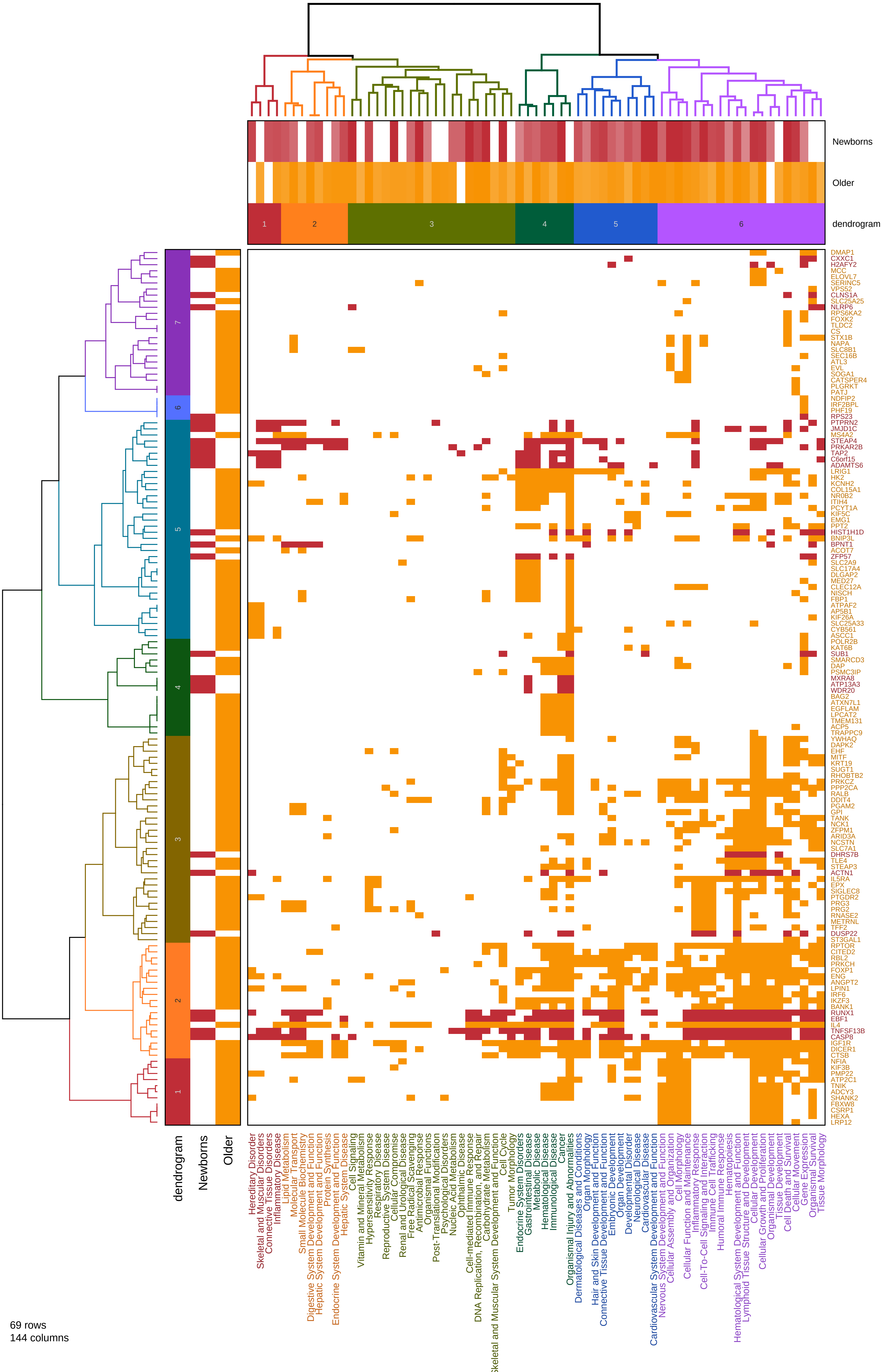
E109 Small Intestine
Cell



Newborns
Older
dendrogram
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2
3
4
5
6
7
DMAP1
CXXC1
H2AFY2
MCC
ELOVL7
SERINC5
VPS52
CLNS1A
SLC25A25
NLRP6
RPS6KA2
FOXK2
TLDC2
CS
STX1B
NAPA
SLC8B1
SEC16B
ATL3
EVL
SOGA1
CATSPER4
PLGRKT
PATJ
NDFIP2
IRF2BPL
PHF19
RPS23
PTPRN2
JMJD1C
MS4A2
STEAP4
PRKAR2B
TAP2
C6orf15
ADAMTS6
LRIG1
HK2
KCNH2
COL15A1
NR0B2
ITIH4
PCYT1A
KIF5C
EMG1
PPT2
HIST1H1D
BNIP3L
BPNT1
ACOT7
ZFP57
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SLC17A4
DLGAP2
MED27
