

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMETHODS

Genome-wide measurement of DNA methylation

For the discovery set, whole blood samples from the multi-site consortia were processed at the Rutgers University Cell and DNA repository (RUCDR) for DNA isolation using Qiagen Autopure LS and the pellets were hydrated in TE buffer. The samples were shipped to JHU for analysis, and DNA integrity and concentration were confirmed by gel electrophoresis and NanoDrop. A total of 3168 samples, randomized for case-control status to minimize batch effects, were hybridized to the Infinium array for the discovery set (including technical replicates from 277 blood samples and liver and placenta samples across every plate for quality control, and blood samples from family members of probands for a separate study). For the replication set, DNA also was isolated at RUCDR. Of those, 516 samples were hybridized to the array (with 16 replicates from liver and placenta). For each sample, 1 µg of genomic DNA was bisulfite-converted using the EZ DNA Methylation™ Kit (Zymo Research, catalog No. D5001), according to the manufacturer's guidelines for the 450K array. DNAm for the discovery and the replication sets was measured using the Infinium HumanMethylation450 BeadChip assay (Illumina, San Diego, CA). We chose to use the same methylation platform for discovery and replication to accurately calculate and model cell proportion differences between cases and controls and maximize data harmonization (see Data processing and statistical modeling section).

Data processing and statistical modeling

Assessment of cell heterogeneity and potential confounders. Several efforts were made to quantify and correct for confounders known to affect DNAm in blood. First, self-reported race was confirmed via multidimensional scaling of beta scale methylation ratios from 65 SNPs selected to discriminate genetic background in the 450K array¹ (**eFigure 1**). For a subset of samples, the 450K race prediction was confirmed with genotyping data (N=374, see genotyping section). Given the large proportion of African American participants, samples were separated in two categories: African American (AA) and non-African American (non-AA). Second, cell proportion estimates for six cell types (CD8+ and CD4+ T cells, B cells, monocytes, granulocytes, and natural killer cells) were calculated for each sample using software available in the *minfi* Bioconductor package, using an adaptation of a published algorithm^{2,3}. Third, we compared gender estimates calculated using software available in *minfi* and from genotype data with self-reported gender. Fourth, self-reported current smoking status was ascertained for all individuals, and samples with missing smoking information were dropped. Moreover, to ensure that potential methylation differences revealed in the present study were not due to residual smoking confounding (even after explicitly modeling smoking in linear regression), we further removed 294 CpGs associated with smoking status in previous publications from our association results^{4,5}. Fifth, we used ANOVA to test the effects of medication on predicted cell proportions, using the following antipsychotic medication categories: 0=No antipsychotics, 1=Typical antipsychotics, 2=Atypical antipsychotics, and 3=Typical and Atypical antipsychotics. Sixth, we applied the "Remove Unwanted Variation, 2-step" (RUV-2) method⁶ to correct potential batch effects by unmeasured factors, using the first two principal components of the raw intensities in the green and red channels of the negative control probes of the 450K array.

Replication analysis. We fit a similar robust linear regression model to that of the discovery set, using the same covariates except for race (all of the samples were identified as non-AA). We considered only the statistically significant DMPs from the discovery results. We applied a threshold of nominal p-value <0.05 and same direction of association to declare replication. We also assessed quadrant correlations (akin to a Kappa statistic) between the discovery and replication regression estimates across these DMPs. Post-hoc analysis to assess the influence of antipsychotic treatment on DNA methylation levels was performed using the 679 cases with complete medication information, correcting for multiple testing using the Sidak test in the *mutoss* package⁷.

Gene ontology and pathway analyses. To investigate the potential biological meaning and functional significance of the SZ-DMPs identified, we undertook gene ontology and pathway analyses. We tested for enrichment of genes for SZ-associated DMPs based on Gene Ontology (Biology Processes database) using the *GOstats* bioconductor package⁸. Network analyses were generated through the use of QIAGEN's Ingenuity Pathway Analysis (IPA®, QIAGEN, Redwood City, www.qiagen.com/ingenuity) and GeneMania (<http://www.genemania.org>).

Illumina genome-wide genotyping and meQTL analysis. A subset of the case-control samples (N=380) were genotyped using the HumanOmni5Exome-4v1 chip. Genotyping was conducted at the Genetic Resources Core Facility, Johns Hopkins Institute of Genetic Medicine, Baltimore, MD. QC was performed following the CHARGE consortium best practices⁹. Samples included for analysis had >99% call rates (N=1 dropped) and consistent inferred and recorded gender (N=5 dropped). SNP filtering eliminated monomorphic SNPs, those with call rates <95%, and duplicated SNPs. This resulted in 3,796,870 autosomal SNPs on 374 samples (165 SZ cases and 209 controls). QC and quantification of population stratification were performed using the package PLINK (<http://pngu.mgh.harvard.edu/purcell/plink/>). To identify meQTL SNPs, 209 control individuals with both DNAm and SNP data were selected, and 456,513 autosomal methylation probes were tested for association with autosomal SNPs. Cis-meQTLs were selected for having a maximum distance of less than 50 Kb between the CpG and the SNP. Analysis was carried out using the package *MatrixEQTL* and a significance level of FDR <0.01¹⁰. The PGC2 SZ-associated SNP set was derived from the published Psychiatric Genomics Consortium latest mega-analysis¹¹. Significance of overlap between SZ-DMPs and PGC2 regions was assessed using Fisher's exact test. To assess replication between these studies, we looked for overlap of significant meQTLs with statistically significant SZ-SNPs reported by the PGC.

Regression modeling formulas for identification of SZ-associated differentially methylated positions (DMSPs).

The formula for the primary regression analysis was:

$$DNAm \sim \beta_0 + \beta_1(\text{Diagnosis}) + \beta_2(\text{sex}) + \beta_3(\text{age}) + \beta_4(\text{current smoking}) + \beta_5(\text{race}) + \beta_6(\text{CD8T}) + \beta_7(\text{CD4T}) + \beta_8(\text{NK}) + \beta_9(\text{B cell}) + \beta_{10}(\text{monocytes}) + \beta_{11}(\text{granulocytes}) + \beta_{12}(\text{PCI negative control probes}) + \beta_{13}(\text{PC2 negative control probes})$$

For the additional analyses stratified by race and gender, the formulae were:

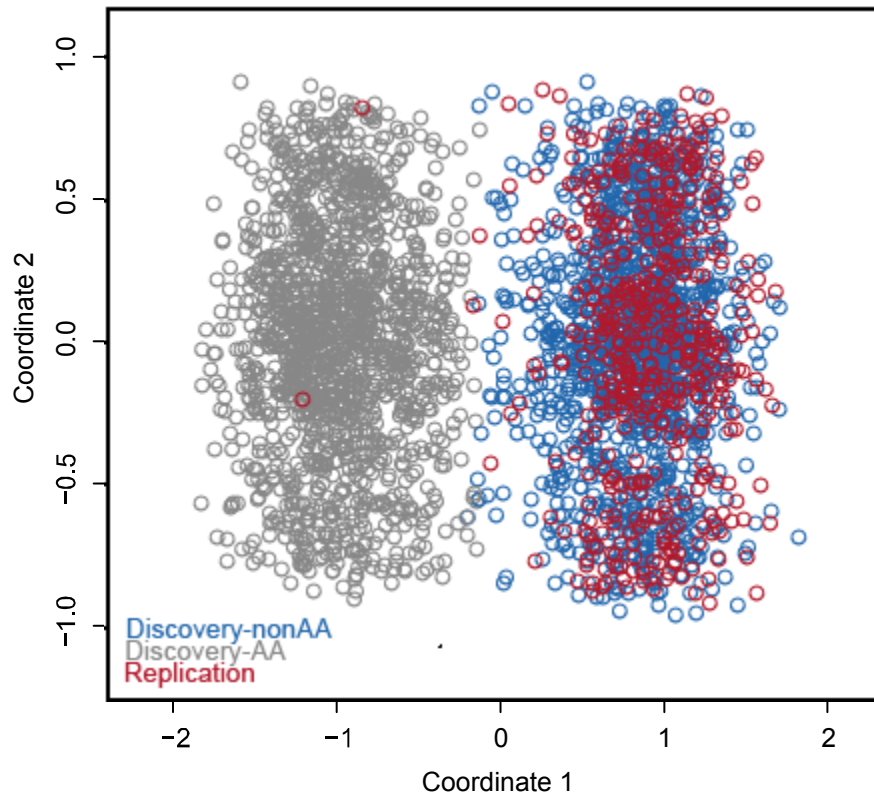
$$DNAm_{AA} \sim \beta_0 + \beta_1(\text{Diagnosis}) + \beta_2(\text{sex}) + \beta_3(\text{age}) + \beta_4(\text{current smoking}) + \beta_5(\text{CD8T}) + \beta_6(\text{CD4T}) + \beta_7(\text{NK}) + \beta_8(\text{B cell}) + \beta_9(\text{monocytes}) + \beta_{10}(\text{granulocytes}) + \beta_{11}(\text{PCI negative control probes}) + \beta_{12}(\text{PC2 negative control probes})$$

$$DNAm_{non-AA} \sim \beta_0 + \beta_1(\text{Diagnosis}) + \beta_2(\text{sex}) + \beta_3(\text{age}) + \beta_4(\text{current smoking}) + \beta_5(\text{CD8T}) + \beta_6(\text{CD4T}) + \beta_7(\text{NK}) + \beta_8(\text{B cell}) + \beta_9(\text{monocytes}) + \beta_{10}(\text{granulocytes}) + \beta_{11}(\text{PCI negative control probes}) + \beta_{12}(\text{PC2 negative control probes})$$

$$\begin{aligned}
 DNAm_{[males]} \sim & \beta_0 + \beta_1(\text{Diagnosis}) + \beta_2(\text{age}) + \beta_3(\text{current} \\
 & \text{smoking}) + \beta_4(\text{race}) + \beta_5(\text{CD8T}) + \beta_6(\text{CD4T}) + \beta_7(\text{NK}) + \beta_8(\text{B cell}) + \beta_9(\text{monocytes}) + \beta_{10}(\text{granulocytes}) + \beta_{11}(\text{PC1} \\
 & \text{negative control probes}) + \beta_{12}(\text{PC2 negative control probes})
 \end{aligned}$$

