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SUPPLEMENTARY INFORMATION

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Dysregulation of the epigenetic landscape of normal aging in Alzheimer's disease

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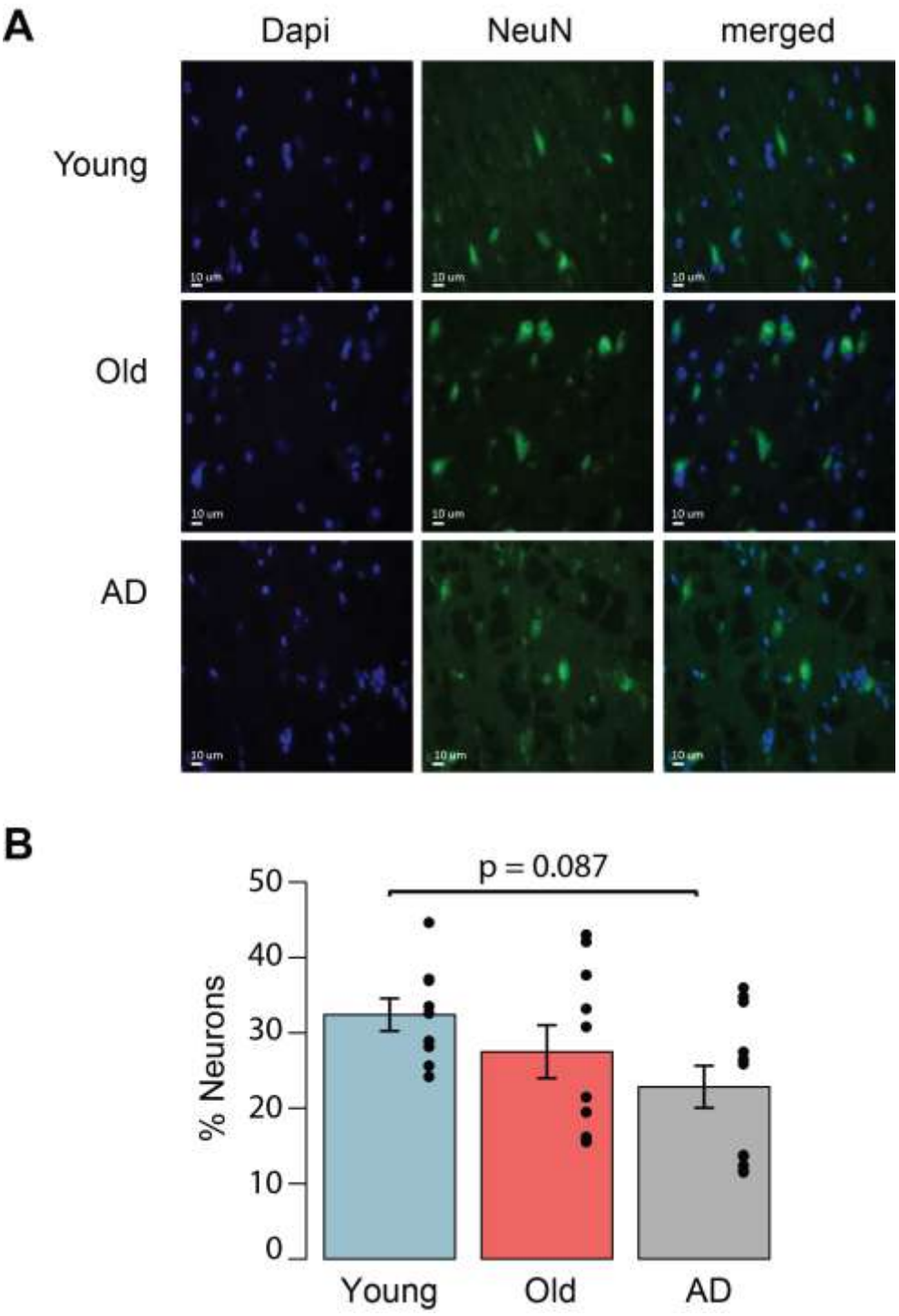
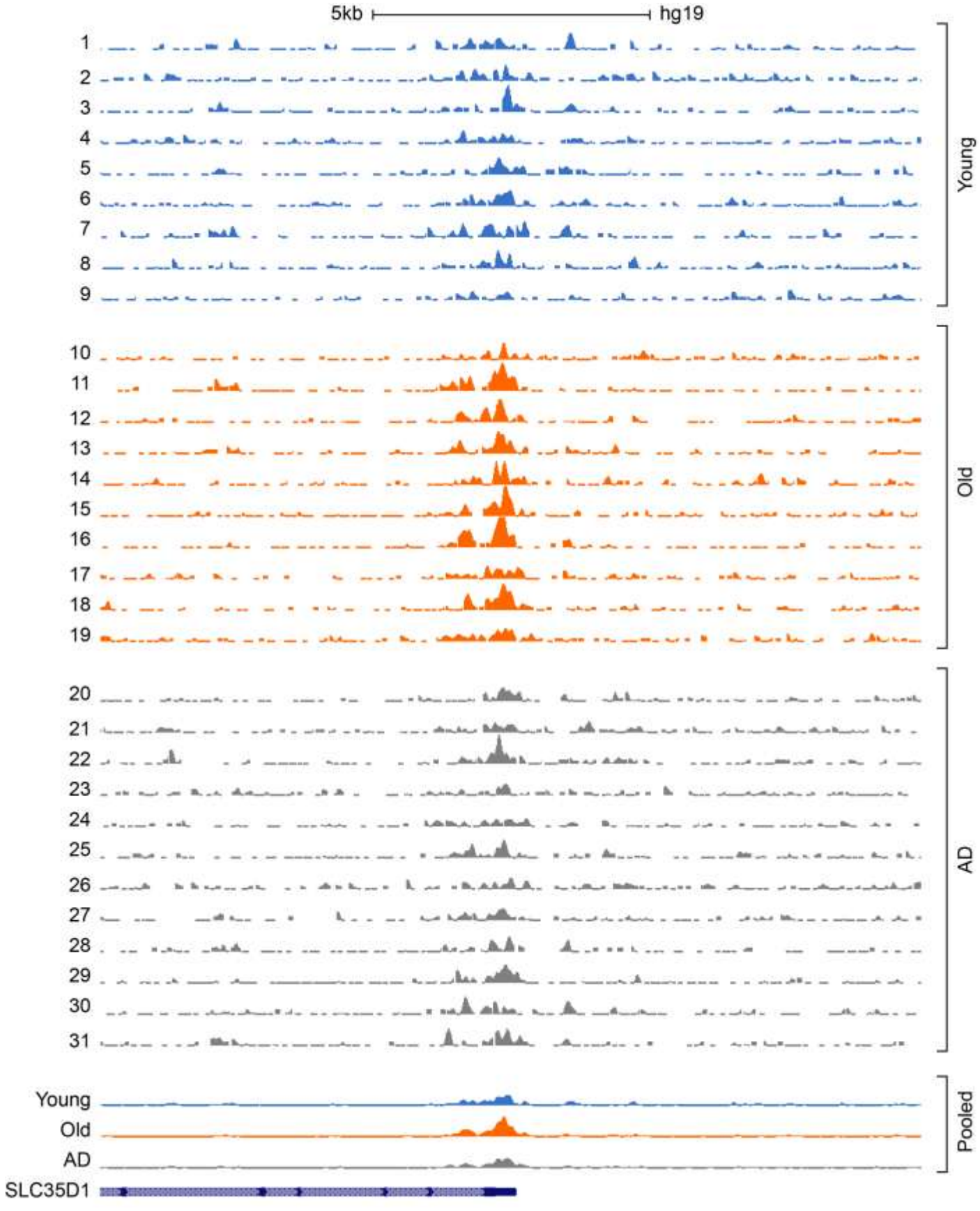


Supplementary Figure 1

Quantification of neurons in temporal cortex of Young, Old and AD subjects.

