

Spatial Transcriptomics of APP/PS1 in Alzheimer's Disease Mouse Models

(Supplementary Materials)

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Supplementary Table 1. Biological pathways enriched by 8,693 differentially expressed genes in AD mice.

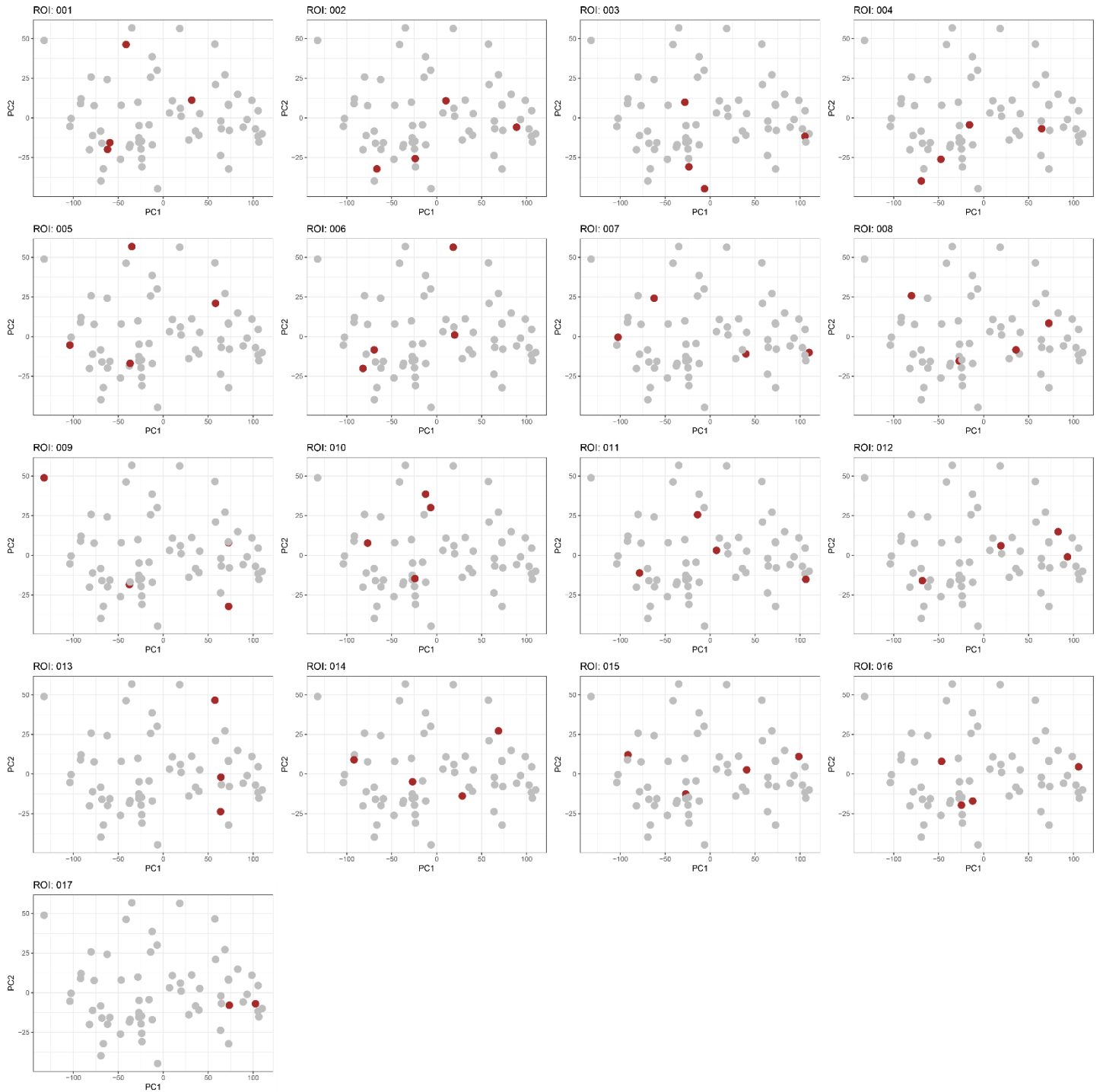
ID	# of genes in pathway	# of common genes	P	FDR
KEGG_SPLICEOSOME	127	89	7.12E-05	0.00265
KEGG_RIBOSOME	88	78	9.44E-13	1.76E-10
KEGG_PROTEASOME	46	38	2.86E-05	0.001328
KEGG_PARKINSONS_DISEASE	130	89	0.000265	0.007044
KEGG_OXIDATIVE_PHOSPHORYLATION	132	97	1.23E-06	0.000114
KEGG_LYSOSOME	121	85	8.96E-05	0.002778
KEGG_HUNTINGTONS_DISEASE	182	127	3.21E-06	0.000199
KEGG_ALZHEIMERS_DISEASE	166	110	0.000397	0.009239
GOMF_TRANSLATION_REGULATOR_ACTIVITY	141	98	5.30E-05	0.013156
GOMF_TRANSLATION_INITIATION_FACTOR_ACTIVITY	51	41	4.83E-05	0.013156
GOMF_TRANSLATION_FACTOR_ACTIVITY_RNA_BINDING	85	64	2.15E-05	0.010501
GOMF_TRANSCRIPTION_COREGULATOR_ACTIVITY	495	312	4.29E-06	0.00373
GOMF_TRANSCRIPTION_COACTIVATOR_ACTIVITY	266	174	3.02E-05	0.010501
GOMF_TAU_PROTEIN_BINDING	43	36	2.61E-05	0.010501
GOMF_STRUCTURAL_CONSTITUENT_OF_RIBOSOME	168	141	2.95E-17	5.12E-14
GOMF_NUCLEOSOME_BINDING	67	51	8.97E-05	0.017323
GOMF_MRNA_5_UTR_BINDING	27	24	8.89E-05	0.017323
GOMF_CADHERIN_BINDING	334	211	0.00012	0.020892
GOCC_VESICLE_COAT	52	40	0.000351	0.009533
GOCC_VACUOLAR_MEMBRANE	452	270	0.002561	0.046008
GOCC_TRANSLATION_PREINITIATION_COMPLEX	18	16	0.001555	0.033287
GOCC_TRANSFERASE_COMPLEX	790	477	1.70E-05	0.000814
GOCC_SPLICEOSOMAL_COMPLEX	192	128	9.26E-05	0.003049
GOCC_SMALL_RIBOSOMAL_SUBUNIT	69	59	1.30E-08	1.09E-06
GOCC_SITE_OF_POLARIZED_GROWTH	167	114	4.76E-05	0.001997
GOCC_SET1C_COMPASS_COMPLEX	15	15	7.63E-05	0.002646
GOCC_RIBOSOME	216	172	3.41E-16	1.71E-13
GOCC_RIBOSOMAL_SUBUNIT	178	151	2.67E-19	2.68E-16
GOCC_RIBONUCLEOPROTEIN_COMPLEX	729	472	6.45E-11	8.11E-09
GOCC_RESPIRASOME	101	71	0.000321	0.008971
GOCC_PROTON_TRANSPORTING_V_TYPE_ATPASE_COMPLEX	27	22	0.002163	0.040552
GOCC_PROTON_TRANSPORTING_TWO_SECTOR_ATPASE_COMPLEX	50	39	0.000248	0.007127
GOCC_PROTEASOME_CORE_COMPLEX	20	18	0.000538	0.013191
GOCC_PROTEASOME_COMPLEX	59	46	7.06E-05	0.002631
GOCC_POLYSOME	65	53	1.64E-06	9.69E-05
GOCC_POLYSOMAL_RIBOSOME	31	25	0.001415	0.030942

