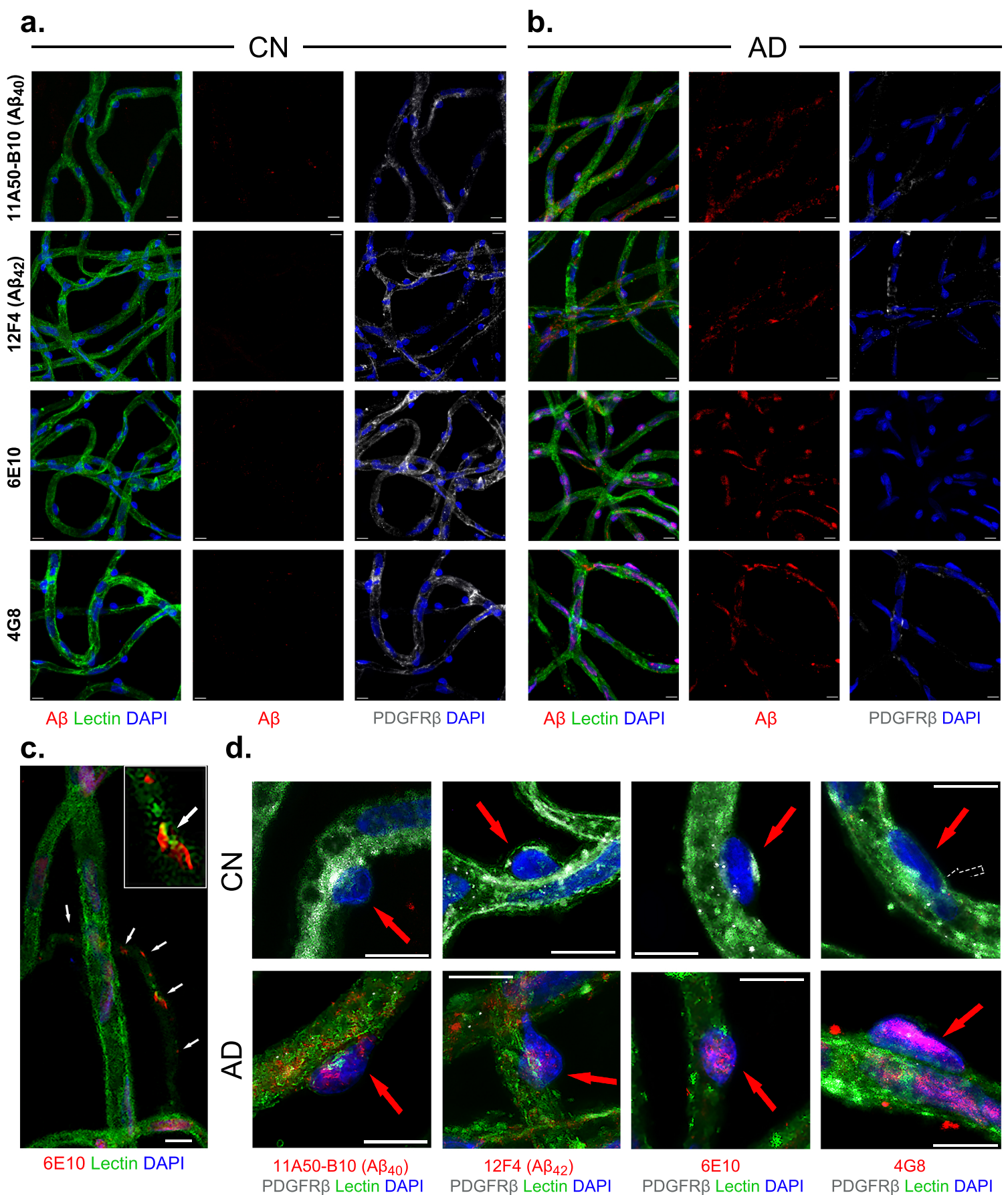


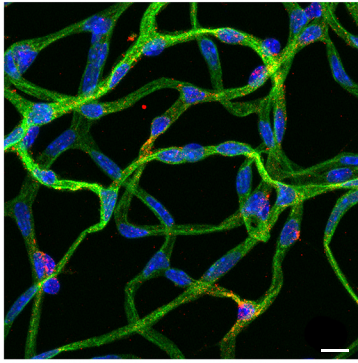
Supplementary Figure 1. Negative controls for all immunofluorescent staining. **a.** Representative images of negative controls (primary antibodies omitted) for isolated vascular staining in figure 1, with secondary antibodies (donkey anti-rabbit Cy3 and anti-mouse Cy5) and DAPI. Scale bar=10 μ m. **b-c.** Representative images of negative controls (primary antibodies omitted) for DAB staining without (w/o) **b.** JRF/cA β 40/28 or **c.** 11A50-B10 (A β ₄₀). Scale bars=20 μ m. **d.** Representative image of negative controls (primary antibodies omitted) for retinal cross-section staining in figure 2, with secondary antibody (donkey anti-rabbit Cy3) and DAPI. Scale bar=10 μ m. **e.** Representative image of negative controls (primary antibodies omitted) for retinal cross-section staining in figure 3 and 4, with secondary antibody (donkey anti-mouse Cy5) and DAPI. Scale bar=10 μ m. **f.** Representative image of negative controls (primary antibodies omitted) for retinal cross-section staining in figures 3 and 4, with secondary antibodies (donkey anti-rabbit Cy3 and anti-mouse Cy5) and DAPI. Scale bar=10 μ m. **g.** Representative image of negative controls (primary antibodies omitted) for retinal cross-section staining in figure 6, with secondary antibodies (donkey anti-goat Cy3 and anti-rabbit Cy5) and DAPI. Scale bar=10 μ m. **h.** Representative images of negative control (without terminal transferase) and positive control (pretreatment with DNaseI) for TUNEL staining experiment in figure 6. Scale bars=10 μ m.



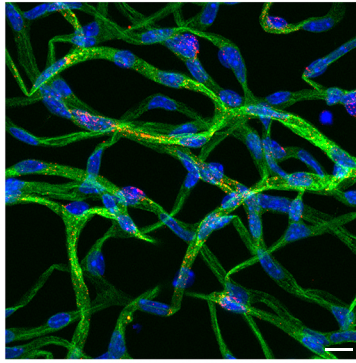
Supplementary Figure 2. Extended representative images for figure 1 on retinal microvascular $A\beta$ and PDGFR β^+ pericytes. **a-b.** Separate channels of representative fluorescent images for $A\beta$ (11A50-B10, 12F4, 6E10 or 4G8 as indicated, red), PDGFR β (pericytes, white), lectin (glycoprotein in blood vessel, green) and DAPI (nuclei, blue) on isolated retinal microvasculature from age and sex-matched human donors with AD (n=5) or cognitively normal (CN, n=5). **c.** $A\beta$ (6E10, red), lectin (green) and DAPI (blue) staining showing $A\beta$ deposits in a degenerated, acellular capillary (indicated by arrows). Upper right image shows zoomed-in image from the original. **d.** Enlarged confocal images of retinal microvascular pericytes from AD and CN donors ($A\beta$ -red, PDGFR β -white, lectin-green, DAPI-blue). Scale bars=10 μ m.

a. ADTg Non-perfused
Mouse [M, 8.5mo]

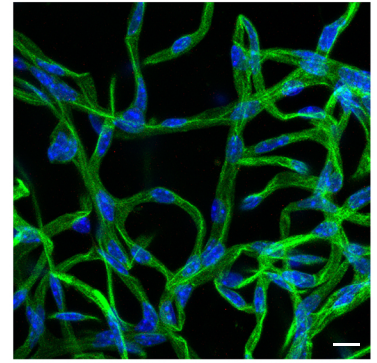
4G8 Lectin DAPI



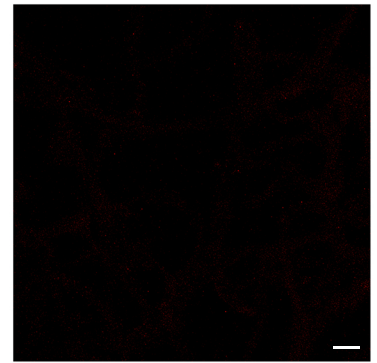
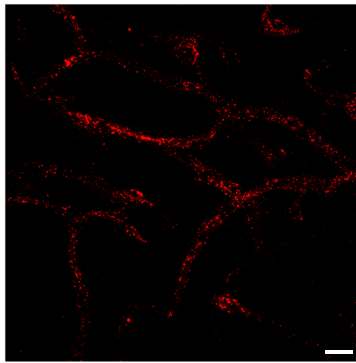
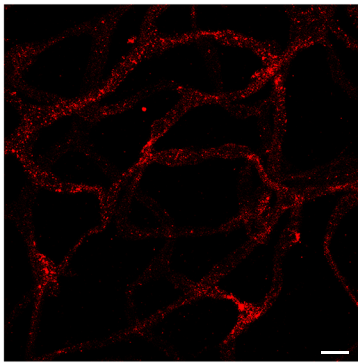
b. ADTg Perfused
Mouse [M, 8.5mo]