(A) Representative IF images showing total nuclei (DAPI-blue, left column), NeuN positive nuclei (green, central column) and merged images (right column) for Young (top row), Old (middle row), AD (bottom row). (B) Barplot (with data points) representing mean ± SEM of neuron percentages quantified by IF (n^o Young = 9; n^o Old = 10; n^o AD = 12). Sample size (n^o) represents individual brain samples. Differences are not significant (*P*=0.087, 1-way ANOVA; F (2,28)=2.669).


5kb
hg19
1
2
3
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6
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8
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Young
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11
12
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16
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Old
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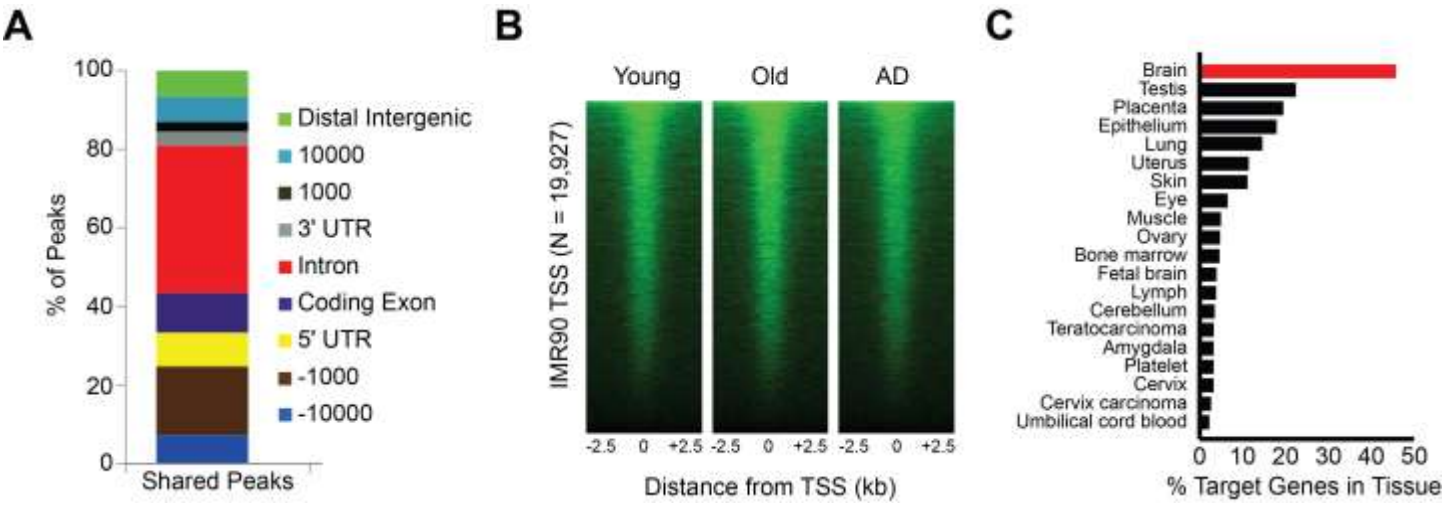
28
29
30
31
AD
Young
Old
AD
SLC35D1
Pooled

Supplementary Figure 2

H4K16ac enrichment in individual and pooled samples.