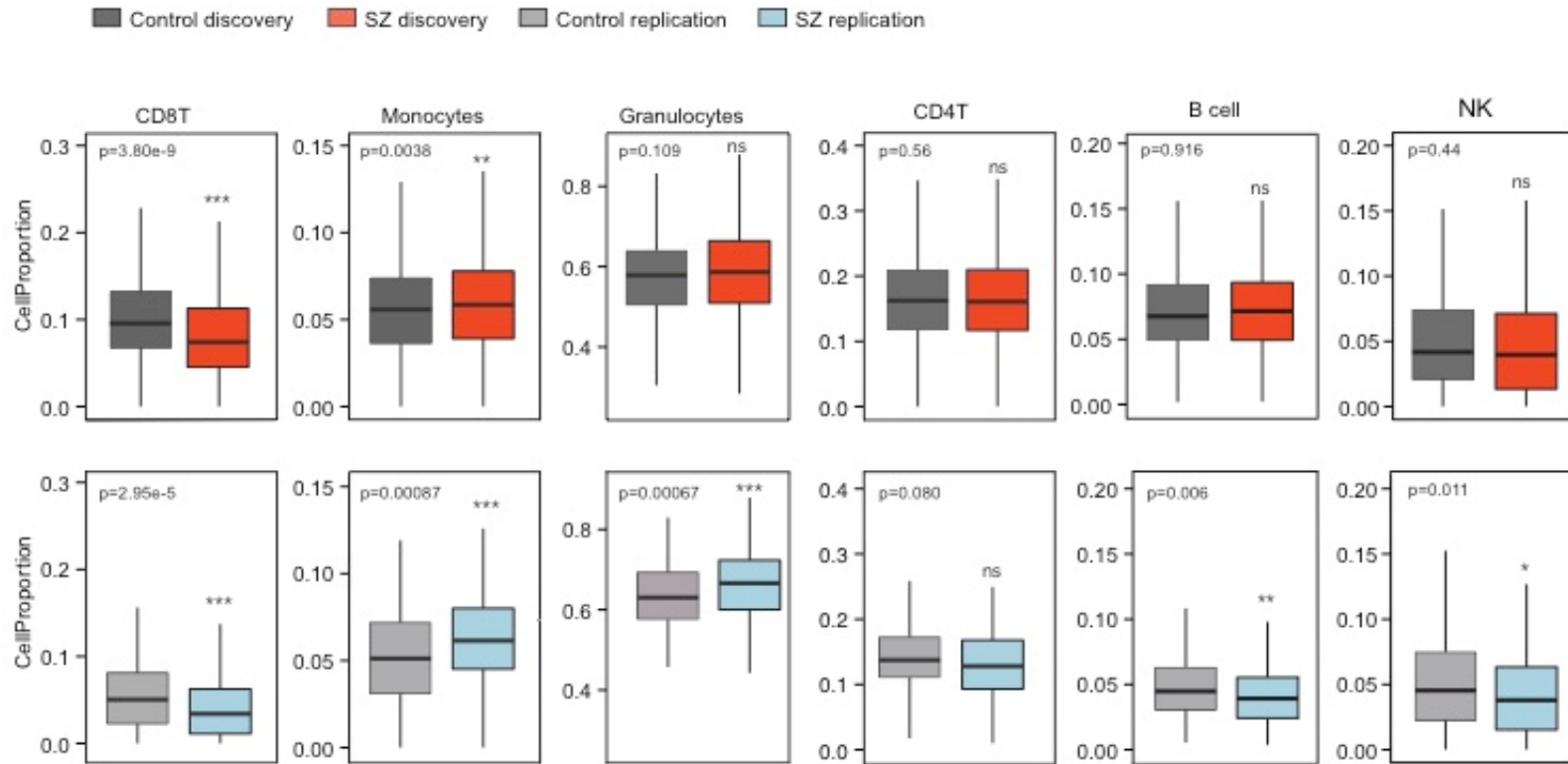
SUPPLEMENTARY FIGURES AND TABLES

eFigure 1



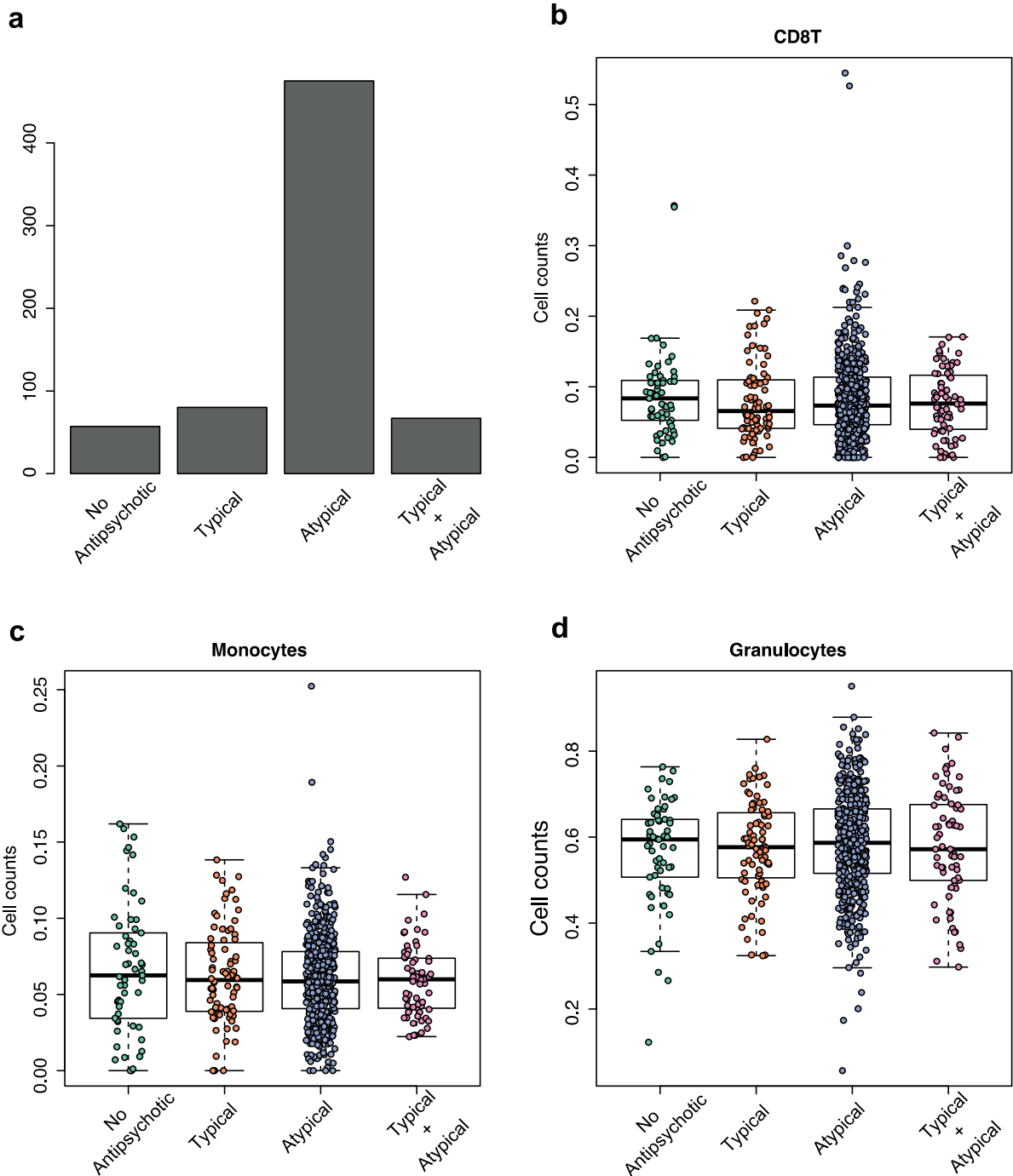
eFigure 1. Self-identified race check using 65 Infinium450K SNPs. MDS plot of beta scale methylation ratios from selected SNPs discriminates African American and non-African American samples. Discovery set African American samples in grey color, Discovery non-African American samples in blue, and replication samples in red. All but 2 replication samples clustered with the non-African American samples.

eFigure 2



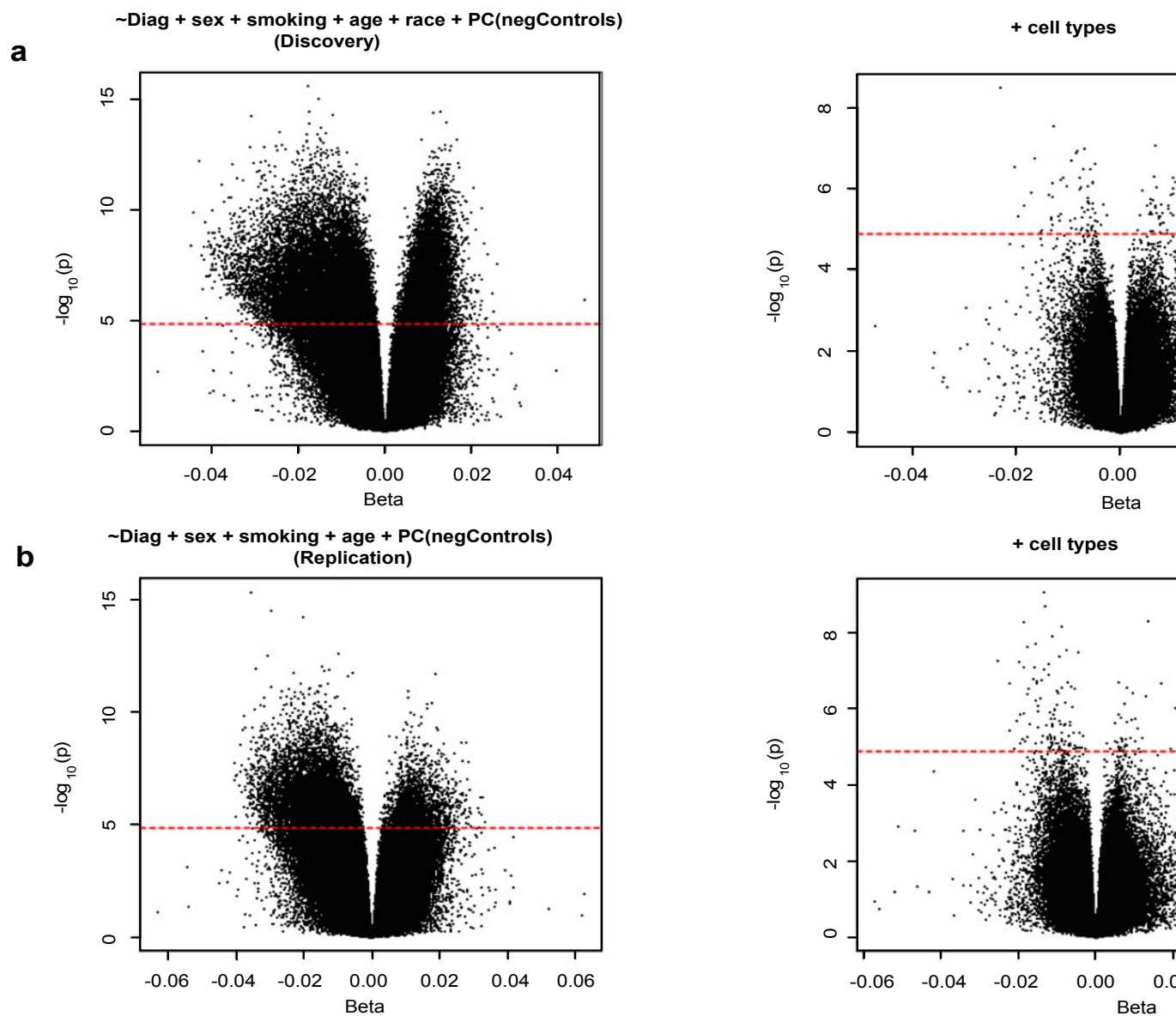
eFigure 2. Estimated cell proportion differences in SZ cases vs. controls. Calculated cell proportions in the discovery set (top panel) and replication set (bottom panel) for six cell types (CD8+ and CD4+ T cells, monocytes, granulocytes, B cells, and natural killer (NK) cells).

eFigure 3



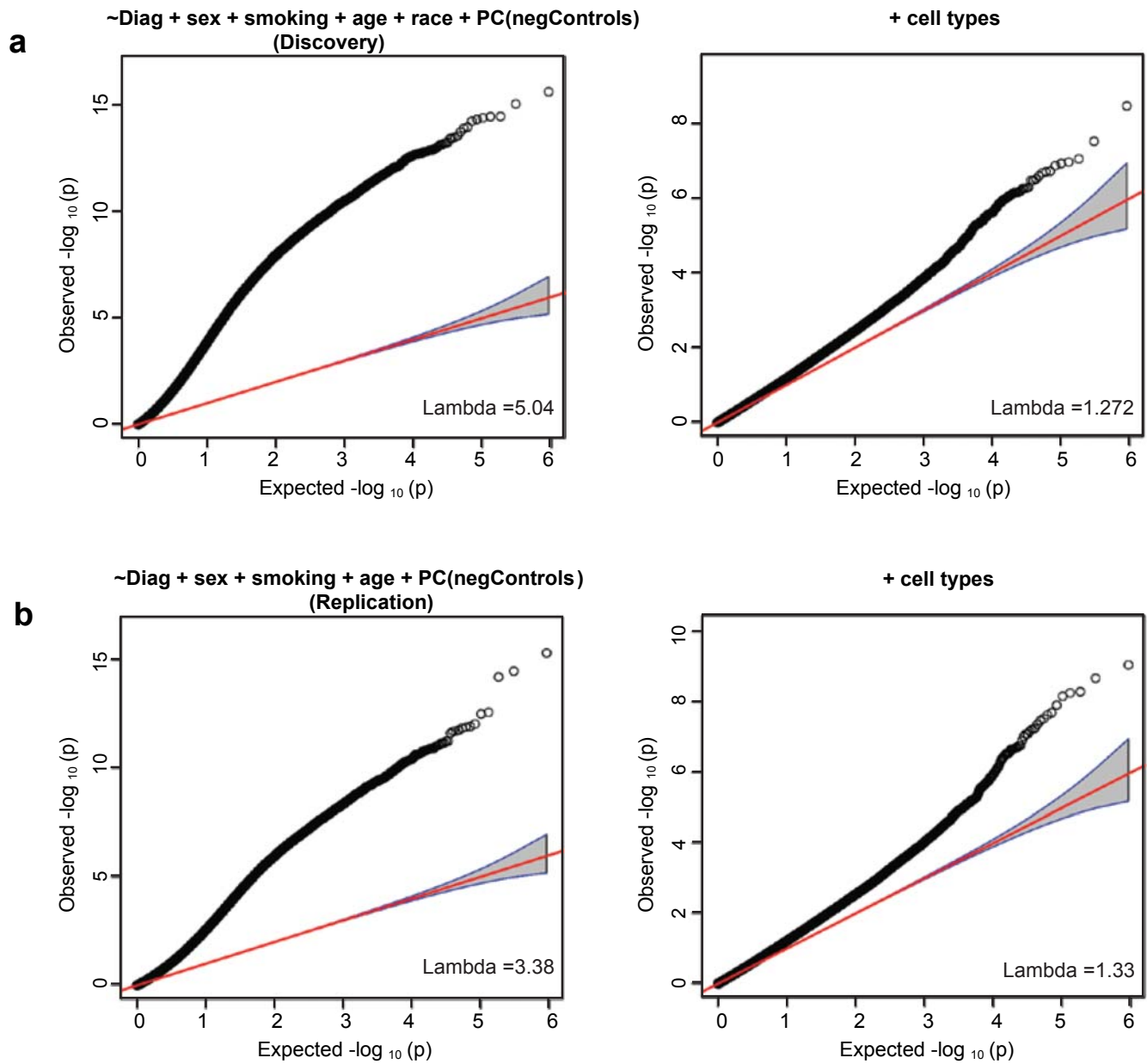
eFigure 3. Association of estimated cell proportions and pharmacological treatment in SZ cases. (a) Distribution of SZ probands by treatment categories (No antipsychotic, typical antipsychotic, atypical antipsychotics, and combination of both typical and atypical). 70% of the probands were treated with atypical antipsychotics. Estimated (b) CD8+T counts (p-value = 0.623), (c) monocytes (p-value= 0.579), and (d) and granulocytes (p-value= 0.535) in each category.

