

## **Supplemental Information**

### **Cholesterol and matrisome pathways dysregulated in *APOE* $\epsilon$ 4 human astrocytes and microglia**

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<i>APOE</i> genotype	Gender	Disease status (CDR at biopsy)	Analysis assigned ID (Randomization)	GRS score	GRS – APOE score	HAPLO1 / HAPLO2	Ethnicity	Age of onset	Age at skin biopsy/ PBMC collection	Source of hiPSC reprogramming	Karyotype	PI HAT of fibroblast and hiPSC (GSA)
33	Female	Control (0)	ID1	0.01831	0.0191	hap.02/ hap.23	Caucasian	-	76	Fibroblasts	Normal	0.9999
33	Female	Control (0)	ID3	-0.00117	-0.00112	hap.09/ hap.09	Caucasian	-	81	Fibroblasts	Normal	1
33	Female	AD (0.5)	ID5	0.00692	0.00722	hap.oth er02/ha p.other 04	Caucasian	82	94	Fibroblasts	Normal	1
33	Female	AD (2)	ID4	0.0074	0.00772	hap.oth er01.ha p.08	Caucasian	78	81	Fibroblasts	Normal	0.9998
33	Male	Control (0)	ID2	-0.00045	-0.00046	hap.02/ hap.20	Caucasian	-	67	Fibroblasts	Normal	1
33	Male	AD (0.5)	ID6	0.01579	0.01647	hap.11/ hap.oth er05	Caucasian	-	87	Fibroblasts	Normal	0.9997
33	Male	Control (0)	ID7	0.0093	0.0097	NA.01/ hap.oth er06	Caucasian	-	83	PBMCs	Normal	1
44	Female	Control (0)	ID9	0.06670	0.01086	hap.oth er03/ha p.other 07	Caucasian	-	76	Fibroblasts	Normal	1
44	Female	AD (2)	ID8	0.05958	0.00343	hap.03/ NA.02	Caucasian	64	72	Fibroblasts	Normal	1
44	Female	AD (2)	ID12	0.06779	0.01203	hap.03/ NA.04	Caucasian	61	72	Fibroblasts	Normal	0.9999
44	Male	AD (0.5)	ID10	0.06078	0.00468	hap.03/ hap.03	Caucasian	77	80	Fibroblasts	Normal	1
44	Male	AD (0.5)	ID11	0.06366	0.00772	hap.17/ NA.03	Caucasian	83	80	Fibroblasts	Normal	1
44	Male	AD (3)	ID13	0.06251	0.00652	hap.17/ hap.17	Caucasian	71	78	Fibroblasts	Normal	0.9997

**Table S1 Genetic and clinical information of the hiPSC lines, Related to Figure 1.**

Abbreviations: *APOE*, apolipoprotein E; GRS, genetic risk score; AD, Alzheimer’s disease; PBMC, peripheral blood mononuclear cell; CDR, clinical dementia rating; HAPLO, *APOE* local haplotype against 1000G common haplotype; GSA, global screening array.

**Microglia: APOE 44 vs 33**

Enriched pathways	Diseases or Functions annotation	p-Value	Predicted Activation State	Activation z-score
Cholesterol biosynthesis	Synthesis of cholesterol	8.63E-42	Increased	2.216
	Metabolism of cholesterol	1.74E-26	Increased	2.216
	Steroid metabolism	3.91E-23	Increased	2.216
	Synthesis of terpenoid	4.54E-18	Increased	2.201
Lysosome	Accumulation of lipid	4.9E-17	Increased	2.805
	Accumulation of cholesterol	9.53E-10	Increased	2.765
	Catabolism of lipid	4.17E-16	Decreased	-2.764
	Cleavage of lipid	1.9E-09	Decreased	-3.364
HDL-mediated lipid transport	Efflux of cholesterol	1.87E-14	Decreased	-2.382
	Cholesterol transport	2.11E-16	Decreased	-2.163
	Removal of lipid	2.79E-14	Decreased	-2.109

Abbreviations: APOE, apolipoprotein E; HDL, high density lipoprotein

**Astrocytes: APOE 44 vs 33**

Enriched pathways	Diseases or Functions annotation	p-Value	Predicted Activation State	Activation z-score
Cholesterol biosynthesis	Synthesis of cholesterol	7.03E-37	Increased	2.216
	Metabolism of cholesterol	4.92E-20	Increased	2.216
	Steroid metabolism	6.43E-18	Increased	2.216
	Synthesis of terpenoid	3.02E-15	Increased	2.201