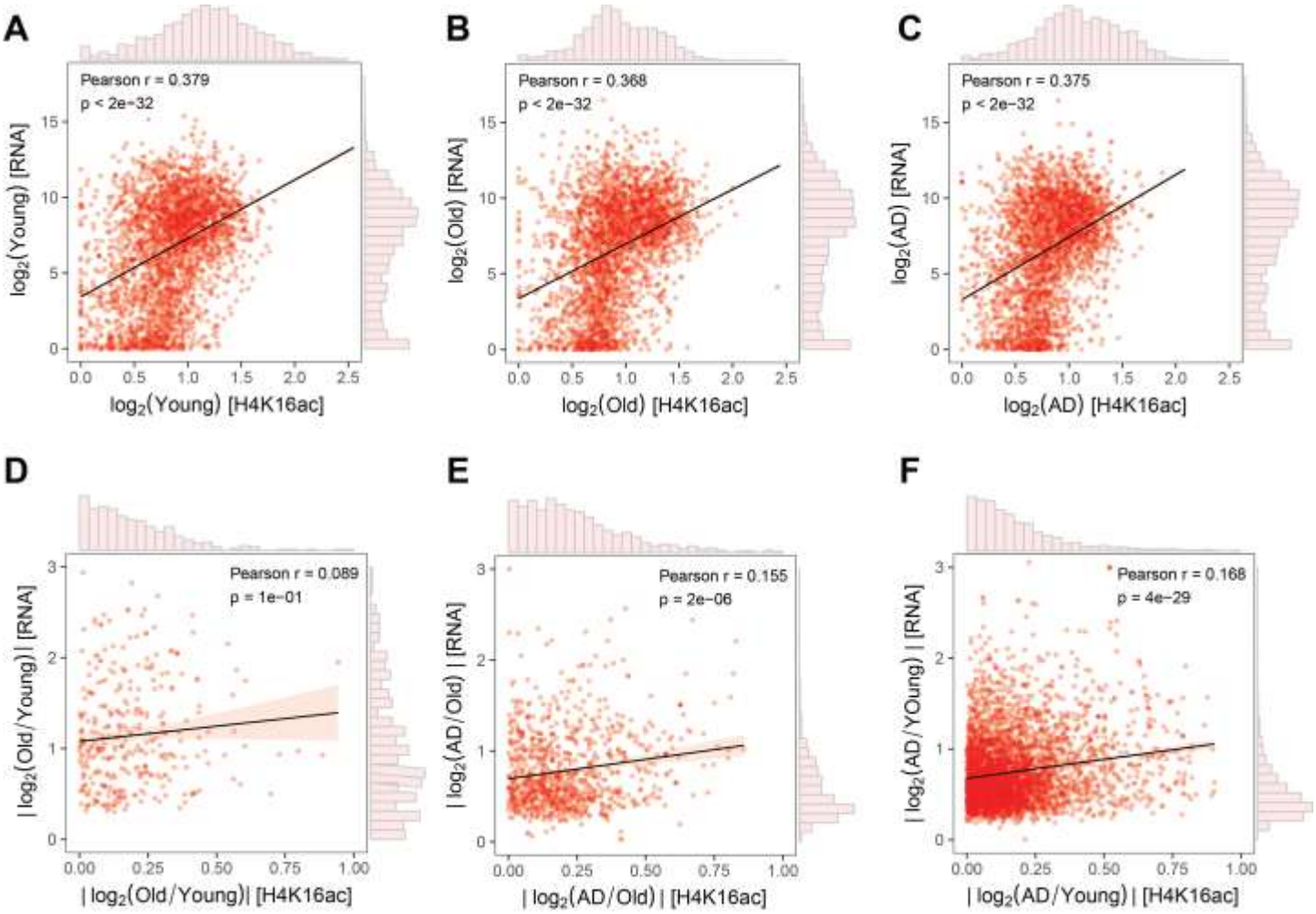
UCSC Genome browser track views of H4K16ac enrichment at the promoter of *SLC35D1* gene in individual Young (blue), Old (orange), AD (gray) samples and corresponding pooled samples. The numbers on the right of each track refer to the sample ID as reported in Table S1.



Supplementary Figure 3

Comparison between H4K16ac peaks detected in the brain and other cell types.