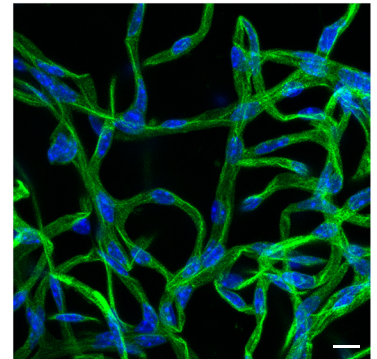
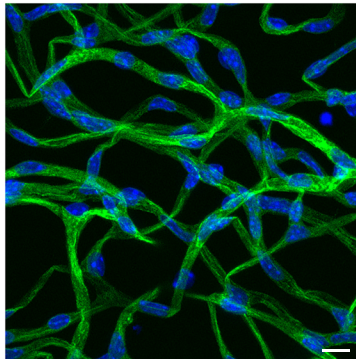
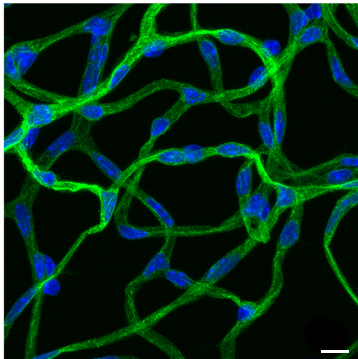
c. WT Perfused
Mouse [M, 8.5mo]



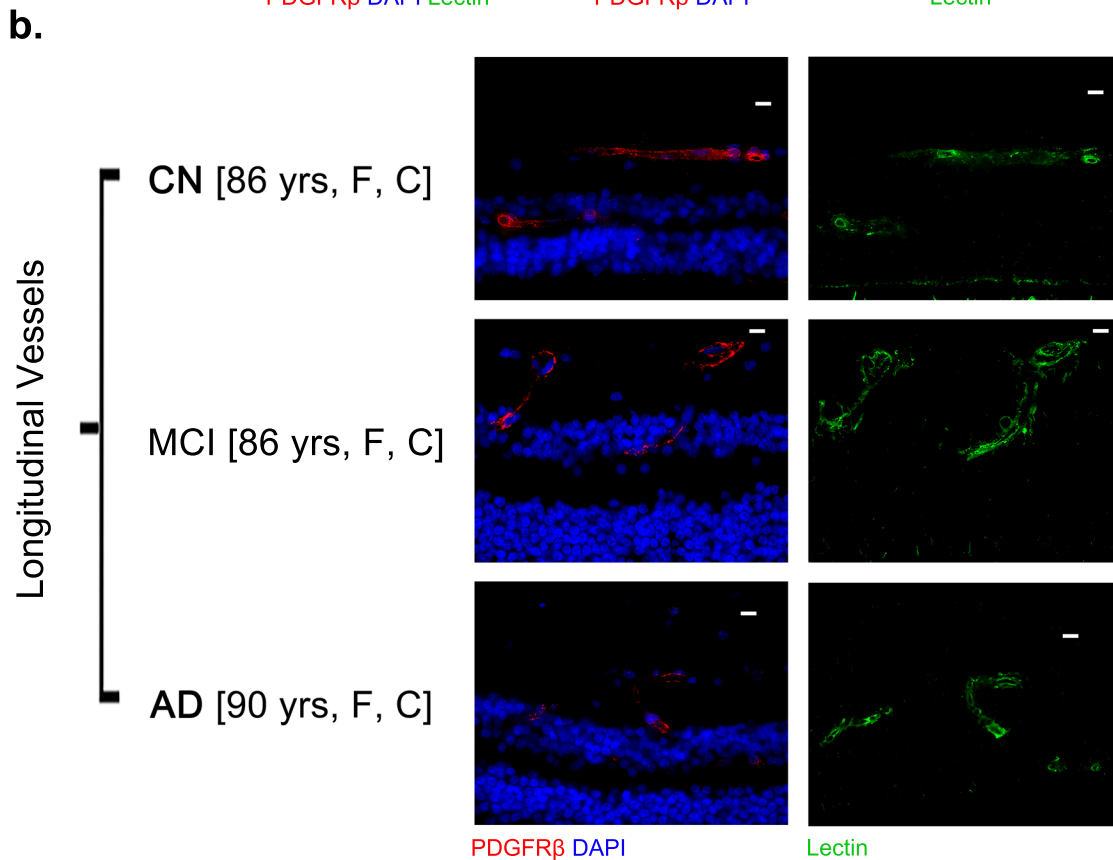
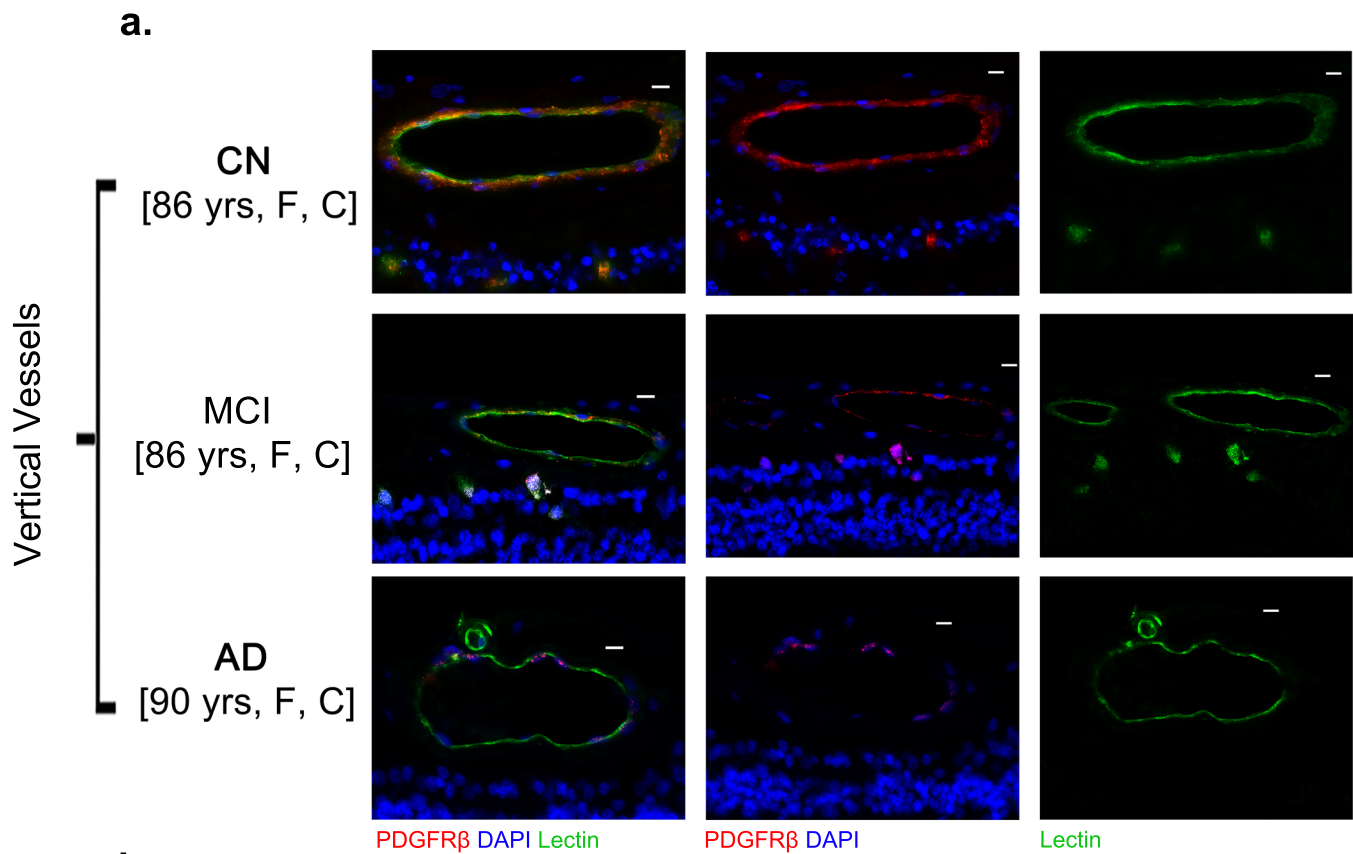
4G8