**Table S2 Ingenuity pathway z-score of enriched pathways from DEG analysis comparing APOE genotype in hiPSC-microglia and astrocytes, Related to Figure 2.**

### hiPSC-mixed cortical cultures (corrected): APOE 44 vs 33

Enriched pathways	Diseases or Functions annotation	p-Value	Predicted Activation State	Activation z-score
Matrisome associated	Chemotaxis	2.9E-31	Increased	5.729
	Chemotaxis of myeloid cells	1.45E-12	Increased	3.976
	Chemotaxis of phagocytes	1.88E-11	Increased	3.721
	Activation of phagocytes	1.41E-17	Increased	3.513
	Inflammatory response	5.39E-26	Increased	4.657
	Synthesis of lipid	4.38E-16	Increased	2.879
	Synthesis of eicosanoid	1.66E-11	Increased	2.397
Core matrisome	Cell movement	5.4E-09	Increased	2.667
	Migration of cells	1.3E-08	Increased	2.257

### AD brains including APOE 44 carriers: Severe vs Mild

Enriched pathways	Diseases or Functions annotation	p-Value	Predicted Activation State	Activation z-score
Matrisome associated	Cell movement of myeloid cells	1.77E-10	Increased	3.152
	Chemotaxis of myeloid cells	2.50E-08	Increased	3.055
	Recruitment of phagocytes	2.28E-10	Increased	2.953
	Cell movement of phagocytes	1.41E-08	Increased	2.918
	Chemotaxis of phagocytes	3.49E-07	Increased	2.73
	Recruitment of myeloid cells	1.15E-07	Increased	2.615
	Activation of cells	1.66E-13	Increased	3.46
	Inflammatory response	1.38E-10	Increased	3.098
	Immune response of cells	1.56E-08	Increased	2.975
	Synthesis of lipid	4.13E-08	Increased	3.285
	Synthesis of fatty acid	4.10E-06	Increased	2.926
	Synthesis of eicosanoid	1.88E-06	Increased	2.759
	Synthesis of prostaglandin	3.29E-06	Increased	2.6
	Synthesis of prostaglandin E2	1.07E-05	Increased	2.408
Synthesis of steroid	5.77E-06	Increased	1.547	
Matrisome	Cell movement of myeloid cells	7.5E-12	Increased	3.376
	Chemotaxis of myeloid cells	5.6E-07	Increased	3.214
	Cell movement of phagocytes	3.2E-10	Increased	3.172
	Recruitment of phagocytes	8E-10	Increased	2.99
	Chemotaxis of phagocytes	4.7E-06	Increased	2.907
	Recruitment of myeloid cells	1.9E-07	Increased	2.673
	Migration of phagocytes	3.5E-12	Increased	2.315
	Inflammatory response	3.1E-11	Increased	3.562
	Activation of cells	3E-11	Increased	3.557
	Immune response of cells	6E-08	Increased	2.719
	Activation of phagocytes	2.4E-07	Increased	2.36
	Synthesis of fatty acid	6E-06	Increased	3.107
	Synthesis of eicosanoid	7.6E-07	Increased	2.956

	Synthesis of prostaglandin	4.2E-06	Increased	2.277
Core matrisome	Cell movement	2.9E-05	Increased	2.378
	Migration of cells	0.00015	Increased	2.299
	Attachment of cells	1.6E-08	Increased	2.217

**Table S3 Ingenuity pathway z-score of enriched pathways from the DEG analysis comparing *APOE* 44 vs. *APOE* 33 in hiPSC-mixed cortical cultures and severe vs. mild dementia in AD brains including *APOE* 4 carriers, Related to Figure 2 and 4.**