GOCC_PIGMENT_GRANULE	109	73	0.00232	0.042438
GOCC_PEPTIDASE_COMPLEX	111	75	0.0014	0.030942
GOCC_OXIDOREDUCTASE_COMPLEX	120	85	5.55E-05	0.002234
GOCC_ORGANELLE_INNER_MEMBRANE	551	376	1.83E-13	4.60E-11
GOCC_ORGANELLAR_RIBOSOME	81	73	7.12E-13	1.19E-10
GOCC_NURD_COMPLEX	14	13	0.001916	0.037801
GOCC_NUCLEAR_PROTEIN_CONTAINING_COMPLEX	1250	721	0.000476	0.012291
GOCC_NEURON_PROJECTION_CYTOPLASM	89	65	9.40E-05	0.003049
GOCC_NADH_DEHYDROGENASE_COMPLEX	49	39	0.000112	0.003523
GOCC_MLL3_4_COMPLEX	14	13	0.001916	0.037801
GOCC_MITOTIC_SPINDLE	159	103	0.001913	0.037801
GOCC_MITOCHONDRION	1648	964	2.60E-06	0.000138
GOCC_MITOCHONDRIAL_SMALL_RIBOSOMAL_SUBUNIT	26	25	1.73E-06	9.69E-05
GOCC_MITOCHONDRIAL_PROTEIN_CONTAINING_COMPLEX	281	213	2.56E-15	8.58E-13
GOCC_MITOCHONDRIAL_MATRIX	473	302	1.22E-06	7.66E-05
GOCC_MITOCHONDRIAL_LARGE_RIBOSOMAL_SUBUNIT	54	47	1.28E-07	9.88E-06
GOCC_MITOCHONDRIAL_ENVELOPE	783	501	2.35E-10	2.62E-08
GOCC_METHYLTRANSFERASE_COMPLEX	92	66	0.000202	0.005967
GOCC_MEMBRANE_COAT	84	59	0.001036	0.023697
GOCC_LYSOSOMAL_LUMEN	97	66	0.002014	0.038968
GOCC_LARGE_RIBOSOMAL_SUBUNIT	112	94	5.94E-12	8.53E-10
GOCC_INTRACELLULAR_PROTEIN_CONTAINING_COMPLEX	741	462	1.53E-07	1.10E-05
GOCC_INNER_MITOCHONDRIAL_MEMBRANE_PROTEIN_COMPLEX	155	112	7.96E-07	5.34E-05
GOCC_HISTONE_METHYLTRANSFERASE_COMPLEX	62	49	2.11E-05	0.000967
GOCC_HISTONE_DEACETYLASE_COMPLEX	72	55	4.01E-05	0.001753
GOCC_GOLGI_ASSOCIATED_VESICLE	84	58	0.002177	0.040552
GOCC_ENVELOPE	1237	755	4.07E-09	4.10E-07
GOCC_ENDOPLASMIC_RETICULUM_PROTEIN_CONTAINING_COMPLEX	125	85	0.000508	0.012781
GOCC_ENDOPEPTIDASE_COMPLEX	79	56	0.000969	0.022663
GOCC_CYTOSOLIC_SMALL_RIBOSOMAL_SUBUNIT	43	34	0.000392	0.010372
GOCC_CYTOSOLIC_RIBOSOME	102	82	8.47E-09	7.75E-07
GOCC_CYTOSOLIC_LARGE_RIBOSOMAL_SUBUNIT	58	47	8.93E-06	0.000449
GOCC_CYTOPLASMIC_STRESS_GRANULE	79	59	6.75E-05	0.002613
GOCC_CLATHRIN_COAT_OF_COATED_PIT	14	13	0.001916	0.037801
GOCC_CATALYTIC_STEP_2_SPLICEOSOME	87	64	7.38E-05	0.002646
GOCC_CATALYTIC_COMPLEX	1430	889	4.22E-13	8.49E-11
GOCC_AXON_CYTOPLASM	62	47	0.000201	0.005967
GOCC_ATPASE_COMPLEX	88	62	0.000686	0.016422
GOBP_TRANSPORT_ALONG_MICROTUBULE	156	105	0.000219	0.03995