eFigure 4

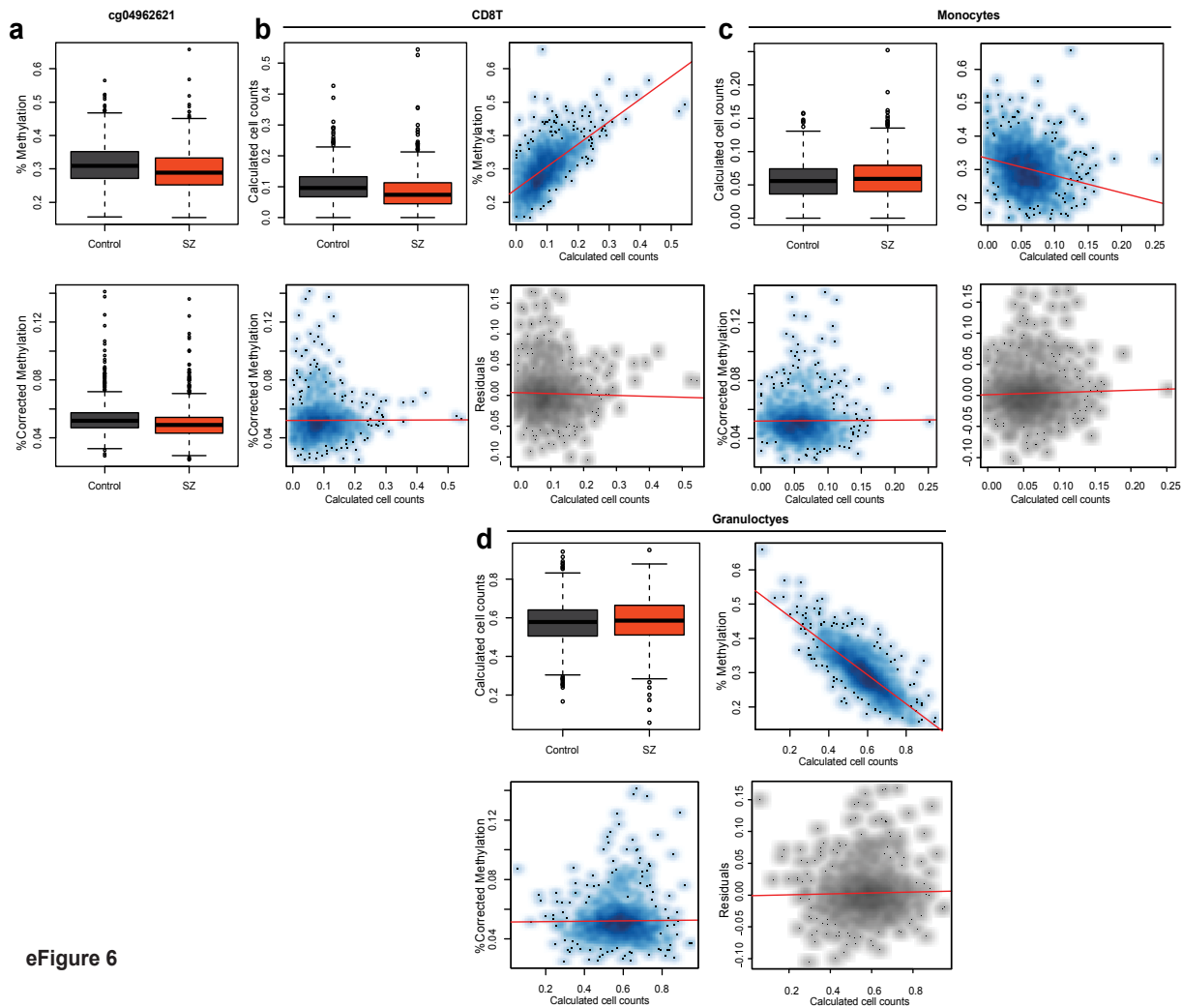


eFigure 4. Volcano plots of DMPs with and without adjusting for cell type. (a) Plots of $-\log_{10}$ (p-value) against beta scale methylation ratios of the methylation difference between SZ cases and controls in the discovery set, without (left) or with (right) cell type adjustment. Both models adjust for sex, smoking, age, race, and batch. (b) Same analysis as in (a), but in the replication set. The dashed line represents the approximate p-value for an FDR = 0.20, the cutoff used in this study.

eFigure 5

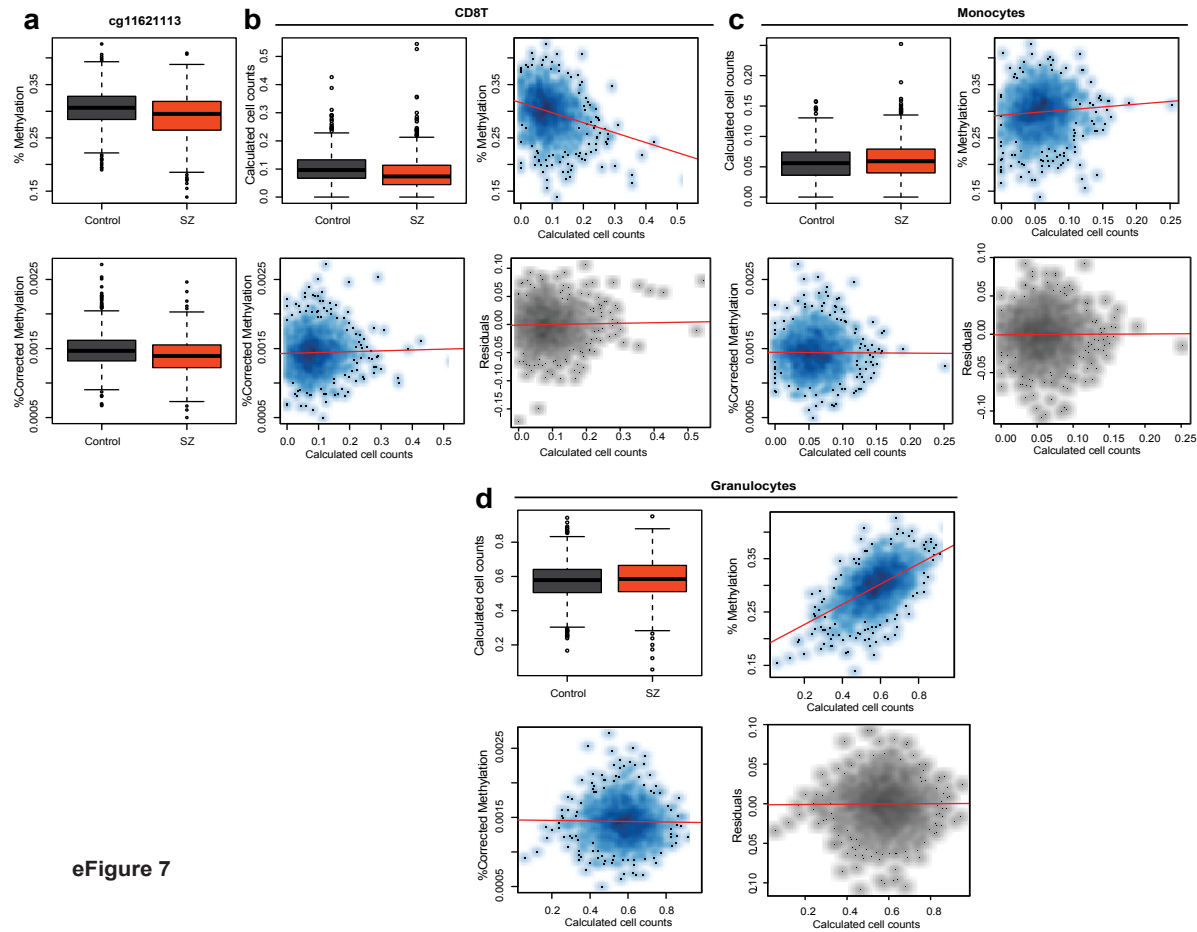


eFigure 5. QQ plots of p-values with and without adjusting for cell type. Expected vs. observed P-value distributions from the case-control analysis, for the discovery **(a)** and replication **(b)** sets. Blue lines represent the 95% confidence intervals for the null distribution. Lambda represents the genomic inflation factor.



eFigure 6

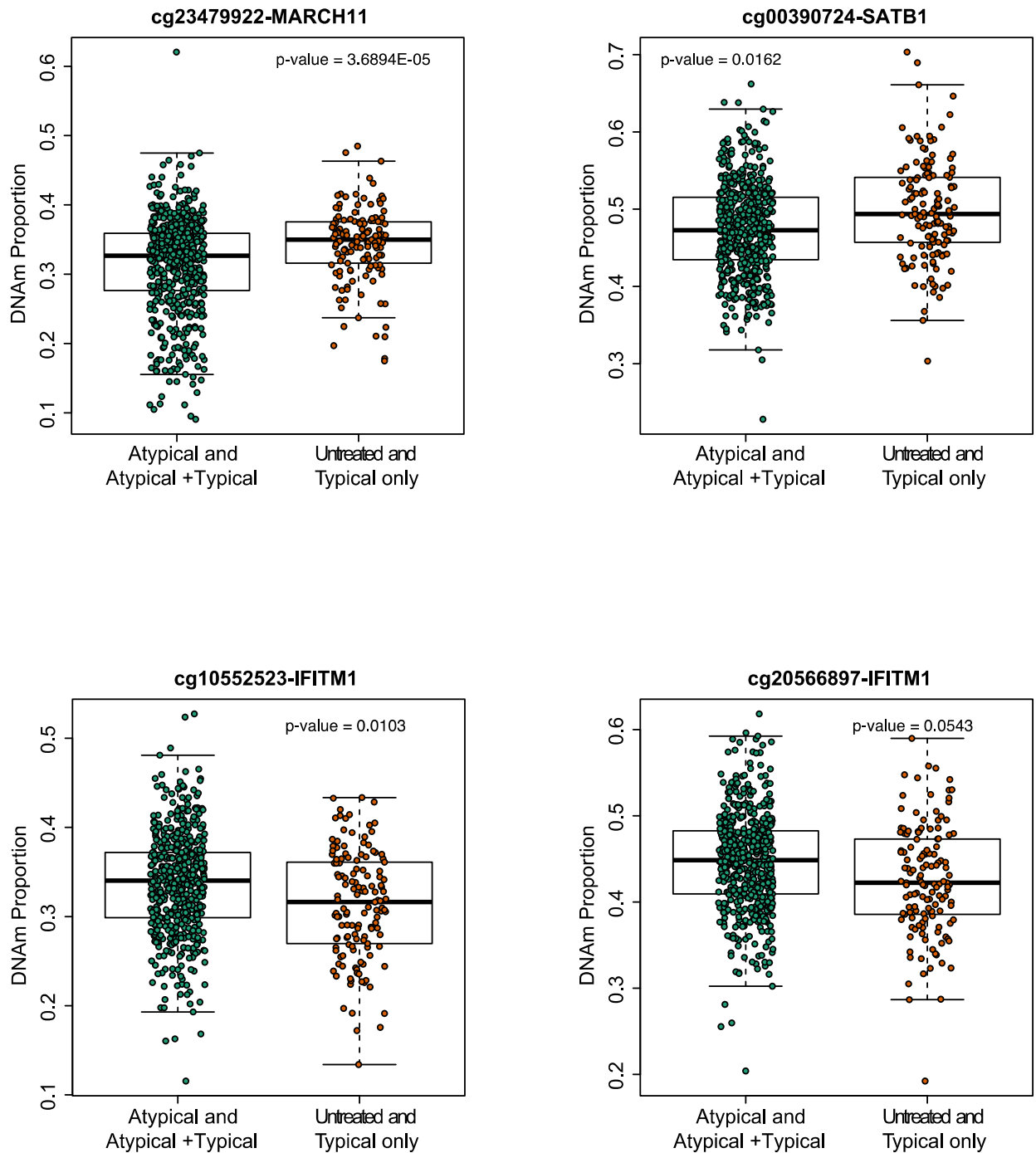
eFigure 6. Testing for residual confounding after regression using loci where CD8+T cell counts and methylation change are positively correlated. (a) Top panel shows unadjusted methylation change for locus cg04962621, bottom panel shows methylation after adjusting for covariates. (b) Top left, calculated CD8+T cell counts by diagnosis; top right: correlation of calculated CD8+T cell counts and unadjusted methylation; bottom left: correlation of calculated CD8+T cell counts and adjusted methylation; bottom right: correlation of calculated CD8+T cell counts and residuals from linear regression. (c) and (d) show the same analysis for monocytes and granulocytes, respectively.