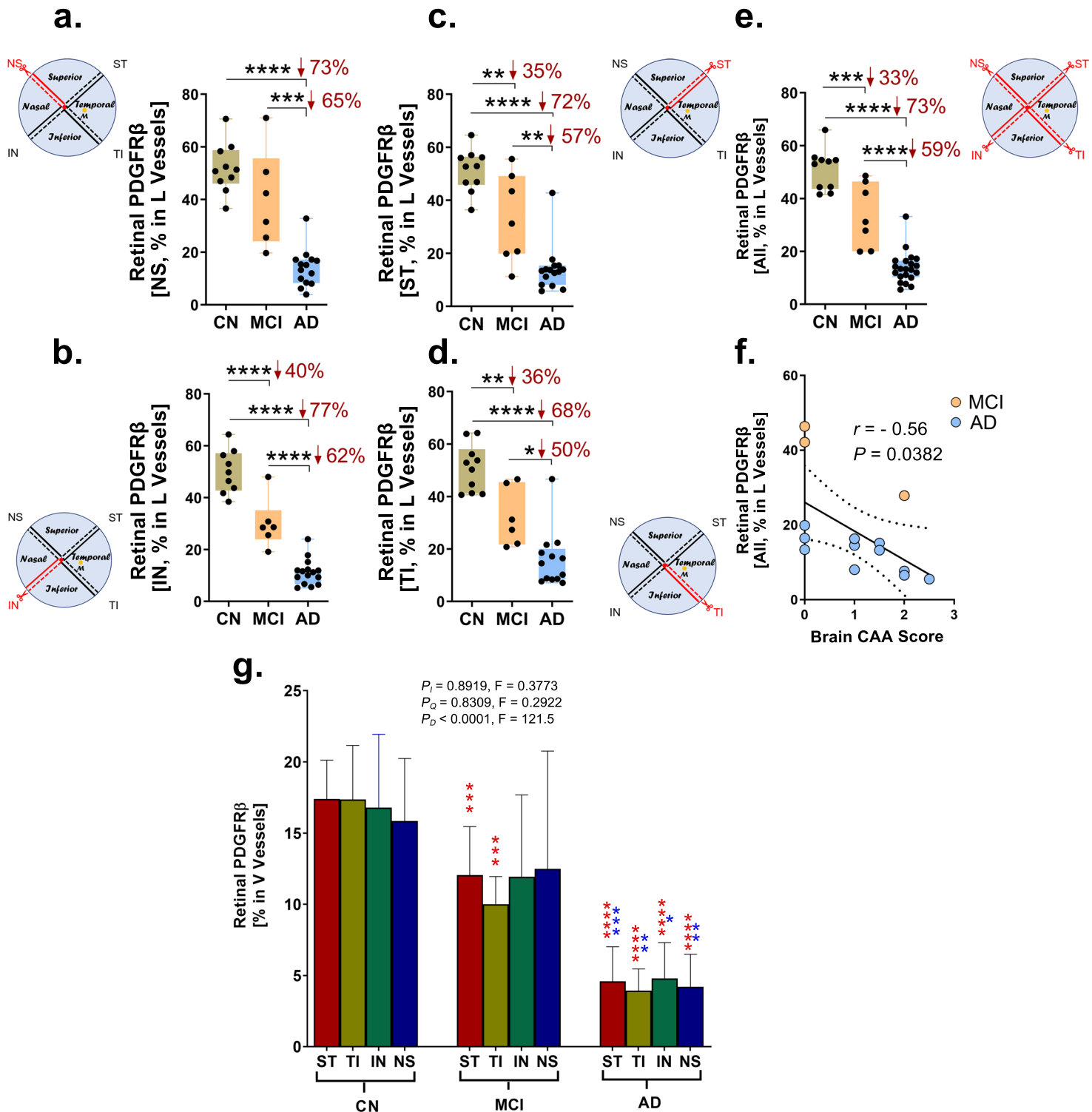
Lectin DAPI



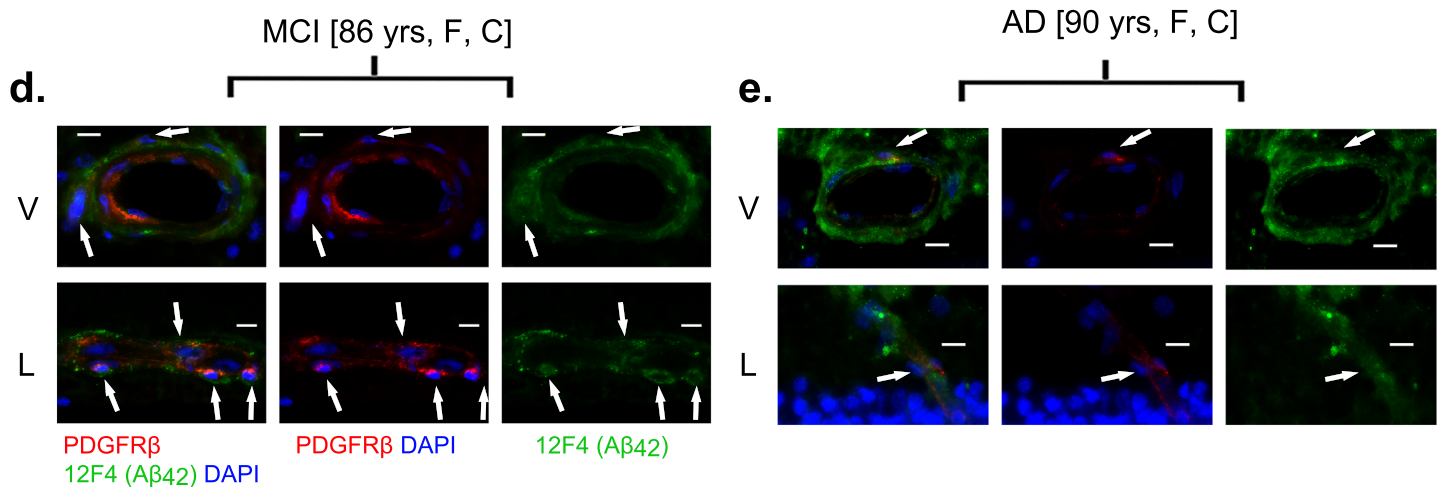
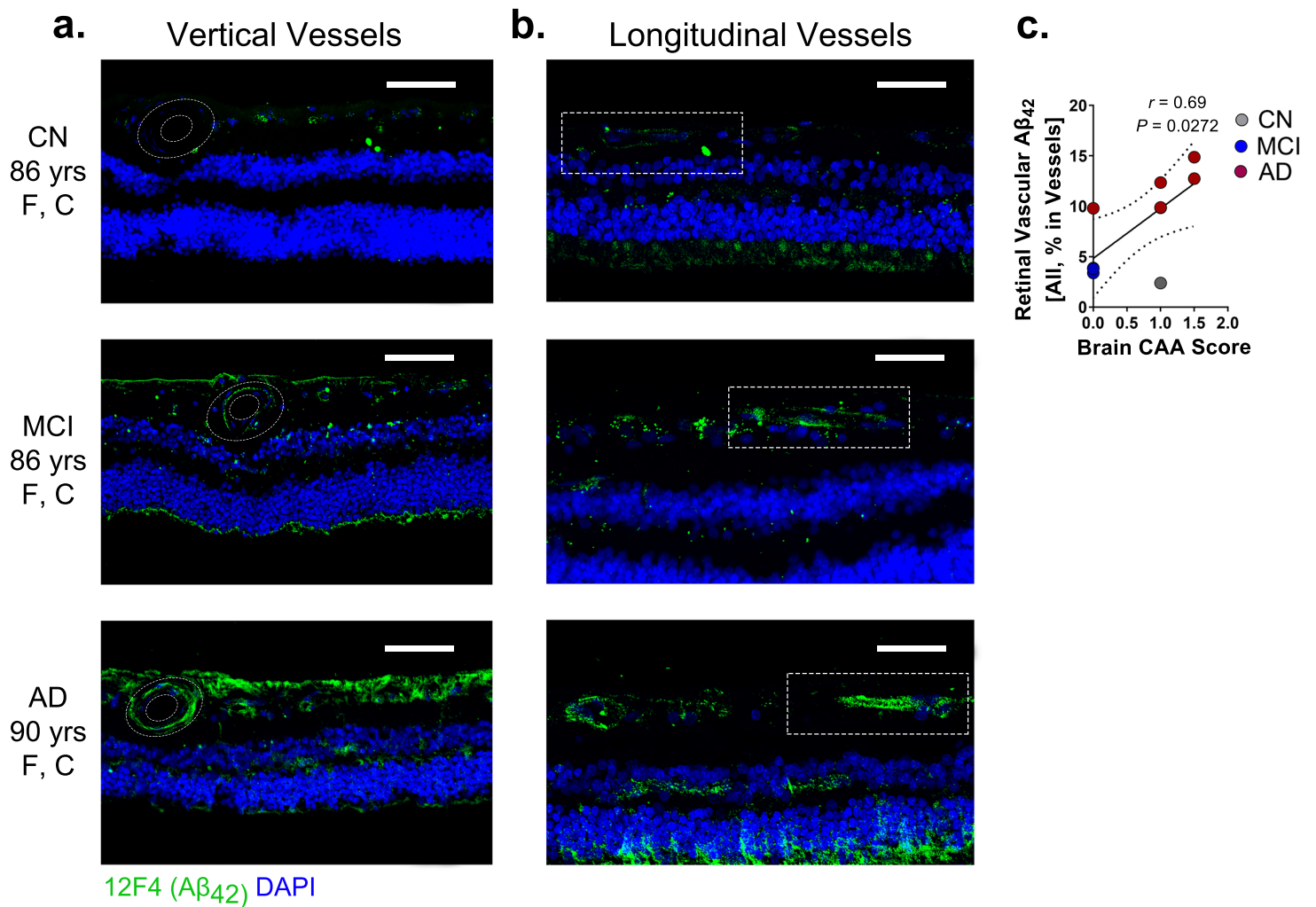
Supplementary Figure 3. Significant retinal vascular A β deposition in perfused transgenic ADTg mice. **a-c.** Representative fluorescent images for A β (4G8, red), lectin (glycoprotein in blood vessel, green) and DAPI (nuclei, blue) on isolated retinal microvasculature from **a.** non-perfused 8.5 month old male ADTg mice, or **b.** perfused 8.5 month old male ADTg mice, and **c.** perfused 8.5 month old male wild type mice. Scale bars=10 μ m.



