Supplementary Material

Supplementary figure 1

Microglia morphology was scored in 40 μm thick sections stained with Iba1 as homeostatic, activated and dystrophic. Percent of homeostatic (a, e, i, m, q, u, y), activated (b, f, j, n, r, v, z) and dystrophic (c, g, k, o, s, w, aa) microglia in the indicated anatomical subregions of the hippocampal formation, with each open circle representing the average score for the indicated region/case. Light grey bars represent the mean and red error bars depict +/- standard error of mean. (d, h, l, p, t, x, bb) Stacked bar graph for anatomical subregions of the hippocampal formation with green bars representing homeostatic microglia, red bars representing activated microglia and black bars representing dystrophic microglia. 1-way ANOVA with Bonferroni posttest was used for statistical analysis. * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Supplementary figure 2

(a) Representative images of CD68 stained sections for hippocampus (upper row), frontal cortex (middle row) and visual cortex (lower row) for the respective experimental groups (listed above images). (b-d) Quantification of % area covered by CD68 staining for hippocampus (b), frontal cortex (c) and visual cortex (d). Each open circle represents one case per experimental group and red error bars depict +/- standard error of mean. (e-g) Linear correlation of % area covered by CD68 staining and % activated microglia for hippocampus (e; $r^2 = 0.2453$, $p=0.0001$), frontal cortex (f; $r^2 = 0.2297$, $p=0.0009$) and visual cortex (g; $r^2 = 0.1775$, $p=0.0014$). Each symbol represents one case. (h) % area covered by CD68 staining for No AD, High AD (represents combined data for High AD and High AD (Trem2) and PART cases in the hippocampus. Each open circle represents one case per experimental group and red error bars depict +/- standard error of mean. (i) % area covered by CD68 staining for No AD, High AD (represents combined data for High AD and High AD (Trem2) and Pathological aging cases in the frontal cortex. Each open circle represents one case per experimental group and red error bars depict +/- standard error of mean. 1-way ANOVA with Bonferroni posttest was used for statistical analysis. ** $p<0.01$.

Supplementary figure 3

(a)Representative overview (upper row) and high magnification (lower row) images of scanned images with annotated cortical regions (frontal cortex) of NAB228 stained slides representing different severity of Aβ-pathology following the commonly used 4-tier scoring system. (b)

Representative overview (upper row) and high magnification (lower row) images of scanned images with annotated cortical regions (frontal cortex) of NAB228 stained slides with representative image of software detected stained area in right images. (c) Representative overview (upper row) and high magnification (lower row) images of scanned images with annotated cortical regions (frontal cortex) of PHF1 stained slides with representative image of software assisted quantification of PHF1-postitive neuritic plaques.

Supplementary figure 4

(a) Graphical representation of average GeoMx quantification data as fold change in TREM2 over HighAD in mask1 (green bars), mask2 (red bars) and mask3 (yellow bars). Dotted red line indicated fold change of 1. (b) Graphical representation of average GeoMx quantification data as fold change in mask1 over masks2-3 in TREM2 (grey bars) and high AD (black bars).

Supplementary figure 5

Average GeoMx protein data normalized to housekeeper and area in high AD and TREM2 for MBP (a), Vcam (b), NMDAR (c), S100B (d) and Calbindin (e). Each red circle represents average data per mask per case. Black and white bars represent the mean for each group and error bars depict the S.E.M. Unpaired t-Test was used for statistical analysis ** $p<0.01$, *** $p<0.001$.

Supplementary figure 6

(a) Raw data counts for genes on nCounter neuropathology panel in dependence of postmortem interval. (b) Linear correlation between gene expression data on the nCounter neuropathology panels for FFPE tissue and corresponding frozen tissue for the same case and anatomical region. (c) Volcano plot of differentially expressed genes in TREM2 cases versus control in frontal cortex samples. Conventional qPCR analysis performed on RNA extracted from corresponding frozen tissue samples for the same case and anatomical region for KCNJ (d), TGFb1 (e) and P2RX7 (f). (g, left panel) Cell type score for microglia derived from the Nanostring nCounter sytem on the Neuropathology panel for High AD and No AD. Each symbol represents one case. (g, right panel) Corresponding histological analysis and representative images used for histological analysis of activated microglia. (h, left panel) Cell type score for neurons derived from the Nanostring nCounter sytem on the Neuropathology panel for High AD and No AD. Each symbol represents one case. (h, right panel) Representative image of

Western blots for synaptophysin (green) and GapDH (red) in No/Low AD, Int. AD and high AD with corresponding quantification. * $p < 0.05$.

Supplementary figure 7

Volcano plot of differentially expressed genes in high AD cases versus control cases in the nCounter neuropathology panel (a, c, e) and Neuroinflammation panel (b, d, e) for frontal cortex samples for hippocampus (a, b), frontal cortex (c, d) and visual cortex (e, f).

Supplementary figure 8

Volcano plot of differentially expressed genes in TREM2 cases versus control cases in the nCounter neuropathology panel (a, c, e) and Neuroinflammation panel (b, d, e) for frontal cortex samples for hippocampus (a, b), frontal cortex (c, d) and visual cortex (e, f).

Supplementary figure 9

Volcano plot of differentially expressed genes in TREM2 cases versus high AD cases in the nCounter neuropathology panel (a, c, e) and Neuroinflammation panel (b, d, e) for frontal cortex samples for hippocampus (a, b), frontal cortex (c, d) and visual cortex (e, f).

Supplementary table 1
Overview of cases used in study

	No AD	Low	Intermed.	High	High AD (TREM2 variant)*	PART	Path. Aging
N	12	14	6	17	17	4	12
Mean age	65.6	70.71	83.67	78.94	76.53	85	86.5
Gender (m/f)	5/7	8/6	3/3	8/9	8/9	1/3	6/6
ApoE 4	5(15)	4(14)	4(6)	15(18)	8(16)	0(2)	2(4)
Mean PMI	17	16	14.33	15.66	12.82	13.5	13.38

Supplementary table 2
Cases used for biochemical analysis

	Gender (m/f)	Mean Age	ApoE 3/3	ApoE 3/4	ApoE 4/4
High AD	3/3	81.33	1	4	1
TREM2	3/3	80	2	3	1

Supplementary table 3
Top 20 differentially expressed genes in TREM2 versus high AD in Hippocampus (Neuropathology panel)