eFigure 7

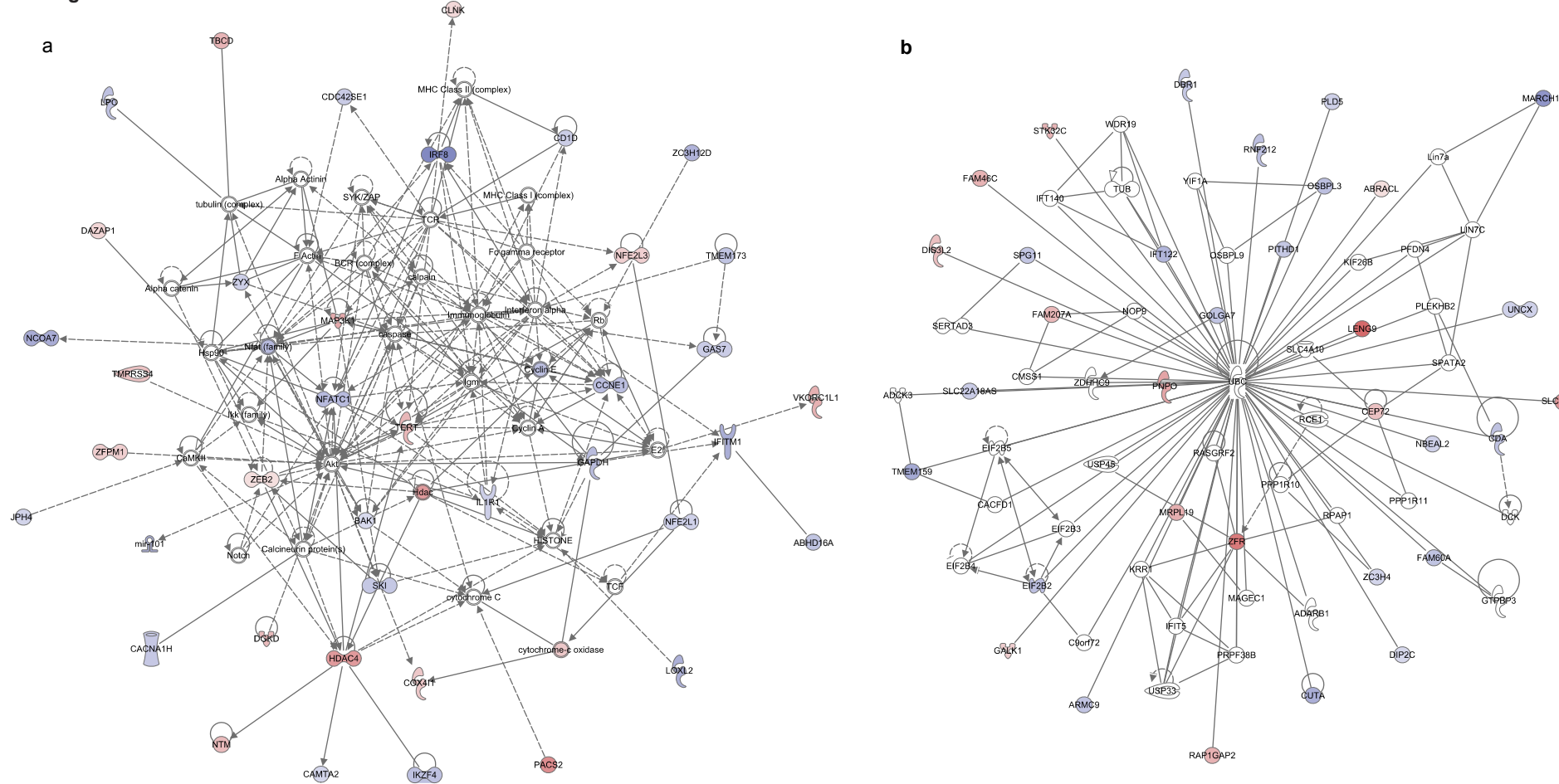
eFigure 7. Testing for residual confounding after regression using loci where CD8T cell counts and methylation change are negatively correlated. (a) Top panel shows unadjusted methylation change for locus cg11621113, bottom panel shows methylation after adjusting for covariates. (b) Top left, calculated CD8+T cell counts by diagnosis; top right: correlation of calculated CD8+T cell counts and unadjusted methylation; bottom left: correlation of calculated CD8+T cell counts and adjusted methylation; bottom right: correlation of calculated CD8+T cell counts and residuals from linear regression. (c) and (d) show the same analysis for monocytes and granulocytes, as in eFigure 6.

eFigure 8



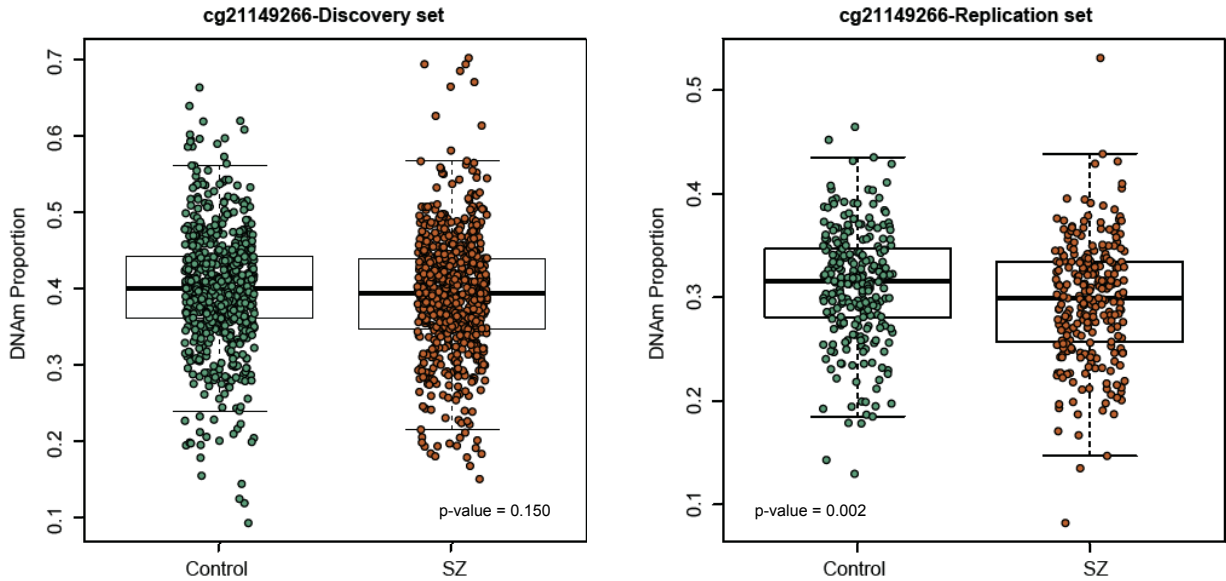
eFigure 8. Post-hoc testing for the effect of atypical antipsychotic medication on methylation levels. The four methylated loci affected by atypical antipsychotic treatment (p -value ≤ 0.05). They correspond to three genes: *MARCH11*, *SATB2*, and *IFITM1*.

eFigure 9



eFigure 9. IPA Network analysis of genes identified in our genome-wide study. Top two regulatory networks included (a) Amino Acid Metabolism, Energy Production, Post-Translational Modification, and (b) Hereditary Disorder, Neurological Disease, Psychological Disorders.

eFigure 10



eFigure 10. Methylation levels at closest locus to Aberg *et al.* MWAS top result *FAM63B*. Methylation levels in the discovery set for cg21149266 in position chr15: 59146882, 126 bp away from the closest validated position at chr15: 59146756. Left, values for discovery set. Right, values for replication set.

| eTable 1. Characteristics of the discovery and replication populations (blood tissue samples) | | | |
|--|-------------------------|--------------|--------------|
| Variable | Controls | Cases | Total |
| Discovery | | | |
| No. Participants | 645 | 689 | 1334 |
| Sex, n (%) | | | |
| Male | 273 (42.3%) | 477 (69.2%) | |
| Female | 372 (57.7%) | 212 (30.8%) | |
| Race/Ethnicity, n (%) | | | |
| non-African American | 419 (65%) | 258 (37.4%) | |
| African American | 226 (35%) | 431 (62.6%) | |
| Study, n (%) | | | |
| Study-Cogs | 412 (63.9%) | 238 (34.5%) | |
| Study-MGI | 84 (13%) | 28 (4.1%) | |
| Study-Paartners | 149 (23.1%) | 423 (61.4%) | |
| Age | 39.53 | 37.65 | |
| Smoking | | | |
| Current Smoker | 97 (15%) | 402 (58.3%) | |
| Psychiatric treatment, n (%) | | | |
| No antipsychotic | 633 ^a (100%) | 57 (8.4%) | |
| Typical antipsychotic | 0 | 80 (11.8%) | |
| Atypical antipsychotic | 0 | 475 (70.0%) | |
| Both typical and atypical antipsychotic | 0 | 67 (9.9%) | |
| Replication | | | |
| No. Participants | 250 | 247 | 497 |
| Sex, n (%) | | | |
| Male | 190 (76%) | 188 (76.1%) | |
| Female | 60 (24%) | 59 (23.9%) | |
| Race/Ethnicity, n (%) | | | |
| non-African American | 250 (100%) | 247 (100%) | |
| Age | 35.1 | 34.96 | |
| Smoker | 125 (50%) | 123 (49.8%) | |

| eTable 2. Summary of discovery and replication results | | | | | | | | | | | |
|--|-----|------------------------|--|-------------|--------|-------|---|-------------|--------|-------|-------------------------|
| Discovery Study | | | Replication Study | | | | | | | | |
| FD R | All | Minus 294 Smoking CpGs | No. CpGs with Δ methylation in same direction | | | | No. CpGs with Δ methylation in different direction | | | | % Replication |
| | | | P<0.05 | P 0.05-0.10 | P>0.10 | Total | P<0.05 | P 0.05-0.10 | P>0.10 | Total | Quadrant Correspondence |
| 0.05 | 120 | 113 | 36 | 8 | 46 | 90 | 1 | 1 | 21 | 23 | 79.65 |
| 0.1 | 248 | 234 | 68 | 17 | 94 | 179 | 3 | 3 | 49 | 55 | 76.50 |
| 0.15 | 547 | 527 | 125 | 29 | 223 | 377 | 9 | 5 | 136 | 150 | 71.54 |
| 0.2 | 945 | 923 | 172 | 48 | 405 | 625 | 16 | 17 | 265 | 298 | 67.71 |