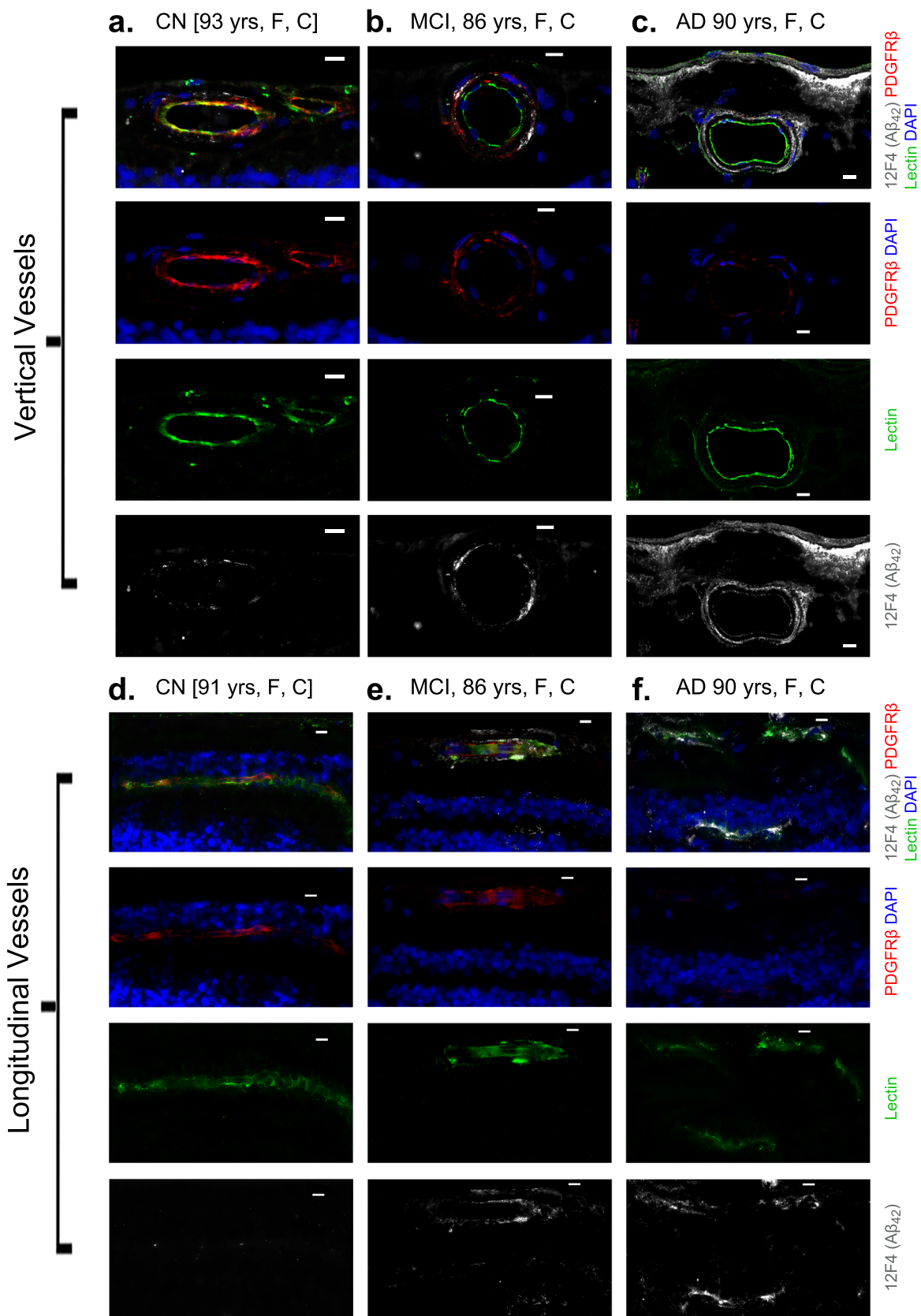
Supplementary Figure 4. Extended representative images for figure 2 on retinal vascular PDGFR β . **a-b.** Merged and separate channels of representative fluorescent images for PDGFR β (red), lectin (glycoprotein in blood vessel, green) and DAPI (nuclei, blue) in paraffin-embedded retinal cross-sections isolated from age and sex-matched human donors with AD, MCI or cognitively normal (CN). **a.** Vertical (V) and **b.** Longitudinal (L) blood vessels are shown. Scale bars=10 μ m.



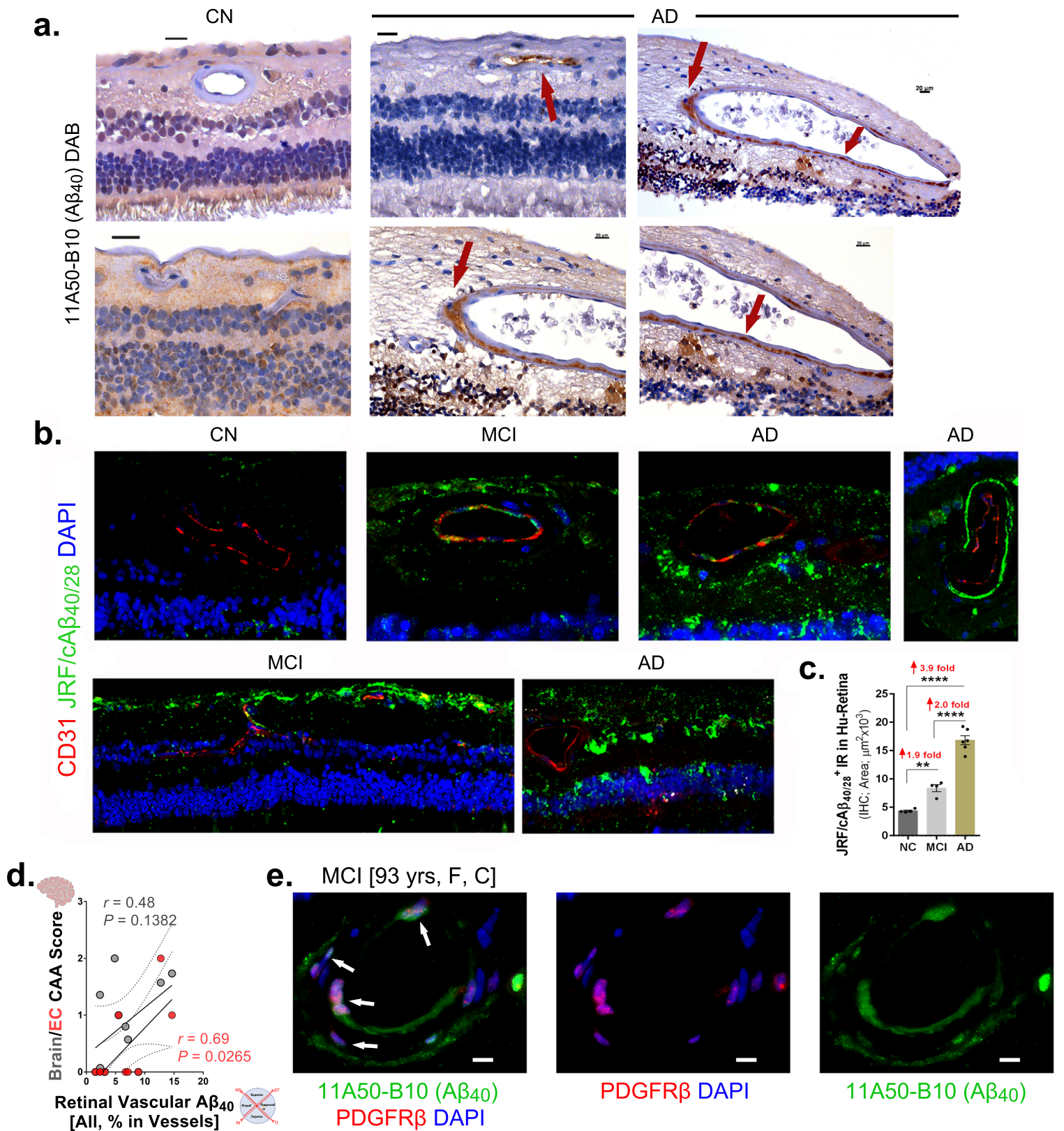
Supplementary Figure 5. Extended data on retinal PDGFR β in longitudinal vasculature from all retinal quadrant regions in AD, MCI and CN human donors and mapping of PDGFR β . **a-d.** Quantitative analysis of % PDGFR β -immunoreactive area in longitudinal (L) vessels from each retinal quadrant separately: **a.** NS, **b.** IN, **c.** ST, **d.** TI in total cohort of AD ($n=21$), MCI ($n=7$) and cognitively normal (CN) ($n=10$) human donors. **e-f.** Quantitative analysis of retinal % PDGFR β immunoreactivity in L vasculature (average of all four quadrants): **e.** subjects stratified by clinical diagnosis ($n=38$) and **f.** Pearson's correlations against brain CAA scores in a subset of this cohort ($n=14$). **g.** Mapping of vertical (V) vascular PDGFR β in four retinal quadrants. (* indicates AD vs. CN, * indicates AD vs. MCI) Data from individuals as well as group means and SEMs are shown. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$, by one-way ANOVA test with Sidak's post-hoc multiple comparison test. Percent change are shown in red.