Individual ID	Analysis assigned fibroblast ID	APOE genotype	Isogenic APOE hiPSC line ID	Transcriptome ID	Karyotype	PI HAT
Indiv1	ID8	33	TCW1E33-1C6	TCW1_33A	Normal	0.9999
		33	TCW1E33-1C8	TCW1_33B	Normal	0.9999
		33	TCW1E33-1F1	TCW1_33C	Normal	1
		44	TCW1E44-2C2	TCW1_44a	Normal	1
		44	TCW1E44-2E3	TCW1_44b	Normal	1
		44	TCW1E44-1D1	TCW1_44c	Normal	0.9999
		KO	TCW1EKO-1A12	TCW1_KO1	Normal	1
		KO	TCW1EKO-1B2	TCW1_KO2	Normal	1
		KO	TCW1EKO-1B12	TCW1_KO3	Normal	1
Indiv2	ID10	33	TCW2E33-2E3	TCW2_33A	Normal	1
		33	TCW2E33-3A5	TCW2_33B	Normal	0.9999
		33	TCW2E33-3D11	TCW2_33C	Normal	0.9999
		44	TCW2E44-4B1	TCW2_44a	Normal	1
		44	TCW2E44-4B4	TCW2_44b	Normal	1
		44	TCW2E44-4B12	TCW2_44c	Normal	1
		KO	TCW2EKO-3A5	TCW2_KO1	Normal	1
		KO	TCW2EKO-3A12	TCW2_KO2	Normal	1
		KO	TCW2EKO-3D10	TCW2_KO3	Normal	1
Indiv3	ID11	33	TCW3E33-RC1B	RC1B_33	Normal	0.9953
		33	TCW3E33-RC1H	RC1H_33	Normal	1
		33	TCW3E33-RC1I	RC1I_33	Normal	0.9968
		44	TCW3E44-CD1D	CD1D_44	Normal	1
		44	TCW3E44-CD1D_2	CD1D_2_44	Normal	1
		44	TCW3E44-CD1F	CD1F_44	Normal	1
Indiv4	ID1	33	TCW4E33-MC2C	MC2C_33	Normal	1
		33	TCW4E33-MC2E	MC2E_33	Normal	1
		33	TCW4E33-MC2F	MC2F_33	Normal	0.9998
		44	TCW4E44-RC2C	RC2C_44	Normal	1
		44	TCW4E44-RC2G	RC2G_44	Normal	1
		44	TCW4E44-RC2I	RC2I_44	Normal	1

**Table S4 Genetic identity-by-descent estimation of genome-edited isogenic APOE hiPSC lines to original source fibroblasts, Related to Figures 3, 6-7.**

haplotype_sequence	TCW_ID	TCW_Hap	1000G haplotype name	1000G Frequency
GCGAATACTCAGTTG	Fibroblast_APOE44_ID.8_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Fibroblast_APOE44_ID.8_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Population_APOE44_ID.8_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Population_APOE44_ID.8_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOE33_TCW1E33-1C6_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOE33_TCW1E33-1C6_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOE33_TCW1E33-1C8_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOE33_TCW1E33-1C8_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOE33_TCW1E33-1F1_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOE33_TCW1E33-1F1_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOE44_TCW1E44-2C2_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOE44_TCW1E44-2C2_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOE44_TCW1E44-2E3_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOE44_TCW1E44-2E3_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOE44_TCW1E44-1D1_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOE44_TCW1E44-1D1_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOEKO_TCW1EKO-1A12_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOEKO_TCW1EKO-1A12_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOEKO_TCW1EKO-1B2_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOEKO_TCW1EKO-1B2_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Isogenic_APOEKO_TCW1EKO-1B12_hap1	HAPLO1	hap.03	34
ATAGAGACTCAGCTA	Isogenic_APOEKO_TCW1EKO-1B12_hap2	HAPLO2	NA.02	NA
GCGAATACTCAGTTG	Fibroblast_APOE44_ID.10_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Fibroblast_APOE44_ID.10_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Population_APOE44_ID.10_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Population_APOE44_ID.10_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE33_TCW2E33-2E3_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE33_TCW2E33-2E3_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE33_TCW2E33-3A5_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE33_TCW2E33-3A5_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE33_TCW2E33-3D11_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE33_TCW2E33-3D11_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE44_TCW2E44-4B1_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE44_TCW2E44-4B1_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE44_TCW2E44-4B4_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE44_TCW2E44-4B4_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE44_TCW2E44-4B12_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOE44_TCW2E44-4B12_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOEKO_TCW2EKO-3A5_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOEKO_TCW2EKO-3A5_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOEKO_TCW2EKO-3A12_hap1	HAPLO1	hap.03	34

