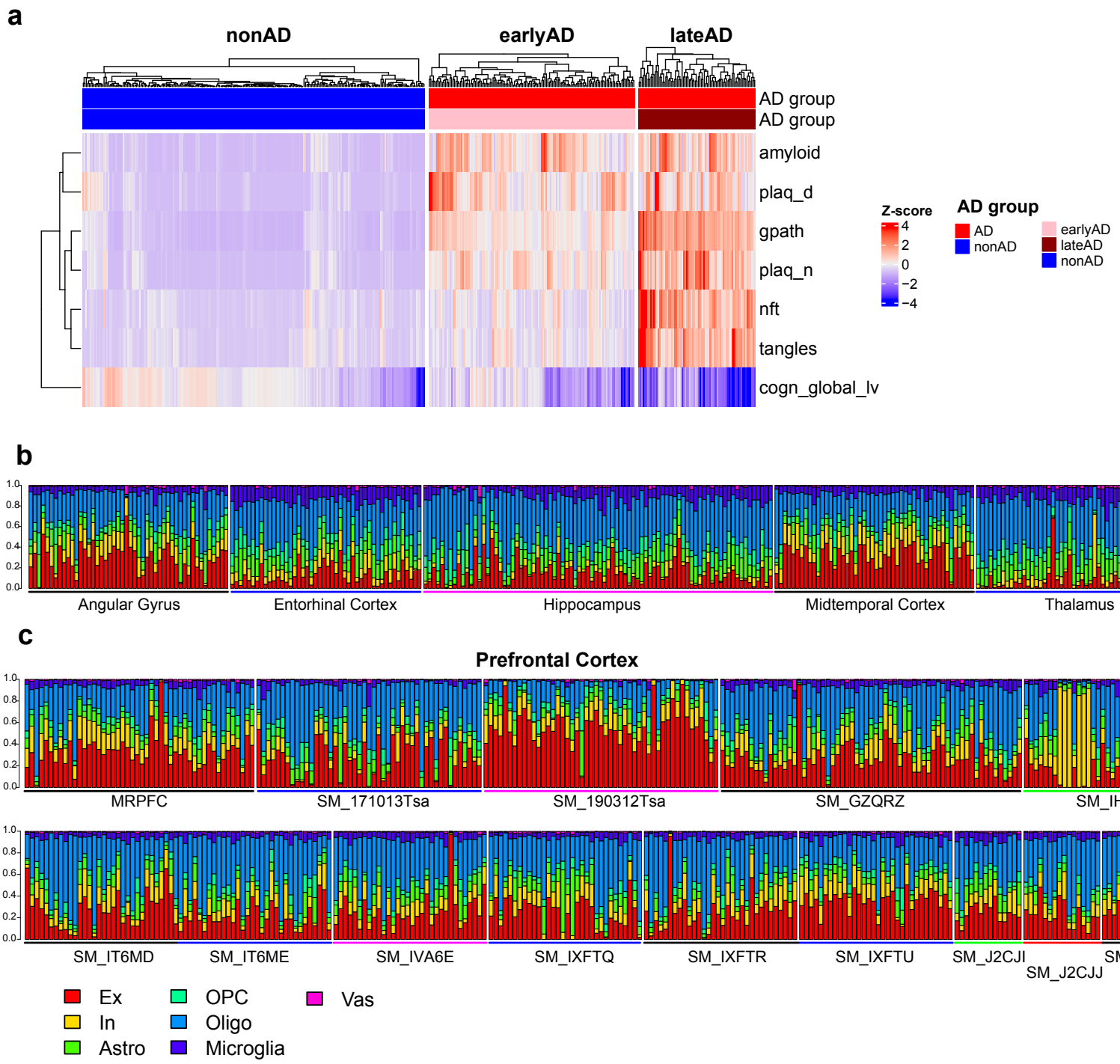
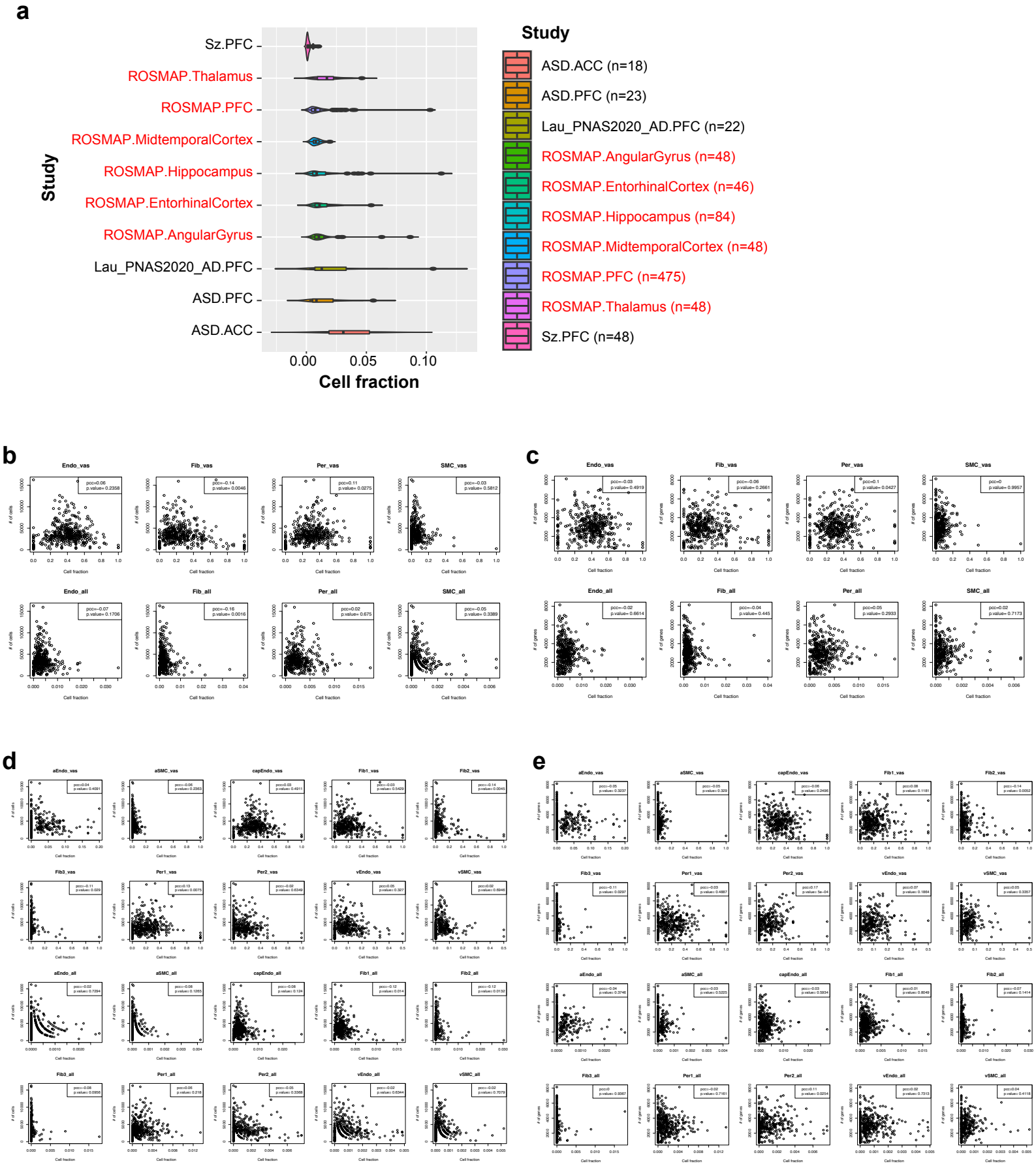
Supplementary Figures

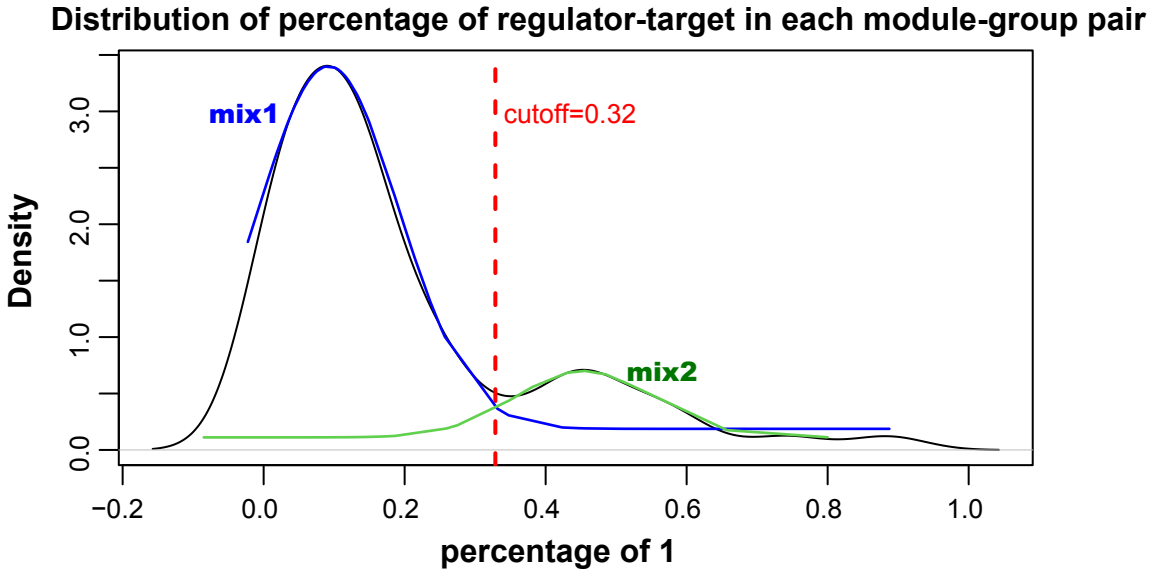
Supplementary Figure 1. Cell type distribution for each individual in six brain regions. a. Heatmap showing the clustering of 428 ROSMAP individuals using seven pathological variables. Three groups (nonAD, earlyAD, and lateAD) are shown. The combined group of earlyAD and lateAD individuals is used as the AD group in this study. **b**. The cell type composition for each individual across five brain regions. **c.** Cell type composition in the prefrontal cortex for multiple batches. Seven major cell types (Ex: excitatory neurons, In: inhibitory neurons, Astro: astrocytes, OPC: oligodendrocyte precursor cells, Oligo: oligodendrocytes, Vas: vascular cells, and Microglia) are shown in the barplot.