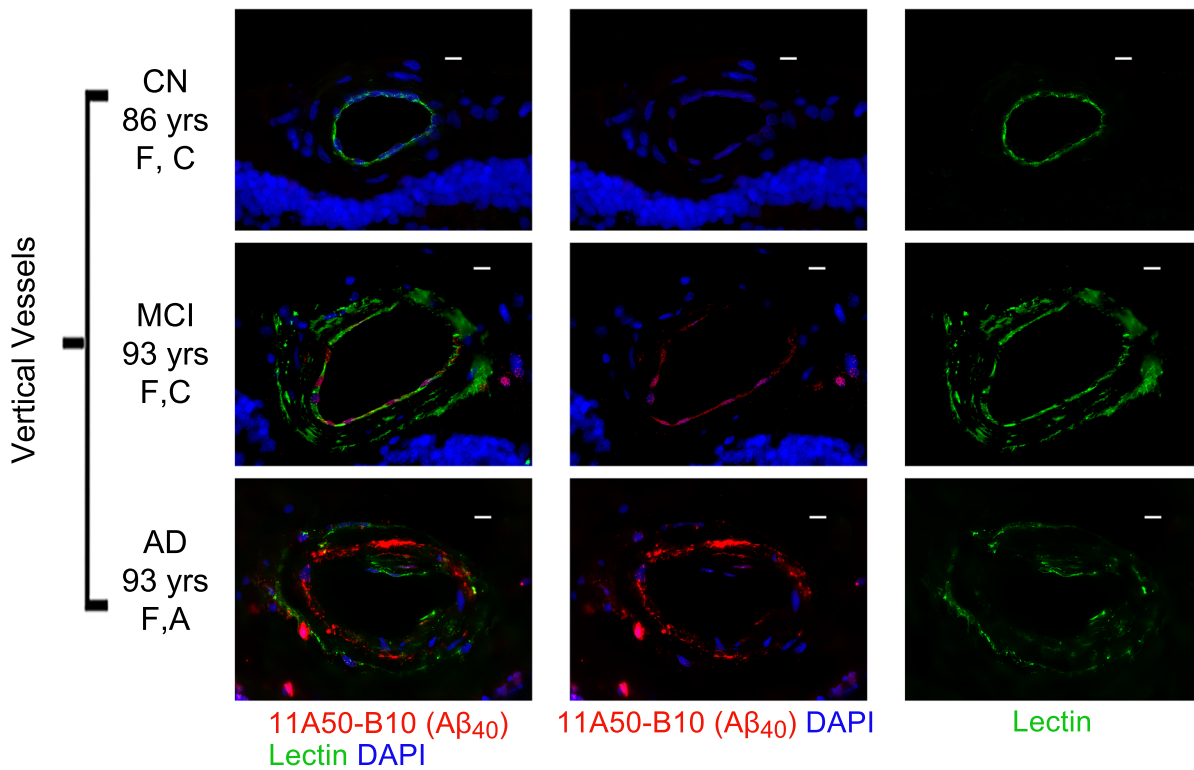
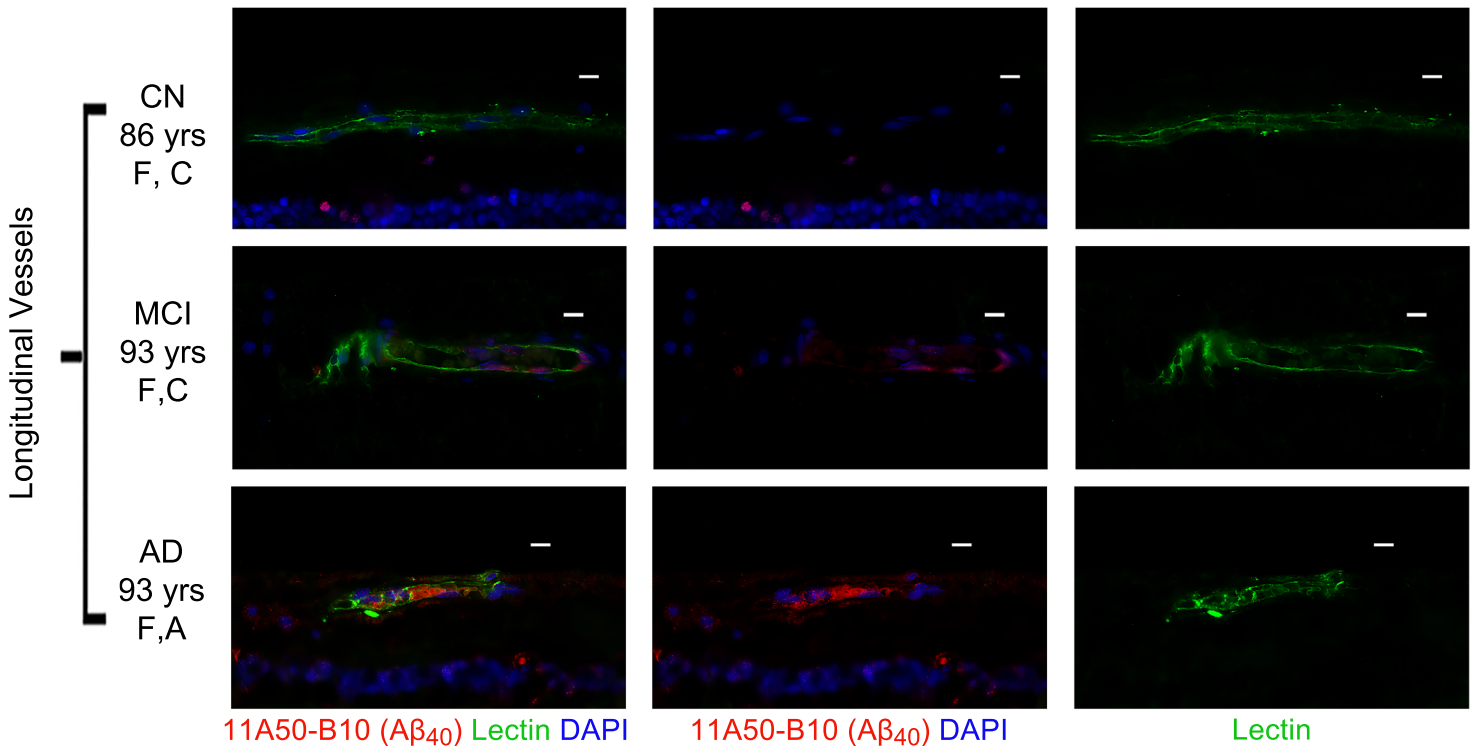
Supplementary Figure 6. Extended representative images for figure 3. **a-b.** Representative fluorescent images of paraffin-embedded retinal cross-sections isolated from age and sex-matched human donors with AD, MCI, or cognitively normal (CN) stained for A β_{42} (12F4, green) and DAPI (nuclei, blue). **a.** Vertical (V) and **b.** longitudinal (L) blood vessels are shown. Dashed geometric shapes (white) indicate pre-defined areas of analysis. Scale bars=50 μ m. **c.** Pearson's coefficient (r) correlation between retinal 12F4⁺ A β_{42} burden in both V and L (All) blood vessels against brain CAA score. **d-e.** Merged and separate channels of representative fluorescent images for 12F4 (A β_{42} , green), PDGFR β (red) and DAPI (nuclei, blue) in paraffin embedded retinal cross-sections isolated from age and sex-matched human subjects with AD and MCI. Arrows point at A β_{42} in PDGFR β ⁺ cells. Both retinal V and L blood vessels in **d.** MCI and **e.** AD patients are shown (yrs=years old; F=female; C=Caucasian). Scale bars=10 μ m.



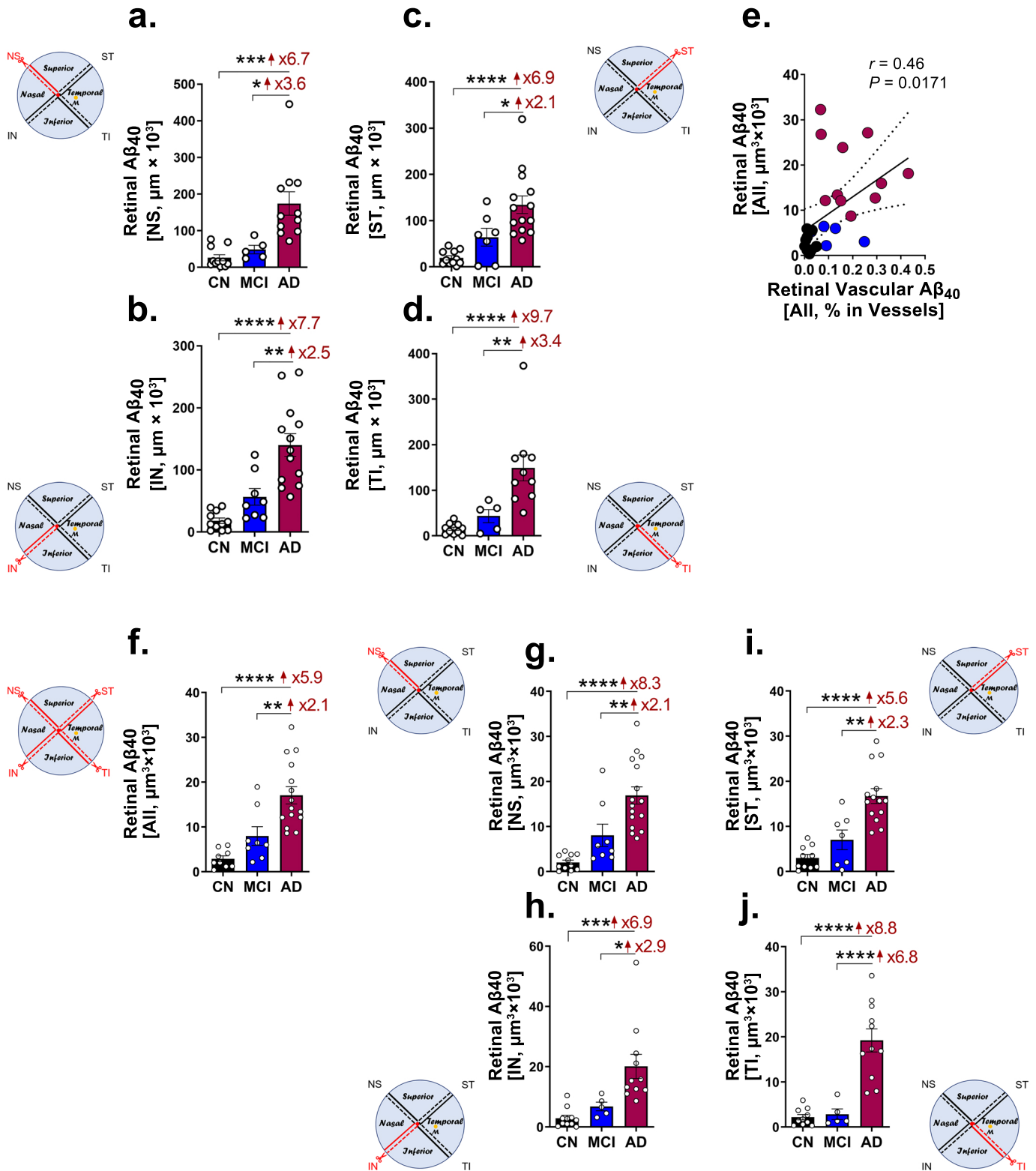
Supplementary Figure 7. Expanded representative images for A β ₄₂, PDGFR β , lectin and DAPI. **a-f.** Merged and separate channels of representative fluorescent images for 12F4 (A β ₄₂, white), PDGFR β (red), lectin (glycoprotein in blood vessel, green) and DAPI (nuclei, blue) in paraffin-embedded retinal cross-sections isolated from age and sex-matched human donors with AD, MCI or cognitively normal (CN). **a-c.** Vertical and **d-f.** Longitudinal vessels are shown (yrs=years old; F=female; C=Caucasian). Scale bars=10 μ m.



