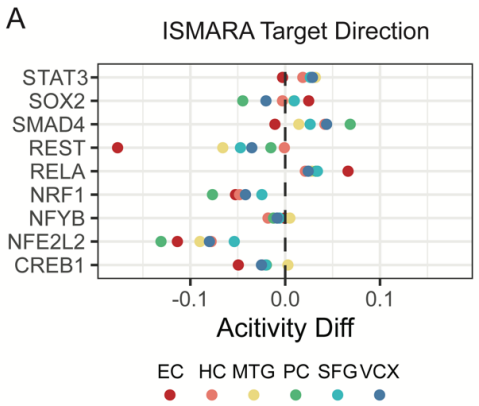
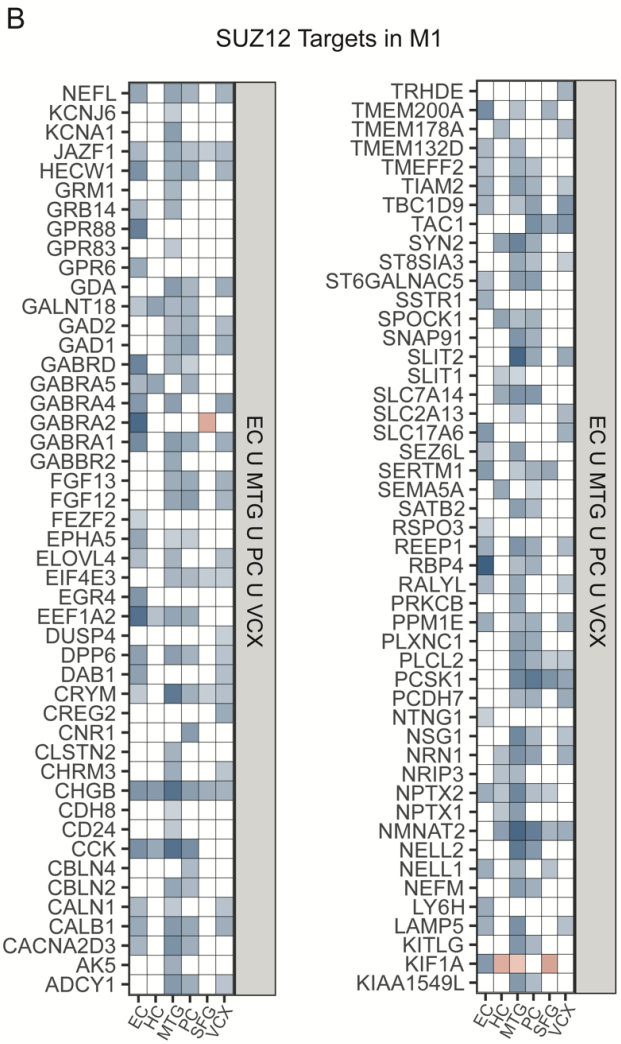
Supplementary Material

Endotype Characterization Reveals Mechanistic Differences Across Brain Regions in Sporadic Alzheimer's Disease

Supplementary File 1. Complete list of DEGs found in study. See PDF.

Supplementary Figure 1. A) *ISMARA* Activity Diff predicted the target direction of canonical TF motifs using the Swiss Regulon database; Activity Diff is the difference in target activity in SAD samples minus NDC samples. B) Differential expression of SUZ12 M1 targets in EC U MTG U PC U VCX; and (up to) top 15 enrichment results from the *tmod* hypergeometric test using Hallmark and GOBP collections performed on (C) REST M1 targets, (D) SUZ12 M1 Targets, (E) SOX2 M3 targets, and (F) NRF1 M4 targets.





C REST M1 Target Enrichment

Title	adj.P.Val
Gobp synaptic signaling	2.21E-21
Gobp cell cell signaling	2.49E-12
Gobp neurotransmitter transport	5.54E-10
Gobp neurotransmitter secretion	2.22E-09
Gobp regulation of neurotransmitter levels	6.04E-09
Gobp vesicle mediated transport in synapse	2.63E-08
Gobp synapse organization	3.57E-08
Gobp regulation of trans synaptic signaling	2.43E-07
Gobp inhibitory synapse assembly	1.19E-05
Gobp behavior	1.19E-05
Gobp synaptic vesicle exocytosis	3.62E-05
Gobp cell junction organization	5.36E-05
Gobp signal release	8.12E-05
Gobp transmembrane transport	0.00012007
Gobp synapse assembly	0.00012007

D SUZ12 M1 Target Enrichment

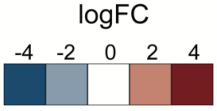
Title	adj.P.Val
Gobp synaptic signaling	8.15E-19
Gobp cell cell signaling	6.58E-16
Gobp axon development	8.45E-08
Gobp cell morphogenesis involved in neuron differentiation	8.45E-08
Gobp behavior	1.60E-07
Gobp cell morphogenesis involved in differentiation	3.64E-07
Gobp cell part morphogenesis	7.12E-07
Gobp nervous system process	8.47E-07
Gobp forebrain development	1.65E-06
Gobp neuron development	1.65E-06
Gobp synaptic transmission gabaergic	1.65E-06
Gobp gamma aminobutyric acid signaling pathway	2.25E-06
Gobp cellular component morphogenesis	2.60E-06
Gobp regulation of trans synaptic signaling	5.16E-06
Gobp cell morphogenesis	6.62E-06