Supplementary Figure 2. Quality control for vascular cells. a. The distributions of vascular cell fractions in this study and public datasets. The data in this study (labeled as "ROSMAP") is shown for each brain region. The public datasets include Sz (schizophrenia) in PFC, AD in PFC from Lau *et al*., and autism (ASD) in two brain regions. There were no statistically significant differences between the data in this study and the other datasets (by t-test). The box starts in the first quantile (25%) and ends in the third (75%). The line inside represents the median. Two whiskers represent the maximum and minimum without outliers. **b**. The correlation between cell fraction and the number of captured cells at the major cell type level. The Pearson correlation coefficient and the p-value by cor.test in R are shown in each panel. The top row uses the cell fraction compared to all vascular cells and the bottom row uses the cell fraction compared to all captured cells. **c**. The correlation between cell fraction and the number of detected genes at the major cell type level. The Pearson correlation coefficient and the p-value by cor.test in R are shown in each panel. The top row uses the cell fraction compared to all vascular cells and the bottom row uses the cell fraction compared to all captured cells. **d**. The correlation between cell fraction and the number of captured cells at the cell subtype level. The Pearson correlation coefficient and the p-value by cor.test in R are shown in each panel. The top two rows use the cell fraction compared to all captured cells and the bottom two rows use the cell fraction compared to all vascular cells. **e**. The correlation between cell fraction and the number of detected genes at the cell subtype level. The Pearson correlation coefficient and the p-value by cor.test in R are shown in each panel. The top two rows use the cell fraction compared to all captured cells and the bottom two rows use the cell fraction compared to all vascular cells.