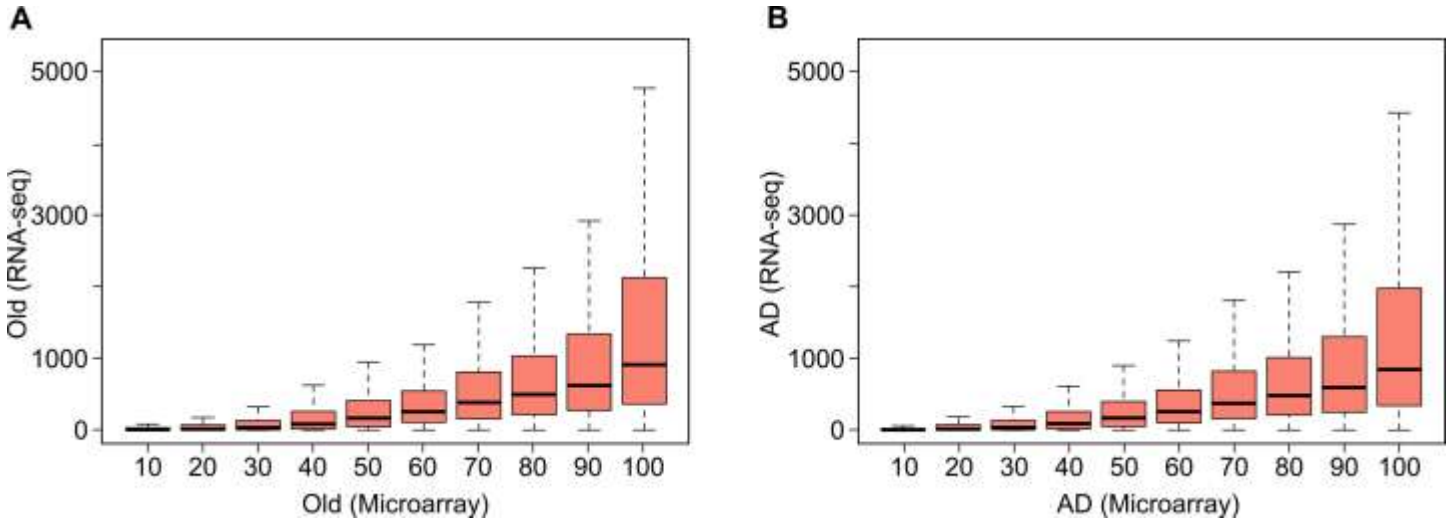
(A) Genomic compartment analysis showing % of H4K16ac shared peaks (in common between Young, Old and AD) is similar to Taylor et al. [20] in mouse ESC and NPC cells. (B) Heatmap showing H4K16ac enrichment in Young, Old and AD over previously mapped H4K16ac peaks in human IMR90 cells [15]. Peaks are sorted in decreasing order of Young brain enrichment. (C). Barplot showing % of tissue-specific expressed genes targeted by H4K16ac (top 10% of Young peaks and up to 1 kb from TSS) for H4K16ac shared peaks (UniProt tissue expression database, DAVID). Tissue terms were filtered by gene count > 200 and FDR < 1%.



Supplementary Figure 4

Correlation between H4K16ac and gene expression in Young, Old and AD subjects.