E SOX2 M3 Target Enrichment

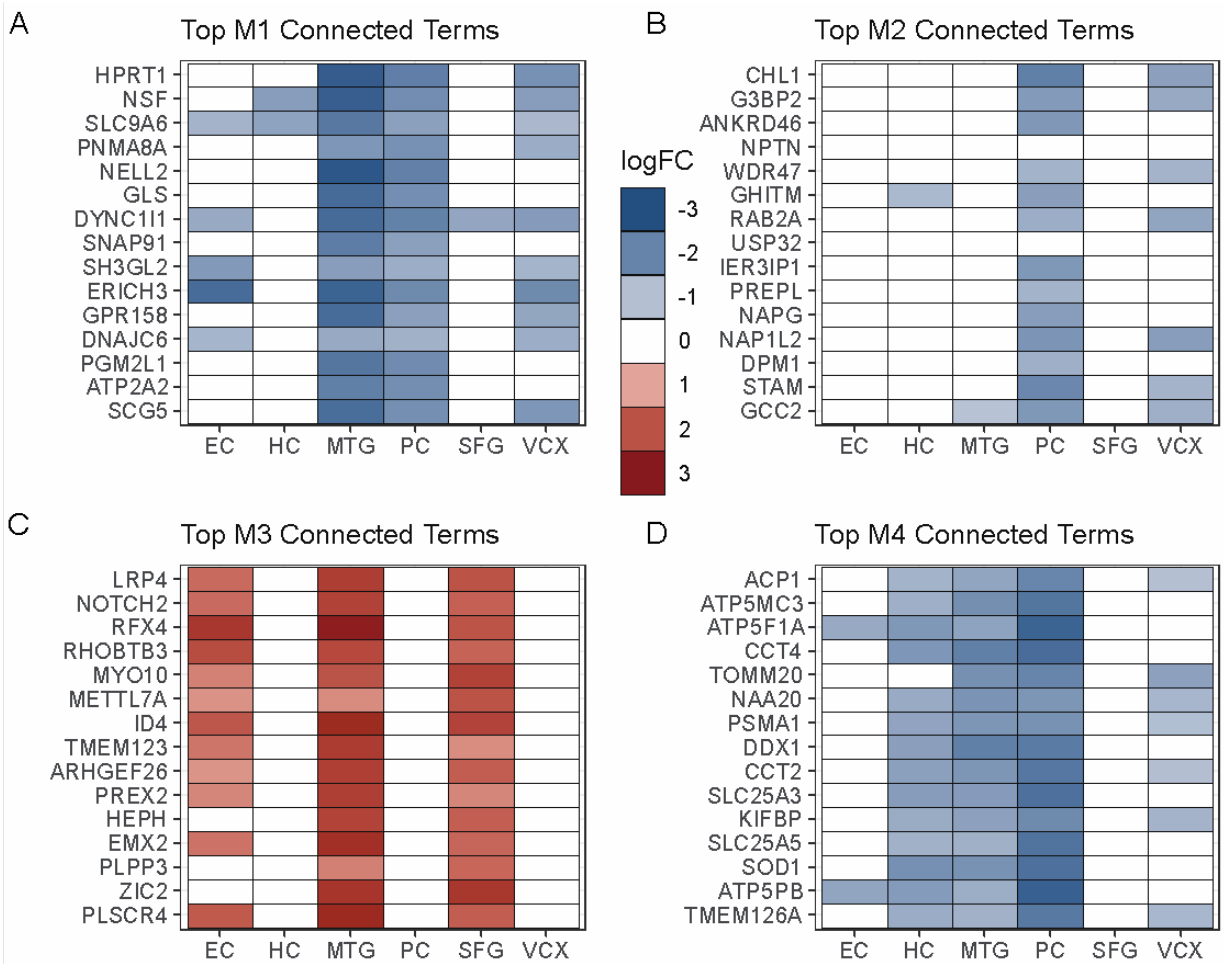
Title	adj.P.Val
Hallmark angiogenesis	5.70E-06
Hallmark epithelial mesenchymal transition	5.70E-06
Gobp regulation of cell differentiation	0.00012458
Gobp anatomical structure formation involved in morphogenesis	0.00014797
Gobp central nervous system development	0.00049898
Gobp tube development	0.00055134
Gobp circulatory system development	0.00061049
Gobp response to lipid	0.00092801
Gobp biological adhesion	0.00092801
Gobp vasculature development	0.00170177
Gobp response to muramyl dipeptide	0.00170177
Gobp regulation of cell adhesion	0.00170177
Gobp gastrulation	0.00170177
Gobp embryo development	0.00170177
Gobp endoderm development	0.00170177

F NRF1 M4 Target Enrichment

Title	adj.P.Val
Hallmark mtorc1 signaling	1.47E-05
Hallmark myc targets v1	9.04E-05
Hallmark oxidative phosphorylation	9.04E-05
Hallmark adipogenesis	0.01276663
Gobp respiratory electron transport chain	0.02240456
Gobp rna dependent dna biosynthetic process	0.04097824
Gobp energy derivation by oxidation of organic compounds	0.04097824
Gobp aerobic respiration	0.04097824
Gobp electron transport chain	0.04097824
Gobp atp synthesis coupled electron transport	0.04097824
Gobp cellular respiration	0.04097824



Supplementary Figure 2. Top 15 hub genes (genes with the highest connectivity) from *CEMiTool* for (A) M1, (B) M2, (C) M3, (D) M4.



Supplementary Figure 3. Venn diagram comparing differentially expressed transcript from this analysis (A) and Liang et al. analysis (B) for each brain region. Number on the bottom right of each indicates probes unique to Liang et al. annotations.