GOBP_TRANSLATIONAL_INITIATION	120	84	0.00012	0.026113
GOBP_TRANSCRIPTION_INITIATION_FROM_RNA_POLYMERASE_II_PROMOTER	80	58	0.000306	0.048009
GOBP_RNA_SPLICING	434	267	0.000229	0.040831
GOBP_RNA_POLYADENYLATION	48	39	4.70E-05	0.013852
GOBP_RIBOSOMAL_LARGE_SUBUNIT_BIOGENESIS	72	53	0.000295	0.048009
GOBP_RESPIRATORY_ELECTRON_TRANSPORT_CHAIN	113	79	0.000202	0.038622
GOBP_REGULATION_OF_RNA_SPLICING	153	114	4.08E-08	0.000104
GOBP_REGULATION_OF_PROTEIN_CATABOLIC_PROCESS	395	250	2.46E-05	0.008829
GOBP_REGULATION_OF_PROTEASOMAL_PROTEIN_CATABOLIC_PROCESS	190	128	4.45E-05	0.01363
GOBP_REGULATION_OF_MRNA_SPLICING_VIA_SPLICEOSOME	103	77	5.13E-06	0.004159
GOBP_REGULATION_OF_MRNA_PROCESSING	139	107	4.91E-09	1.88E-05
GOBP_REGULATION_OF_MRNA_METABOLIC_PROCESS	293	199	1.59E-07	0.000243
GOBP_REGULATION_OF_MRNA_3_END_PROCESSING	28	24	0.000307	0.048009
GOBP_REGULATION_OF_MICROTUBULE_POLYMERIZATION_OR_DEPOLYMERIZATION	88	63	0.000307	0.048009
GOBP_REGULATION_OF_MACROAUTOPHAGY	158	110	1.68E-05	0.008063
GOBP_REGULATION_OF_DNA_TEMPLATED_TRANSCRIPTION_ELONGATION	57	44	0.000154	0.031946
GOBP_REGULATION_OF_CELLULAR_PROTEIN_CATABOLIC_PROCESS	258	169	3.48E-05	0.011596
GOBP_REGULATION_OF_CATABOLIC_PROCESS	980	596	3.93E-07	0.00043
GOBP_PROTEIN_LOCALIZATION_TO_ORGANELLE	872	522	2.54E-05	0.008829
GOBP_PROTEIN_CATABOLIC_PROCESS	977	582	1.92E-05	0.008222
GOBP_PROTEASOME_MEDIATED_UBIQUITIN_DEPENDENT_PROTEIN_CATABOLIC_PROCESS	413	261	1.93E-05	0.008222
GOBP_PROTEASOMAL_PROTEIN_CATABOLIC_PROCESS	494	319	1.25E-07	0.000239
GOBP_PROCESS_UTILIZING_AUTOPHAGIC_MECHANISM	543	333	5.90E-05	0.014605
GOBP_POSITIVE_REGULATION_OF_MRNA_PROCESSING	32	27	0.000217	0.03995
GOBP_PEPTIDE_METABOLIC_PROCESS	908	533	0.000321	0.049163
GOBP_PEPTIDE_BIOSYNTHETIC_PROCESS	740	448	2.12E-05	0.008558
GOBP_ORGANELLE_TRANSPORT_ALONG_MICROTUBULE	85	63	5.73E-05	0.014605
GOBP_MRNA_PROCESSING	496	306	6.17E-05	0.014764
GOBP_MRNA_METABOLIC_PROCESS	725	433	0.000163	0.03264
GOBP_MRNA_3_END_PROCESSING	63	50	1.40E-05	0.007167
GOBP_MODIFICATION_DEPENDENT_MACROMOLECULE_CATABOLIC_PROCESS	666	408	1.04E-05	0.006006
GOBP_MITOCHONDRION_LOCALIZATION	50	39	0.000248	0.043154
GOBP_MITOCHONDRIAL_ELECTRON_TRANSPORT_NADH_TO_UBIQUINONE	51	40	0.000166	0.03264
GOBP_MACROMOLECULE_CATABOLIC_PROCESS	1331	782	1.10E-05	0.006006
GOBP_MACROAUTOPHAGY	310	197	0.000123	0.026113
GOBP_INTRACELLULAR_TRANSPORT	1546	915	3.32E-07	0.000423
GOBP_INTRACELLULAR_PROTEIN_TRANSPORT	849	505	8.36E-05	0.018819

GOBP_HISTONE_MODIFICATION	498	303	0.000274	0.0466
GOBP_ESTABLISHMENT_OF_PROTEIN_LOCALIZATION	1652	957	2.31E-05	0.008829
GOBP_DNA_TEMPLATED_TRANSCRIPTION_ELONGATION	83	62	4.39E-05	0.01363
GOBP_CYTOPLASMIC_TRANSLATION	148	127	2.65E-17	2.03E-13
GOBP_CELLULAR_RESPIRATION	231	156	5.57E-06	0.004159
GOBP_CELLULAR_PROTEIN_CATABOLIC_PROCESS	819	500	1.87E-06	0.001795
GOBP_CELLULAR_MACROMOLECULE_LOCALIZATION	1683	980	5.97E-06	0.004159
GOBP_AXONAL_TRANSPORT	65	50	6.50E-05	0.015091
GOBP_AXO_DENDRITIC_TRANSPORT	77	58	5.09E-05	0.014449
GOBP_ATP_METABOLIC_PROCESS	273	177	5.48E-05	0.014605
GOBP_AMIDE_BIOSYNTHETIC_PROCESS	870	518	5.91E-05	0.014605
GOBP_AEROBIC_RESPIRATION	187	129	6.88E-06	0.004393

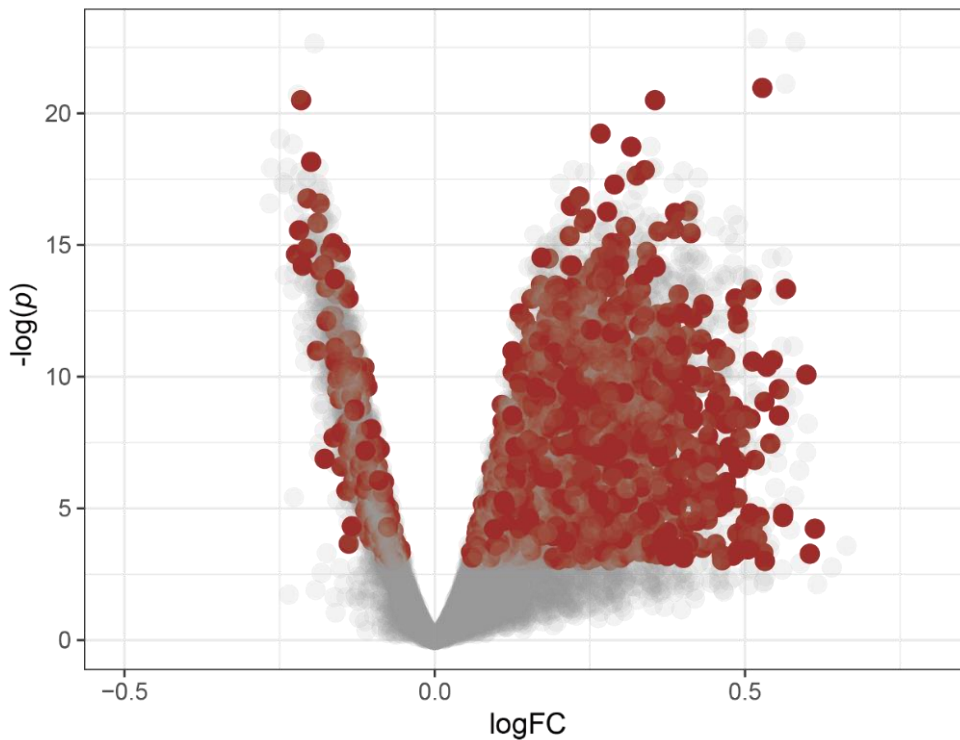
Supplementary Figure 1. Principal Component Analysis (PCA)-based analysis of the large-scale structure in the gene expression data according to ROI.



