

Supplementary figures for the article *Risperidone response in patients with schizophrenia drives DNA methylation changes in the immune and neuronal systems*

**Supplementary figures legends**

**Supplementary Figure 1. PCA based on the blood cell composition data estimated from the methylation values for both visits.** PC1 is used as a proxy for the cell type composition in the statistical analysis (for details s. Methods section). Samples from the same individual are connected by a line. Good responders are shown in blue, the bad ones in orange. Dots denote baseline visit (VA), triangles the follow-up (VB). CD4+ T = helper T-cells, CD8+T = killer T-cells, NK = natural killer cells.

**Supplementary Figure 2. Factor Analysis (FA) of variables describing unwanted variation (control matrix, chip identity, position on the chip, and sampling centre).** A) The first two FA axes showing the unwanted variation variables significantly associated with those axes; B) contribution of the unwanted variation components to the construction of the first two FA axes. The red line denotes the threshold above which the variables are considered to have contributed to the axes construction more than expected by chance. Slide = chip identity, array = position on the chip, ctrlMat\_\* = different components of the control matrix (for details s. Methods section).

**Supplementary Figure 3. PCA of within-normalized 39,239 variable autosomal probes from all 56 samples.** A) PC1 & PC2 and B) PC1 & PC3. Two outlier individuals were detected: P9 along the PC2 and P14 along the PC3. Both individuals were excluded from further analysis.

**Supplementary Figure 4. Treemaps showing prioritized GO CC terms enriched in A) PC1-, B) PC1+, C) PC2- and D) PC2+ groups, grouped by semantic similarity.** The size of rectangles is proportional to the significance of the corresponding term. Sets of semantically similar terms are divided from each other by thicker border lines.

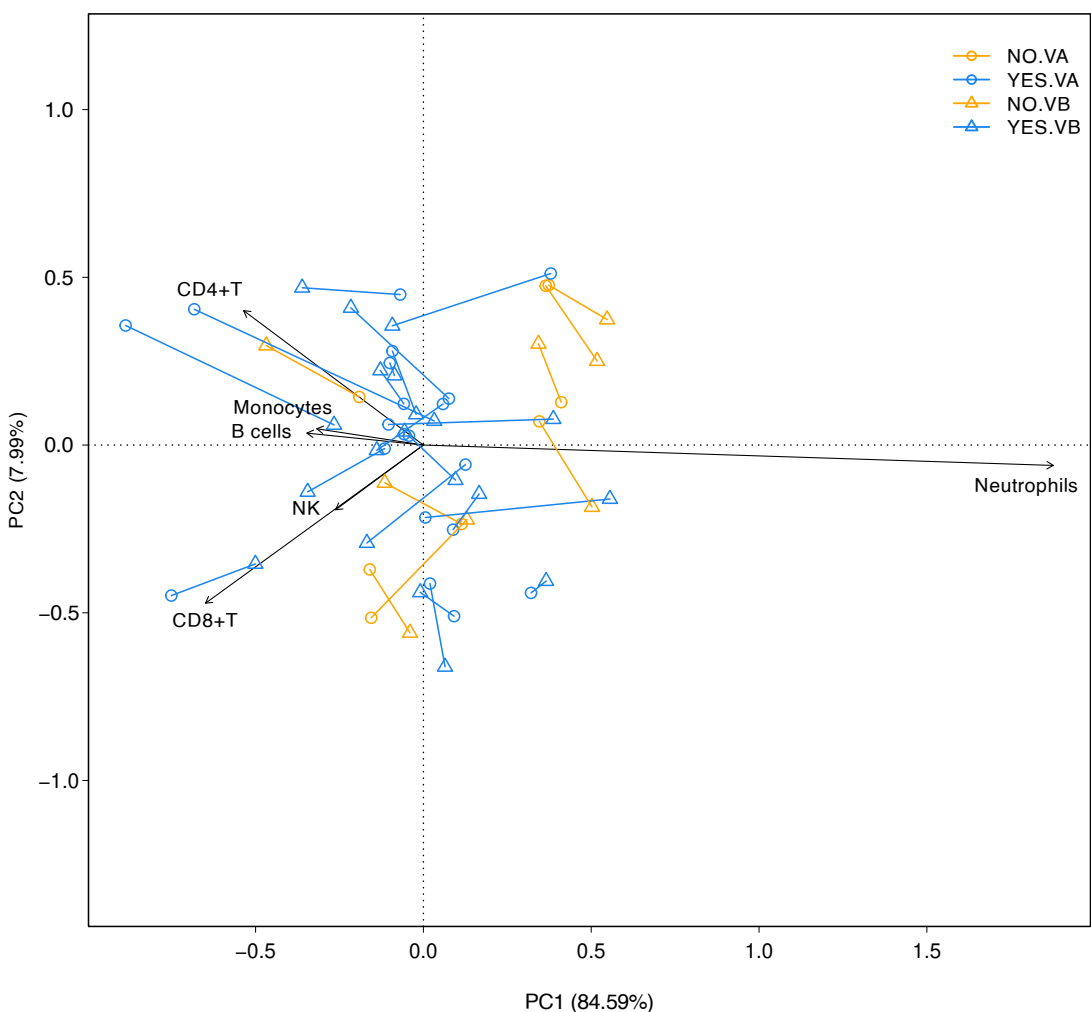
**Supplementary Figure 5. Treemaps showing prioritized GO MF terms enriched in A) PC1-, B) PC1+, C) PC2- and D) PC2+ groups, grouped by semantic similarity.** The size of rectangles is proportional to the significance of the corresponding term. Sets of semantically similar terms are divided from each other by thicker border lines.