	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	Linear fold change	Lower confidence limit (linear)	Upper confidence limit (linear)	P-value	BY.p.value	method	Gene.sets	probe.ID
SF3B2-mRNA	0.398	0.0867	0.228	0.568	1.32	1.17	1.48	0.000986	1	loglinear	Transcription and Splicing	NM_006842.2:2364
FAM126A-mRNA	-0.401	0.108	-0.612	-0.19	0.757	0.654	0.876	0.0039	1	loglinear	Growth Factor Signaling, Myelination	XM_006715799.2:4296
NELFA-mRNA	-0.324	0.1	-0.52	-0.128	0.799	0.697	0.915	0.00885	1	loglinear	Chromatin Modification	NM_005663.3:547
DGKB-mRNA	-0.231	0.0759	-0.38	-0.0826	0.852	0.768	0.944	0.0123	1	loglinear	Lipid Metabolism	NM_004080.1:680
CDK5RAP3-mRNA	-0.233	0.0806	-0.391	-0.0751	0.851	0.762	0.949	0.0161	1	loglinear	Disease Association, Unfolded Protein Response	NM_176096.2:1402
JUN-mRNA	-0.541	0.188	-0.909	-0.173	0.687	0.533	0.887	0.0164	1	lm.nb	Angiogenesis, Apoptosis, Disease Association, Growth Factor Signaling, Oxidative Stress, Transmitter Response and Reuptake, Trophic Factors	NM_002228.3:140
PLEKHO2-mRNA	-0.37	0.13	-0.625	-0.115	0.774	0.649	0.923	0.0173	1	lm.nb	Cytokines	NM_025201.4:2500
SNRPA-mRNA	-0.309	0.116	-0.535	-0.082	0.807	0.69	0.945	0.0235	1	lm.nb	Transcription and Splicing	NM_004596.3:456
ACAA1-mRNA	0.449	0.173	0.11	0.788	1.37	1.08	1.73	0.0267	1	lm.nb	Lipid Metabolism	NM_001130410.1:1090
ATM-mRNA	-0.425	0.165	-0.748	-0.102	0.745	0.595	0.931	0.0273	1	lm.nb	Apoptosis, Chromatin Modification, Disease Association, Growth Factor Signaling	NM_138292.3:1323
LSM2-mRNA	-0.449	0.175	-0.792	-0.106	0.733	0.577	0.929	0.0282	1	lm.nb	Transcription and Splicing	NM_021177.3:325
STX2-mRNA	-0.32	0.126	-0.567	-0.0724	0.801	0.675	0.951	0.0297	1	lm.nb	Neural Connectivity, Oxidative Stress, Transmitter Synthesis and Storage, Vesicle Trafficking	NM_194356.2:440
MAPK3-mRNA	-0.269	0.109	-0.482	-0.0556	0.83	0.716	0.962	0.033	1	lm.nb	Apoptosis, Chromatin Modification, Disease Association, Growth Factor Signaling, Transmitter Release, Transmitter Response and Reuptake, Trophic Factors	NM_001040056.1:580
PLA2G16-mRNA	-0.424	0.172	-0.761	-0.0859	0.746	0.59	0.942	0.0338	1	lm.nb	Growth Factor Signaling, Lipid Metabolism	NM_007069.3:847
PMP22-mRNA	-0.497	0.207	-0.902	-0.0926	0.708	0.535	0.938	0.0368	1	lm.nb	Myelination, Vesicle Trafficking	NM_000304.3:417
SIRT1-mRNA	-0.245	0.102	-0.445	-0.045	0.844	0.735	0.969	0.0372	1	loglinear	Angiogenesis, Carbohydrate Metabolism, Chromatin Modification, Disease Association, Oxidative Stress	NM_012238.4:840
PSMB9-mRNA	-0.402	0.168	-0.73	-0.073	0.757	0.603	0.951	0.0376	1	lm.nb	Activated Microglia, Disease Association, Unfolded Protein Response	NM_002800.4:455
ATP2B3-mRNA	0.423	0.188	0.054	0.791	1.34	1.04	1.73	0.0484	1	lm.nb	Transmitter Release, Transmitter Response and Reuptake	NM_001001344.2:1280
NTNG1-mRNA	1.11	0.495	0.139	2.08	2.16	1.1	4.22	0.0489	1	lm.nb	Disease Association, Growth Factor Signaling, Tissue Integrity	NM_014917.2:160
DDIT3-mRNA	-0.43	0.193	-0.808	-0.0525	0.742	0.571	0.964	0.0496	1	lm.nb	Apoptosis, Disease Association, Growth Factor Signaling, Oxidative Stress, Unfolded Protein Response	NM_004083.4:40

Supplementary table 4
Top 20 differentially expressed genes in TREM2 versus high AD in frontal cortex (Neuropathology panel)

	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	Linear fold change	Lower confidence limit (linear)	Upper confidence limit (linear)	P-value	BY.p.value	method	Gene.sets	probe.ID
KATNA1-mRNA	-0.356	0.0943	-0.541	-0.171	0.781	0.687	0.888	0.00436	1	Wald	Axon and Dendrite Structure, Neuronal Cytoskeleton	NM_001204076.1:406
LCLAT1-mRNA	-0.251	0.0694	-0.387	-0.115	0.84	0.765	0.923	0.00465	1	loglinear	Lipid Metabolism	NM_001002257.1:326
GAD2-mRNA	0.448	0.132	0.189	0.708	1.36	1.14	1.63	0.00693	1	lm.nb	Axon and Dendrite Structure, Neural Connectivity, Transmitter Release, Transmitter Synthesis and Storage, Vesicle Trafficking	NM_000818.2:1245
SIRT2-mRNA	-0.321	0.0955	-0.509	-0.134	0.8	0.703	0.911	0.00717	1	loglinear	Axon and Dendrite Structure, Chromatin Modification, Disease Association, Myelination, Oxidative Stress	NM_012237.3:610
CHRNB2-mRNA	0.5	0.15	0.207	0.794	1.41	1.15	1.73	0.0075	1	lm.nb	Neural Connectivity, Transmitter Release, Transmitter Response and Reuptake, Transmitter Synthesis and Storage, Vesicle Trafficking	NM_000748.2:3865
ATP13A2-mRNA	0.287	0.0905	0.109	0.464	1.22	1.08	1.38	0.01	1	loglinear	Oxidative Stress	NM_001141974.1:925
RHOA-mRNA	0.337	0.108	0.125	0.549	1.26	1.09	1.46	0.0109	1	lm.nb	Angiogenesis, Growth Factor Signaling, Transmitter Response and Reuptake, Trophic Factors	NM_001664.2:1230
DNM1L-mRNA	0.301	0.0993	0.106	0.495	1.23	1.08	1.41	0.0127	1	lm.nb	Activated Microglia, Neural Connectivity	NM_001278463.1:1396
ATP6V0E2-mRNA	0.431	0.144	0.148	0.715	1.35	1.11	1.64	0.0137	1	lm.nb	Transmitter Synthesis and Storage	NR_110612.1:2509
ATM-mRNA	-0.308	0.109	-0.521	-0.0947	0.808	0.697	0.936	0.0178	1	lm.nb	Apoptosis, Chromatin Modification, Disease Association, Growth Factor Signaling	NM_138292.3:1323
SPAST-mRNA	-0.241	0.0863	-0.41	-0.072	0.846	0.753	0.951	0.019	1	loglinear	Axon and Dendrite Structure	NM_014946.3:698
NEFH-mRNA	0.832	0.299	0.247	1.42	1.78	1.19	2.67	0.0192	1	lm.nb	Axon and Dendrite Structure, Disease Association, Neuronal Cytoskeleton, Oxidative Stress	NM_021076.3:1350
NELL2-mRNA	0.449	0.164	0.128	0.771	1.37	1.09	1.71	0.0209	1	lm.nb	Axon and Dendrite Structure	NM_006159.1:180
SF3B2-mRNA	0.303	0.113	0.0805	0.525	1.23	1.06	1.44	0.0235	1	lm.nb	Transcription and Splicing	NM_006842.2:2364
P2RX7-mRNA	-0.369	0.139	-0.641	-0.0962	0.775	0.641	0.935	0.0242	1	lm.nb	Disease Association, Neural Connectivity, Transmitter Release, Transmitter Response and Reuptake, Vesicle Trafficking	NM_002562.5:780
SH3TC2-mRNA	-0.322	0.123	-0.562	-0.0809	0.8	0.677	0.945	0.0256	1	lm.nb	Myelination	NM_024577.3:2178
AKT3-mRNA	-0.475	0.188	-0.843	-0.107	0.719	0.557	0.929	0.0299	1	lm.nb	Apoptosis, Carbohydrate Metabolism, Growth Factor Signaling, Transmitter Release, Transmitter Response and Reuptake, Trophic Factors	NM_005465.4:287
CDK5RAP3-mRNA	-0.242	0.0958	-0.43	-0.0545	0.845	0.742	0.963	0.03	1	lm.nb	Disease Association, Unfolded Protein Response	NM_176096.2:1402
JUN-mRNA	-0.378	0.152	-0.676	-0.0804	0.769	0.626	0.946	0.032	1	lm.nb	Angiogenesis, Apoptosis, Disease Association, Growth Factor Signaling, Oxidative Stress, Transmitter Response and Reuptake, Trophic Factors	NM_002228.3:140
GAA-mRNA	0.291	0.119	0.0566	0.524	1.22	1.04	1.44	0.0352	1	lm.nb	Activated Microglia, Autophagy	NM_000152.3:3166