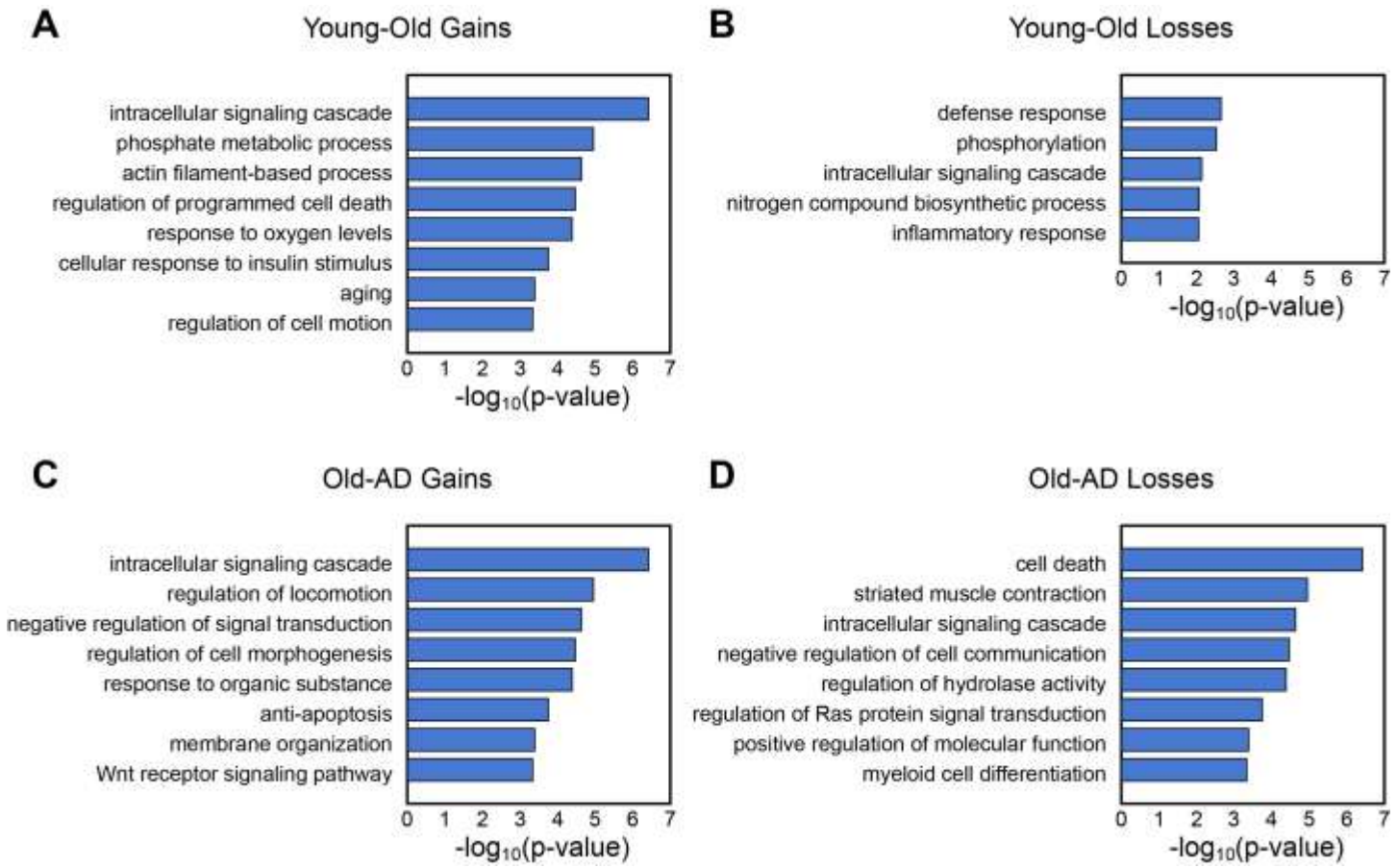
(A-C) Scatter plot of H4K16ac peak enrichment (log_2 AUC +1) vs gene expression (log_2 DESeq-score +1) of genes expressed in (A) Young, (B) Old and (C) AD considering the closest peak from the TSS. For graphical representation, 3000 randomly chosen points are shown in each panel. (D-F) Absolute H4K16ac fold-changes (closest peak from the TSS) vs absolute gene expression changes for the significantly ($P < 0.05$, FDR< 0.05) differentially expressed genes for the comparisons (D) Young to Old, (E) Old to AD and (F) Young to AD. Linear regression trendlines and Pearson correlation coefficients are indicated.



Supplementary Figure 5

Comparison between RNA-seq and published microarray data (Blalock et al. 2011) in Old and AD subjects.