**Supplementary Figure 6. Treemaps showing prioritized A) BP, B) CC and C) MF GO terms enriched in the variable autosomal CpG subset compared to the all the CpGs on the EPIC chip.** Terms are grouped by semantic similarity. The size of rectangles is proportional to the significance of the corresponding term. Sets of semantically similar terms are divided from each other by thicker border lines.

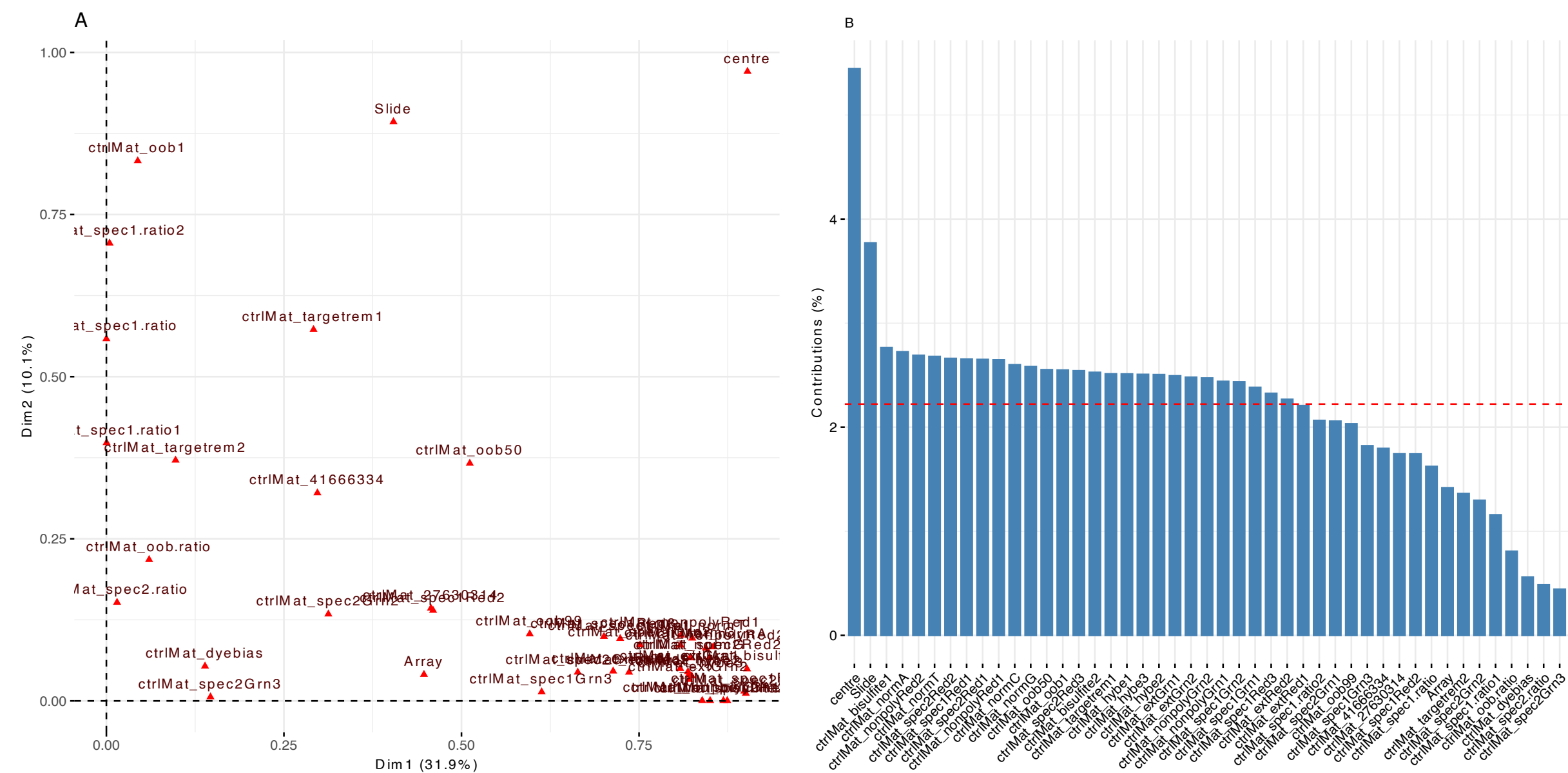
**Supplementary Figure 7. KEGG pathways enriched in A) PC1-, B) PC1+ and C) PC2+ groups with the corresponding differentially methylated genes.**