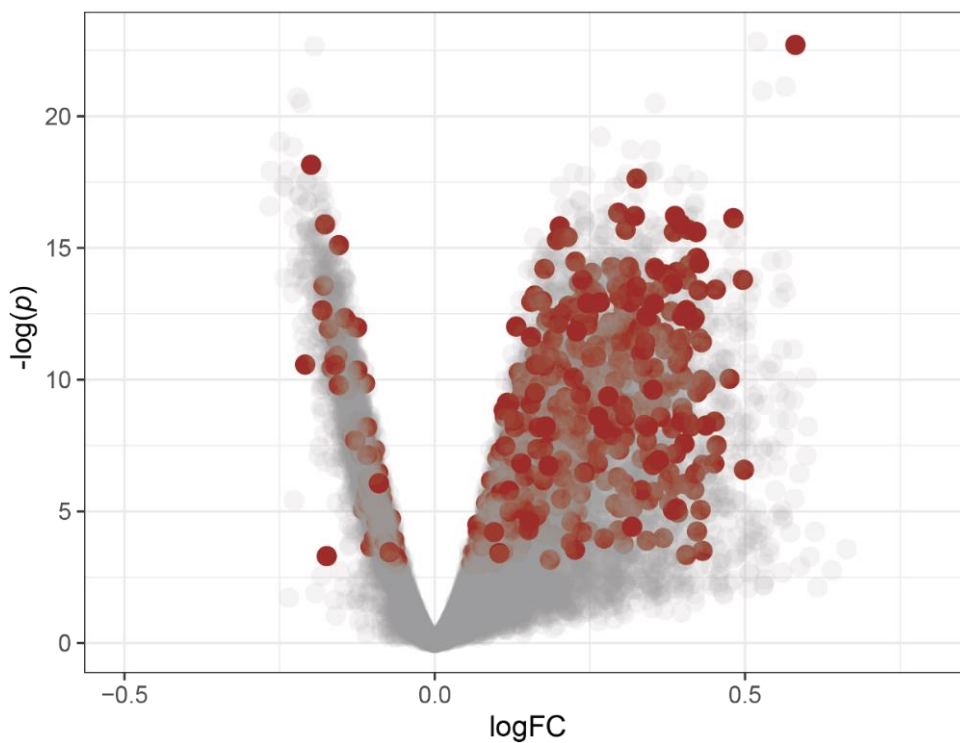
Supplementary Figure 2. Comparative analyses of AD-DEGs obtained from mice brain, human brain, and human blood.

Grey colored points indicate genes exhibiting AD-related signatures (i.e., FC values between AD and control and their p-values) obtained from AD mice (Spatial transcriptome). Brown colored points in the upper part of plots indicate DEGs in all three human brain transcriptomic datasets (GSE5281, GSE33000, and GSE48350). Brown colored points in the lower part of plots denote DEGs in all three human blood transcriptomic datasets (GSE63060, GSE63061, and ROSMAP).

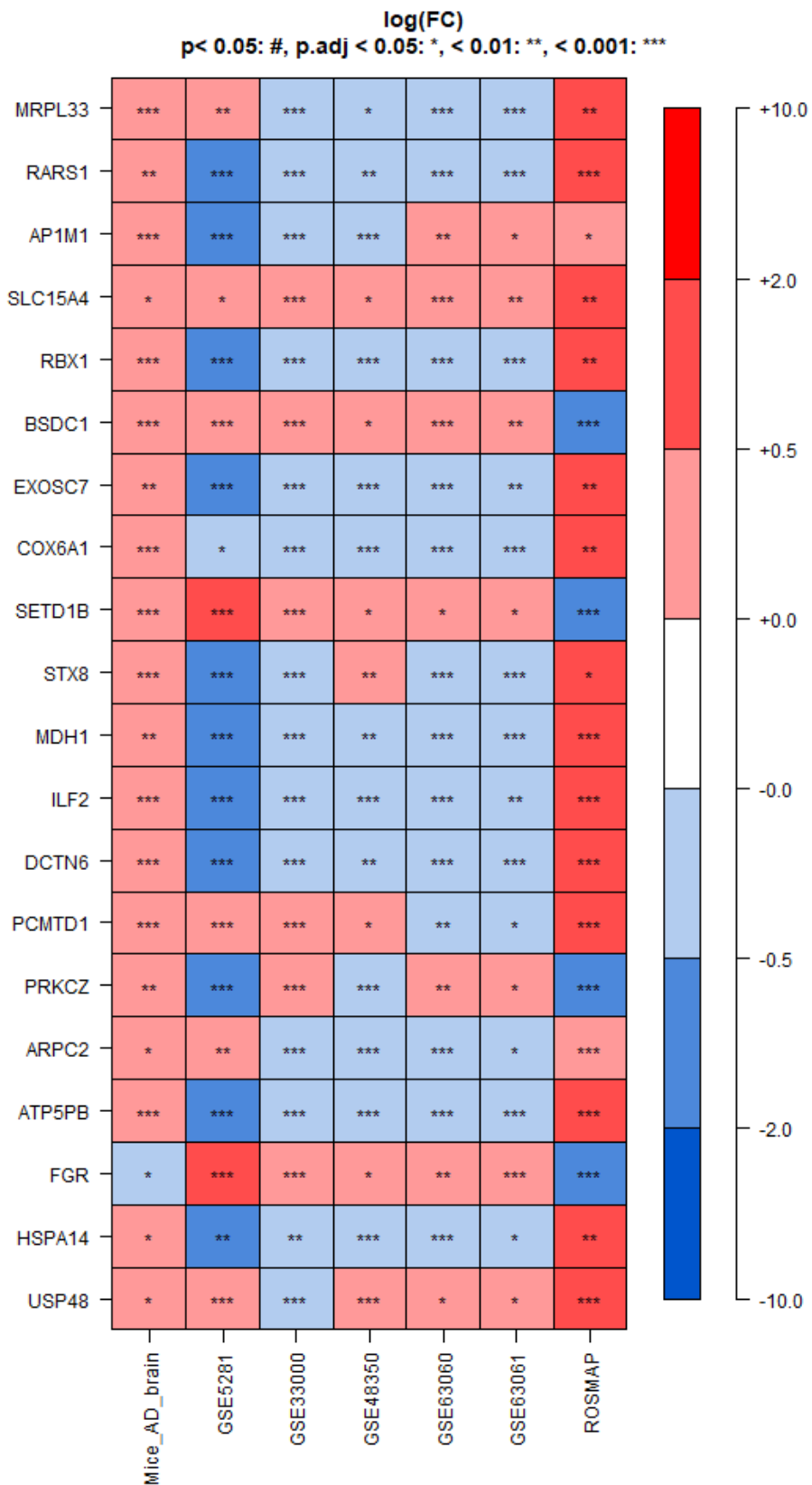
Mouse brain versus Human brain datasets (# of common DEGs = 1,937)