GCGAATACTCAGTTG	Isogenic_APOEKO_TCW2EKO-3A12_hap2	HAPLO2	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOEKO_TCW2EKO-3D10_hap1	HAPLO1	hap.03	34
GCGAATACTCAGTTG	Isogenic_APOEKO_TCW2EKO-3D10_hap2	HAPLO2	hap.03	34
GCGAATACTCAGCGA	Fibroblast_APOE44_ID.11_hap1	HAPLO1	hap.17	12
GTGGATACTCAGCGA	Fibroblast_APOE44_ID.11_hap2	HAPLO2	NA.03	NA
GCGAATACTCAGCGA	Population_APOE44_ID.11_hap1	HAPLO1	hap.17	12
GTGGATACTCAGCGA	Population_APOE44_ID.11_hap2	HAPLO2	NA.03	NA
GCGAATACTCAGCGA	Isogenic_APOE33_TCW3E33-RC1B_hap1	HAPLO1	hap.17	12
GTGGATACTCAGCGA	Isogenic_APOE33_TCW3E33-RC1B_hap2	HAPLO2	NA.03	NA
GCGAATACTCAGCGA	Isogenic_APOE33_TCW3E33-RC1H_hap1	HAPLO1	hap.17	12
GTGGATACTCAGCGA	Isogenic_APOE33_TCW3E33-RC1H_hap2	HAPLO2	NA.03	NA
GCGAATACTCAGCGA	Isogenic_APOE33_TCW3E33-RC1I_hap1	HAPLO1	hap.17	12
GTGGATACTCAGCGA	Isogenic_APOE33_TCW3E33-RC1I_hap2	HAPLO2	NA.03	NA
GCGAATACTCAGCGA	Isogenic_APOE44_TCW3E44-CD1D_hap1	HAPLO1	hap.17	12
GTGGATACTCAGCGA	Isogenic_APOE44_TCW3E44-CD1D_hap2	HAPLO2	NA.03	NA
GCGAATACTCAGCGA	Isogenic_APOE44_TCW3E44-CD1F_hap1	HAPLO1	hap.17	12
GTGGATACTCAGCGA	Isogenic_APOE44_TCW3E44-CD1F_hap2	HAPLO2	NA.03	NA
GCGAAGGTGCGATTG	Fibroblast_APOE33_ID.1_hap1	HAPLO1	hap.02	47
GTAGAGGTGCGACGA	Fibroblast_APOE33_ID.1_hap2	HAPLO2	hap.23	10
GCGAAGGTGCGATTG	Population_APOE33_ID.1_hap1	HAPLO1	hap.02	47
GTAGAGGTGCGACGA	Population_APOE33_ID.1_hap2	HAPLO2	hap.23	10
GCGAAGGTGCGATTG	Isogenic_APOE33_TCW4E33-MC2C_hap1	HAPLO1	hap.02	47
GTAGAGGTGCGACGA	Isogenic_APOE33_TCW4E33-MC2C_hap2	HAPLO2	hap.23	10
GCGAAGGTGCGATTG	Isogenic_APOE33_TCW4E33-MC2E_hap1	HAPLO1	hap.02	47
GTAGAGGTGCGACGA	Isogenic_APOE33_TCW4E33-MC2E_hap2	HAPLO2	hap.23	10
GCGAAGGTGCGATTG	Isogenic_APOE33_TCW4E33-MC2F_hap1	HAPLO1	hap.02	47
GTAGAGGTGCGACGA	Isogenic_APOE33_TCW4E33-MC2F_hap2	HAPLO2	hap.23	10
GCGAAGGTGCGATTG	Isogenic_APOE44_TCW4E44-RC2C_hap1	HAPLO1	hap.02	47
GTAGAGGTGCGACGA	Isogenic_APOE44_TCW4E44-RC2C_hap2	HAPLO2	hap.23	10
GCGAAGGTGCGATTG	Isogenic_APOE44_TCW4E44-RC2G_hap1	HAPLO1	hap.02	47
GTAGAGGTGCGACGA	Isogenic_APOE44_TCW4E44-RC2G_hap2	HAPLO2	hap.23	10
GCGAAGGTGCGATTG	Isogenic_APOE44_TCW4E44-RC2I_hap1	HAPLO1	hap.02	47
GTAGAGGTGCGACGA	Isogenic_APOE44_TCW4E44-RC2I_hap2	HAPLO2	hap.23	10

**Table S5 APOE local haplotype sequences and frequency of TCW lines (fibroblasts, population iPSCs, isogenic iPSCs), Related to Figures 1 and 3.**

Abbreviations: TCW\_Hap, Haplotype definition of TCW lines; NA, not applicable. See Table S8 for a list and description of all APOE local haplotypes from the 1000G project. See Table S8 for the 1000G reference sequences.