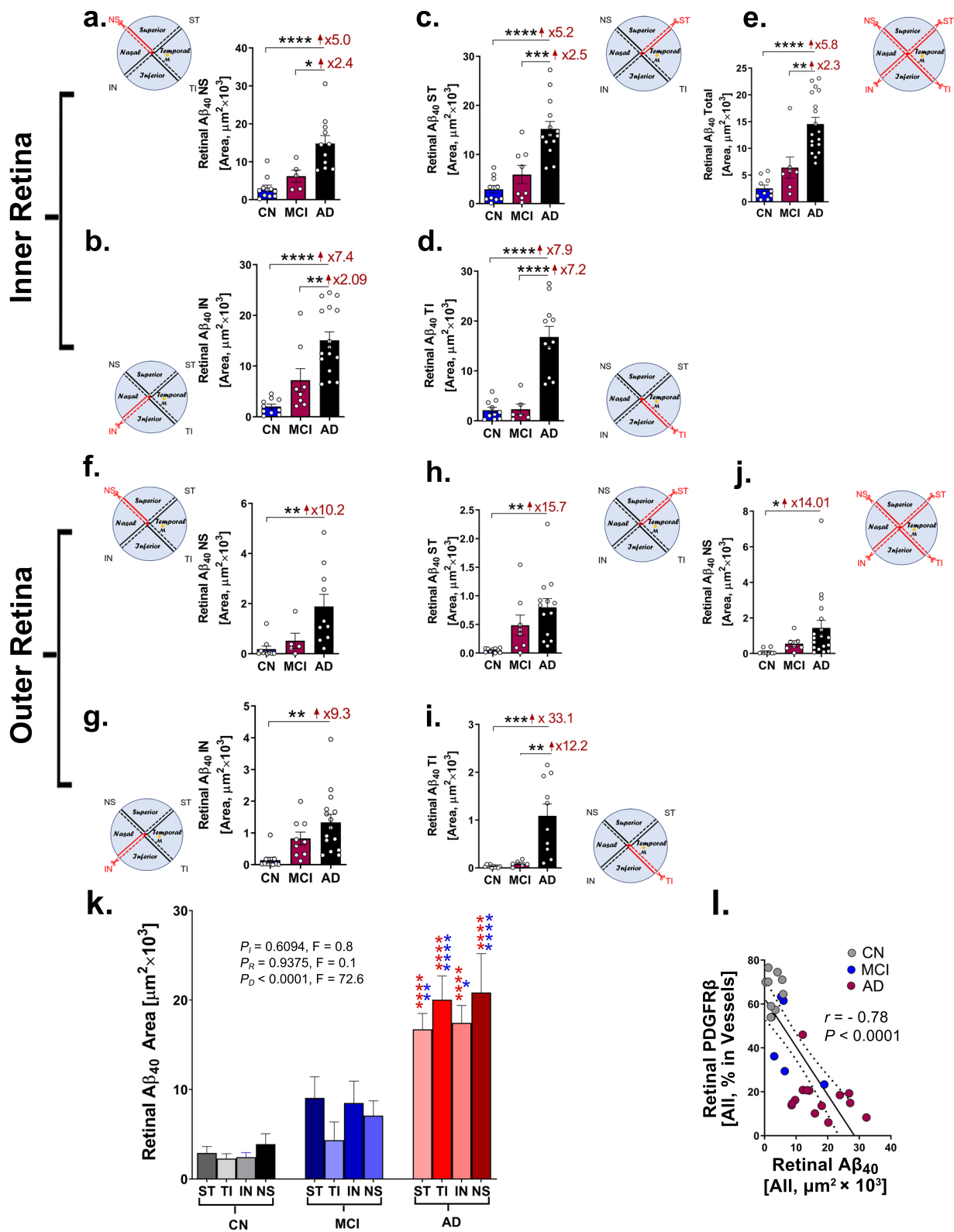
Supplementary Figure 8. Extended data on retinal vascular Aβ₄₀ deposits from MCI and AD human donors compared to cognitively normal controls. **a.** Representative horseradish peroxidase and 3,3'-Diaminobenzidine (DAB) staining of images for 11A50-B10-Aβ₄₀ in retinas from AD and cognitively normal (CN) subjects. Arrows indicate vascular Aβ₄₀ staining in tunica intima and media. Scale bars = 20 μm. **b.** Representative fluorescent microscope images of paraffin-embedded retinal cross-sections from AD, MCI and CN stained against Aβ₄₀ (JRF/cAβ 40/28 antibody; green), endothelial cells (CD31; red) and nuclei (DAPI, blue). **c.** Quantitative analysis of retinal vascular Aβ₄₀-IR area in a subset of MCI (n=4), AD (n=6) and CN (n=4) human donors. Data from individual human donors as well as group means and SEMs are shown. ***p* < 0.01, *****p* < 0.0001, by one-way ANOVA test with Sidak's post-hoc multiple comparison test. Fold change are shown in red. **d.** Pearson's coefficient (*r*) correlation between retinal Aβ₄₀ burden (11A50-B10-IR area) in both vertical and longitudinal vasculature (average) against CAA score in parenchymal brain average (grey) and entorhinal cortex (EC, red), within a subset of subjects with AD, MCI and CN (n=10). **e.** High-magnification images showing co-localization of vascular Aβ₄₀ (green) and PDGFRβ (red; co-localization indicated by arrows) in a MCI subject (yrs=years old; F=female; C=Caucasian). Scale bars = 10 μm.