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| eTable 3. SZ-associated DMPs (all samples) | | | | | | | | |
|---|------------------------------------|-------|-----------|------------------------|----------|-------|-------------------------|----------|
| Probe | Illumina annotation (nearest gene) | chr | position | Discovery set (N=1334) | | | Replication set (N=497) | |
| | | | | Δ Beta | P Value | FDR | Δ Beta | P Value |
| cg04792777 | KIAA0125 | chr14 | 106322429 | -0.007 | 1.06E-07 | 0.010 | -0.008 | 2.13E-04 |
| cg13092108 | RPS6KA1 | chr1 | 26857284 | -0.008 | 1.16E-07 | 0.010 | -0.009 | 4.38E-05 |
| cg04962621 | MGRN1 | chr16 | 4714733 | -0.009 | 1.32E-07 | 0.010 | -0.007 | 6.95E-05 |
| cg13997435 | S100A2 | chr1 | 153538406 | -0.007 | 3.26E-07 | 0.011 | -0.005 | 2.77E-02 |
| cg26385126 | NCOR2 | chr12 | 124912021 | 0.006 | 4.99E-07 | 0.014 | 0.010 | 3.91E-07 |
| cg07458272 | KIAA0355 | chr19 | 34744396 | 0.010 | 5.39E-07 | 0.014 | 0.007 | 2.10E-02 |
| cg13549638 | RPTOR | chr17 | 78860076 | 0.013 | 6.70E-07 | 0.014 | 0.008 | 3.72E-02 |
| cg10975863 | RAD51B | chr14 | 68830704 | 0.011 | 6.90E-07 | 0.014 | 0.010 | 1.62E-02 |
| cg22891595 | RP11-699L21.1 | chr3 | 193570256 | 0.011 | 6.94E-07 | 0.014 | 0.006 | 4.98E-02 |
| cg06996599 | C6orf136 | chr6 | 30619232 | 0.007 | 9.39E-07 | 0.015 | 0.006 | 3.28E-03 |
| cg23387863 | PEAK1 | chr15 | 77472416 | 0.010 | 1.02E-06 | 0.015 | 0.011 | 6.62E-04 |
| cg25323444 | MAD1L1 | chr7 | 2111060 | 0.011 | 1.07E-06 | 0.016 | 0.011 | 2.32E-04 |
| cg11621113 | MAN2B1 | chr19 | 12776725 | -0.008 | 1.09E-06 | 0.016 | -0.013 | 8.72E-10 |
| cg23009327 | TCF3 | chr19 | 1630248 | 0.010 | 1.32E-06 | 0.017 | 0.007 | 7.92E-03 |
| cg12939085 | PPP1CA | chr11 | 67166104 | 0.008 | 2.45E-06 | 0.023 | 0.006 | 4.65E-03 |
| cg06721411 | AUP1 | chr2 | 74753759 | 0.009 | 2.67E-06 | 0.023 | 0.006 | 3.72E-02 |
| cg12619262 | CHST12 | chr7 | 2480493 | 0.016 | 2.85E-06 | 0.024 | 0.012 | 7.44E-03 |
| cg03038262 | IFITM1 | chr11 | 315262 | -0.007 | 3.02E-06 | 0.024 | -0.006 | 2.27E-02 |
| cg19769147 | PACS2 | chr14 | 105860954 | 0.009 | 3.08E-06 | 0.024 | 0.007 | 2.27E-02 |
| cg16038738 | FAM102B | chr1 | 109103731 | -0.006 | 3.27E-06 | 0.025 | -0.005 | 1.23E-03 |
| cg14827056 | AGO2 | chr8 | 141550539 | 0.006 | 3.78E-06 | 0.028 | 0.004 | 4.65E-02 |
| cg25792439 | CARD14 | chr17 | 78163268 | 0.007 | 4.89E-06 | 0.029 | 0.006 | 2.28E-02 |
| cg11186858 | SEC14L1 | chr17 | 75096382 | 0.011 | 4.93E-06 | 0.029 | 0.014 | 1.38E-04 |
| cg13390284 | MIR101-1 | chr1 | 65531864 | -0.007 | 5.11E-06 | 0.029 | -0.004 | 2.76E-02 |
| cg00417304 | PRDM11 | chr11 | 45124456 | -0.009 | 5.39E-06 | 0.030 | -0.013 | 2.95E-05 |
| cg04535902 | GFI1 | chr1 | 92947332 | -0.013 | 5.73E-06 | 0.031 | -0.011 | 1.90E-02 |
| cg27457201 | RPTOR | chr17 | 78854232 | 0.008 | 7.92E-06 | 0.038 | 0.009 | 8.35E-03 |
| cg04232128 | TMEM173 | chr5 | 138861241 | -0.005 | 8.39E-06 | 0.040 | -0.003 | 2.49E-02 |
| cg20359445 | IKZF4 | chr12 | 56415591 | -0.006 | 9.06E-06 | 0.042 | -0.004 | 1.69E-03 |
| cg24489015 | LPO | chr17 | 56316162 | -0.006 | 9.34E-06 | 0.043 | -0.006 | 1.04E-04 |
| cg11977605 | RNF212 | chr4 | 1076247 | -0.006 | 1.04E-05 | 0.045 | -0.005 | 7.14E-04 |
| cg00994936 | DAZAP1 | chr19 | 1423902 | 0.003 | 1.08E-05 | 0.045 | 0.004 | 2.61E-02 |
| cg14114377 | MARK4 | chr19 | 45756845 | -0.008 | 1.07E-05 | 0.045 | -0.008 | 1.31E-03 |
| cg13451416 | AGAP1 | chr2 | 236671149 | -0.005 | 1.15E-05 | 0.046 | -0.005 | 7.72E-03 |
| cg03497652 | ANKS3 | chr16 | 4751569 | 0.009 | 1.26E-05 | 0.049 | 0.012 | 7.00E-05 |
| cg24517501 | GFI1 | chr1 | 92952702 | -0.008 | 1.30E-05 | 0.050 | -0.008 | 4.99E-04 |
| cg07333545 | MCM3 | chr6 | 52170606 | -0.011 | 1.44E-05 | 0.052 | -0.009 | 1.12E-02 |
| cg11597902 | SEC14L1 | chr17 | 75096239 | 0.010 | 1.49E-05 | 0.054 | 0.011 | 4.65E-04 |
| cg27093918 | MIR1538 | chr16 | 69564625 | -0.012 | 1.71E-05 | 0.059 | -0.015 | 7.17E-05 |

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| | | | | | | | | |
|------------|---------|-------|-----------|--------|----------|-------|--------|----------|
| cg23542902 | HES1 | chr3 | 193807749 | -0.005 | 1.73E-05 | 0.059 | -0.004 | 1.47E-02 |
| cg08940169 | ZFPM1 | chr16 | 88540241 | 0.004 | 1.89E-05 | 0.063 | 0.006 | 2.87E-05 |
| cg26581729 | NPDC1 | chr9 | 139939792 | -0.010 | 1.95E-05 | 0.063 | -0.016 | 1.72E-07 |
| cg08869118 | MLXIP | chr12 | 122617908 | 0.004 | 1.99E-05 | 0.064 | 0.003 | 2.36E-02 |
| cg09308580 | ZFP36L2 | chr2 | 43405947 | -0.006 | 2.31E-05 | 0.066 | -0.004 | 8.91E-03 |
| cg27431877 | NCOR2 | chr12 | 124911924 | 0.005 | 2.29E-05 | 0.066 | 0.008 | 1.64E-04 |
| cg10397932 | SKI | chr1 | 2166155 | -0.005 | 2.33E-05 | 0.066 | -0.003 | 2.37E-02 |
| cg21581415 | SCAP | chr3 | 47460784 | 0.006 | 2.38E-05 | 0.067 | 0.005 | 1.94E-02 |
| cg22887491 | NTM | chr11 | 131618277 | 0.005 | 2.43E-05 | 0.067 | 0.002 | 3.22E-02 |
| cg05036937 | ITGA2 | chr5 | 52283760 | -0.006 | 2.50E-05 | 0.068 | -0.005 | 6.13E-03 |
| cg03078690 | VPS52 | chr6 | 33235504 | 0.006 | 2.97E-05 | 0.074 | 0.006 | 5.65E-03 |
| cg17901584 | DHCR24 | chr1 | 55353706 | -0.010 | 3.14E-05 | 0.076 | -0.011 | 6.95E-03 |
| cg01115923 | KIFC3 | chr16 | 57793728 | -0.005 | 3.16E-05 | 0.076 | -0.003 | 4.81E-02 |
| cg01765406 | HS6ST1 | chr2 | 129231478 | -0.007 | 3.35E-05 | 0.077 | -0.006 | 1.46E-02 |
| cg16111190 | DDR1 | chr6 | 30860887 | 0.011 | 3.78E-05 | 0.084 | 0.009 | 1.27E-02 |
| cg01676795 | POR | chr7 | 75586348 | 0.011 | 4.03E-05 | 0.086 | 0.010 | 2.46E-02 |
| cg26253134 | TGFA | chr2 | 70751721 | -0.006 | 4.15E-05 | 0.088 | -0.005 | 9.43E-04 |
| cg04359840 | XYLT1 | chr16 | 17563300 | -0.011 | 4.14E-05 | 0.088 | -0.017 | 2.28E-05 |
| cg00066663 | CHD3 | chr17 | 7792674 | -0.004 | 4.38E-05 | 0.091 | -0.003 | 5.23E-03 |
| cg20384132 | RANBP3L | chr5 | 36302349 | 0.009 | 4.39E-05 | 0.091 | 0.007 | 2.03E-02 |
| cg06315217 | GMDS | chr6 | 1629850 | 0.006 | 4.51E-05 | 0.093 | 0.006 | 4.58E-03 |
| cg03762242 | GAS7 | chr17 | 9940004 | -0.005 | 4.76E-05 | 0.096 | -0.003 | 2.69E-02 |
| cg27115863 | CARD10 | chr22 | 37921640 | -0.010 | 4.77E-05 | 0.096 | -0.011 | 1.30E-03 |
| cg02117086 | B3GNT7 | chr2 | 232265670 | 0.010 | 4.90E-05 | 0.097 | 0.006 | 4.79E-02 |
| cg19148201 | DDR1 | chr6 | 30860237 | 0.011 | 5.09E-05 | 0.098 | 0.009 | 4.53E-02 |
| cg04462774 | AQP6 | chr12 | 50368110 | 0.005 | 5.22E-05 | 0.098 | 0.005 | 3.32E-02 |
| cg00812833 | PLD5 | chr1 | 242687412 | -0.004 | 5.20E-05 | 0.098 | -0.003 | 3.34E-02 |
| cg25722983 | STK40 | chr1 | 36840028 | -0.007 | 5.27E-05 | 0.098 | -0.012 | 4.95E-06 |
| cg14741228 | FAM60A | chr12 | 31476479 | -0.005 | 5.36E-05 | 0.099 | -0.005 | 1.33E-03 |
| cg10236687 | EMP2 | chr16 | 10626884 | -0.011 | 5.65E-05 | 0.102 | -0.009 | 1.94E-02 |
| cg10839385 | VSIG8 | chr1 | 159825049 | 0.006 | 5.68E-05 | 0.102 | 0.004 | 8.76E-03 |
| cg23479922 | MARCH11 | chr5 | 16179633 | -0.010 | 5.85E-05 | 0.103 | -0.009 | 1.43E-02 |
| cg11356547 | ZFR | chr5 | 32355062 | 0.010 | 5.96E-05 | 0.103 | 0.007 | 2.89E-02 |
| cg04189320 | KLF13 | chr15 | 31691214 | -0.005 | 5.98E-05 | 0.103 | -0.005 | 1.72E-02 |
| cg20143111 | CLNK | chr4 | 10673188 | 0.003 | 5.98E-05 | 0.103 | 0.002 | 4.81E-02 |
| cg16660971 | RPTOR | chr17 | 78860029 | 0.011 | 5.97E-05 | 0.103 | 0.017 | 1.03E-04 |
| cg19235307 | IFT122 | chr3 | 129160154 | -0.007 | 6.25E-05 | 0.104 | -0.006 | 4.67E-03 |
| cg15246238 | FSCN1 | chr7 | 5635134 | -0.010 | 6.41E-05 | 0.105 | -0.019 | 1.32E-06 |
| cg07791897 | MAP3K1 | chr5 | 55897584 | 0.007 | 6.39E-05 | 0.105 | 0.006 | 1.03E-02 |
| cg13442969 | DYRK2 | chr12 | 68044208 | -0.007 | 6.52E-05 | 0.105 | -0.006 | 1.18E-02 |
| cg09277709 | FBXO46 | chr19 | 46224285 | 0.007 | 6.52E-05 | 0.105 | 0.009 | 1.87E-03 |
| cg07552087 | MLST8 | chr16 | 2258457 | 0.005 | 6.62E-05 | 0.105 | 0.005 | 9.28E-03 |
| cg11311053 | NCOR2 | chr12 | 124912049 | 0.006 | 6.70E-05 | 0.105 | 0.013 | 5.07E-09 |
| cg10626063 | SPRED3 | chr19 | 38881032 | 0.011 | 6.87E-05 | 0.106 | 0.023 | 1.86E-06 |