Supplementary table 5
Top 20 differentially expressed genes in TREM2 versus high AD in visual cortex (Neuropathology panel)

	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	Linear fold change	Lower confidence limit (linear)	Upper confidence limit (linear)	P-value	BY.p.value	method	Gene.sets	probe.ID
PPP3CC-mRNA	0.296	0.0694	0.16	0.433	1.23	1.12	1.35	0.00163	1	loglinear	Disease Association, Growth Factor Signaling, Transmitter Release, Transmitter Response and Reuptake	NM_005605.4:1058
NRG1-mRNA	0.635	0.167	0.308	0.963	1.55	1.24	1.95	0.00335	1	lm.nb	Axon and Dendrite Structure, Growth Factor Signaling, Myelination, Neural Connectivity	NM_013959.2:1405
ATP6V0E2-mRNA	0.448	0.131	0.19	0.706	1.36	1.14	1.63	0.00667	1	lm.nb	Transmitter Synthesis and Storage	NR_110612.1:2509
DNM1L-mRNA	0.426	0.13	0.171	0.681	1.34	1.13	1.6	0.00832	1	lm.nb	Activated Microglia, Neural Connectivity	NM_001278463.1:1396
KATNA1-mRNA	-0.376	0.115	-0.602	-0.149	0.771	0.659	0.902	0.00995	1	Wald	Axon and Dendrite Structure, Neuronal Cytoskeleton	NM_001204076.1:406
NTNG1-mRNA	0.788	0.25	0.298	1.28	1.73	1.23	2.42	0.0103	1	lm.nb	Disease Association, Growth Factor Signaling, Tissue Integrity	NM_014917.2:160
PMP22-mRNA	-0.781	0.252	-1.28	-0.287	0.582	0.413	0.82	0.0113	1	lm.nb	Myelination, Vesicle Trafficking	NM_000304.3:417
PLA2G16-mRNA	-0.829	0.281	-1.38	-0.279	0.563	0.384	0.824	0.0145	1	lm.nb	Growth Factor Signaling, Lipid Metabolism	NM_007069.3:847
EFNA1-mRNA	-0.68	0.232	-1.14	-0.225	0.624	0.455	0.856	0.0151	1	lm.nb	Angiogenesis, Disease Association, Growth Factor Signaling, Tissue Integrity	NM_004428.2:650
CA2-mRNA	-0.596	0.204	-0.997	-0.196	0.662	0.501	0.873	0.0154	1	lm.nb	Axon and Dendrite Structure, Disease Association, Vesicle Trafficking	NM_000067.2:575
PRKCB-mRNA	0.462	0.16	0.149	0.775	1.38	1.11	1.71	0.016	1	lm.nb	Angiogenesis, Chromatin Modification, Growth Factor Signaling, Transmitter Release, Transmitter Response and Reuptake	NM_212535.1:1750
PLCL2-mRNA	0.386	0.139	0.114	0.658	1.31	1.08	1.58	0.0195	1	lm.nb	Activated Microglia, Vesicle Trafficking	NM_015184.5:2785
GRIN1-mRNA	0.679	0.247	0.195	1.16	1.6	1.14	2.24	0.0205	1	lm.nb	Axon and Dendrite Structure, Disease Association, Neural Connectivity, Transmitter Release, Transmitter Response and Reuptake, Vesicle Trafficking	NM_000832.5:1290
GRIN2A-mRNA	0.682	0.248	0.195	1.17	1.6	1.15	2.25	0.0206	1	lm.nb	Disease Association, Neural Connectivity, Transmitter Release, Transmitter Response and Reuptake, Transmitter Synthesis and Storage, Vesicle Trafficking	NM_000833.3:4497
SIRT2-mRNA	-0.467	0.173	-0.806	-0.128	0.724	0.572	0.915	0.0223	1	lm.nb	Axon and Dendrite Structure, Chromatin Modification, Disease Association, Myelination, Oxidative Stress	NM_012237.3:610
CNTNAP1-mRNA	0.422	0.157	0.116	0.729	1.34	1.08	1.66	0.0224	1	lm.nb	Axon and Dendrite Structure, Myelination, Tissue Integrity	NM_003632.2:4050
PTPRR-mRNA	0.365	0.136	0.0985	0.631	1.29	1.07	1.55	0.0229	1	lm.nb	Disease Association, Growth Factor Signaling	NM_001207015.1:642
GNAO1-mRNA	-0.372	0.139	-0.643	-0.0999	0.773	0.64	0.933	0.0231	1	lm.nb	Axon and Dendrite Structure, Oxidative Stress, Transmitter Release, Transmitter Response and Reuptake	NM_020988.2:1422
SF3B2-mRNA	0.268	0.101	0.0705	0.466	1.2	1.05	1.38	0.024	1	lm.nb	Transcription and Splicing	NM_006842.2:2364
CACNA1C-mRNA	0.622	0.237	0.157	1.09	1.54	1.12	2.12	0.0254	1	lm.nb	Disease Association, Growth Factor Signaling, Neural Connectivity, Transmitter Release, Transmitter Response and Reuptake	NM_000719.6:40

Supplementary table 6
Top 20 differentially expressed genes in TREM2 versus high AD in hippocampus (Neuroinflammation panel)

	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	Linear fold change	Lower confidence limit (linear)	Upper confidence limit (linear)	P-value	BY.p.value	method	Gene.sets	probe.ID
RB1CC1-mRNA	-0.366	0.115	-0.592	-0.139	0.776	0.663	0.908	0.00899	1	loglinear	Autophagy, Cellular Stress	NM_001083617.1:1860
P2RY12-mRNA	0.52	0.171	0.186	0.854	1.43	1.14	1.81	0.011	1	lm.nb	All DAM, Homeostatic Microglia, Microglia Function, Stage 1 DAM	NM_022788.3:230
CSF3R-mRNA	0.64	0.212	0.224	1.05	1.56	1.17	2.08	0.0117	1	lm.nb	Cytokine Signaling, Growth Factor Signaling	NM_000760.3:2066
ITGA7-mRNA	0.478	0.169	0.146	0.809	1.39	1.11	1.75	0.0165	1	lm.nb	Astrocyte Function, Growth Factor Signaling, Matrix Remodeling	NM_002206.1:1170
ITGAX-mRNA	0.741	0.263	0.225	1.26	1.67	1.17	2.39	0.0168	1	lm.nb	All DAM, Matrix Remodeling, Microglia Function, Stage 2 DAM	NM_000887.4:561
MAN2B1-mRNA	0.458	0.164	0.136	0.779	1.37	1.1	1.72	0.0175	1	lm.nb	Microglia Function	NM_001173498.1:380
ATG14-mRNA	0.297	0.109	0.0839	0.511	1.23	1.06	1.43	0.0196	1	loglinear	Autophagy, Cellular Stress	NM_014924.3:4520
CALR-mRNA	-0.406	0.151	-0.703	-0.109	0.755	0.614	0.927	0.0213	1	lm.nb	Adaptive Immune Response, Autophagy, Neurons and Neurotransmission	NM_004343.2:965
TNFSF4-mRNA	0.382	0.157	0.0745	0.689	1.3	1.05	1.61	0.0351	1	Wald	Cytokine Signaling, Inflammatory Signaling, NF-kB	NM_003326.2:545
FADD-mRNA	0.478	0.198	0.0903	0.866	1.39	1.06	1.82	0.0363	1	Wald	Apoptosis, Innate Immune Response	NM_003824.2:1560
FLT1-mRNA	-0.846	0.38	-1.59	-0.101	0.556	0.332	0.932	0.0479	1	lm.nb	Angiogenesis, Cytokine Signaling, Growth Factor Signaling, Microglia Function	NM_002019.4:530
IFNAR1-mRNA	-0.41	0.19	-0.783	-0.0381	0.752	0.581	0.974	0.0536	1	lm.nb	Cytokine Signaling, Growth Factor Signaling, Inflammatory Signaling, Innate Immune Response	NM_000629.2:782
VEGFA-mRNA	-0.999	0.462	-1.91	-0.0926	0.5	0.267	0.938	0.0537	1	lm.nb	Angiogenesis, Cellular Stress, Cytokine Signaling, Growth Factor Signaling, Microglia Function	NM_001025366.1:1325
TLR2-mRNA	0.431	0.2	0.0397	0.823	1.35	1.03	1.77	0.0538	1	lm.nb	Growth Factor Signaling, Innate Immune Response, Microglia Function	NM_003264.3:2402
DAPK1-mRNA	0.292	0.136	0.0262	0.559	1.22	1.02	1.47	0.0544	1	lm.nb	Apoptosis, Autophagy	NM_001288729.1:1810
PTEN-mRNA	-0.193	0.0914	-0.372	-0.0139	0.875	0.773	0.99	0.0584	1	loglinear	Adaptive Immune Response, Autophagy, DNA Damage, Growth Factor Signaling, Lipid Metabolism	NM_000314.3:1675
CDKN1C-mRNA	0.462	0.225	0.0209	0.903	1.38	1.01	1.87	0.0647	1	lm.nb	Cell Cycle, DNA Damage	NM_001122631.1:1102
MAG-mRNA	0.64	0.322	0.00945	1.27	1.56	1.01	2.41	0.0721	1	lm.nb	Growth Factor Signaling, Matrix Remodeling, Oligodendrocyte Function	NM_001199216.1:2250
RPL28-mRNA	-0.354	0.181	-0.709	0.00141	0.782	0.612	1	0.0768	1	lm.nb	Microglia Function	NM_000991.3:70
IFITM2-mRNA	-0.557	0.285	-1.12	0.00222	0.68	0.461	1	0.0768	1	lm.nb	Adaptive Immune Response, Inflammatory Signaling	NM_006435.2:390