a.**b.**

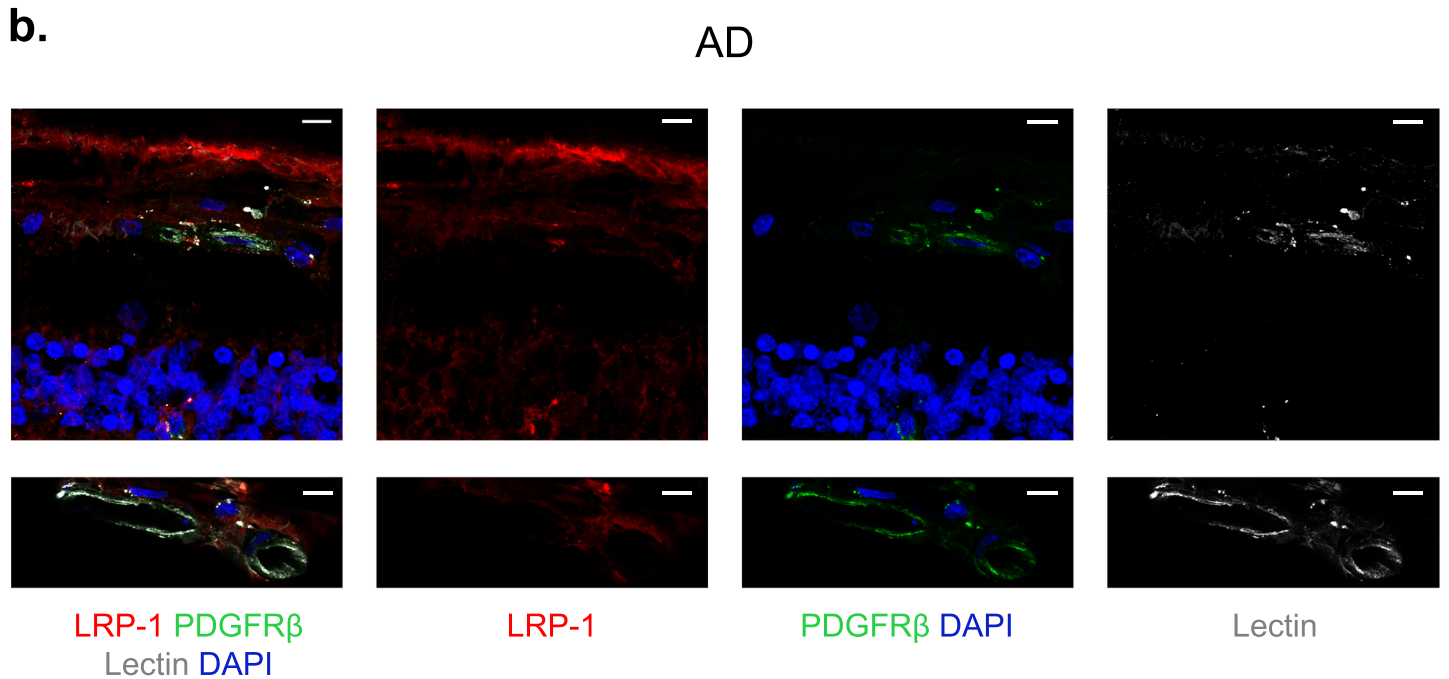
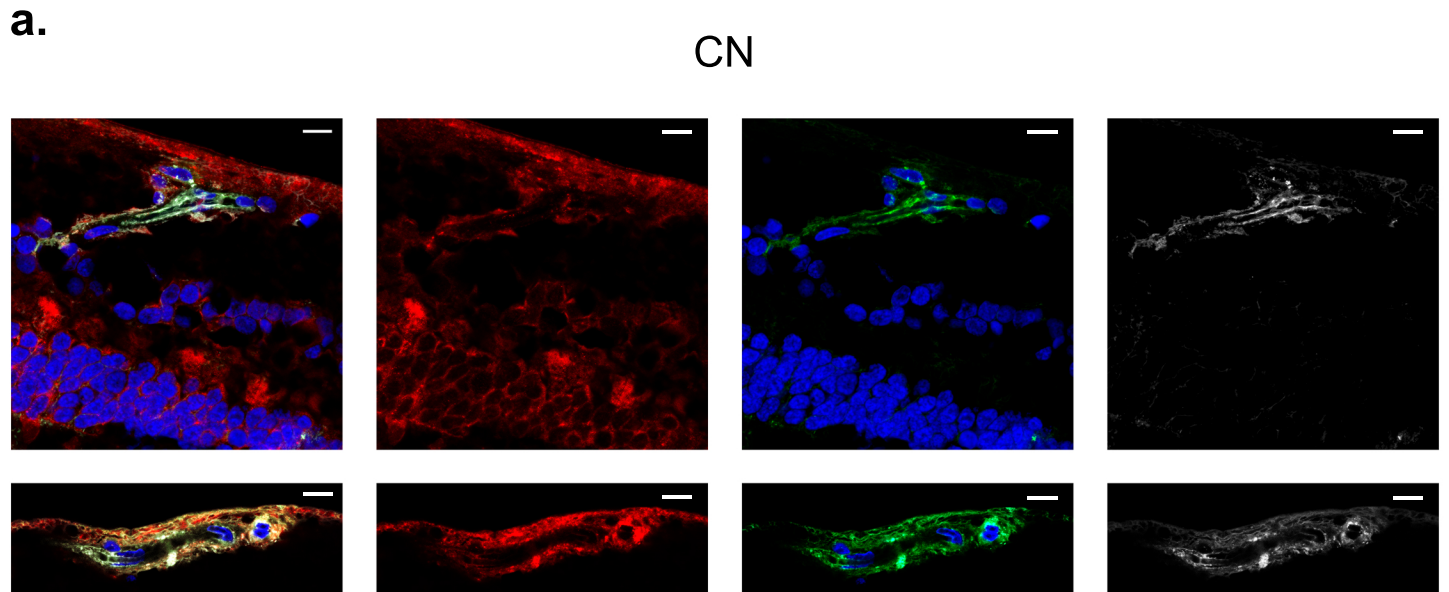
Supplementary Figure 9. Extended representative images for retinal $A\beta_{40}$. **a-b.** Merged and separate channels of representative fluorescent images for 11A50-B10 ($A\beta_{40}$, red), lectin (glycoprotein in blood vessel, green) and DAPI (nuclei, blue) in paraffin-embedded retinal cross-sections isolated from age and sex-matched human donors with AD, MCI or cognitively normal (CN). **a.** Vertical and **b.** Longitudinal vessels are shown (yrs=years old; F=female; C=Caucasian; A=Asian). Scale bars=10 μ m.



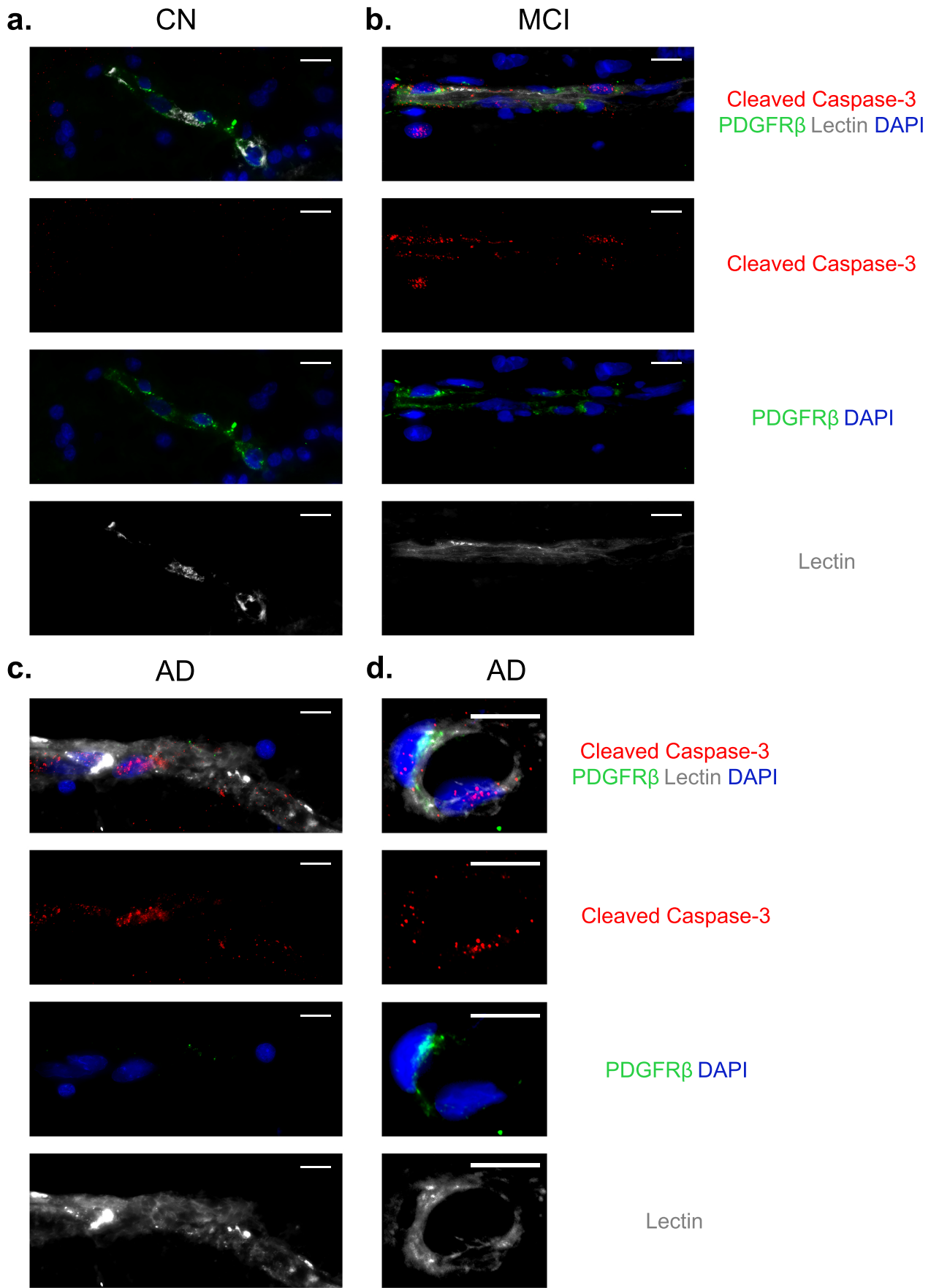
Supplementary Figure 10. Supplementary information for quantification of A β_{40} in human retina. **a-d.** Quantitative analysis of 11A50-B10 (A β_{40}) immunoreactive (IR) area (normalized by retinal thickness) in retinal layers (from inner to outer limiting membrane) from each retinal quadrant separately: **a.** NS, **b.** IN, **c.** ST, **d.** TI in AD (n=17), MCI (n=8), and CN (n=11) human donors. **e.** Pearson's coefficient (r) correlation between A β_{40} IR area and retinal A β_{40} burden in blood vessels (n=26). **f-j.** Quantitative analysis of raw data of 11A50-B10 (A β_{40})-IR area in retinal layers from each retinal quadrant separately and all quadrants together: **f.** all retinal quadrants, **g.** NS, **h.** IN, **i.** ST and **j.** TI in AD (n=17), MCI (n=8) and CN (n=11) human donors. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$, by one-way ANOVA test with Sidak's post-hoc multiple comparison test. Fold changes are shown in red.