<b>Brain banks</b>	<b>MSBB</b>				<b>ROSMAP</b>
Brain regions	PFC	STG	PHG	IFG	DLPFC
Number of <i>APOE</i> 44 AD	9	10	7	8	5
Number of <i>APOE</i> 33 AD	46	44	42	45	55
Number of <i>APOE</i> 33 Control	15	12	13	11	55
Age (years)	85.2±9.6	85.0±9.6	85.0±9.7	85.3±9.7	86.7±4.5
Male (%)	35.6	37.5	38.1	36.0	35.8
Number of CDR = 0	35	33	32	27	198
Number of CDR = 0.5	39	33	32	38	167
Number of CDR >= 1	187	174	151	157	246
Total	261	240	215	222	623

**Table S6 Demographics and disease status of the brain bank cohorts, Related to Figure 4.**

Abbreviations: *APOE*, apolipoprotein E; AD, Alzheimer's disease; MSBB, Mount Sinai Brain Bank; ROSMAP, the Religious Orders Study (ROS) and the Memory and Aging Project (MAP); PFC, prefrontal cortex, STG, superior temporal gyrus; PHG, parahippocampal gyrus; IFG, inferior frontal gyrus; DLPFC, dorsolateral prefrontal cortex; CDR, Clinical Dementia Rating.

Cell	Region	Comparison	p-value	FDR
mic	BA10	APOE 44 AD vs APOE 33 AD	0.272	0.612
mic	BA10	APOE 44 AD vs APOE 33 Control	0.223	0.582
mic	BA10	APOE 33 AD vs APOE 33 Control	0.586	0.823
mic	BA22	APOE 44 AD vs APOE 33 AD	0.049	0.330
mic	BA22	APOE 44 AD vs APOE 33 Control	0.018	0.221
mic	BA22	APOE 33 AD vs APOE 33 Control	0.306	0.612
mic	BA36	APOE 44 AD vs APOE 33 AD	0.604	0.823
mic	BA36	APOE 44 AD vs APOE 33 Control	0.033	0.288
mic	BA36	APOE 33 AD vs APOE 33 Control	0.013	0.199
mic	BA44	APOE 44 AD vs APOE 33 AD	0.198	0.566
mic	BA44	APOE 44 AD vs APOE 33 Control	0.116	0.439
mic	BA44	APOE 33 AD vs APOE 33 Control	0.393	0.674

Cell	Region	Comparison	p-value	FDR
neu	BA10	APOE 44 AD vs APOE 33 AD	0.944	0.973
neu	BA10	APOE 44 AD vs APOE 33 Control	0.265	0.612
neu	BA10	APOE 33 AD vs APOE 33 Control	0.219	0.582
neu	BA22	APOE 44 AD vs APOE 33 AD	0.814	0.921
neu	BA22	APOE 44 AD vs APOE 33 Control	0.160	0.483
neu	BA22	APOE 33 AD vs APOE 33 Control	0.041*	0.311
neu	BA36	APOE 44 AD vs APOE 33 AD	0.441	0.679
neu	BA36	APOE 44 AD vs APOE 33 Control	0.111	0.439
neu	BA36	APOE 33 AD vs APOE 33 Control	0.006*	0.148
neu	BA44	APOE 4 AD vs APOE 33 AD	0.441	0.679
neu	BA44	APOE 44 AD vs APOE 33 Control	0.957	0.973
neu	BA44	APOE 33 AD vs APOE 33 Control	0.644	0.829

Cell	Region	Comparison	p-value	FDR
ast	BA10	APOE 44 AD vs APOE 33 AD	0.694	0.852
ast	BA10	APOE 44 AD vs APOE 33 Control	0.288	0.612
ast	BA10	APOE 33 AD vs APOE 33 Control	0.422	0.679
ast	BA22	APOE 44 AD vs APOE 33 AD	0.088	0.438
ast	BA22	APOE44 AD vs APOE 33 Control	0.466	0.699
ast	BA22	APOE 33 AD vs APOE33 Control	0.696	0.852
ast	BA36	APOE 44 AD vs APOE 33 AD	0.026	0.260
ast	BA36	APOE 44 AD vs APOE 33 Control	0.347	0.632
ast	BA36	APOE 33 AD vs APOE 33 Control	0.093	0.438
ast	BA44	APOE 44 AD vs APOE 33 AD	0.121	0.439
ast	BA44	APOE 44 AD vs APOE 33 Control	0.161	0.483
ast	BA44	APOE 33 AD vs APOE 33 Control	0.417	0.679