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| | | | | | | | | |
|------------|---------------|-------|-----------|--------|----------|-------|--------|----------|
| cg20930290 | RPS6KA4 | chr11 | 64138764 | 0.007 | 7.30E-05 | 0.108 | 0.004 | 3.42E-02 |
| cg20610950 | SEC14L1 | chr17 | 75096202 | 0.012 | 7.93E-05 | 0.112 | 0.021 | 9.21E-05 |
| cg05919456 | PXDC1 | chr6 | 3722818 | -0.009 | 8.02E-05 | 0.113 | -0.008 | 2.65E-02 |
| cg10836392 | SULT4A1 | chr22 | 44258132 | -0.008 | 8.86E-05 | 0.118 | -0.007 | 2.85E-02 |
| cg16815625 | TRAPPC9 | chr8 | 141229477 | 0.011 | 9.19E-05 | 0.119 | 0.009 | 3.89E-02 |
| cg13871900 | SLC38A10 | chr17 | 79235968 | 0.008 | 9.14E-05 | 0.119 | 0.008 | 1.03E-02 |
| cg23565821 | CUTA | chr6 | 33385056 | -0.007 | 9.36E-05 | 0.119 | -0.016 | 8.09E-08 |
| cg07781445 | RAP1GAP2 | chr17 | 2886250 | 0.006 | 9.35E-05 | 0.119 | 0.007 | 6.06E-03 |
| cg04172533 | NOD2 | chr16 | 50743027 | -0.005 | 9.43E-05 | 0.119 | -0.004 | 3.26E-02 |
| cg00159243 | SELPLG | chr12 | 109023799 | -0.007 | 9.61E-05 | 0.119 | -0.011 | 1.10E-06 |
| cg04777348 | GFI1 | chr1 | 92952897 | -0.007 | 9.77E-05 | 0.120 | -0.012 | 3.10E-05 |
| cg02027561 | NCOA7 | chr6 | 126110790 | -0.008 | 1.01E-04 | 0.121 | -0.006 | 4.69E-02 |
| cg17879299 | DDR1 | chr6 | 30860300 | 0.015 | 9.97E-05 | 0.120 | 0.019 | 1.91E-03 |
| cg06636316 | CCNE1 | chr19 | 30303495 | -0.006 | 1.07E-04 | 0.123 | -0.006 | 9.50E-04 |
| cg05006142 | RP5-1086L22.1 | chr6 | 170536124 | 0.011 | 1.08E-04 | 0.124 | 0.015 | 1.69E-04 |
| cg00695799 | ZC3H12D | chr6 | 149803087 | -0.007 | 1.09E-04 | 0.125 | -0.007 | 4.55E-05 |
| cg03897436 | UNKL | chr16 | 1425469 | 0.004 | 1.20E-04 | 0.131 | 0.004 | 2.59E-02 |
| cg00390724 | SATB1 | chr3 | 18484742 | -0.013 | 1.22E-04 | 0.132 | -0.010 | 4.03E-02 |
| cg10552523 | IFITM1 | chr11 | 313478 | -0.010 | 1.24E-04 | 0.132 | -0.009 | 1.43E-02 |
| cg06902929 | PPT2 | chr6 | 32123258 | -0.004 | 1.27E-04 | 0.134 | -0.005 | 9.64E-03 |
| cg07558761 | SLC7A5 | chr16 | 87866696 | 0.007 | 1.32E-04 | 0.135 | 0.008 | 1.48E-02 |
| cg26687842 | FOXO1 | chr13 | 41055491 | 0.007 | 1.36E-04 | 0.136 | 0.011 | 7.66E-05 |
| cg18431951 | PUF60 | chr8 | 144906507 | 0.008 | 1.39E-04 | 0.136 | 0.007 | 3.72E-02 |
| cg10134910 | RNF212 | chr4 | 1076041 | -0.006 | 1.42E-04 | 0.139 | -0.009 | 1.63E-03 |
| cg00834988 | AUTS2 | chr7 | 70060153 | 0.008 | 1.42E-04 | 0.139 | 0.006 | 2.22E-02 |
| cg07021906 | SLC7A5 | chr16 | 87866833 | 0.008 | 1.43E-04 | 0.139 | 0.014 | 1.76E-04 |
| cg25338134 | GXYLT2 | chr3 | 72940510 | -0.006 | 1.45E-04 | 0.139 | -0.006 | 3.99E-03 |
| cg09778958 | LRFN3 | chr19 | 36427721 | -0.006 | 1.46E-04 | 0.139 | -0.006 | 7.65E-03 |
| cg02203067 | SLC7A5 | chr16 | 87866800 | 0.006 | 1.47E-04 | 0.139 | 0.006 | 1.49E-02 |
| cg22091236 | RPTOR | chr17 | 78853966 | 0.007 | 1.52E-04 | 0.141 | 0.005 | 3.48E-02 |
| cg03620886 | FDX1L | chr19 | 10420353 | -0.003 | 1.52E-04 | 0.141 | -0.003 | 3.93E-02 |
| cg10987503 | GET4 | chr7 | 922825 | 0.006 | 1.52E-04 | 0.141 | 0.009 | 2.34E-03 |
| cg15742245 | CD177 | chr19 | 43857717 | 0.011 | 1.55E-04 | 0.142 | 0.014 | 7.99E-03 |
| cg21302812 | CDC37 | chr19 | 10506915 | 0.004 | 1.59E-04 | 0.142 | 0.005 | 1.16E-02 |
| cg06647844 | MRPL19 | chr2 | 75888565 | 0.006 | 1.59E-04 | 0.142 | 0.007 | 3.19E-02 |
| cg07328664 | DIS3L2 | chr2 | 233125062 | 0.005 | 1.62E-04 | 0.143 | 0.004 | 3.79E-02 |
| cg00933443 | DBR1 | chr3 | 137892432 | -0.005 | 1.62E-04 | 0.143 | -0.004 | 4.99E-02 |
| cg19190163 | PSMB8 | chr6 | 32810785 | -0.007 | 1.63E-04 | 0.143 | -0.007 | 7.63E-03 |
| cg02731632 | UNCX | chr7 | 1328627 | -0.004 | 1.64E-04 | 0.143 | -0.004 | 8.03E-03 |
| cg25290355 | LENG9 | chr19 | 54975087 | 0.012 | 1.71E-04 | 0.147 | 0.007 | 1.43E-02 |
| cg23606421 | ENTPD8 | chr9 | 140330621 | -0.005 | 1.73E-04 | 0.148 | -0.007 | 6.13E-03 |
| cg21220247 | KIAA0125 | chr14 | 106321936 | -0.008 | 1.77E-04 | 0.149 | -0.010 | 1.86E-03 |
| cg00916854 | VPS37B | chr12 | 123350361 | 0.005 | 1.85E-04 | 0.152 | 0.005 | 1.82E-02 |
| cg12754982 | IGF2R | chr6 | 160409942 | 0.008 | 1.86E-04 | 0.152 | 0.008 | 2.42E-02 |

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| | | | | | | | | |
|------------|------------|-------|-----------|--------|----------|-------|--------|----------|
| cg07336872 | ULBP3 | chr6 | 150393535 | -0.008 | 1.88E-04 | 0.152 | -0.007 | 2.63E-02 |
| cg21746997 | BMPR1B | chr4 | 95679381 | -0.007 | 1.96E-04 | 0.155 | -0.005 | 4.27E-02 |
| cg13171679 | GOLGA7 | chr8 | 41258634 | -0.005 | 1.98E-04 | 0.155 | -0.004 | 1.93E-02 |
| cg17636309 | EEF1D | chr8 | 144672242 | 0.007 | 2.06E-04 | 0.158 | 0.007 | 2.96E-02 |
| cg03370704 | MIR143HG | chr5 | 148785408 | -0.015 | 2.11E-04 | 0.159 | -0.013 | 4.08E-02 |
| cg14078053 | IRS1 | chr2 | 227661656 | 0.006 | 2.15E-04 | 0.160 | 0.011 | 1.20E-04 |
| cg05028773 | LOC284454 | chr19 | 13947162 | -0.004 | 2.15E-04 | 0.160 | -0.004 | 9.82E-03 |
| cg20566897 | IFITM1 | chr11 | 313527 | -0.010 | 2.18E-04 | 0.160 | -0.008 | 1.48E-02 |
| cg21019522 | SLC22A18AS | chr11 | 2920789 | -0.005 | 2.27E-04 | 0.164 | -0.005 | 1.22E-03 |
| cg24502330 | CDA | chr1 | 20914028 | -0.006 | 2.32E-04 | 0.164 | -0.005 | 1.56E-02 |
| cg16931076 | WNT5B | chr12 | 1702001 | -0.007 | 2.31E-04 | 0.164 | -0.012 | 1.23E-06 |
| cg07979747 | DDR1 | chr6 | 30860136 | 0.007 | 2.31E-04 | 0.164 | 0.007 | 4.54E-02 |
| cg25647583 | FES | chr15 | 91427184 | -0.005 | 2.33E-04 | 0.164 | -0.003 | 1.26E-02 |
| cg03940776 | SYNJ2 | chr6 | 158490013 | -0.005 | 2.40E-04 | 0.167 | -0.004 | 3.11E-02 |
| cg22964469 | SORL1 | chr11 | 121337508 | -0.005 | 2.49E-04 | 0.170 | -0.006 | 6.97E-04 |
| cg09665571 | TBCD | chr17 | 80861008 | 0.006 | 2.48E-04 | 0.170 | 0.007 | 3.89E-03 |
| cg07722722 | C1orf228 | chr1 | 45187551 | 0.009 | 2.55E-04 | 0.171 | 0.004 | 4.90E-02 |
| cg20562447 | CPT1A | chr11 | 68611596 | 0.004 | 2.53E-04 | 0.171 | 0.003 | 2.43E-02 |
| cg14986464 | ABHD16A | chr6 | 31669902 | -0.005 | 2.60E-04 | 0.172 | -0.009 | 3.85E-05 |
| cg00294109 | CRBN | chr3 | 3219781 | -0.004 | 2.60E-04 | 0.172 | -0.003 | 3.12E-02 |
| cg27241044 | BASP1P1 | chr13 | 23499838 | -0.007 | 2.64E-04 | 0.172 | -0.009 | 9.35E-03 |
| cg17368760 | THBD | chr20 | 23029287 | -0.007 | 2.68E-04 | 0.173 | -0.006 | 7.17E-03 |
| cg18532239 | CEP72 | chr5 | 619883 | 0.005 | 2.64E-04 | 0.172 | 0.004 | 2.20E-02 |
| cg25767870 | FAM46C | chr1 | 118188756 | 0.006 | 2.69E-04 | 0.173 | 0.006 | 1.56E-02 |
| cg05541096 | TTL11 | chr9 | 124854664 | -0.005 | 2.86E-04 | 0.177 | -0.010 | 3.76E-07 |
| cg16568360 | TAOK2 | chr16 | 29987261 | -0.005 | 2.86E-04 | 0.177 | -0.006 | 1.02E-03 |
| cg20054248 | IKZF4 | chr12 | 56414508 | -0.004 | 2.89E-04 | 0.177 | -0.003 | 1.60E-02 |
| cg22675767 | ACAP3 | chr1 | 1234367 | 0.005 | 2.97E-04 | 0.179 | 0.004 | 3.88E-02 |
| cg12002745 | FAM83A | chr8 | 124179875 | -0.004 | 3.10E-04 | 0.182 | -0.004 | 7.12E-03 |
| cg17126555 | ICAM3 | chr19 | 10445516 | 0.006 | 3.17E-04 | 0.183 | 0.006 | 2.21E-02 |
| cg17343451 | AP2M1 | chr3 | 183899704 | 0.006 | 3.20E-04 | 0.184 | 0.007 | 7.39E-03 |
| cg20817228 | LINC00623 | chr1 | 149614778 | 0.007 | 3.33E-04 | 0.186 | 0.008 | 1.86E-02 |
| cg26076905 | PIK3R1 | chr5 | 67522298 | 0.006 | 3.44E-04 | 0.191 | 0.005 | 1.38E-02 |
| cg09801824 | DNAJB12 | chr10 | 74076930 | -0.005 | 3.54E-04 | 0.193 | -0.004 | 2.07E-03 |
| cg03459202 | DIP2C | chr10 | 676740 | -0.003 | 3.57E-04 | 0.193 | -0.004 | 1.10E-02 |
| cg23344523 | IGF2R | chr6 | 160380572 | 0.006 | 3.60E-04 | 0.193 | 0.007 | 4.45E-03 |
| cg22996004 | PNPO | chr17 | 46018654 | 0.007 | 3.63E-04 | 0.193 | 0.006 | 6.19E-03 |
| cg15943584 | EIF2B2 | chr14 | 75472643 | -0.006 | 3.63E-04 | 0.193 | -0.006 | 8.71E-03 |
| cg06784563 | NFATC1 | chr18 | 77284509 | -0.006 | 3.67E-04 | 0.193 | -0.007 | 1.29E-03 |
| cg23622878 | PWWP2B | chr10 | 134225120 | 0.006 | 3.70E-04 | 0.193 | 0.005 | 3.33E-02 |
| cg08933467 | FCRL1 | chr1 | 157776690 | -0.004 | 3.69E-04 | 0.193 | -0.005 | 2.31E-03 |
| cg27225680 | GALK1 | chr17 | 73760817 | 0.004 | 3.92E-04 | 0.197 | 0.003 | 8.12E-04 |
| cg27300045 | ZC3H4 | chr19 | 47610813 | -0.004 | 3.93E-04 | 0.197 | -0.004 | 1.58E-03 |
| cg09868768 | ASPRV1 | chr2 | 70188605 | 0.007 | 3.98E-04 | 0.198 | 0.006 | 2.97E-02 |