CLEC12A
NISCH
FBP1
ATPAF2
AP5B1
KIF26A
SLC25A33
CYB561
ASCC1
POLR2B
KAT6B
SUB1
SMARCD3
DAP
PSMC3IP
MXRA8
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WDR20
BAG2
ATXN7L1
EGFLAM
LPCAT2
TMEM131
ACP5
TRAPPC9
YWHAQ
DAPK2
EHF
MITF
KRT19
SUGT1
RHOBTB2
PRKCZ
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PGAM2
GPI
TANK
NCK1
ZFPM1
ARID3A
NCSTN
SLC7A1
DHRS7B
TLE4
STEAP3
ACTN1
IL5RA
EPX
SIGLEC8
PTGDR2
PRG3
PRG2
RNASE2
METRNL
TFF2
DUSP22
ST3GAL1
RPTOR
CITED2
RBL2
PRKCH
FOXP1
ENG
ANGPT2
LPIN1
IRF6
IKZF3
BANK1
RUNX1
EBF1
IL4
TNFSF13B
CASP8
IGF1R
DICER1
CTSB
NFIA
KIF3B
PMP22
ATP2C1
TNIK
ADCY3
SHANK2
FBXW8
CSRP1
HEXA
LRP12
Hereditary Disorder
Skeletal and Muscular Disorders
Connective Tissue Disorders
Inflammatory Disease
Lipid Metabolism
Molecular Transport
Small Molecule Biochemistry
Digestive System Development and Function
Hepatic System Development and Function
Protein Synthesis
Endocrine System Development and Function
Hepatic System Disease
Cell Signaling
Vitamin and Mineral Metabolism
Hypersensitivity Response
Respiratory Disease
Reproductive System Disease
Cellular Compromise
Renal and Urological Disease