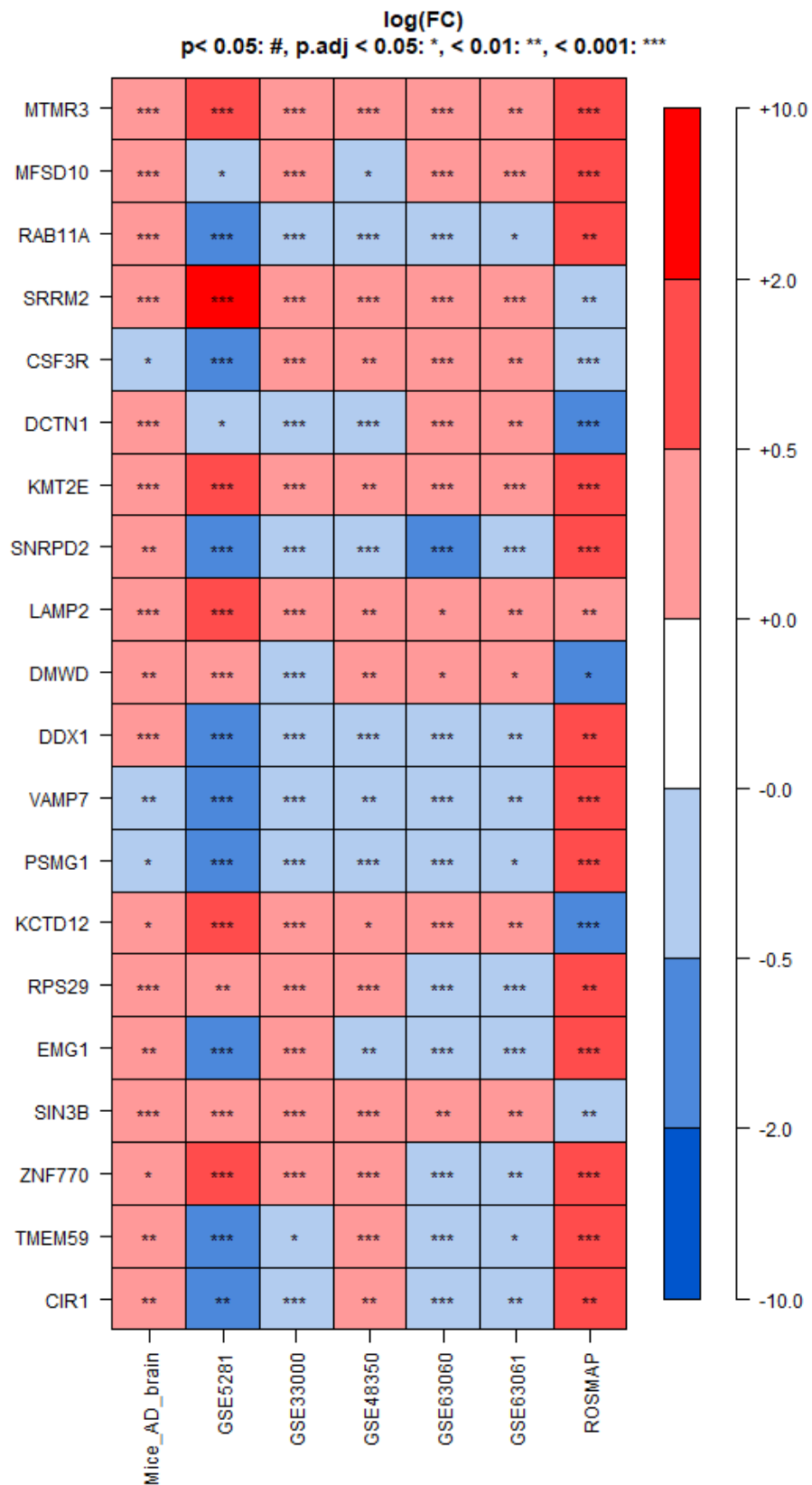
Mouse brain versus Human blood datasets (# of common DEGs = 697)



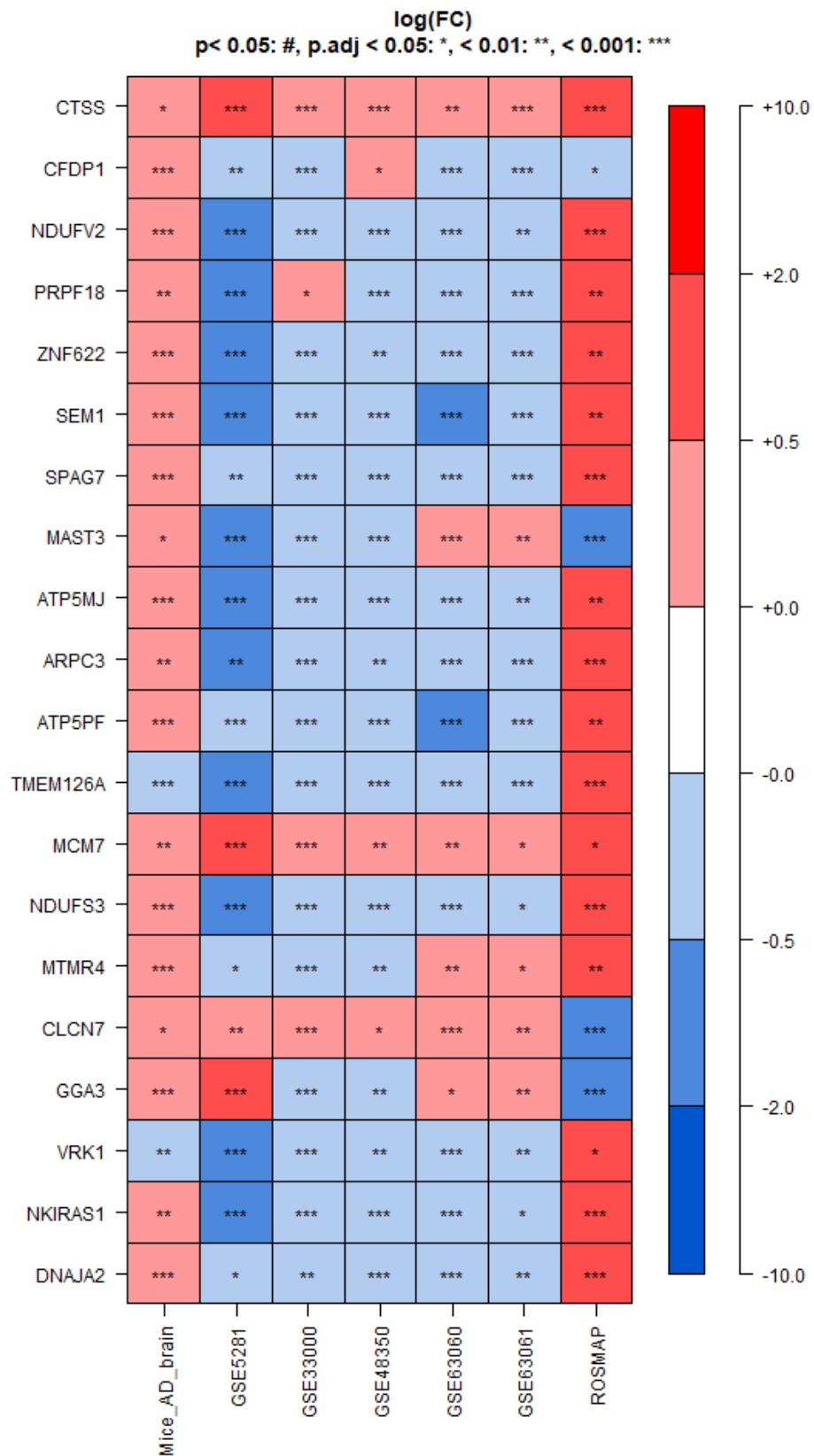
Supplementary Figure 3. Common AD-DEGs in mouse brain, human brain, and human blood. (*MRPL33*, *RARS1*, *AP1M1*, *SLC15A4*, *RBX1*, *BSDC1*, *EXOSC7*, *COX6A1*, *SETD1B*, *STX8*, *MDH1*, *ILF2*, *DCTN6*, *PCMTD1*, *PRKCZ*, *ARPC2*, *ATP5PB*, *FGR*, *HSPA14*, *USP48*). Asterisks indicate the level of significance in the correlations, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.