Supplementary table 7

Top 20 differentially expressed genes in TREM2 versus high AD in frontal cortex (Neuroinflammation panel)

	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	Linear fold change	Lower confidence limit (linear)	Upper confidence limit (linear)	P-value	BY.p.value	method	Gene.sets	probe.ID
COTL1-mRNA	0.338	0.0938	0.154	0.521	1.26	1.11	1.44	0.00115	1	lm.nb	Microglia Function	NM_021149.2:1200
BRD2-mRNA	0.283	0.082	0.123	0.444	1.22	1.09	1.36	0.00215	1	lm.nb	Epigenetic Regulation	NM_005104.2:1890
MBD2-mRNA	0.224	0.0724	0.0819	0.366	1.17	1.06	1.29	0.00515	1	lm.nb	Epigenetic Regulation	NM_003927.3:745
FOS-mRNA	1.42	0.504	0.427	2.4	2.67	1.34	5.3	0.01	1	lm.nb	Adaptive Immune Response, Cellular Stress, Growth Factor Signaling, Innate Immune Response, Neurons and Neurotransmission	NM_005252.2:1475
SIN3A-mRNA	0.284	0.102	0.0847	0.483	1.22	1.06	1.4	0.0103	1	lm.nb	Epigenetic Regulation	NM_015477.1:1605
KDM5A-mRNA	0.181	0.0674	0.0492	0.313	1.13	1.03	1.24	0.0131	1	loglinear	Epigenetic Regulation	NM_001042603.1:1962
PADI2-mRNA	0.414	0.161	0.0984	0.729	1.33	1.07	1.66	0.0171	1	lm.nb	Astrocyte Function, Epigenetic Regulation	NM_007365.2:2825
CDKN1C-mRNA	0.704	0.278	0.16	1.25	1.63	1.12	2.38	0.0185	1	lm.nb	Cell Cycle, DNA Damage	NM_001122631.1:1102
LMNA-mRNA	0.438	0.181	0.082	0.793	1.35	1.06	1.73	0.0242	1	lm.nb	Apoptosis, Cell Cycle, Microglia Function	NM_005572.2:1580
IKBKG-mRNA	0.278	0.118	0.0477	0.509	1.21	1.03	1.42	0.0268	1	lm.nb	Adaptive Immune Response, Apoptosis, Cytokine Signaling, Growth Factor Signaling, Inflammatory Signaling, Innate Immune Response, NF-kB	NM_003639.2:470
NFKBIA-mRNA	0.448	0.19	0.0764	0.82	1.36	1.05	1.77	0.027	1	lm.nb	Adaptive Immune Response, Apoptosis, Growth Factor Signaling, Inflammatory Signaling, Innate Immune Response, NF-kB	NM_020529.1:945
HMGB1-mRNA	0.442	0.189	0.0721	0.812	1.36	1.05	1.76	0.0282	1	lm.nb	Apoptosis, Autophagy, Inflammatory Signaling, Innate Immune Response	NM_002128.4:2916
SOCS3-mRNA	0.991	0.424	0.161	1.82	1.99	1.12	3.53	0.0283	1	lm.nb	Adaptive Immune Response, Astrocyte Function, Cytokine Signaling, Inflammatory Signaling, Innate Immune Response	NM_003955.3:1870
ASH2L-mRNA	0.227	0.0975	0.0355	0.418	1.17	1.02	1.34	0.0293	1	lm.nb	Epigenetic Regulation, Wnt	NM_001105214.2:1530
ITGAV-mRNA	0.338	0.147	0.0503	0.626	1.26	1.04	1.54	0.0307	1	lm.nb	Adaptive Immune Response, Angiogenesis, Autophagy, Growth Factor Signaling, Matrix Remodeling	NM_002210.2:2615
APC-mRNA	0.165	0.0723	0.023	0.306	1.12	1.02	1.24	0.0323	1	lm.nb	Apoptosis, Astrocyte Function, Wnt	NM_000038.3:6850
TGFB1-mRNA	0.424	0.19	0.0527	0.796	1.34	1.04	1.74	0.0352	1	lm.nb	Cell Cycle, Cytokine Signaling, Growth Factor Signaling, Matrix Remodeling, Microglia Function	NM_000660.3:1260
C4A-mRNA	0.778	0.349	0.0952	1.46	1.72	1.07	2.75	0.0356	1	lm.nb	Astrocyte Function	NM_007293.2:1217
KDM6A-mRNA	0.443	0.205	0.0397	0.845	1.36	1.03	1.8	0.042	1	lm.nb	Epigenetic Regulation	NM_021140.2:2590
KCNJ10-mRNA	0.377	0.175	0.0335	0.72	1.3	1.02	1.65	0.0422	1	lm.nb	Astrocyte Function, Neurons and Neurotransmission	NM_002241.4:4740

Supplementary table 8
Top 20 differentially expressed genes in TREM2 versus high AD in visual cortex (Neuroinflammation panel)