Free Radical Scavenging
Antimicrobial Response
Organismal Functions
Post-Translational Modification
Psychological Disorders
Nucleic Acid Metabolism
Ophthalmic Disease
Cell-mediated Immune Response
DNA Replication, Recombination, and Repair
Carbohydrate Metabolism
Skeletal and Muscular System Development and Function
Cell Cycle
Tumor Morphology
Endocrine System Disorders
Gastrointestinal Disease
Metabolic Disease
Hematological Disease
Immunological Disease
Cancer
Organismal Injury and Abnormalities
Dermatological Diseases and Conditions
Organ Morphology
Hair and Skin Development and Function
Connective Tissue Development and Function
Embryonic Development
Organ Development
Developmental Disorder
Neurological Disease
Cardiovascular Disease
Cardiovascular System Development and Function
Nervous System Development and Function
Cellular Assembly and Organization
Cell Morphology
Cellular Function and Maintenance
Inflammatory Response
Cell-To-Cell Signaling and Interaction
Immune Cell Trafficking
Humoral Immune Response
Hematopoiesis
Hematological System Development and Function
Lymphoid Tissue Structure and Development
Cellular Development
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Organismal Development
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Cell Death and Survival
Cellular Movement
Gene Expression
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Tissue Morphology
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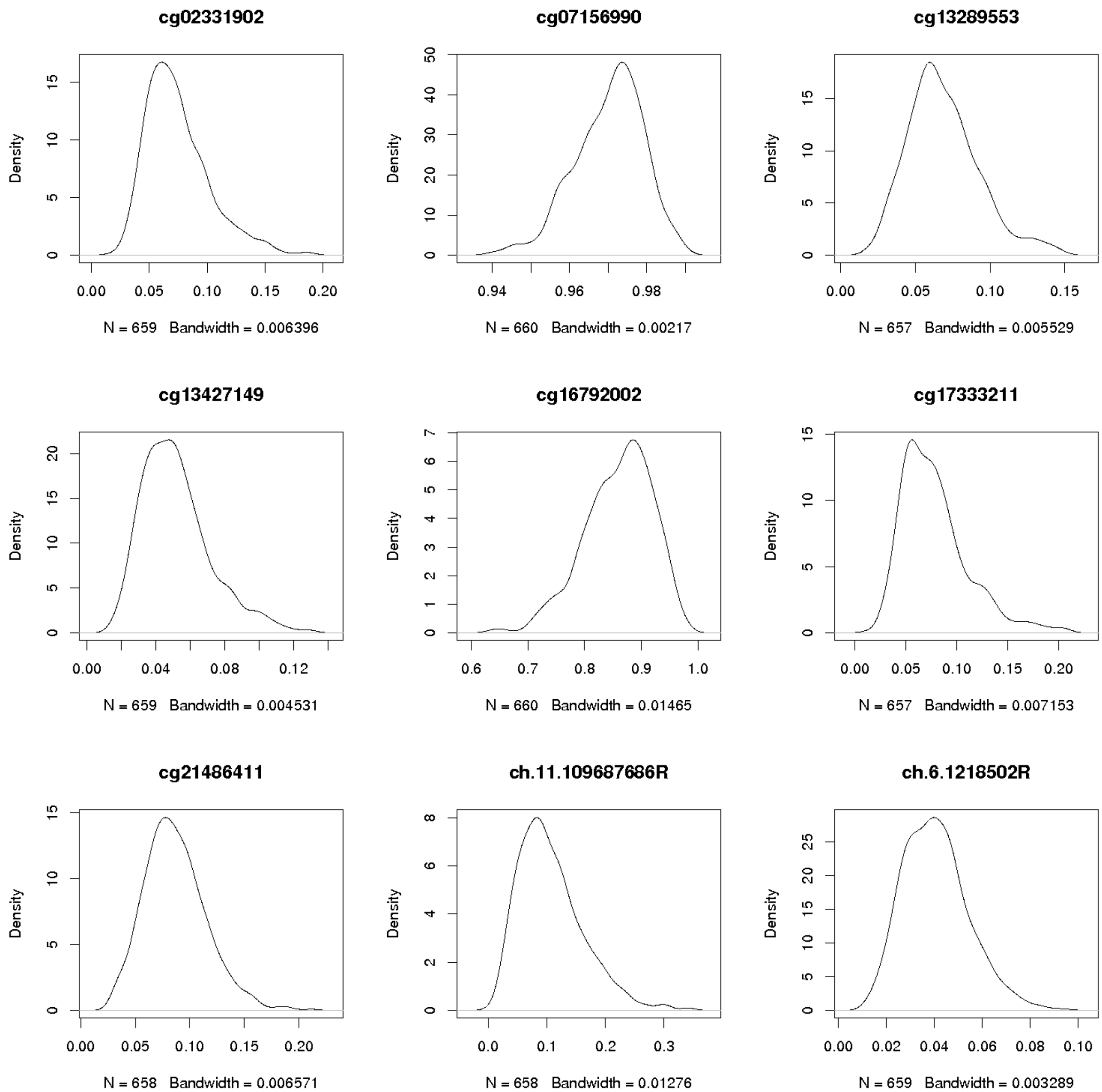
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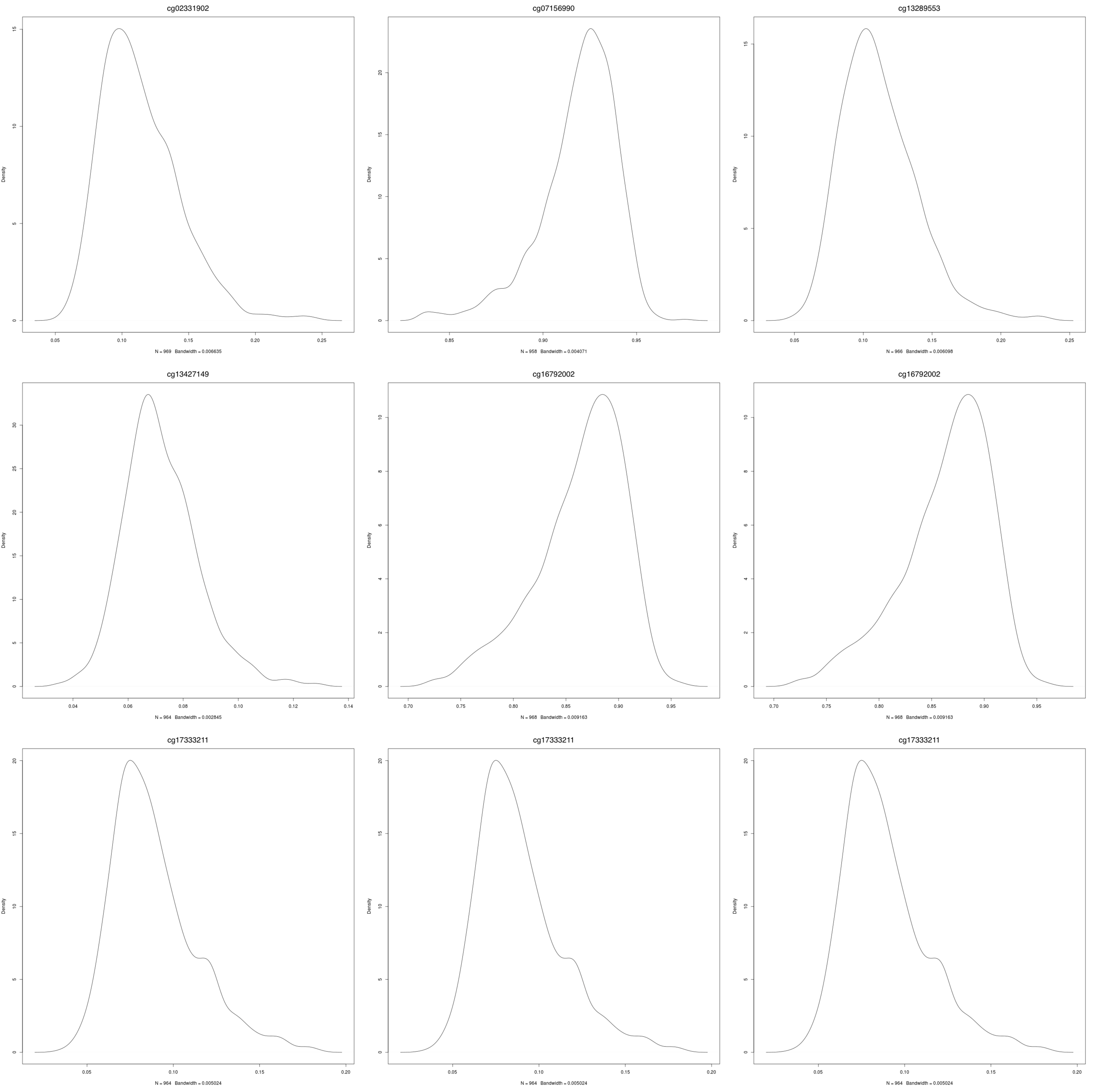
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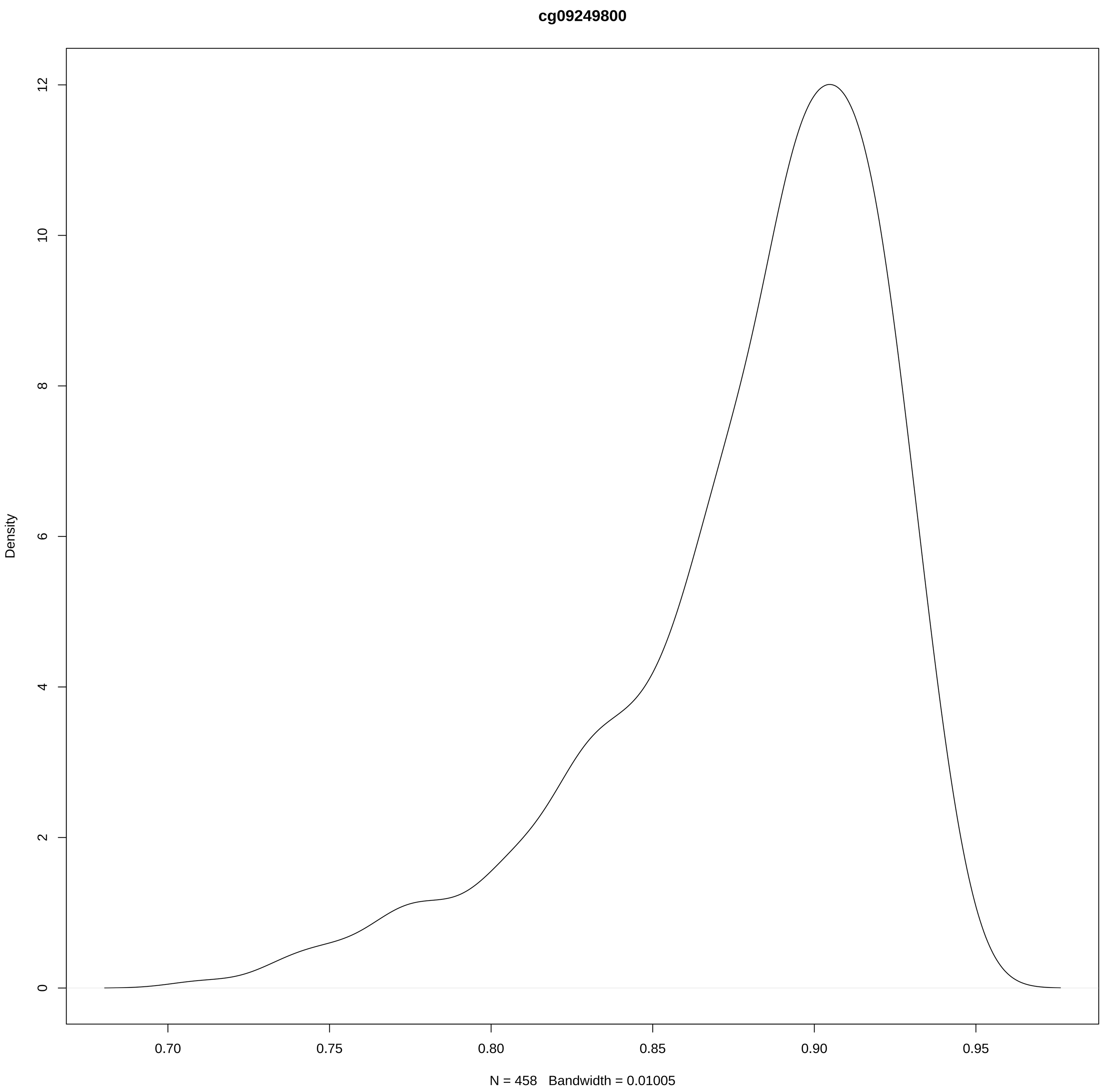