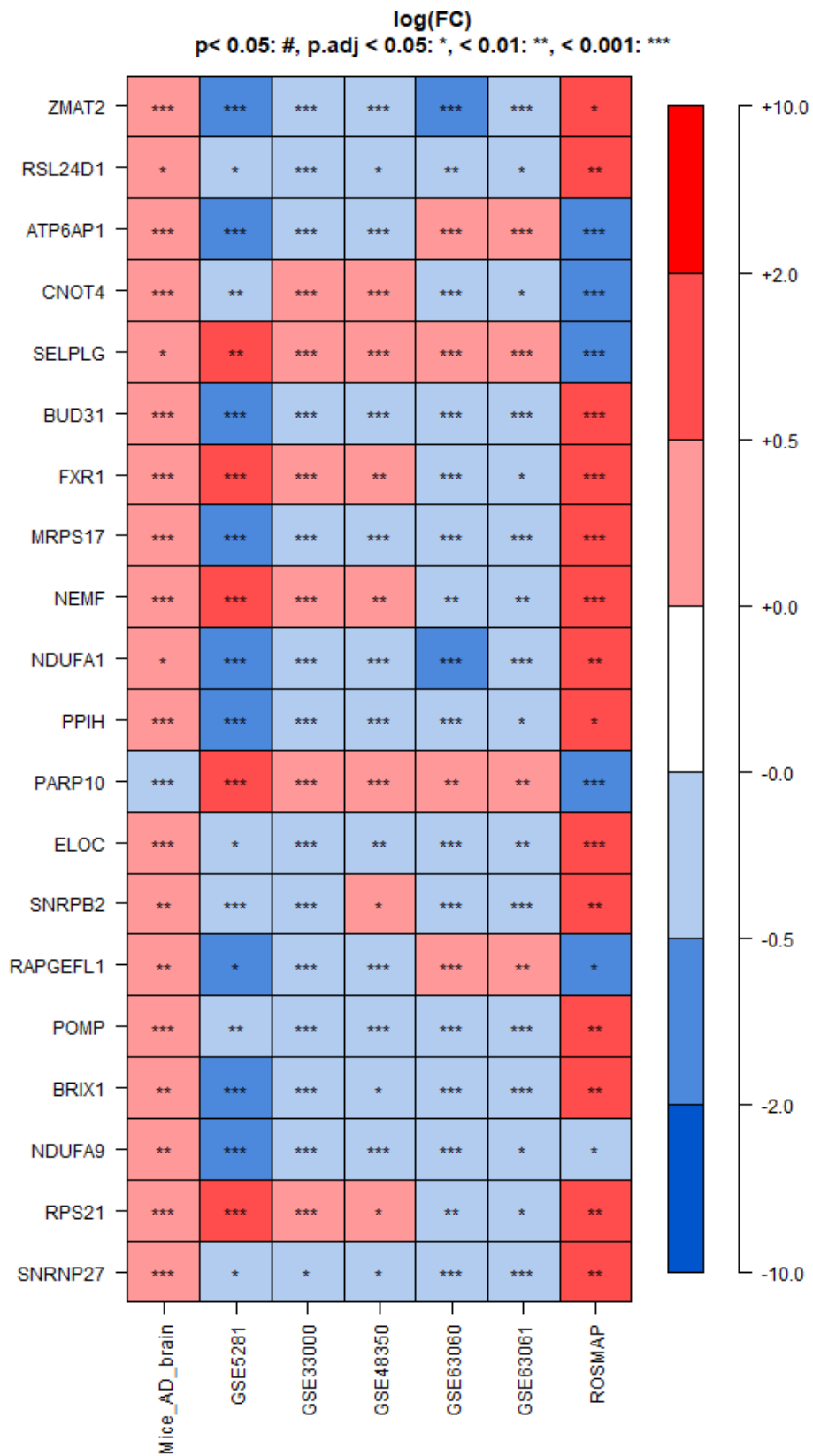
Supplementary Figure 3. Common AD-DEGs in mouse brain, human brain, and human blood, continued (*MTMR3*, *MFSD10*, *RAB11A*, *SRRM2*, *CSF3R*, *DCTN1*, *KMT2E*, *SNRPD2*, *LAMP2*, *DMWD*, *DDX1*, *VAMP7*, *PSMG1*, *KCTD12*, *RPS29*, *EMG1*, *SIN3B*, *ZNF770*, *TMEM59*, *CIR1*). Asterisks indicate the level of significance in the correlations, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.