	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	Linear fold change	Lower confidence limit (linear)	Upper confidence limit (linear)	P-value	BY.p.value	method	Gene.sets	probe.ID
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ASH2L-mRNA	0.227	0.0975	0.0355	0.418	1.17	1.02	1.34	0.0293	1	lm.nb	Epigenetic Regulation, Wnt	NM_001105214.2:1530
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TGFB1-mRNA	0.424	0.19	0.0527	0.796	1.34	1.04	1.74	0.0352	1	lm.nb	Cell Cycle, Cytokine Signaling, Growth Factor Signaling, Matrix Remodeling, Microglia Function	NM_000660.3:1260
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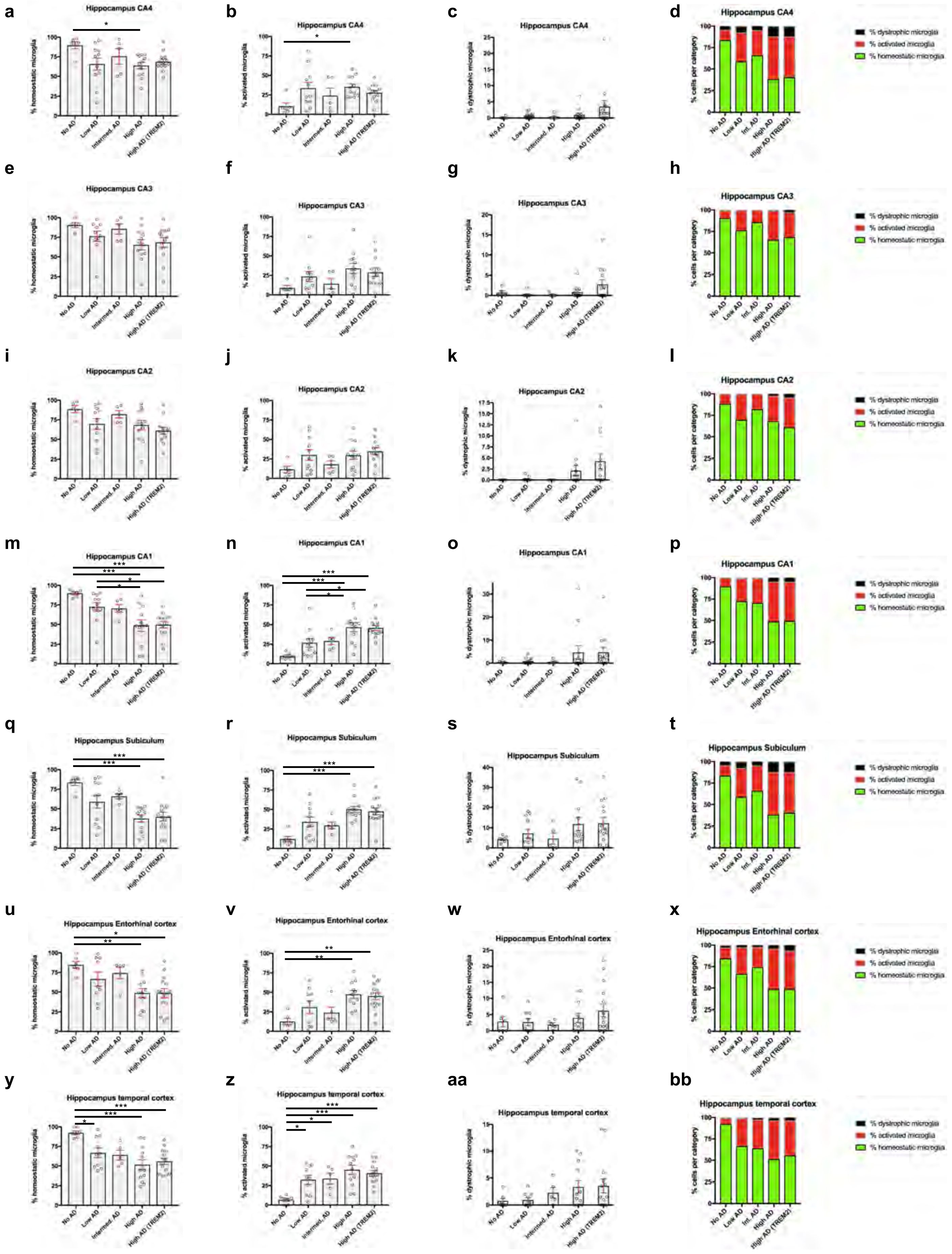
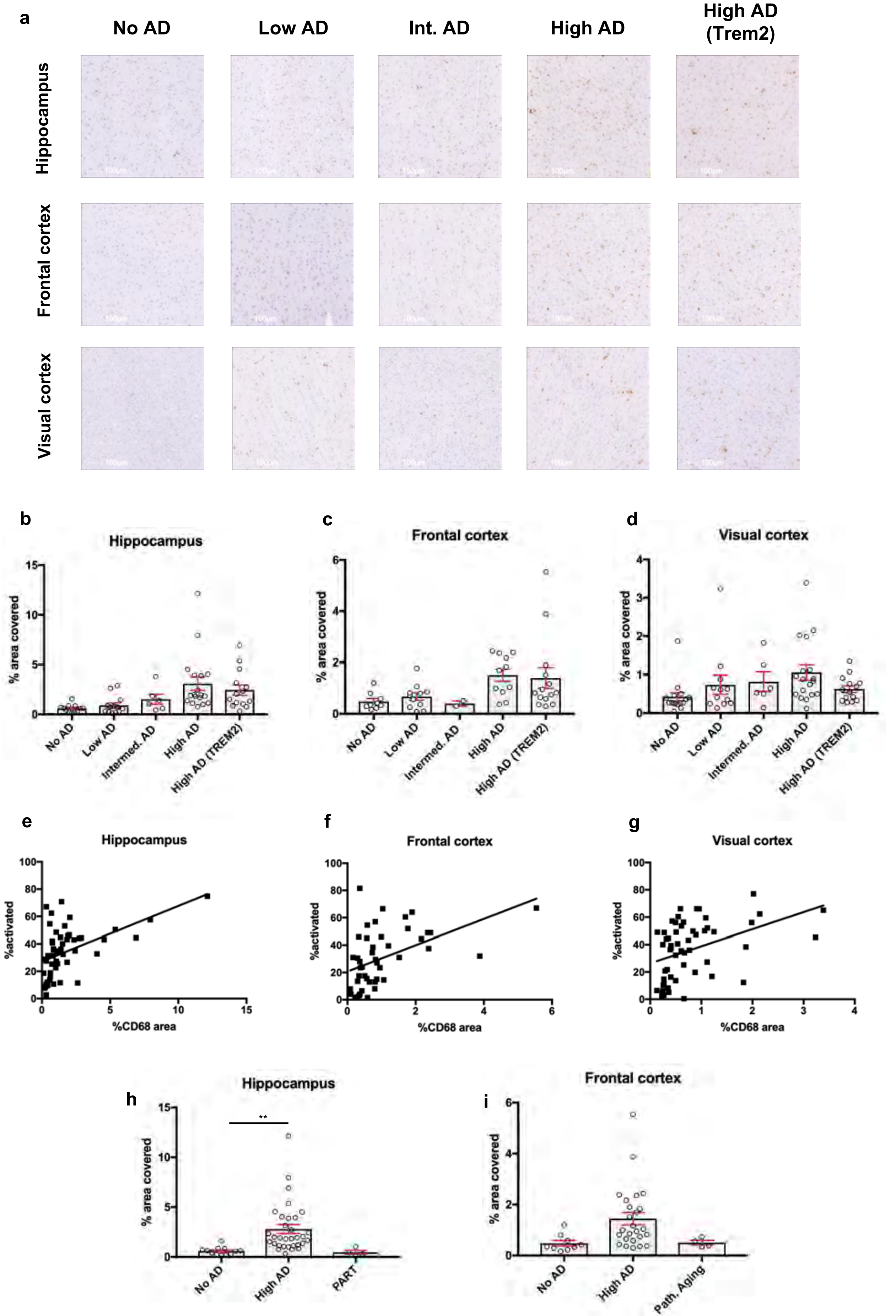
KDM6A-mRNA	0.443	0.205	0.0397	0.845	1.36	1.03	1.8	0.042	1	lm.nb	Epigenetic Regulation	NM_021140.2:2590
KCNJ10-mRNA	0.377	0.175	0.0335	0.72	1.3	1.02	1.65	0.0422	1	lm.nb	Astrocyte Function, Neurons and Neurotransmission	NM_002241.4:4740