**Supplementary Figure 8. Characteristics of top CpGs (absolute coefficient estimate  $\geq 0.18$ ) differentially methylated between good and bad responders.** Number of significant vs. total number of CpGs annotated to the gene are shown in the parentheses. Estimate values in the heatmap are capped to 5% and 95% quantiles for better visualisation, the exact values with 95% confidence intervals are shown in the plot on the left.

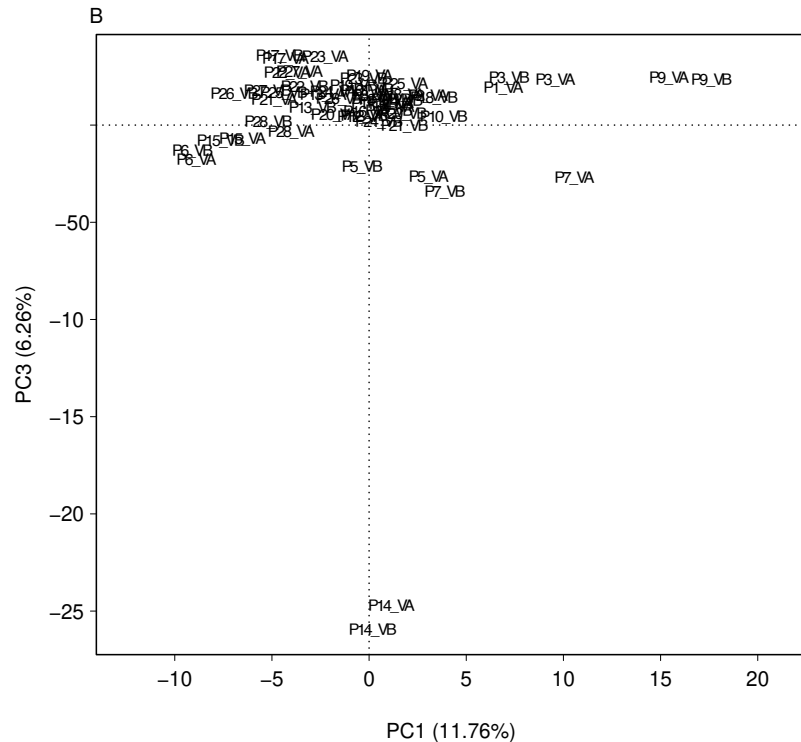
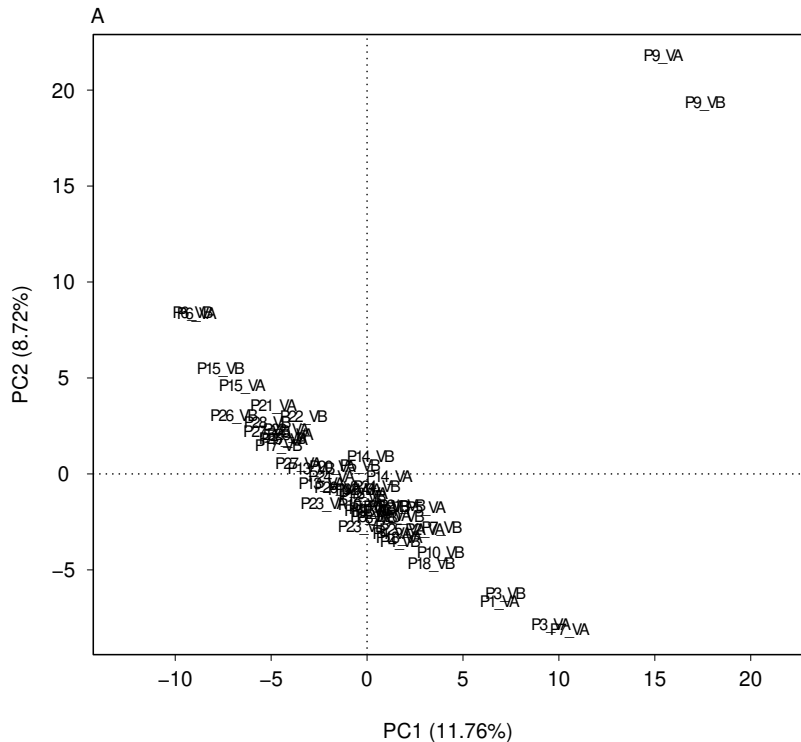
**Supplementary Figure 9. Characteristics of top CpGs (absolute coefficient estimate  $\geq 0.18$ ) with different temporal dynamics between good and bad responders.** Number of significant vs. total number of CpGs annotated to the gene are shown in the parentheses. Estimate values in the heatmap are capped to 5% and 95% quantiles for better visualisation, the exact values with 95% confidence intervals are shown in the plot on the left. None of the CpGs were correlated with PC1- or PC2-. Also, none was significant for the main effect of response nor had any known blood-brain methylation correlation. Finally, the coefficients are from models that all had adjusted p-value  $\leq 0.05$ . That is why those columns are omitted (compare with Supplementary Figure 8).