Cell	Region	Comparison	p-value	FDR
end	BA10	APOE 44 AD vs APOE 33 AD	0.979	0.979
end	BA10	APOE 44 AD vs APOE 33 Control	0.378	0.667

end	BA10	<i>APOE</i> 33 AD vs <i>APOE</i> 33 Control	0.302	0.612
end	BA22	<i>APOE</i> 44 AD vs <i>APOE</i> 33 AD	0.900	0.948
end	BA22	<i>APOE</i> 44 AD vs <i>APOE</i> 33 Control	0.007	0.148
end	BA22	<i>APOE</i> 33 AD vs <i>APOE</i> 33 Control	0.003	0.148
end	BA36	<i>APOE</i> 44 AD vs <i>APOE</i> 33 AD	0.732	0.861
end	BA36	<i>APOE</i> 44 AD vs <i>APOE</i> 33 Control	0.347	0.632
end	BA36	<i>APOE</i> 33 AD vs <i>APOE</i> 33 Control	0.278	0.612
end	BA44	<i>APOE</i> 44 AD vs <i>APOE</i> 33 AD	0.145	0.483
end	BA44	<i>APOE</i> 44 AD vs <i>APOE</i> 33 Control	0.124	0.439
end	BA44	<i>APOE</i> 33 AD vs <i>APOE</i> 33 Control	0.649	0.829

  

Cell	Region	Comparison	p-value	FDR
oli	BA10	<i>APOE</i> 44 AD vs <i>APOE</i> 33 AD	0.852	0.929
oli	BA10	<i>APOE</i> 44 AD vs <i>APOE</i> 33 Control	0.532	0.779
oli	BA10	<i>APOE</i> 33 AD vs <i>APOE</i> 33 Control	0.618	0.825
oli	BA22	<i>APOE</i> 44 AD vs <i>APOE</i> 33 AD	0.339	0.632
oli	BA22	<i>APOE</i> 44 AD vs <i>APOE</i> 33 Control	0.598	0.823
oli	BA22	<i>APOE</i> 33 AD vs <i>APOE</i> 33 Control	0.233	0.582
oli	BA36	<i>APOE</i> 44 AD vs <i>APOE</i> 33 AD	0.094	0.438
oli	BA36	<i>APOE</i> 44 AD vs <i>APOE</i> 33 Control	0.069	0.415
oli	BA36	<i>APOE</i> 33 AD vs <i>APOE</i> 33 Control	0.720	0.861
oli	BA44	<i>APOE</i> 44 AD vs <i>APOE</i> 33 AD	0.882	0.945
oli	BA44	<i>APOE</i> 44 AD vs <i>APOE</i> 33 Control	0.847	0.929
oli	BA44	<i>APOE</i> 33 AD vs <i>APOE</i> 33 Control	0.749	0.865

**Table S7 Cell type proportion changes by *APOE* genotype or AD phenotype, Related to Figure 4.**

Abbreviations: BA, Brodmann Area, mic, microglia; neu, neurons; ast, astrocytes; end, endothelial cells; oli, oligodendrocytes.

<i>APOE</i> genotype	Sex	Dx	Ethnicity	Age of death, year	PMI, hour	Tangle Stage	Plaque Stage
33	Female	AD	Caucasian	89	4.08	Stage 6	Stage C
33	Female	AD	Other	90	6.58	Stage 6	Stage C
33	Male	AD	Caucasian	71	4	Stage 4	Stage B
33	Male	AD	Caucasian	76	3.75	Stage 6	Stage C
44	Female	AD	Caucasian	89	8.3	Stage 4	Stage B
44	Female	AD	Caucasian	89	3.67	Stage 5	Stage C
44	Male	AD	Caucasian	71	3.83	Stage 4	Stage C
44	Male	AD	Caucasian	71	5.62	Stage 4	Stage C
<i>APOE</i> genotype	Total subjects = Male+ Female			Average Age of death	Average PMI	Average Stage	
33	4 = 2 + 2			81.5	4.60	5.5	
44	4 = 2 + 2			80.0	5.35	4.3	

**Table S8 Phenotype of selected *APOE* AD individuals for post-mortem brain analysis, Related to Figure 6.**