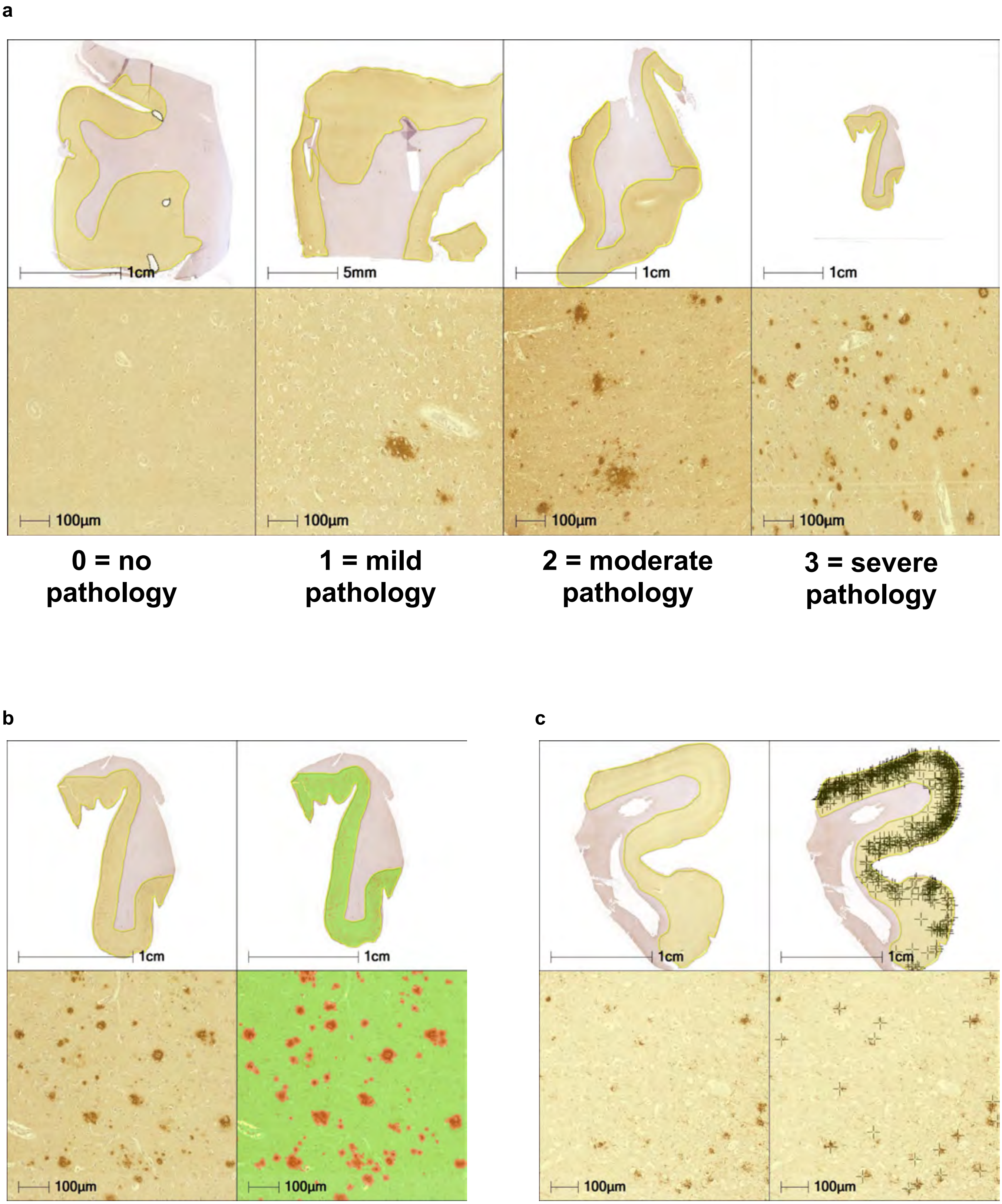
Supplementary figure 1



Supplementary figure 2



Supplementary figure 3



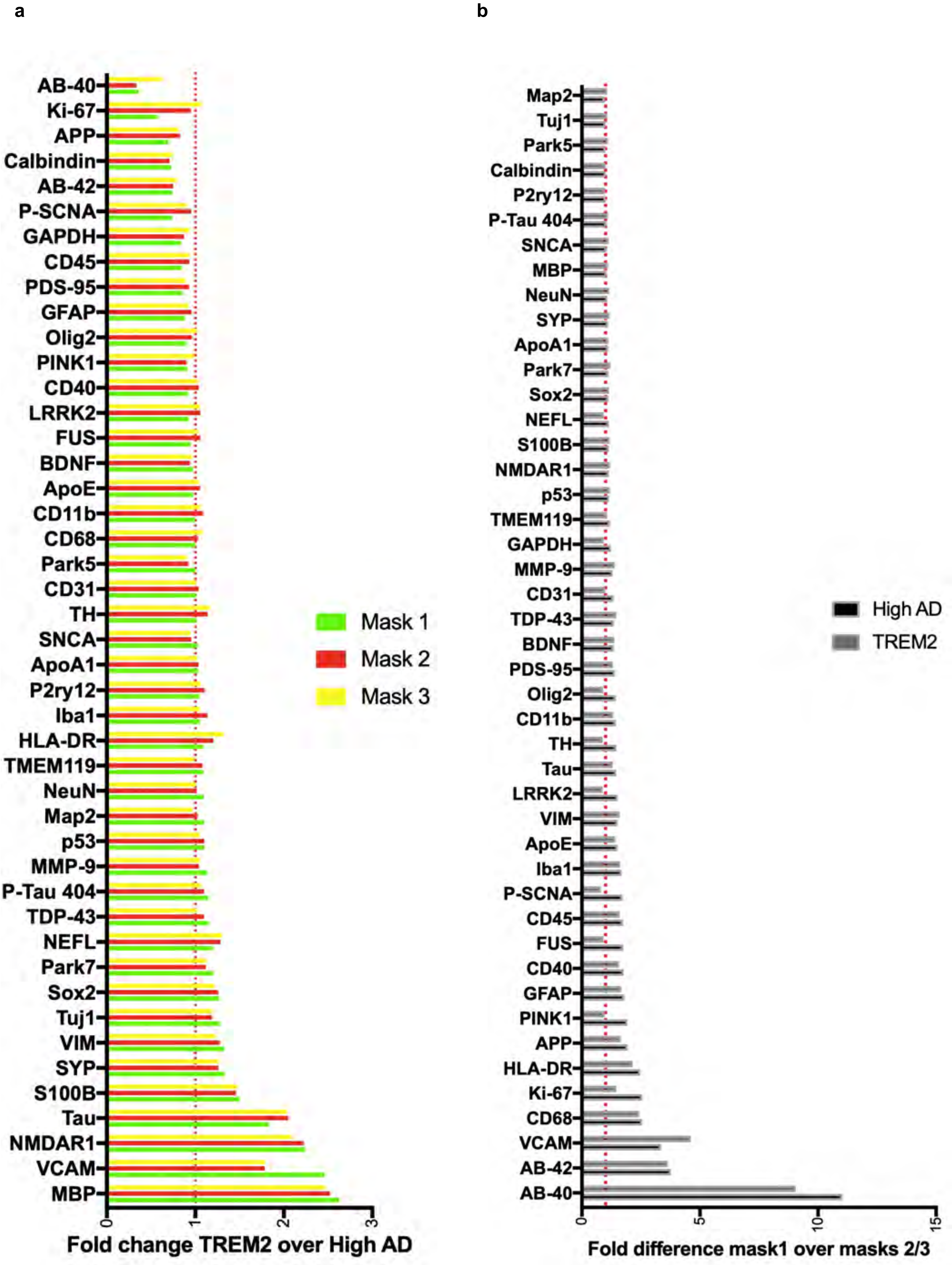
0 = no pathology