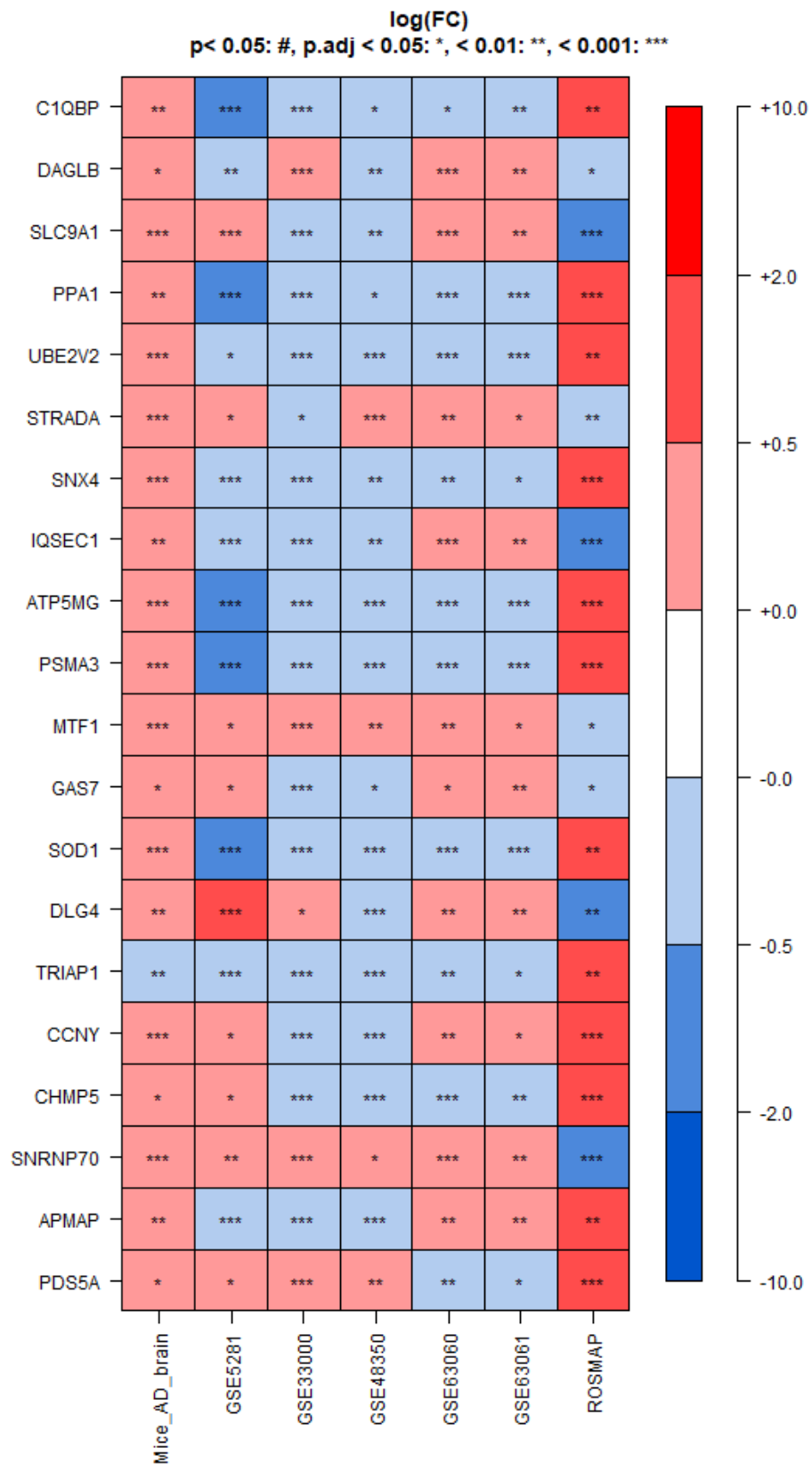
Supplementary Figure 3. Common AD-DEGs in mouse brain, human brain, and human blood, continued (*CTSS*, *CFDP1*, *NDUFV2*, *PRPF18*, *ZNF622*, *SEM1*, *SPAG7*, *MAST3*, *ATP5MJ*, *ARPC3*, *ATP5PF*, *TMEM126A*, *MCM7*, *NDUFS3*, *MTMR4*, *CLCN7*, *GGA3*, *VRK1*, *NKIRAS1*, *DNAJA2*). Asterisks indicate the level of significance in the correlations, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.



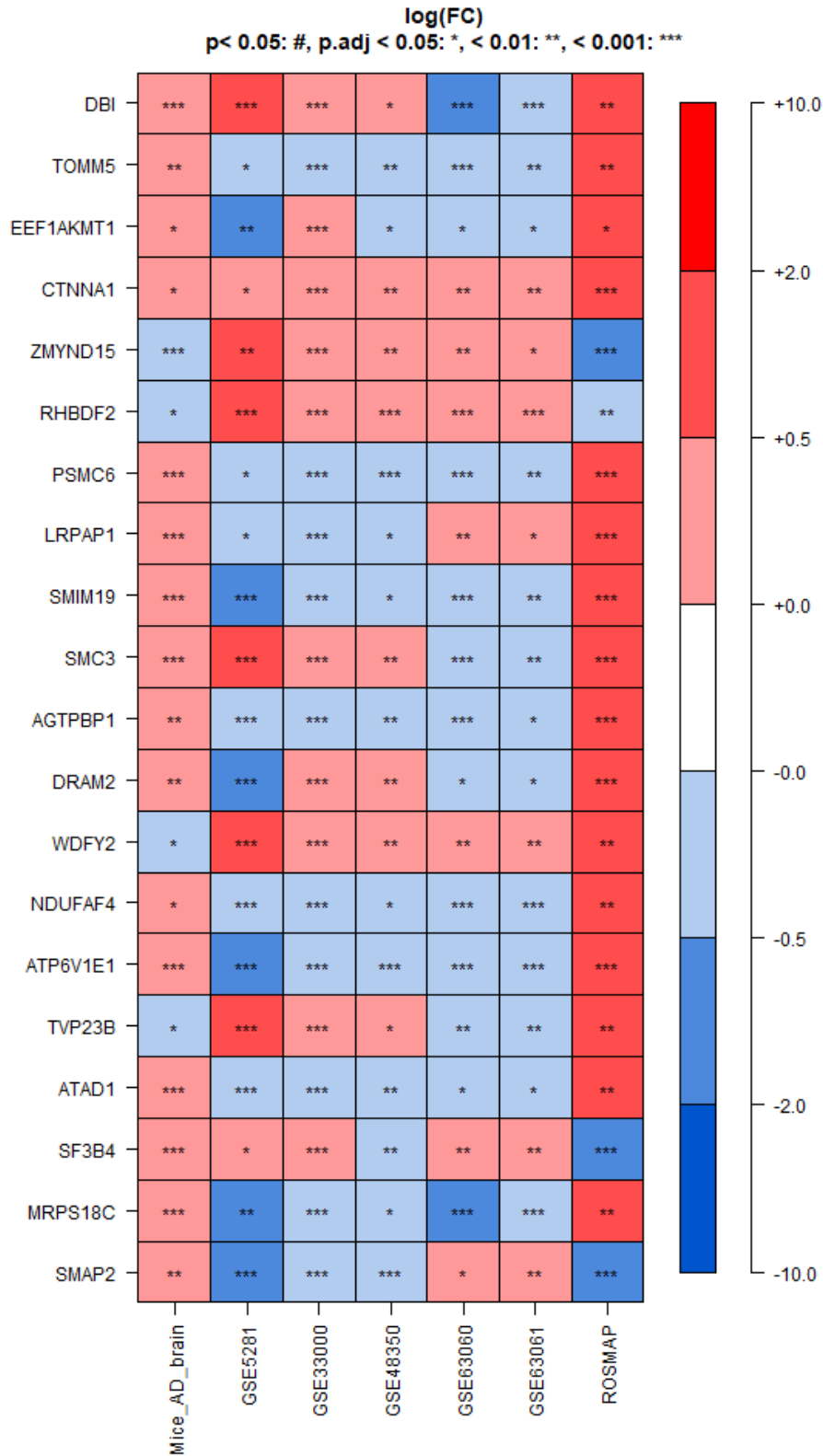
Supplementary Figure 3. Common AD-DEGs in mouse brain, human brain, and human blood, continued (*ZMAT2*, *RSL24D1*, *ATP6AP1*, *CNOT4*, *SELPLG*, *BUD31*, *FXR1*, *MRPS17*, *NEMF*, *NDUFA1*, *PPIH*, *PARP10*, *ELOC*, *SNRBP2*, *RAPGEFL1*, *POMP*, *BRX1*, *NDUFA9*, *RPS21*, *SNRNP27*). Asterisks indicate the level of significance in the correlations, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.