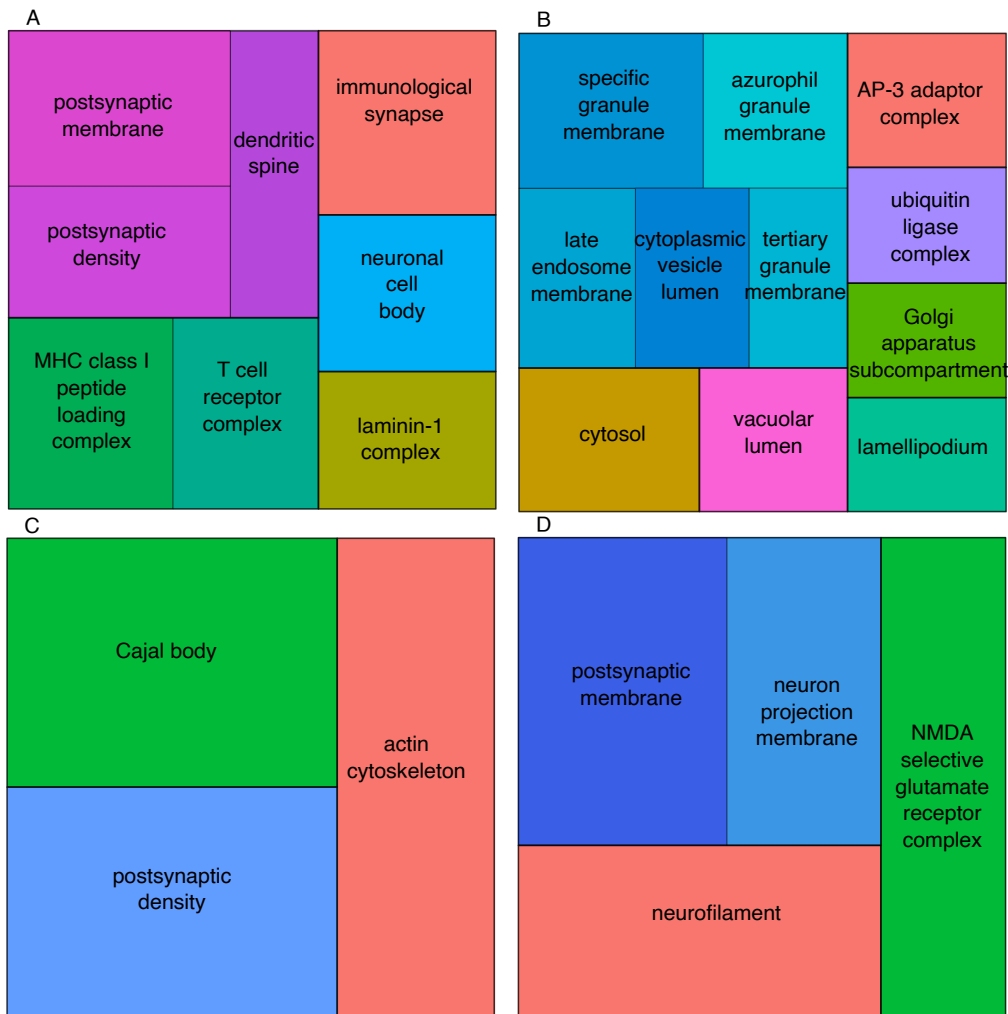
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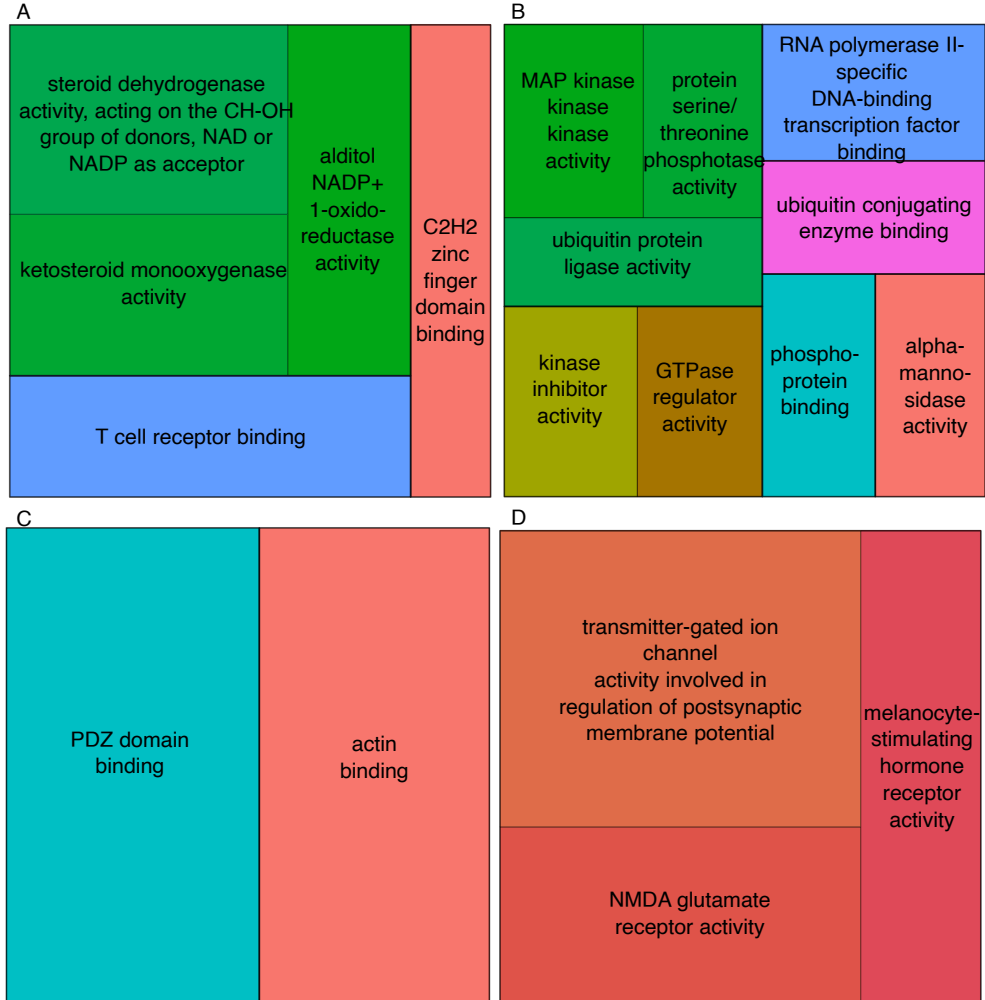