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|------------|-------|------|----------|--------|----------|-------|--------|----------|
| cg20914572 | PRRT1 | chr6 | 32119874 | -0.006 | 4.04E-04 | 0.198 | -0.005 | 4.71E-03 |
|------------|-------|------|----------|--------|----------|-------|--------|----------|

eTable 4. SZ-associated DMPs (stratified analysis, males only)

| Probe | Illumina annotation (nearest gene) | chr | position | Discovery set (N=750) | | | Replication set (N=497) | |
|------------|---------------------------------------|-------|-----------|-----------------------|----------|-------|----------------------------|----------|
| | | | | Δ Beta | P Value | FDR | Δ Beta | P Value |
| cg13092108 | RPS6KA1 | chr1 | 26857284 | -0.011 | 5.64E-08 | 0.009 | -0.008 | 9.80E-04 |
| cg04792777 | KIAA0125 | chr14 | 106322429 | -0.008 | 5.52E-06 | 0.094 | -0.007 | 5.45E-03 |
| cg23565821 | CUTA | chr6 | 33385056 | -0.011 | 6.71E-06 | 0.096 | -0.013 | 1.88E-04 |
| cg14986464 | ABHD16A | chr6 | 31669902 | -0.008 | 6.84E-06 | 0.096 | -0.008 | 2.32E-03 |
| cg14326196 | KIF12 | chr9 | 116860650 | -0.023 | 8.44E-06 | 0.096 | -0.013 | 3.48E-02 |
| cg10626063 | SPRED3 | chr19 | 38881032 | 0.016 | 9.87E-06 | 0.104 | 0.027 | 4.23E-07 |
| cg04962621 | MGRN1 | chr16 | 4714733 | -0.009 | 1.27E-05 | 0.109 | -0.007 | 3.02E-04 |
| cg08933467 | FCRL1 | chr1 | 157776690 | -0.006 | 1.65E-05 | 0.126 | -0.005 | 4.32E-03 |
| cg10785394 | FAM20B | chr1 | 178993006 | -0.009 | 1.83E-05 | 0.127 | -0.007 | 8.24E-03 |
| cg05541096 | TTL1 | chr9 | 124854664 | -0.008 | 1.85E-05 | 0.127 | -0.011 | 7.00E-07 |
| cg16660971 | RPTOR | chr17 | 78860029 | 0.015 | 1.92E-05 | 0.129 | 0.016 | 1.95E-03 |
| cg11621113 | MAN2B1 | chr19 | 12776725 | -0.009 | 1.94E-05 | 0.129 | -0.012 | 1.83E-06 |
| cg10615591 | RTEL1 | chr20 | 62318433 | -0.008 | 2.51E-05 | 0.133 | -0.007 | 1.50E-02 |
| cg09778958 | LRFN3 | chr19 | 36427721 | -0.009 | 2.64E-05 | 0.133 | -0.006 | 1.60E-02 |
| cg11597902 | SEC14L1 | chr17 | 75096239 | 0.012 | 2.97E-05 | 0.137 | 0.010 | 3.41E-03 |
| cg06096184 | LRIG1 | chr3 | 66549732 | -0.009 | 4.24E-05 | 0.155 | -0.005 | 2.75E-02 |
| cg06682039 | RP5-1086L22.1 | chr6 | 170536047 | 0.014 | 4.45E-05 | 0.156 | 0.008 | 2.58E-02 |
| cg25647583 | FES | chr15 | 91427184 | -0.007 | 4.96E-05 | 0.159 | -0.004 | 8.06E-03 |
| cg16568360 | TAOK2 | chr16 | 29987261 | -0.007 | 5.66E-05 | 0.166 | -0.007 | 1.47E-03 |
| cg10836392 | SULT4A1 | chr22 | 44258132 | -0.010 | 5.74E-05 | 0.166 | -0.010 | 1.31E-02 |
| cg14239983 | SORL1 | chr11 | 121337384 | -0.008 | 8.16E-05 | 0.186 | -0.008 | 2.73E-03 |
| cg23968113 | SNTG2 | chr2 | 1234756 | -0.004 | 8.99E-05 | 0.190 | -0.003 | 4.39E-02 |
| cg05006142 | RP5-1086L22.1 | chr6 | 170536124 | 0.014 | 9.94E-05 | 0.194 | 0.018 | 1.64E-04 |

eTable 5. SZ-associated DMPs (stratified analysis, only non-African Americans)

| Probe | Illumina annotation (nearest gene) | chr | position | Discovery set (N=677) | | | Replication set (N=497) | |
|------------|------------------------------------|-------|-----------|-----------------------|-------------|-------|-------------------------|----------|
| | | | | Δ Beta | P Value | FDR | Δ Beta | P Value |
| cg15132169 | ZC3H12D | chr6 | 149805995 | -0.017 | 4.92081E-07 | 0.028 | -0.008 | 1.93E-02 |
| cg22891595 | RP11-699L21.1 | chr3 | 193570256 | 0.013 | 7.33932E-06 | 0.073 | 0.006 | 4.98E-02 |
| cg09502149 | SLC2A1 | chr1 | 43406792 | 0.011 | 1.08666E-05 | 0.087 | 0.006 | 2.23E-02 |
| cg11699125 | ACOT7 | chr1 | 6341327 | 0.006 | 0.000011777 | 0.090 | 0.004 | 6.32E-03 |
| cg13549638 | RPTOR | chr17 | 78860076 | 0.014 | 1.26229E-05 | 0.090 | 0.008 | 3.72E-02 |
| cg09249800 | ACOT7 | chr1 | 6341287 | 0.005 | 1.38433E-05 | 0.090 | 0.003 | 9.78E-03 |
| cg13136655 | ZC3H12D | chr6 | 149806131 | -0.012 | 0.000014062 | 0.090 | -0.005 | 2.12E-02 |
| cg04983687 | ZFPM1 | chr16 | 88558223 | 0.007 | 1.81063E-05 | 0.098 | 0.006 | 4.61E-04 |
| cg09802688 | TRAF3IP3 | chr1 | 209942066 | -0.011 | 1.95438E-05 | 0.099 | -0.007 | 1.55E-03 |
| cg22344793 | TRIM29 | chr11 | 120039642 | -0.008 | 2.23543E-05 | 0.104 | -0.003 | 3.92E-02 |
| cg00390724 | SATB1 | chr3 | 18484742 | -0.021 | 2.22985E-05 | 0.104 | -0.010 | 4.03E-02 |
| cg16660971 | RPTOR | chr17 | 78860029 | 0.016 | 2.32846E-05 | 0.104 | 0.017 | 1.03E-04 |
| cg18082788 | ZC3H12D | chr6 | 149806339 | -0.017 | 2.56209E-05 | 0.105 | -0.008 | 3.61E-02 |
| cg23479922 | MARCH11 | chr5 | 16179633 | -0.017 | 3.17613E-05 | 0.116 | -0.009 | 1.43E-02 |
| cg09391371 | PDCD1 | chr2 | 242790370 | -0.005 | 3.36901E-05 | 0.120 | -0.004 | 1.35E-03 |
| cg13997435 | S100A2 | chr1 | 153538406 | -0.008 | 3.90229E-05 | 0.130 | -0.005 | 2.77E-02 |
| cg14389122 | EDC3 | chr15 | 74945851 | -0.009 | 4.38037E-05 | 0.136 | -0.007 | 3.89E-03 |
| cg10836392 | SULT4A1 | chr22 | 44258132 | -0.012 | 4.44516E-05 | 0.136 | -0.007 | 2.85E-02 |
| cg00812833 | PLD5 | chr1 | 242687412 | -0.006 | 6.16995E-05 | 0.152 | -0.003 | 3.34E-02 |
| cg21019522 | SLC22A18AS | chr11 | 2920789 | -0.007 | 7.18738E-05 | 0.161 | -0.005 | 1.22E-03 |
| cg19003304 | TOX | chr8 | 60029914 | 0.006 | 7.35323E-05 | 0.161 | 0.003 | 2.22E-02 |
| cg12946371 | NDUFC2-KCTD14 | chr11 | 77757383 | 0.004 | 0.000090358 | 0.168 | 0.002 | 2.95E-02 |
| cg00682367 | RP11-290F20.1 | chr20 | 48963280 | -0.007 | 9.40389E-05 | 0.168 | -0.004 | 2.00E-03 |
| cg13046440 | UBE3A | chr15 | 25684837 | 0.008 | 9.44532E-05 | 0.168 | 0.004 | 7.85E-03 |
| cg08940169 | ZFPM1 | chr16 | 88540241 | 0.005 | 9.75324E-05 | 0.169 | 0.006 | 2.87E-05 |
| cg09308580 | ZFP36L2 | chr2 | 43405947 | -0.007 | 0.000110849 | 0.172 | -0.004 | 8.91E-03 |
| cg07458272 | KIAA0355 | chr19 | 34744396 | 0.011 | 0.000130475 | 0.184 | 0.007 | 2.10E-02 |
| cg04276536 | CCDC102A | chr16 | 57567813 | -0.006 | 0.000134158 | 0.186 | -0.005 | 9.43E-04 |
| cg22887491 | NTM | chr11 | 131618277 | 0.006 | 0.000150868 | 0.193 | 0.002 | 3.22E-02 |

eTable 6. SZ-associated DMPs (stratified analysis, only African Americans, first 100 DMPs)

| Probe | Illumina annotation (nearest gene) | chr | position | Discovery study (N=657) | | | Replication study (N=497) | |
|------------|---------------------------------------|-------|-----------|-------------------------|----------|-------|------------------------------|----------|
| | | | | Δ Beta | P Value | FDR | Δ Beta | P Value |
| cg23565821 | CUTA | chr6 | 33385056 | -0.014 | 5.30E-08 | 0.004 | -0.016 | 8.09E-08 |
| cg14114377 | MARK4 | chr19 | 45756845 | -0.013 | 1.55E-07 | 0.006 | -0.008 | 1.31E-03 |
| cg12939085 | PPP1CA | chr11 | 67166104 | 0.012 | 2.87E-07 | 0.008 | 0.006 | 4.65E-03 |
| cg07722722 | C1orf228 | chr1 | 45187551 | 0.018 | 2.96E-07 | 0.008 | 0.004 | 4.90E-02 |
| cg05419096 | LINC00443 | chr13 | 107467865 | -0.010 | 4.17E-07 | 0.009 | -0.005 | 1.73E-02 |
| cg19190163 | PSMB8 | chr6 | 32810785 | -0.014 | 4.87E-07 | 0.010 | -0.007 | 7.63E-03 |
| cg12582905 | IFITM2 | chr11 | 310771 | -0.006 | 7.88E-07 | 0.012 | -0.002 | 2.00E-02 |
| cg20170777 | COX10-AS1 | chr17 | 13972099 | -0.015 | 8.89E-07 | 0.014 | -0.009 | 1.47E-02 |
| cg07622001 | AC008697.1 | chr5 | 158758903 | -0.009 | 1.11E-06 | 0.014 | -0.005 | 5.56E-04 |
| cg19465320 | STAT5B | chr17 | 40426890 | -0.012 | 1.29E-06 | 0.015 | -0.010 | 1.29E-04 |
| cg11977605 | RNF212 | chr4 | 1076247 | -0.010 | 1.86E-06 | 0.017 | -0.005 | 7.14E-04 |
| cg03762242 | GAS7 | chr17 | 9940004 | -0.008 | 3.99E-06 | 0.025 | -0.003 | 2.69E-02 |
| cg01435039 | PTCHD3P1 | chr10 | 29700804 | -0.008 | 4.68E-06 | 0.026 | -0.006 | 7.95E-04 |
| cg19939130 | IFI16 | chr1 | 158978468 | -0.012 | 5.30E-06 | 0.028 | -0.006 | 3.23E-02 |
| cg23429047 | HS6ST1 | chr2 | 129028542 | 0.009 | 5.63E-06 | 0.028 | 0.004 | 1.48E-02 |
| cg00417304 | PRDM11 | chr11 | 45124456 | -0.014 | 5.58E-06 | 0.028 | -0.013 | 2.95E-05 |
| cg18906043 | GRAP | chr17 | 18967111 | -0.007 | 5.96E-06 | 0.028 | -0.003 | 5.15E-03 |
| cg07678266 | GLT1D1 | chr12 | 129444630 | 0.021 | 8.37E-06 | 0.034 | 0.011 | 4.42E-02 |
| cg03147185 | NCAPH | chr2 | 97008030 | -0.009 | 8.82E-06 | 0.035 | -0.007 | 8.75E-04 |
| cg25247520 | PVT1 | chr8 | 128808017 | -0.011 | 9.87E-06 | 0.037 | -0.010 | 3.04E-04 |
| cg03438552 | TAP2 | chr6 | 32805548 | -0.013 | 1.01E-05 | 0.037 | -0.006 | 4.11E-02 |
| cg00094412 | GABBR1 | chr6 | 29592854 | -0.013 | 1.04E-05 | 0.037 | -0.007 | 2.34E-02 |
| cg13092108 | RPS6KA1 | chr1 | 26857284 | -0.011 | 1.09E-05 | 0.037 | -0.009 | 4.38E-05 |
| cg09605818 | TRPV1 | chr17 | 3489147 | 0.006 | 1.10E-05 | 0.037 | 0.004 | 8.14E-03 |
| cg19235307 | IFT122 | chr3 | 129160154 | -0.013 | 1.15E-05 | 0.037 | -0.006 | 4.67E-03 |
| cg16472834 | AC098823.3 | chr2 | 231533021 | -0.014 | 1.18E-05 | 0.037 | -0.005 | 3.96E-02 |
| cg26581729 | NPDC1 | chr9 | 139939792 | -0.014 | 1.22E-05 | 0.037 | -0.016 | 1.72E-07 |
| cg11356290 | ZCWPW2 | chr3 | 28390998 | -0.002 | 1.25E-05 | 0.037 | -0.001 | 4.13E-02 |
| cg20930290 | RPS6KA4 | chr11 | 64138764 | 0.010 | 1.39E-05 | 0.039 | 0.004 | 3.42E-02 |
| cg01062024 | IMPDH2 | chr3 | 49065979 | -0.013 | 1.48E-05 | 0.039 | -0.008 | 7.77E-03 |
| cg02220008 | PHACTR1 | chr6 | 13192742 | -0.011 | 1.51E-05 | 0.039 | -0.007 | 2.21E-02 |
| cg24351076 | ITPRIPL1 | chr2 | 96992044 | -0.010 | 1.55E-05 | 0.039 | -0.005 | 2.11E-02 |
| cg20842997 | UGDH-AS1 | chr4 | 39529386 | -0.008 | 1.58E-05 | 0.039 | -0.003 | 3.28E-02 |
| cg16778018 | MGRN1 | chr16 | 4736225 | 0.011 | 1.70E-05 | 0.041 | 0.006 | 4.31E-02 |
| cg23965590 | CBL | chr11 | 119133451 | -0.010 | 1.78E-05 | 0.042 | -0.008 | 6.70E-04 |
| cg14827056 | AGO2 | chr8 | 141550539 | 0.008 | 1.81E-05 | 0.042 | 0.004 | 4.65E-02 |
| cg20384132 | RANBP3L | chr5 | 36302349 | 0.016 | 1.81E-05 | 0.042 | 0.007 | 2.03E-02 |
| cg11186858 | SEC14L1 | chr17 | 75096382 | 0.014 | 2.03E-05 | 0.045 | 0.014 | 1.38E-04 |
| cg19845878 | TACC3 | chr4 | 1742857 | 0.009 | 2.19E-05 | 0.046 | 0.008 | 1.74E-03 |