Supplementary Figure 3. Distribution of percentage of regulator-target in each module-group pair. The black line represents the distribution of percentage of regulator-target pairs in each module-group block shown in Fig. 3f. The blue and green lines represent the inferred normal distributions based on the Gaussian mixture model using mixtools in R. The percentage 32%, the intersection point of two normal distributions (the red dashed line), is used as a cutoff to determine if the target cluster was regulated by a regulator module.


a
nonAD
earlyAD
lateAD
AD group
AD group
amyloid
plaq_d
gpath
plaq_n
nft
tangles
cogn_global_lv
Z-score
4
2
0
−2
−4
AD group
AD
nonAD
earlyAD
lateAD
nonAD
b
1.0
0.8
0.6
0.4
0.2
0.0
Angular Gyrus
Entorhinal Cortex
Hippocampus
Midtemporal Cortex
Thalamus
c
Prefrontal Cortex
MRPFC
SM_171013Tsa
SM_190312Tsa
SM_GZQRZ
SM_IHLAS
SM_IT6MD
SM_IT6ME
SM_IVA6E
SM_IXFTQ
SM_IXFTR
SM_IXFTU
SM_J2CJI
SM_J2CJJ
SM_Last16
Ex
In
Astro
OPC
Oligo
Microglia
Vas


a
Study
Sz.PFC
ROSMAP.Thalamus
ROSMAP.PFC
ROSMAP.MidtemporalCortex
ROSMAP.Hippocampus
ROSMAP.EntorhinalCortex
ROSMAP.AngularGyrus
Lau_PNAS2020_AD.PFC
ASD.PFC
ASD.ACC
0.00
0.05
0.10
Cell fraction
Study
ASD.ACC (n=18)
ASD.PFC (n=23)
Lau_PNAS2020_AD.PFC (n=22)
ROSMAP.AngularGyrus (n=48)
ROSMAP.EntorhinalCortex (n=46)
ROSMAP.Hippocampus (n=84)
ROSMAP.MidtemporalCortex (n=48)
ROSMAP.PFC (n=475)
ROSMAP.Thalamus (n=48)
Sz.PFC (n=48)
b
Endo_vas
Fib_vas
Per_vas
SMC_vas
Endo_all
Fib_all
Per_all
SMC_all
# of cells
Cell fraction
c
Endo_vas
Fib_vas
Per_vas
SMC_vas
Endo_all
Fib_all
Per_all
SMC_all
# of genes
Cell fraction
d
aEndo_vas
aSMC_vas
capEndo_vas
Fib1_vas
Fib2_vas
Fib3_vas
Per1_vas
Per2_vas
vEndo_vas
vSMC_vas
aEndo_all
aSMC_all
capEndo_all
Fib1_all
Fib2_all
Fib3_all
Per1_all
Per2_all
vEndo_all
vSMC_all
# of cells
Cell fraction
e
aEndo_vas
aSMC_vas
capEndo_vas
Fib1_vas
Fib2_vas
Fib3_vas
Per1_vas
Per2_vas
vEndo_vas
vSMC_vas
aEndo_all
aSMC_all
capEndo_all
Fib1_all
Fib2_all
Fib3_all
Per1_all
Per2_all
vEndo_all
vSMC_all
# of genes
Cell fraction


Distribution of percentage of regulator-target in each module-group pair
mix1
cutoff=0.32
mix2
Density
0.0
1.0
2.0
3.0
−0.2
0.0
0.2
0.4
0.6
0.8
1.0
percentage of 1