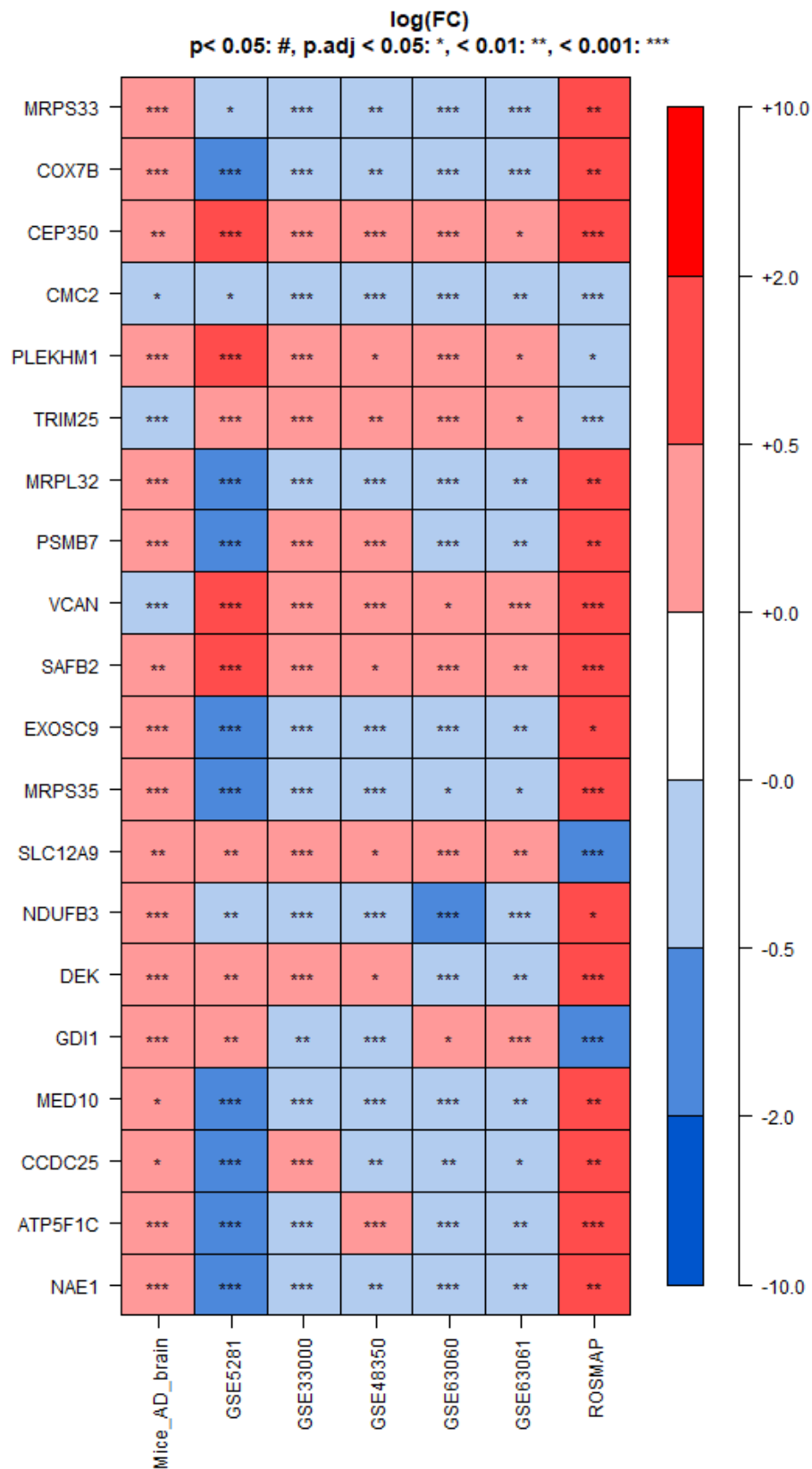
Supplementary Figure 3. Common AD-DEGs in mouse brain, human brain, and human blood, continued (*C1QBP*, *DAGLB*, *SLC9A1*, *PPA1*, *UBE2V2*, *STRADA*, *SNX4*, *IQSEC1*, *ATP5MG*, *PSMA3*, *MTF1*, *GAS7*, *SOD1*, *DLG4*, *TRIAP1*, *CCNY*, *CHMP5*, *SNRNP70*, *APMAP*, *PDS5A*). Asterisks indicate the level of significance in the correlations, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.



Supplementary Figure 3. Common AD-DEGs in mouse brain, human brain, and human blood, continued (*DBI*, *TOMM5*, *EEF1AKMT1*, *CTNNA1*, *ZMYND15*, *RHBDF2*, *PSMC6*, *LRPAP1*, *SMIM19*, *SMC3*, *AGTPBP1*, *DRAM2*, *WDFY2*, *NDUFAF4*, *ATP6V1E1*, *TVP23B*, *ATAD1*, *SF3B4*, *MRPS18C*, *SMAP2*). Asterisks indicate the level of significance in the correlations, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.



Supplementary Figure 3. Common AD-DEGs in mouse brain, human brain, and human blood, continued (*MRPS33*, *COX7B*, *CEP350*, *CMC2*, *PLEKHM1*, *TRIM25*, *MRPL32*, *PSMB7*, *VCAN*, *SAFB2*, *EXOSC9*, *MRPS35*, *SLC12A9*, *NDUFB3*, *DEK*, *GDI1*, *MED10*, *CCDC25*, *ATP5F1C*, *NAE1*). Asterisks indicate the level of significance in the correlations, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.



Supplementary Figure 3. Common AD-DEGs in mouse brain, human brain, and human blood, continued (*TSPOAP1*, *P2RX7*, *PAM16*, *PCBP2*, *HIGD1A*, *DPY30*, *AKIRIN2*, *HSBP1*, *PTBP1*, *DYNLT3*, *AP2A2*, *MRPL46*, *PLOD3*, *MMADHC*, *LASP1*, *NDUFS4*, *SF3B5*, *MRPS22*, *CAPNS1*, *BCKDK*). Asterisks indicate the level of significance in the correlations, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