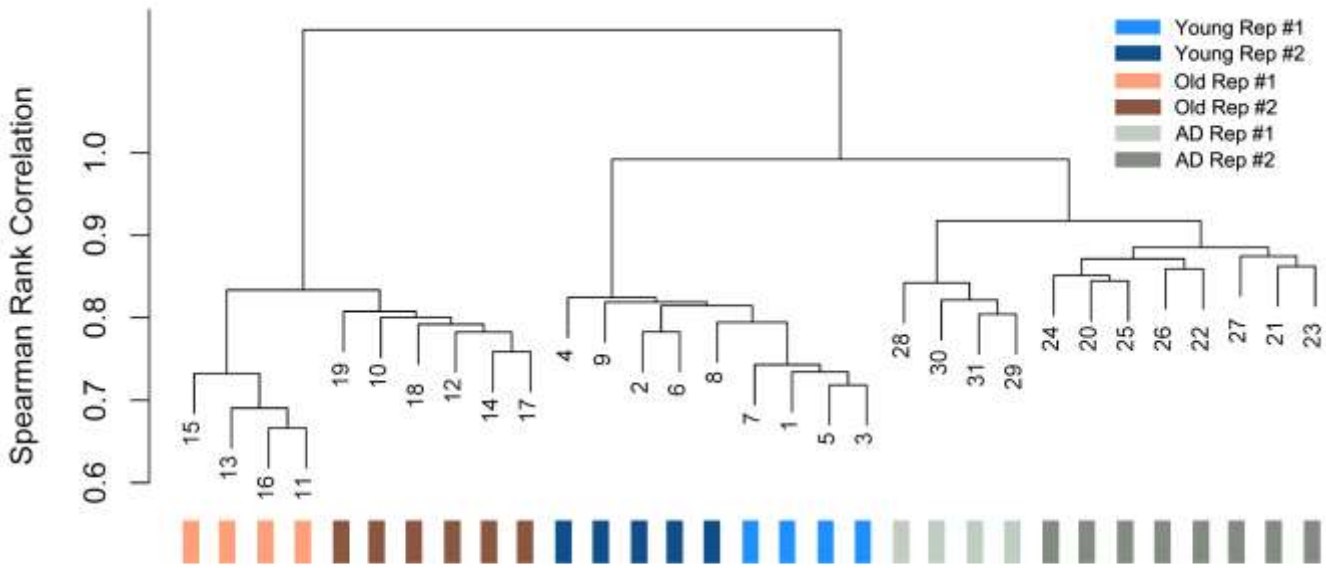
Boxplot showing RNA-seq gene expression (DEseq-scores) in Old (A) or AD (B) for genes identified in a published AD microarray study [21] from human hippocampus. All expressed genes from the published microarray data (control Old and AD) were sorted into ten groups of increasing expression and compared to Old (A) or AD (B) in our RNA-seq data.



Supplementary Figure 6

GO analysis of genes with H4K16ac changes in aging and AD subjects.