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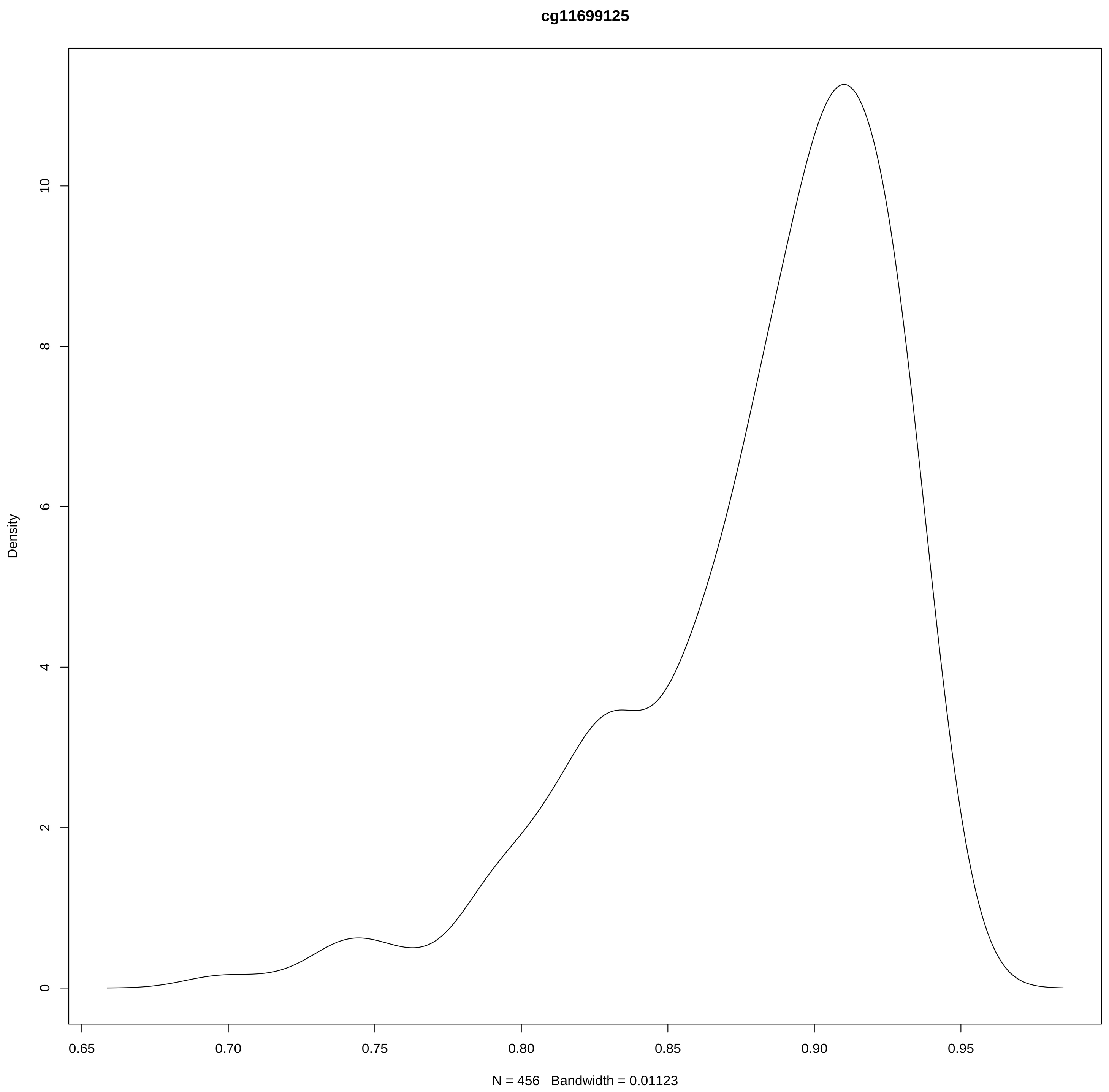
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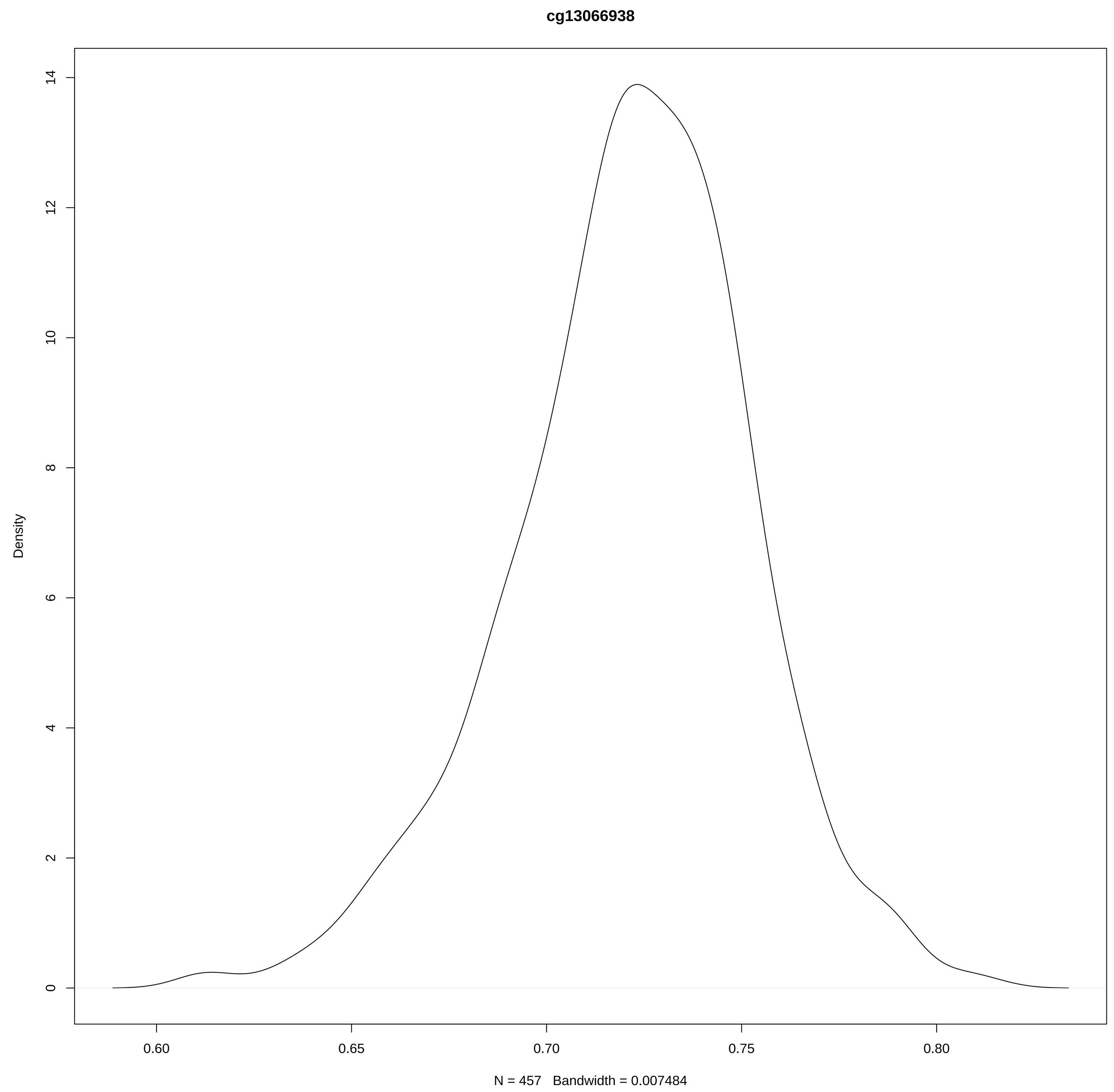
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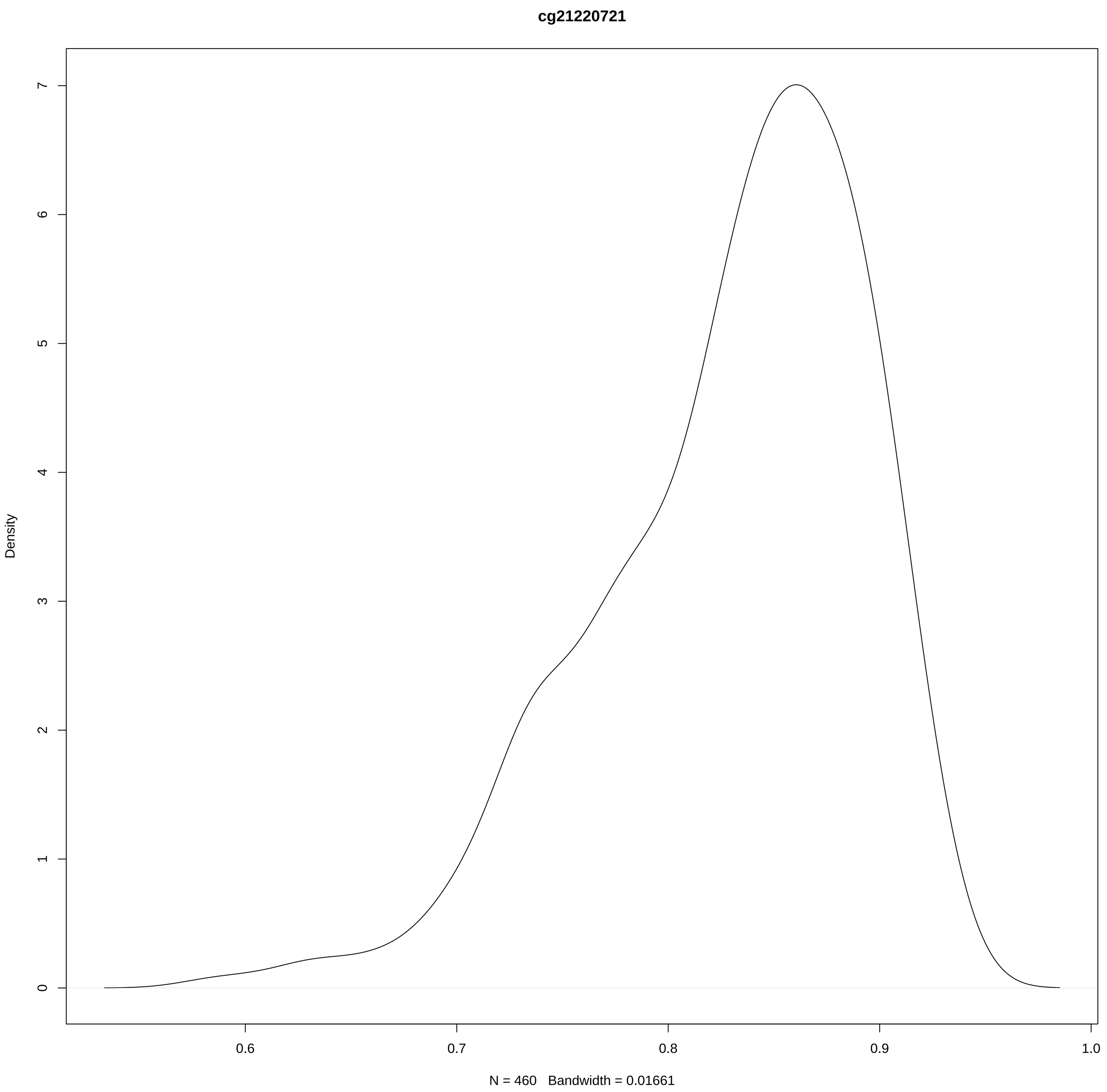
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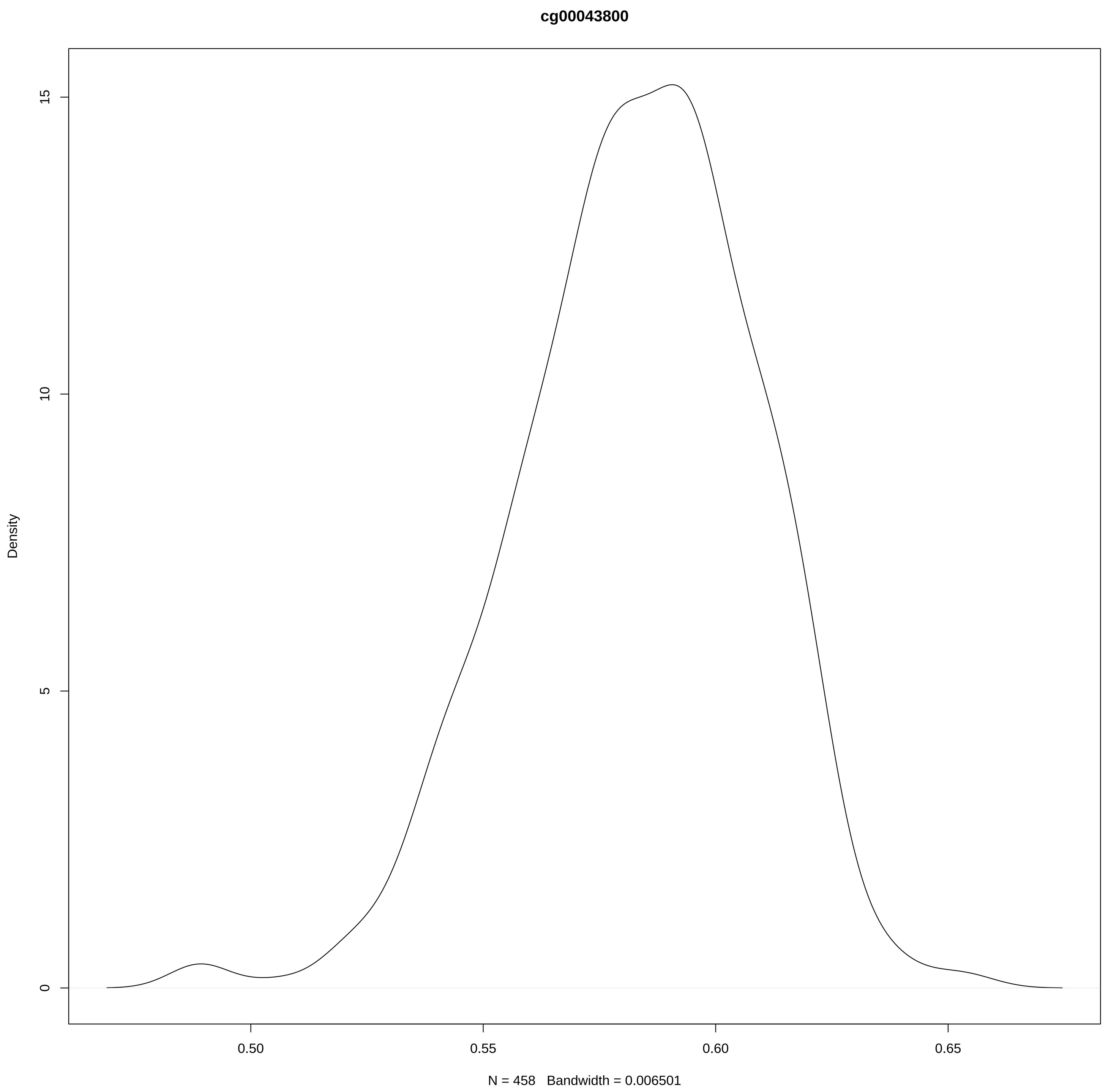
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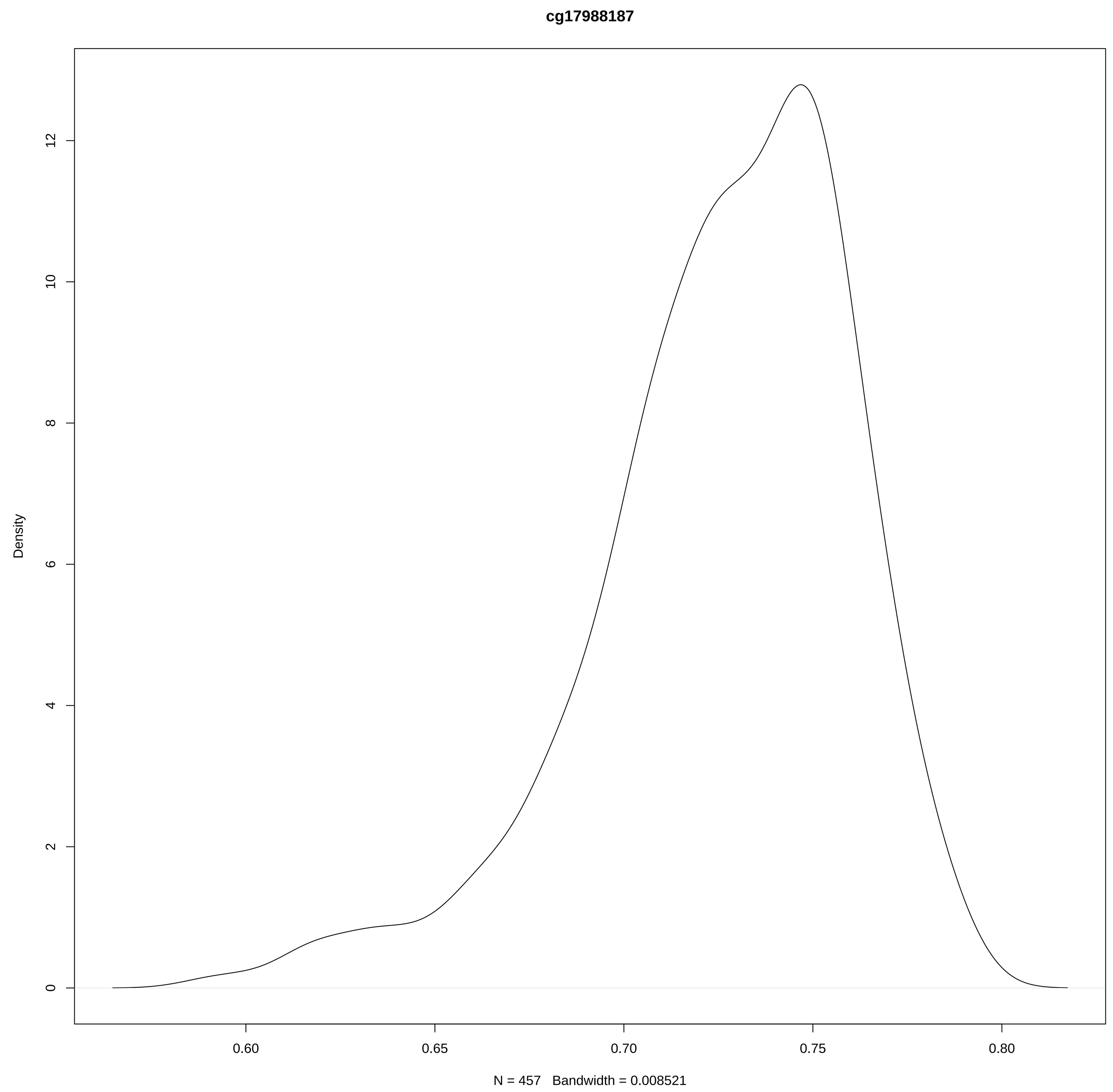
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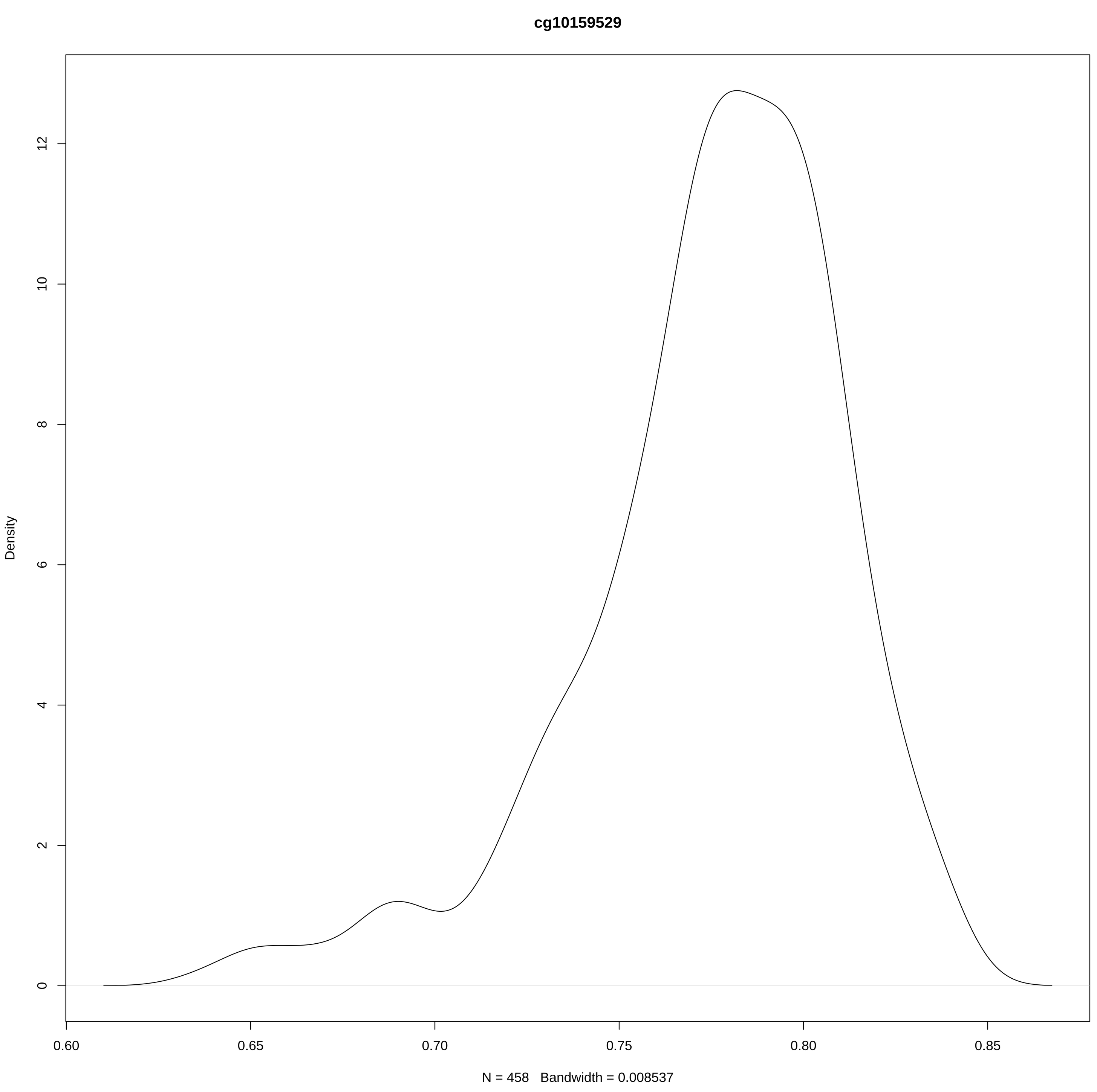