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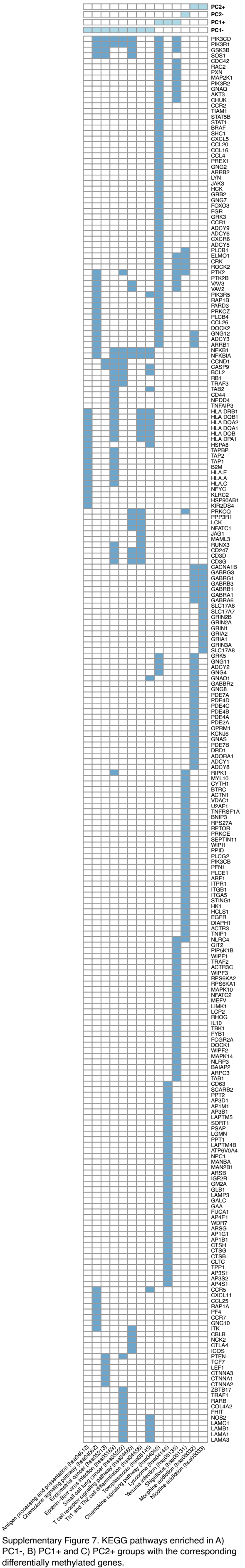
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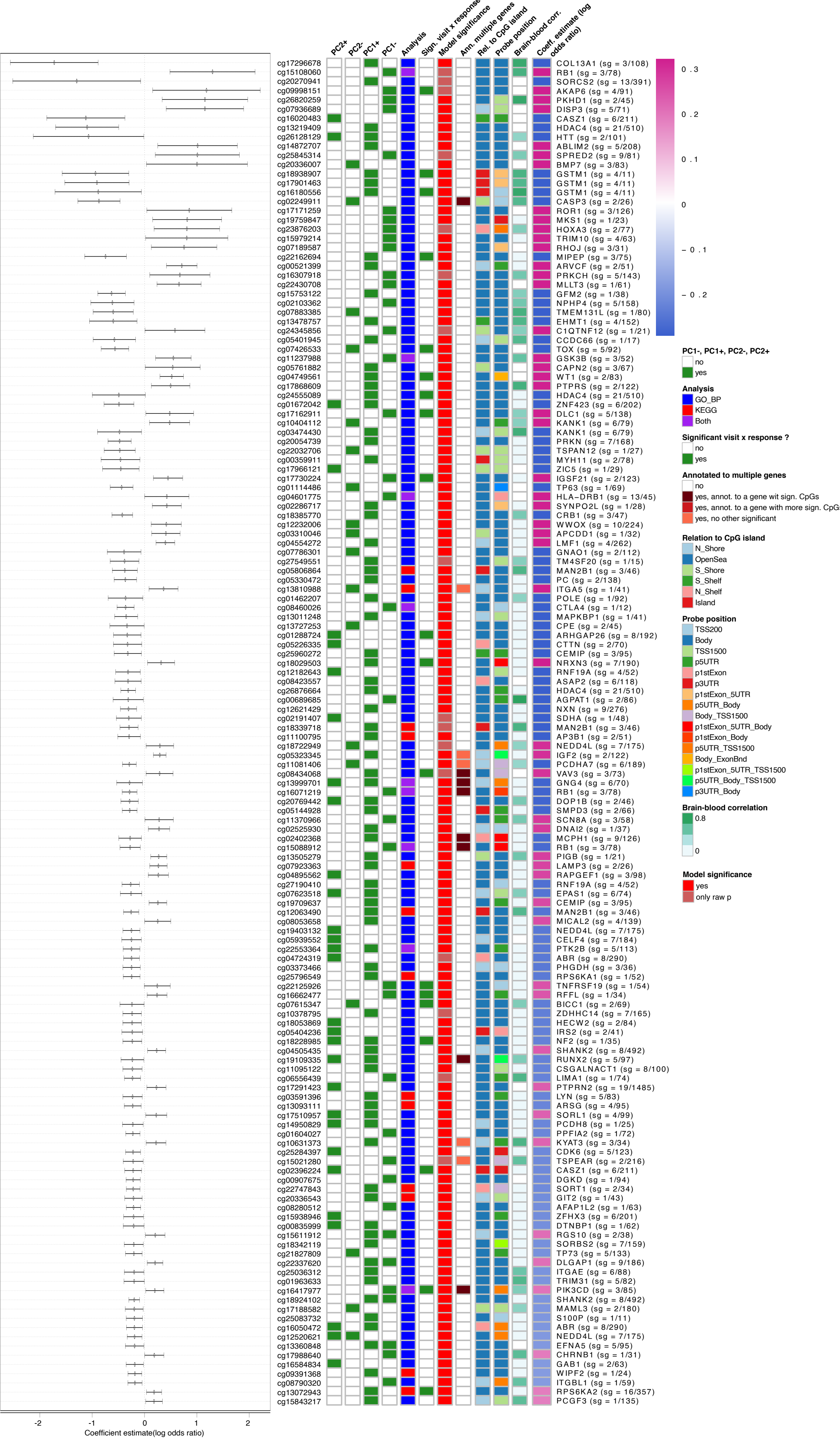