1 = mild pathology

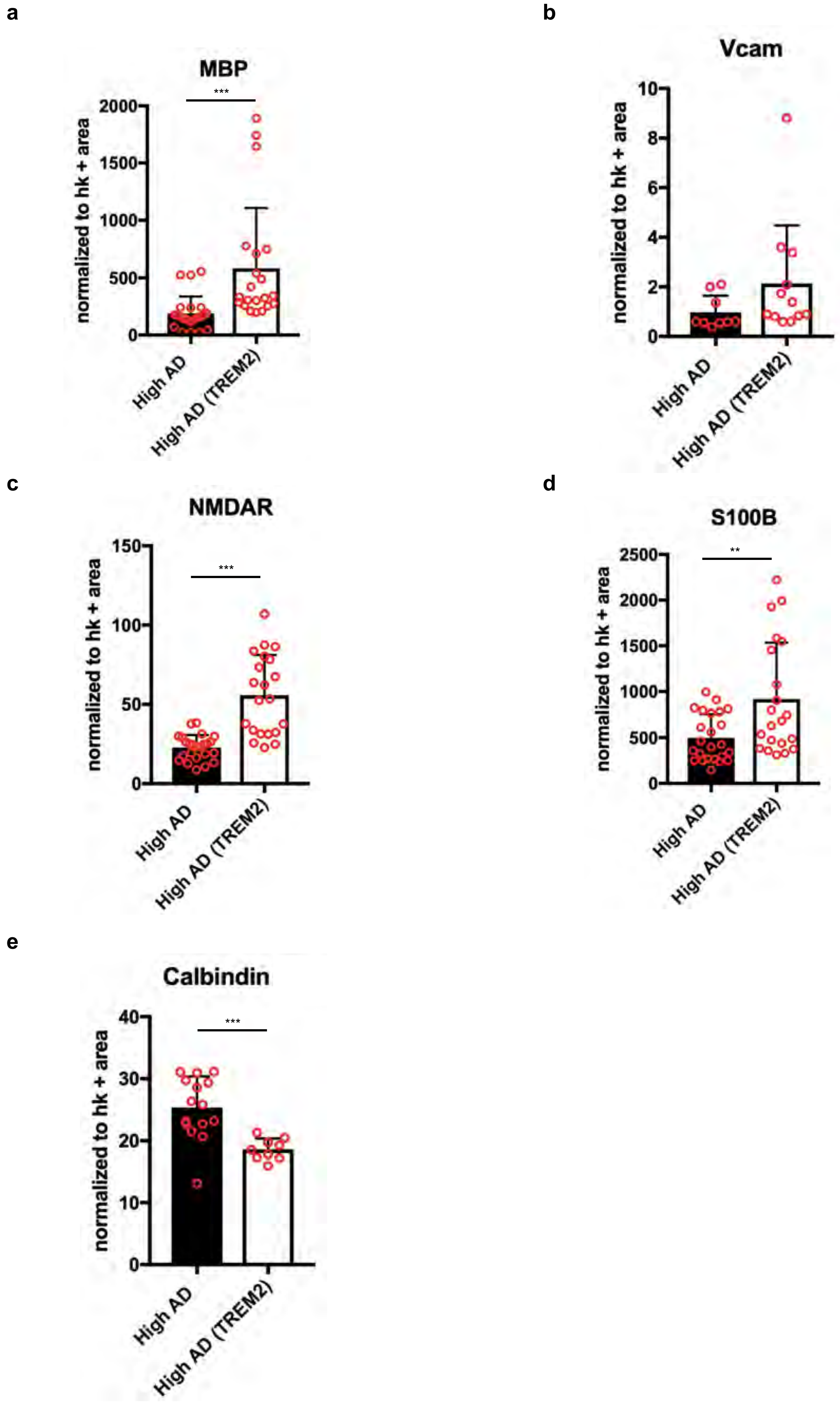
2 = moderate pathology

3 = severe pathology

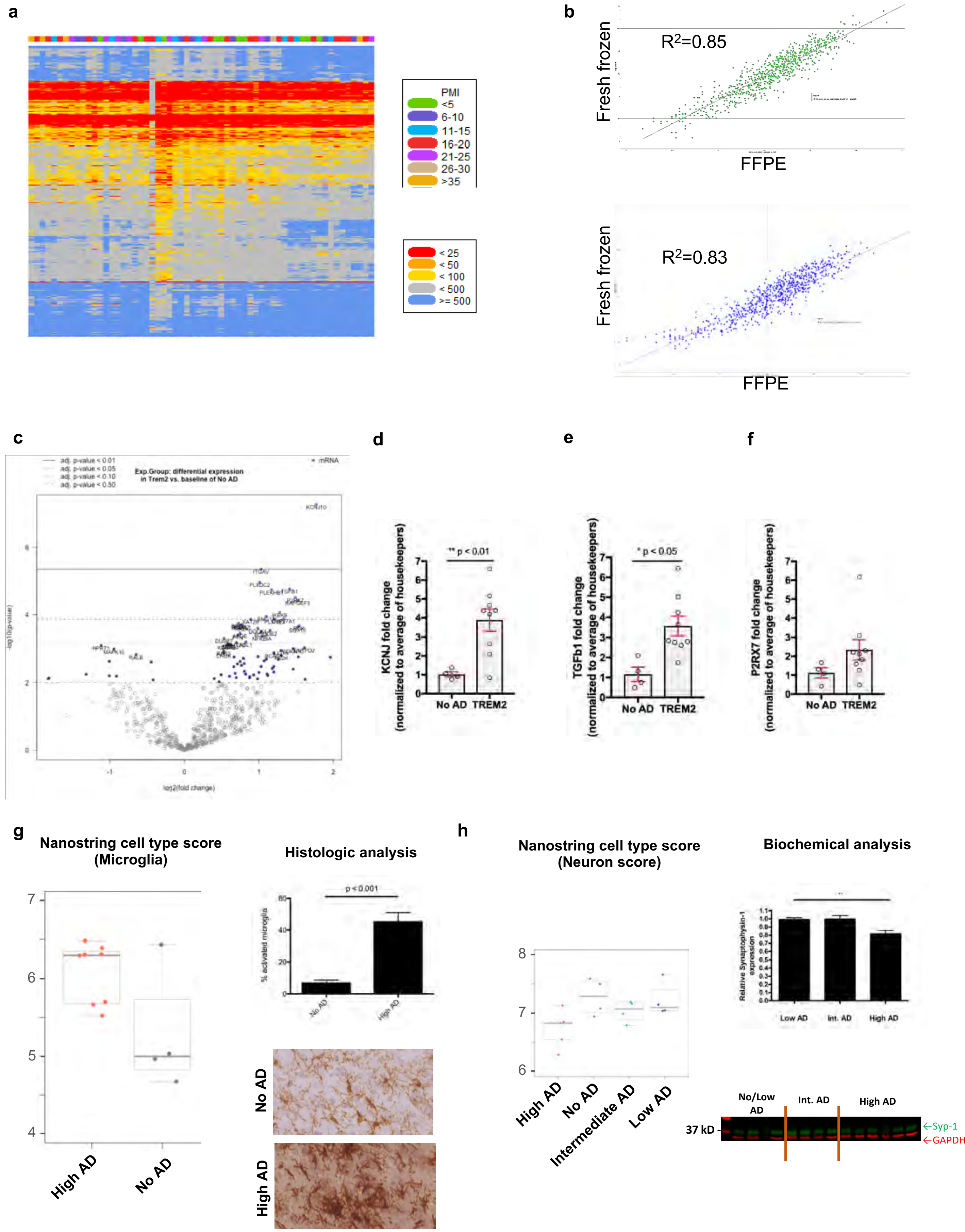
Supplementary figure 4



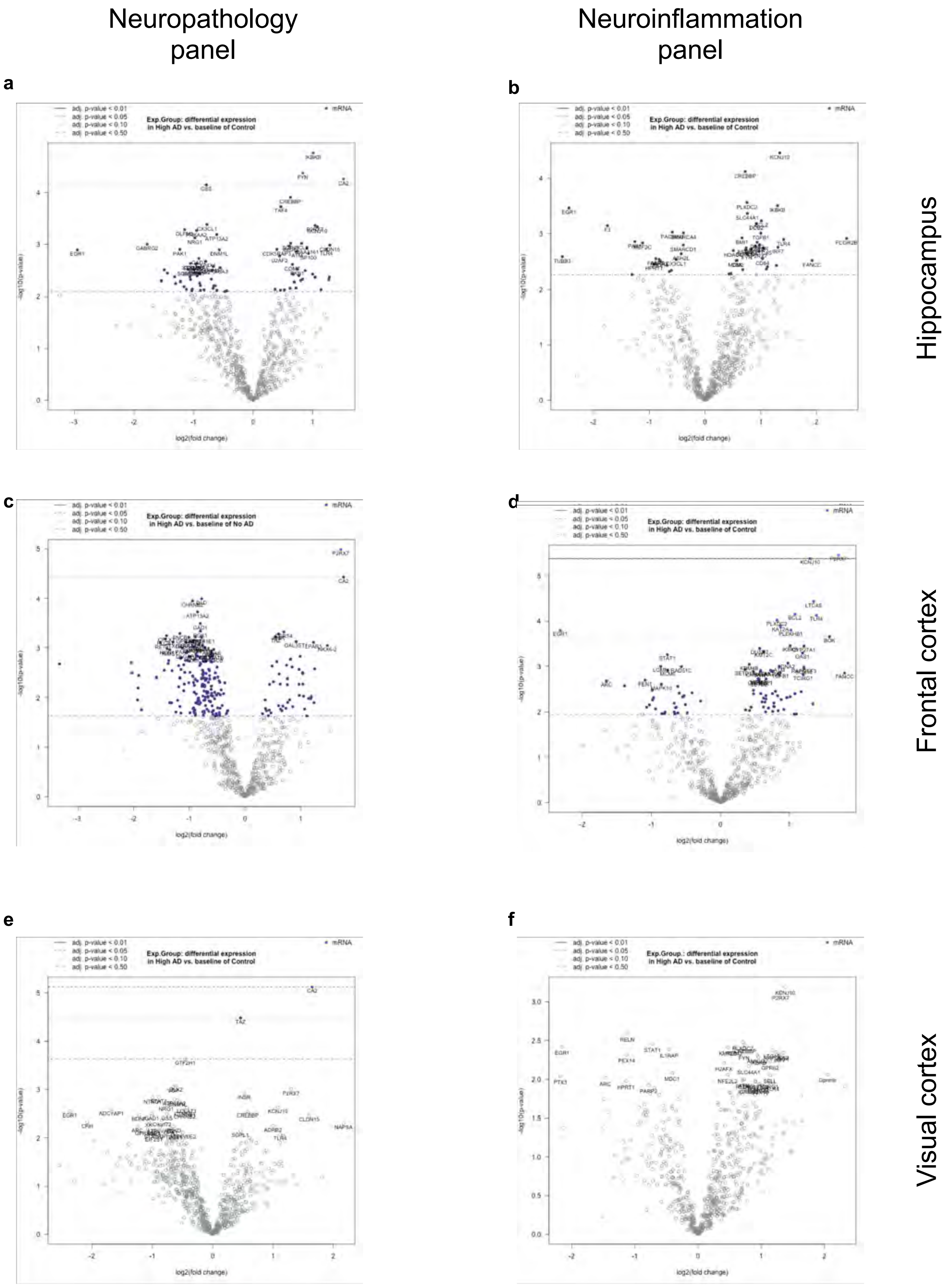