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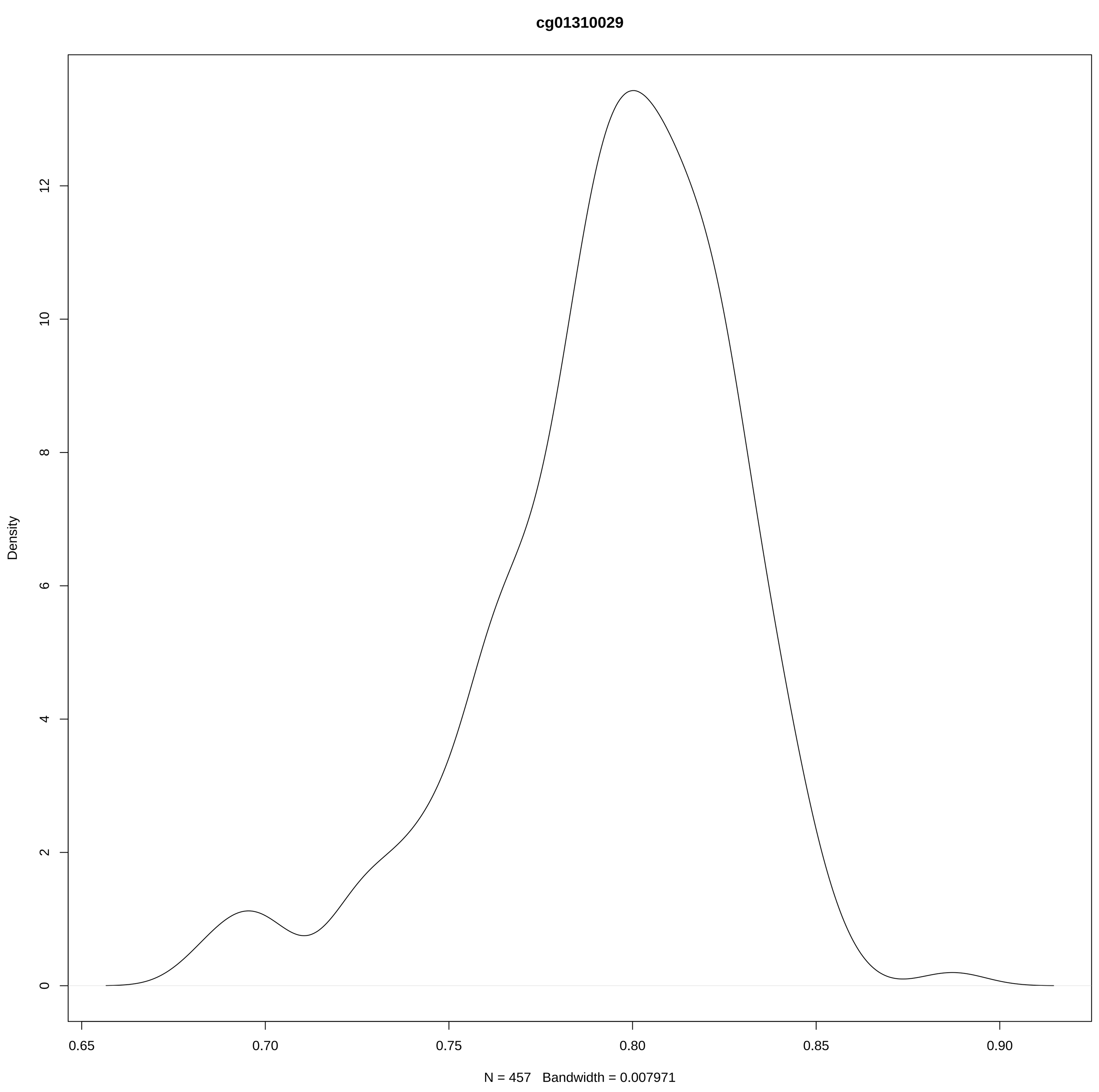
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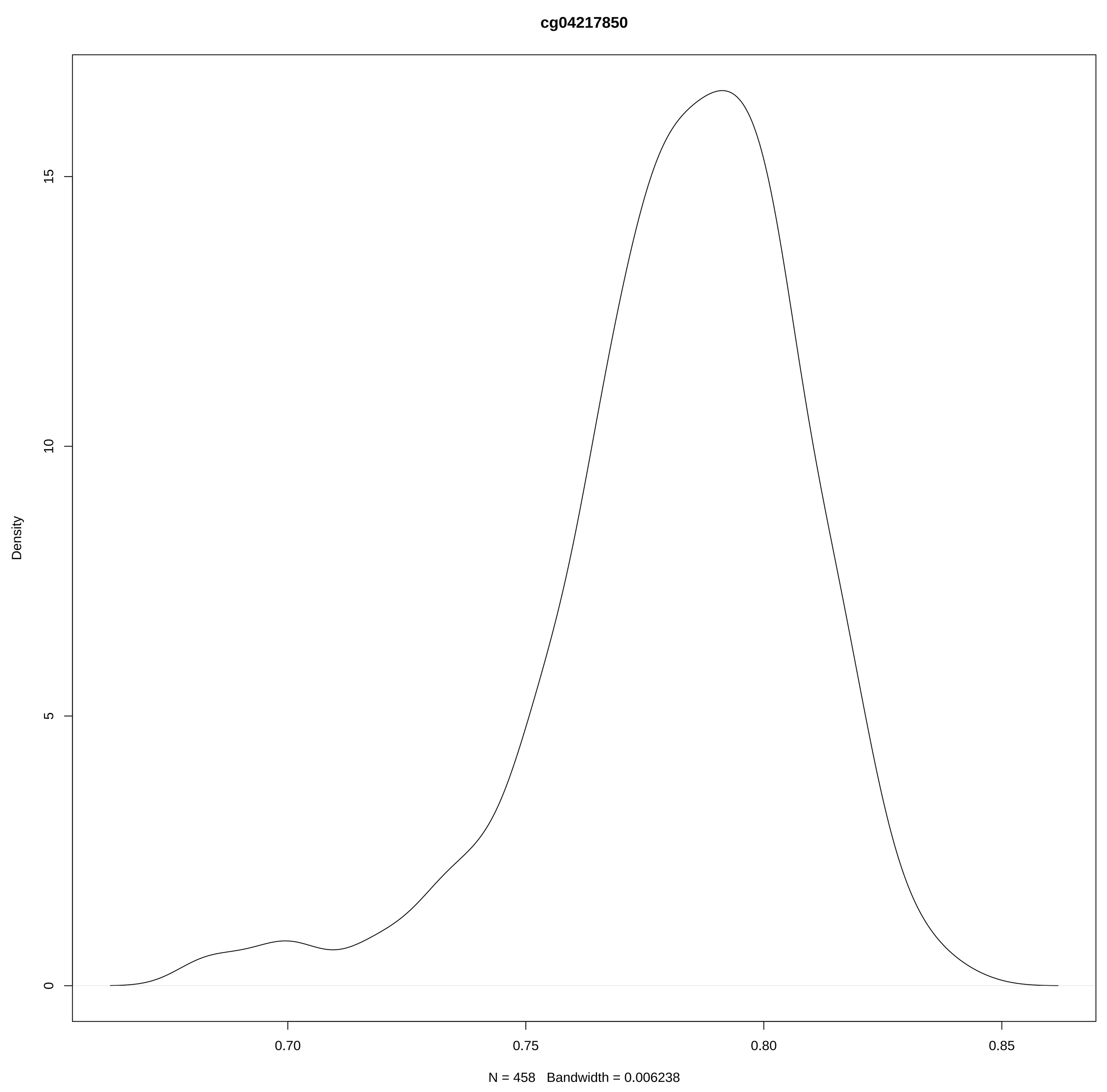
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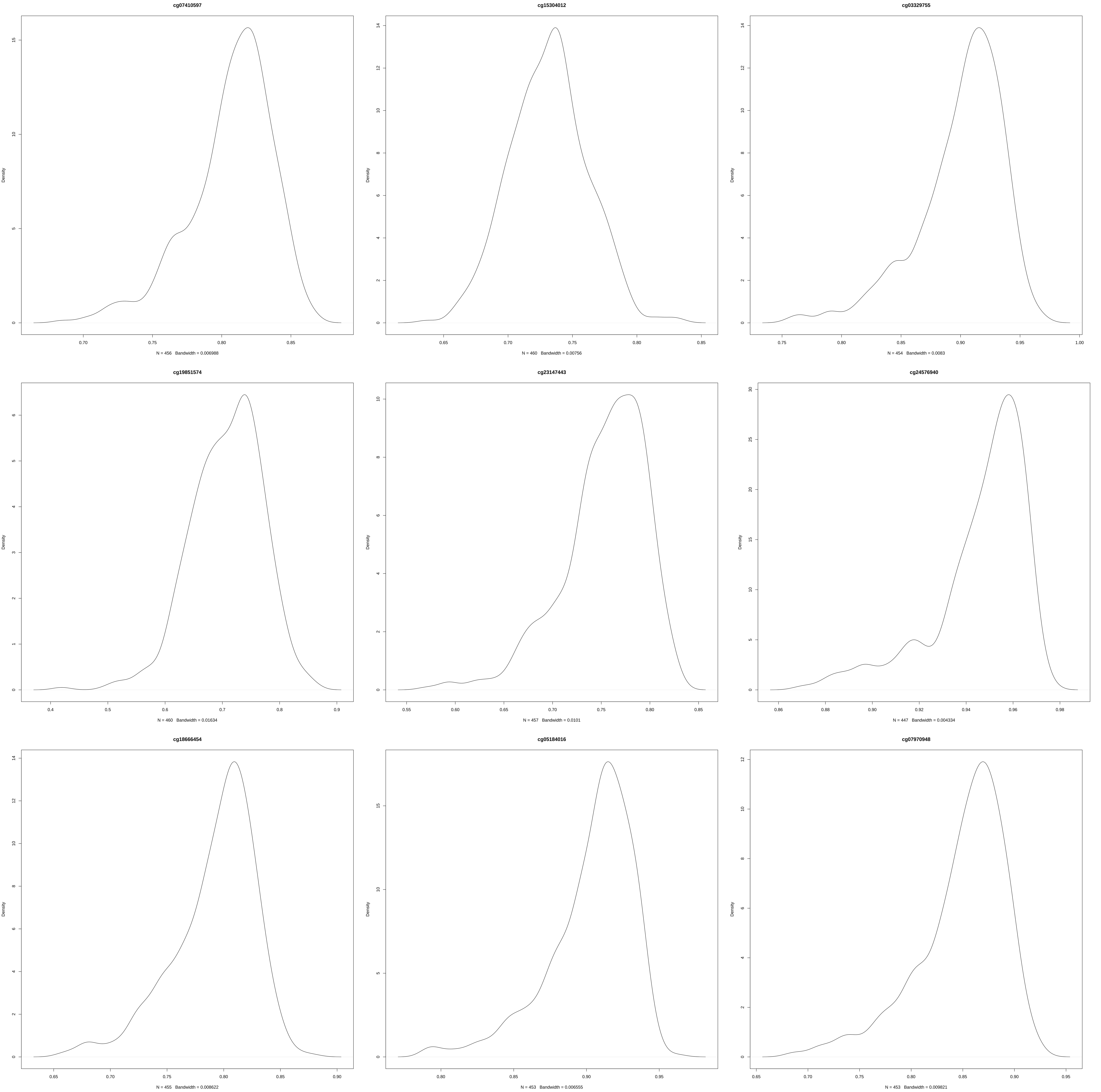
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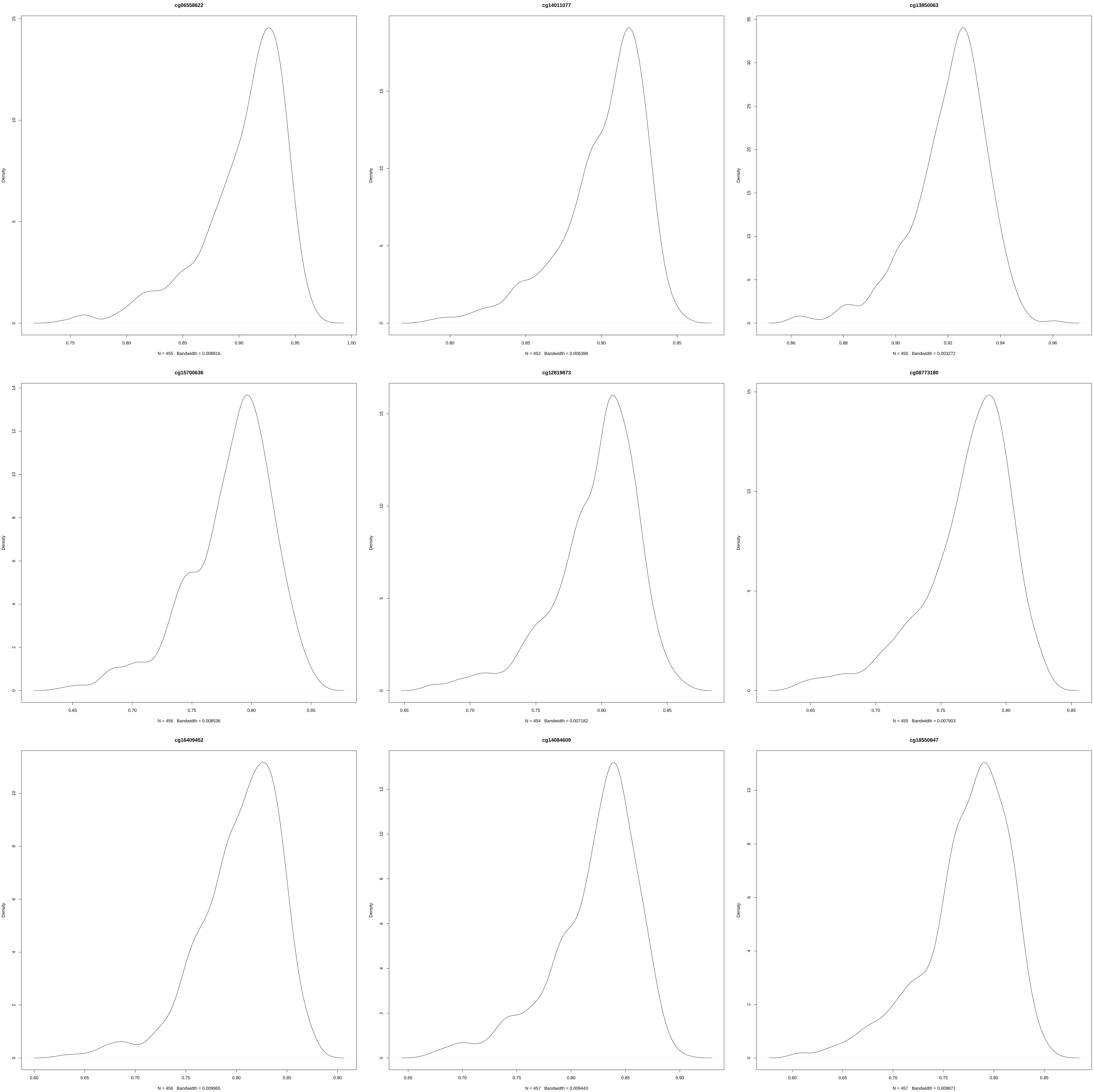
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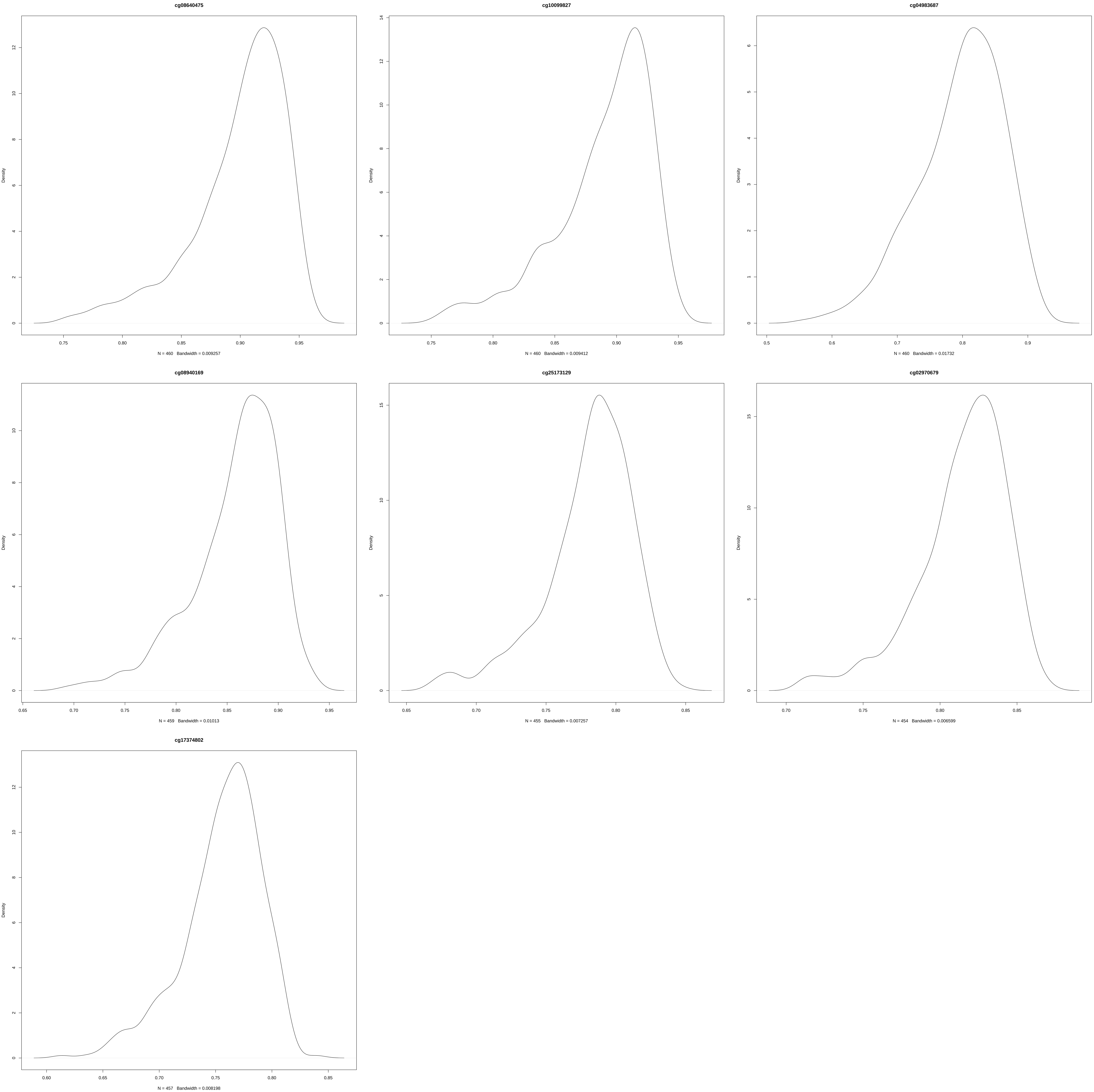
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