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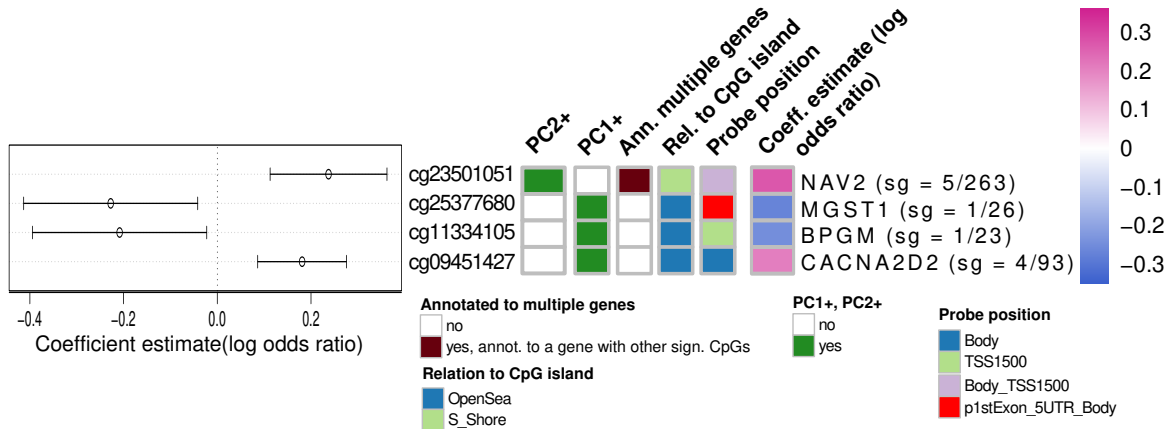


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