Supplementary figure 5



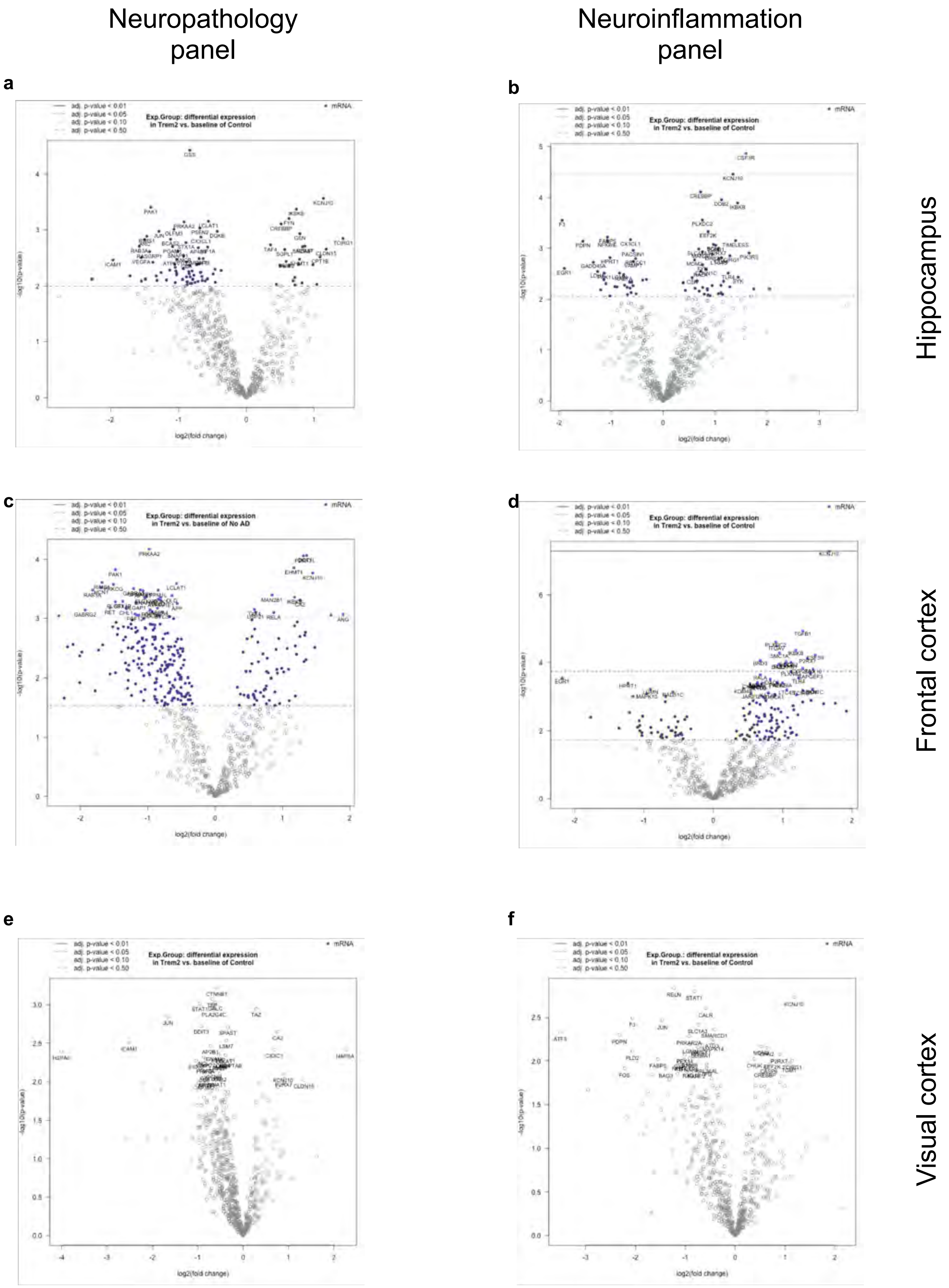
Supplementary figure 6



Supplementary figure 7



Supplementary figure 8



Supplementary figure 9