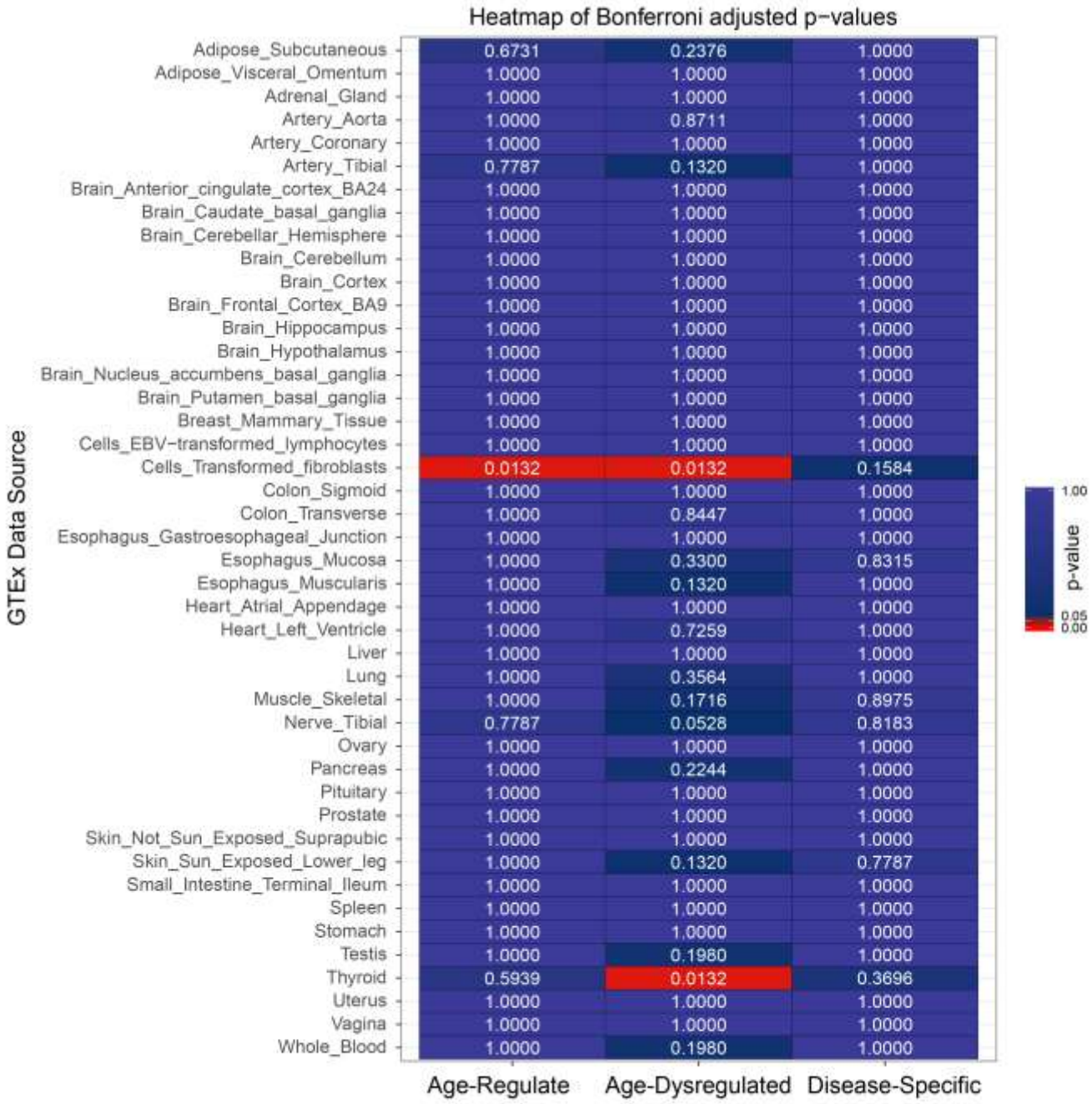
(A-D) Bar plot for top eight most significantly enriched GO terms (BP; DAVID) for genes with significant ($P < 0.05$, Welch's t-test, two-sided) H4K16ac (A) gains or (B) losses during aging (Young-Old comparison) and H4K16ac (C) gains or (D) losses in AD (Old-AD comparison). Reported GO terms contain > 20 genes and FDR < 10%.



Supplementary Figure 7

Correlation across patients at the three classes of H4K16ac changes.

Dendrogram of Spearman Rank Correlation across patients (rep1 and rep2) for the three classes of peaks (Age-regulate, Age-dysregulated and Disease-specific; $P < 0.05$, 1-way Anova) showing patients clustering according to study group (Young, Old and AD). The numbers for each patient refer to the sample ID as reported in Table S1.



Supplementary Figure 8

H4K16ac overlap analysis with tissue eQTLs from the GTEx project.

Heatmap of Bonferroni adjusted p-values for sampling-based analysis of H4K16ac overlap (the three classes of changes) with tissue eQTLs from the GTEx project.