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| | | | | | | | | |
|---------------------|-----------|-------|-----------|--------|----------|-------|--------|----------|
| cg04172533 | NOD2 | chr16 | 50743027 | -0.008 | 2.36E-05 | 0.048 | -0.004 | 3.26E-02 |
| cg08880817 | TXNDC5 | chr6 | 7909642 | -0.009 | 2.50E-05 | 0.049 | -0.003 | 4.46E-02 |
| cg11356547 | ZFR | chr5 | 32355062 | 0.016 | 2.50E-05 | 0.049 | 0.007 | 2.89E-02 |
| cg02505676 | ACSF3 | chr16 | 89220516 | 0.005 | 2.55E-05 | 0.049 | 0.003 | 3.80E-03 |
| cg25628989 | SSRP1 | chr11 | 57093345 | -0.017 | 2.64E-05 | 0.049 | -0.010 | 3.73E-02 |
| cg19769147 | PACS2 | chr14 | 105860954 | 0.013 | 2.90E-05 | 0.051 | 0.007 | 2.27E-02 |
| cg05438719 | CMIP | chr16 | 81476518 | -0.008 | 2.96E-05 | 0.051 | -0.004 | 4.56E-02 |
| cg18529294 | CENPO | chr2 | 25016799 | -0.004 | 3.09E-05 | 0.052 | -0.002 | 3.52E-02 |
| cg23962746 | MIR205HG | chr1 | 209105888 | -0.010 | 3.17E-05 | 0.053 | -0.005 | 4.53E-02 |
| ch.3.638689 R | GADL1 | chr3 | 31240746 | -0.003 | 3.25E-05 | 0.054 | -0.001 | 4.28E-02 |
| cg15922057 | KSR1 | chr17 | 25784714 | -0.010 | 3.36E-05 | 0.055 | -0.004 | 1.31E-02 |
| cg14741228 | FAM60A | chr12 | 31476479 | -0.008 | 3.41E-05 | 0.055 | -0.005 | 1.33E-03 |
| cg24143729 | RASA3 | chr13 | 114820861 | 0.007 | 3.47E-05 | 0.055 | 0.007 | 1.61E-03 |
| cg26812615 | MAP1LC3B2 | chr12 | 116996773 | -0.008 | 3.67E-05 | 0.056 | -0.007 | 5.41E-03 |
| cg08932533 | CD47 | chr3 | 107812758 | 0.008 | 3.68E-05 | 0.056 | 0.004 | 3.30E-02 |
| cg11003133 | AIM2 | chr1 | 159046391 | -0.013 | 3.75E-05 | 0.056 | -0.008 | 1.33E-02 |
| cg21742048 | NEURL1B | chr5 | 172099681 | -0.010 | 3.79E-05 | 0.056 | -0.005 | 4.42E-02 |
| cg23222278 | LINC00312 | chr3 | 8623867 | -0.007 | 3.83E-05 | 0.056 | -0.004 | 1.40E-02 |
| cg19668951 | SLC39A13 | chr11 | 47430812 | -0.009 | 3.94E-05 | 0.057 | -0.010 | 7.69E-07 |
| cg09132240 | NCOR2 | chr12 | 124922727 | 0.008 | 4.58E-05 | 0.061 | 0.006 | 2.97E-03 |
| cg12619262 | CHST12 | chr7 | 2480493 | 0.021 | 4.69E-05 | 0.061 | 0.012 | 7.44E-03 |
| ch.2.113772 948R | PAX8 | chr2 | 114056478 | -0.005 | 4.88E-05 | 0.062 | -0.001 | 3.27E-02 |
| cg16111190 | DDR1 | chr6 | 30860887 | 0.016 | 5.40E-05 | 0.065 | 0.009 | 1.27E-02 |
| cg05146536 | FAM47E | chr4 | 77140678 | -0.007 | 5.46E-05 | 0.065 | -0.003 | 2.91E-02 |
| cg04962621 | MGRN1 | chr16 | 4714733 | -0.011 | 5.93E-05 | 0.066 | -0.007 | 6.95E-05 |
| cg01408817 | FXD3 | chr19 | 35606534 | -0.008 | 5.88E-05 | 0.066 | -0.005 | 1.48E-02 |
| cg15072976 | GAL3ST2 | chr2 | 242715549 | 0.011 | 6.12E-05 | 0.067 | 0.006 | 2.10E-02 |
| cg08112313 | XRCC1 | chr19 | 44079105 | -0.008 | 6.67E-05 | 0.070 | -0.005 | 2.54E-02 |
| cg16568360 | TAOK2 | chr16 | 29987261 | -0.008 | 6.66E-05 | 0.070 | -0.006 | 1.02E-03 |
| cg02772266 | PARP11 | chr12 | 4060781 | 0.008 | 6.91E-05 | 0.070 | 0.005 | 1.13E-02 |
| cg04239024 | CENPE | chr4 | 104119155 | -0.005 | 6.98E-05 | 0.070 | -0.002 | 2.18E-02 |
| cg14986464 | ABHD16A | chr6 | 31669902 | -0.009 | 6.97E-05 | 0.070 | -0.009 | 3.85E-05 |
| cg15921436 | ARL17A | chr17 | 44337874 | -0.008 | 7.01E-05 | 0.070 | -0.006 | 4.76E-02 |
| cg23542902 | HES1 | chr3 | 193807749 | -0.008 | 7.20E-05 | 0.070 | -0.004 | 1.47E-02 |
| cg19835796 | ZNF608 | chr5 | 123637793 | -0.006 | 7.17E-05 | 0.070 | -0.004 | 4.51E-02 |
| cg02100497 | DAPK1 | chr9 | 90273707 | -0.007 | 7.39E-05 | 0.070 | -0.004 | 3.47E-02 |
| cg10921517 | MOB2 | chr11 | 1520881 | 0.006 | 7.43E-05 | 0.070 | 0.003 | 4.92E-02 |
| cg27115863 | CARD10 | chr22 | 37921640 | -0.016 | 7.48E-05 | 0.070 | -0.011 | 1.30E-03 |
| cg05809481 | ISG20L2 | chr1 | 156696467 | -0.012 | 7.53E-05 | 0.071 | -0.006 | 2.68E-02 |
| cg02023550 | GPC1 | chr2 | 241294007 | -0.007 | 7.73E-05 | 0.071 | -0.005 | 3.70E-03 |
| cg22515589 | BAHCC1 | chr17 | 79426432 | 0.011 | 7.85E-05 | 0.071 | 0.007 | 2.73E-02 |
| cg09247619 | PTPRC | chr1 | 198648849 | -0.009 | 7.95E-05 | 0.071 | -0.006 | 6.09E-03 |
| cg22422264 | USP8 | chr15 | 50792856 | 0.014 | 7.98E-05 | 0.071 | 0.012 | 1.64E-03 |

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| | | | | | | | | |
|------------|--------|-------|-----------|--------|----------|-------|--------|----------|
| cg23009327 | TCF3 | chr19 | 1630248 | 0.012 | 8.12E-05 | 0.071 | 0.007 | 7.92E-03 |
| cg03897436 | UNKL | chr16 | 1425469 | 0.007 | 8.49E-05 | 0.073 | 0.004 | 2.59E-02 |
| cg01511901 | HMGB1 | chr13 | 31004719 | -0.011 | 8.83E-05 | 0.073 | -0.006 | 1.76E-02 |
| cg16759443 | ACSF3 | chr16 | 89200506 | 0.005 | 8.90E-05 | 0.073 | 0.003 | 4.57E-02 |
| cg13442969 | DYRK2 | chr12 | 68044208 | -0.011 | 8.92E-05 | 0.073 | -0.006 | 1.18E-02 |
| cg22052056 | DNMT3B | chr20 | 31351813 | -0.010 | 9.10E-05 | 0.073 | -0.006 | 4.55E-02 |
| cg06696905 | PDE12 | chr3 | 57539284 | -0.007 | 9.48E-05 | 0.075 | -0.004 | 3.08E-02 |
| cg26385126 | NCOR2 | chr12 | 124912021 | 0.007 | 9.96E-05 | 0.077 | 0.010 | 3.91E-07 |
| cg14819242 | GRAMD3 | chr5 | 125782749 | -0.008 | 1.02E-04 | 0.077 | -0.005 | 1.05E-02 |
| cg22129111 | ALOXE3 | chr17 | 8009699 | -0.008 | 1.02E-04 | 0.077 | -0.005 | 1.89E-02 |
| cg01765406 | HS6ST1 | chr2 | 129231478 | -0.009 | 1.04E-04 | 0.077 | -0.006 | 1.46E-02 |
| cg22940798 | TAP2 | chr6 | 32805554 | -0.011 | 1.07E-04 | 0.078 | -0.006 | 3.53E-02 |
| cg10919344 | OR5A1 | chr11 | 59210634 | -0.010 | 1.12E-04 | 0.079 | -0.006 | 2.74E-02 |
| cg09186031 | METTL9 | chr16 | 21677966 | -0.010 | 1.12E-04 | 0.079 | -0.008 | 5.02E-05 |
| cg12378753 | ABLIM1 | chr10 | 116527201 | -0.011 | 1.14E-04 | 0.079 | -0.011 | 3.99E-04 |
| cg11344352 | ERCC1 | chr19 | 45927696 | -0.013 | 1.15E-04 | 0.080 | -0.008 | 6.94E-07 |
| cg13463033 | SEC16A | chr9 | 139360276 | 0.007 | 1.16E-04 | 0.080 | 0.005 | 5.66E-03 |
| cg08348165 | OR2A12 | chr7 | 143791397 | 0.010 | 1.19E-04 | 0.081 | 0.008 | 1.60E-02 |

eTable 7. Gene Ontology characterization of SZ-associated DMPs in blood

| | GO.ID | Term | Annotated | Significant | Expected | Odds Ratio | p-value (FDR) |
|----|------------|--|-----------|-------------|----------|------------|---------------|
| 1 | GO:0051056 | regulation of small GTPase mediated signal transduction | 546 | 15 | 4.69 | 3.56 | 0.114 |
| 2 | GO:0031929 | TOR signaling | 60 | 5 | 0.51 | 10.88 | 0.114 |
| 3 | GO:0009966 | regulation of signal transduction | 2487 | 38 | 21.34 | 2.12 | 0.114 |
| 4 | GO:0023051 | regulation of signaling | 2773 | 41 | 23.80 | 2.07 | 0.114 |
| 5 | GO:0010646 | regulation of cell communication | 2786 | 41 | 23.91 | 2.06 | 0.114 |
| 6 | GO:0061462 | protein localization to lysosome | 16 | 3 | 0.14 | 27.26 | 0.148 |
| 7 | GO:0051058 | negative regulation of small GTPase mediated signal transduction | 41 | 4 | 0.35 | 12.85 | 0.163 |
| 8 | GO:0046578 | regulation of Ras protein signal transduction | 520 | 13 | 4.46 | 3.18 | 0.185 |
| 9 | GO:0097264 | self proteolysis | 5 | 2 | 0.04 | 78.20 | 0.191 |
| 10 | GO:0035556 | intracellular signal transduction | 2194 | 33 | 18.83 | 2.02 | 0.191 |
| 11 | GO:0032006 | regulation of TOR signaling | 48 | 4 | 0.41 | 10.80 | 0.191 |
| 12 | GO:0032007 | negative regulation of TOR signaling | 22 | 3 | 0.19 | 18.65 | 0.196 |
| 13 | GO:0035023 | regulation of Rho protein signal transduction | 486 | 12 | 4.17 | 3.12 | 0.199 |
| 14 | GO:0007264 | small GTPase mediated signal transduction | 488 | 12 | 4.19 | 3.11 | 0.199 |
| 15 | GO:0008216 | spermidine metabolic process | 6 | 2 | 0.05 | 58.64 | 0.199 |

eTable 8. meQTLs that overlap with SZ-SNPs from PGC

| Probe | P Value | FDR | chr | position | SNPs | PGC Ranks |
|--------------|----------------|------------|------------|-----------------|-------------|------------------|
| cg25647583 | 2.29E-07 | 2.55E-05 | 15 | 91428636 | rs7177338 | 11 |
| cg25647583 | 7.89E-06 | 0.000621 | 15 | 91428197 | rs2071382 | 11 |

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