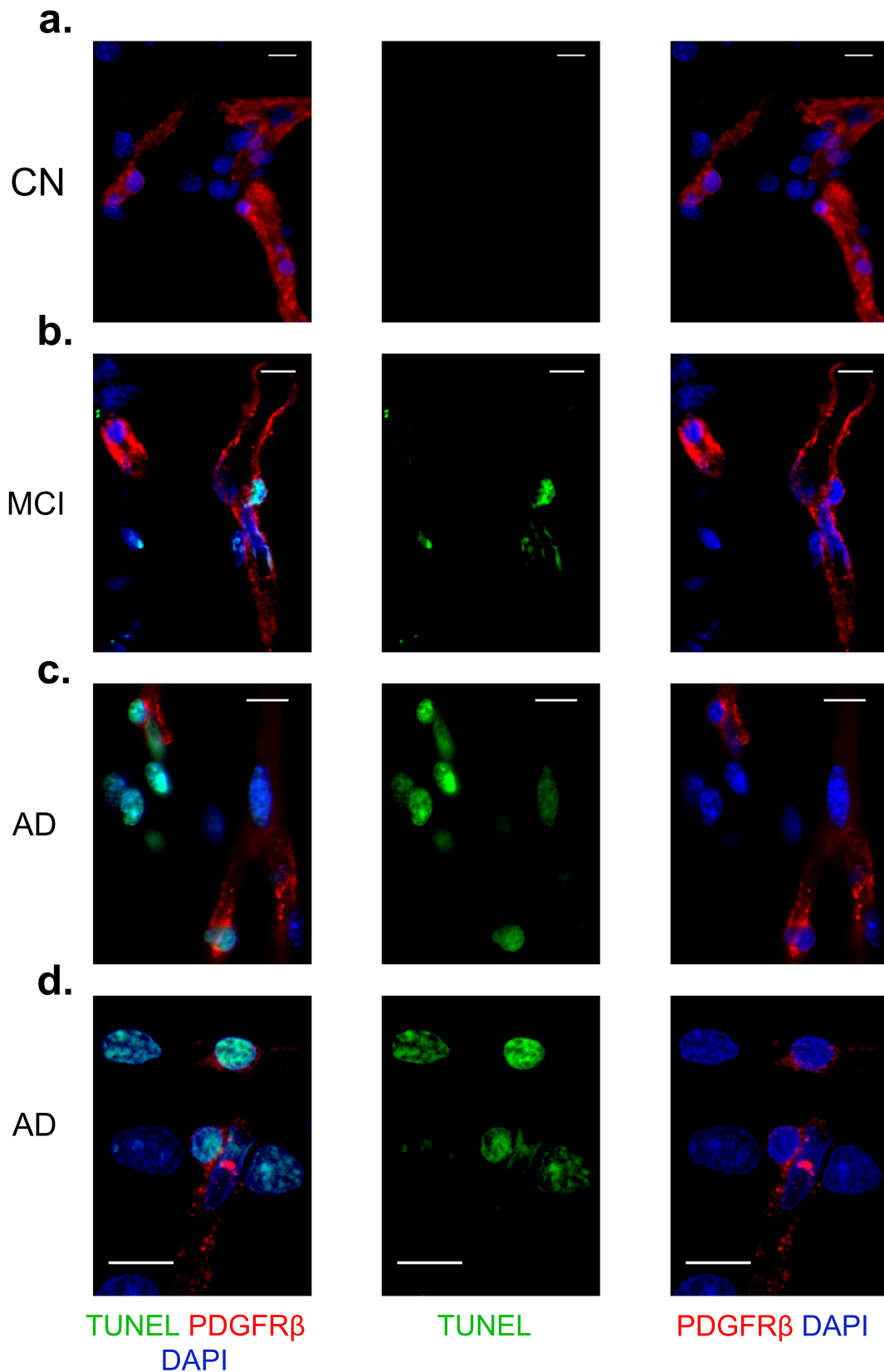
Supplementary Figure 11. Extended data of inner vs. outer retinal A β_{40} and mapping for all four retinal quadrants. **a-e.** Quantitative analysis of raw data of A β_{40} -immunoreactive (IR) area in inner retinal layers from each retinal quadrant separately and all quadrants together: **a.** NS, **b.** IN, **c.** ST, **d.** TI, **e.** all, in AD ($n=17$), MCI ($n=8$) and CN ($n=11$) human donors. **f-j.** Quantitative analysis of raw data of A β_{40} -IR area in outer retinal layers from each retinal quadrant separately and all quadrants together: **f.** NS, **g.** IN, **h.** ST, **i.** TI, **j.** all, in AD ($n=17$), MCI ($n=8$) and CN ($n=11$) human donors. **k.** Mapping of A β_{40} in four retinal quadrants (* indicates AD vs. CN, * indicates AD vs. MCI). **l.** Pearson's coefficient (r) correlation between A β_{40} IR area against % PDGFR β -IR area in vessels ($n=28$). Data from individual human donor as well as group means and SEMs are shown. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$, by one-way or two-way ANOVA test with Sidak's post-hoc multiple comparison test. Fold changes are shown in red.



Supplementary Figure 12. Extended representative images for LRP-1 in figure 6. **a-b.** Merged and separate channels of representative fluorescent images for LRP-1 (red), PDGFR β (green), lectin (glycoprotein in blood vessel, white) and DAPI (nuclei, blue) in paraffin-embedded retinal cross-sections isolated from age and sex-matched human donors with AD or cognitively normal (CN). **a.** CN and **b.** AD are shown. Scale bars=10 μ m.



Supplementary Figure 13. Extended representative images for cleaved caspase-3 in figure 6. **a-d.** Merged and separate channels of fluorescent images for cleaved caspase-3 (red), PDGFR β (green), lectin (glycoprotein in blood vessel, white) and DAPI (nuclei, blue) in paraffin-embedded retinal cross-sections isolated from age and sex-matched human donors with AD, MCI or cognitively normal (CN). **a.** CN, **b.** MCI and **c-d.** AD are shown. Scale bars=10 μ m.



Supplementary Figure 14. Extended representative images for TUNEL staining in figure 6. **a-d.** Merged and separate channels of fluorescent images for TUNEL (green), PDGFR β (red), and DAPI (nuclei, blue) in paraffin-embedded retinal cross-sections isolated from age and sex-matched human donors with AD, MCI or cognitively normal (CN). **a.** CN, **b.** MCI and **c-d.** AD are shown. Scale bars=10 μ m.

Table S1. Demographic data on human eye donors evaluated by retinal cross-section.

	CN	MCI	AD	F	P
No. of Subjects (n=46)	14	11	21	-	-
	(9F, 5M)	(5F, 6M)	(13F, 8M)		
Age ± SD	79.14 ± 10.5	87.09 ± 5.4	81.81 ± 14.9	1.404	0.2567
[Years]	F: 79.78 ± 12.3	F, 90.2 ± 3.6	F, 85.61 ± 12.6		
	M: 78.0 ± 7.3	M, 84.5 ± 5.5	M, 67.2 ± 16.7		
Race	13C (92.9%)	7C (81.8%)	16C (76.2%)	-	-
(%)	1B (7.1%)	1H (9.1%)	1B (4.8%)		
		1B (9.1%)	4A (19%)		
PMI	7.5 ± 2.3	9.5 ± 5.0	7.6 ± 3.7	1.120	0.3355
[Hours]					

CN cognitively normal; MCI, mild cognitive impairment; AD, Alzheimer’s disease; F, female, M, male; SD, standard deviation; C, Caucasian; B, Black; H, Hispanic; A, Asian, UK Unknown; PMI, post-mortem interval; Values are presented as mean ± SD. F and P values were determined by one-way ANOVA with Sidak’s multiple comparison test.

Table S2. Neuropathological evaluation in a subset of human donors evaluated by retinal cross-section.

Brain Scores	CN* (n=1)	MCI (n=7)	AD (n=17)
CAA	1	0.7 ± 0.97	1.3 ± 0.75
A β Plaque	0.545	2.11 ± 0.77	2.8 ± 0.93
Neurofibrillary Tangle	0.98	1.46 ± 0.99	2.5 ± 1.3
Neuropil Thread	0.86	1.1 ± 0.93	1.13 ± 1.2
Atrophy	0.8	1.09 ± 1.08	2.05 ± 1.2

CN cognitively normal; MCI, mild cognitive impairment; AD, Alzheimer's disease; A neuropathological score from one CN donor. CAA, cerebral amyloid angiopathy.

Table S3. Multiple correlation analysis between % retinal PDGF β area in vessels and neuropathological parameters

		Neuritic Plaques	Immature Plaques	Diffuse Plaque	NFTs (Silver)	Neuropil Threads
All Brain	<i>r</i>	-0.50	-0.36	-0.45	-0.07	-0.03
	<i>P</i>	0.0264	0.1224	0.0443	0.7801	0.9022
Hippocampus	<i>r</i>	-0.61	-0.40	-0.38	-0.17	0.12
	<i>P</i>	0.0046	0.0802	0.0986	0.4622	0.6184
Entorhinal Cortex	<i>r</i>	0.26	-0.01	0.35	0.15	-0.23
	<i>P</i>	0.0433	0.2598	0.3403	0.4902	0.5154
Frontal Cortex	<i>r</i>	-0.01	-0.30	-0.04	-0.38	-0.34
	<i>P</i>	0.9543	0.1990	0.8586	0.1027	0.1396
Temporal Cortex	<i>r</i>	-0.06	-0.33	-0.35	-0.09	-0.18
	<i>P</i>	0.8066	0.1551	0.1265	0.7234	0.4504
Parietal Cortex	<i>r</i>	0.05	0.01	-0.28	-0.33	-0.39
	<i>P</i>	0.8431	0.9769	0.2280	0.1511	0.0938
PV. Ctx. A-17	<i>r</i>	-0.32	-0.35	-0.46	-0.25	-0.55
	<i>P</i>	0.2134	0.1540	0.0568	0.3412	0.0175
VA. Ctx. A-18	<i>r</i>	-0.74	-0.30	-0.58	-0.39	-0.46
	<i>P</i>	0.0015	0.2598	0.0192	0.1457	0.0872

Correlations between retinal % area of PDGF β in vessels and the corresponding neuropathological measurements: neuritic plaques, immature plaques, diffuse plaques, neurofibrillary tangles (NFTs; by Gallyas Silver stain), neuropil threads by silver stain. Scores are given as: 0 = None, 1 = Sparse (-5), 3 = Moderate (6-20), 5 = Frequent (21-30 or above) based on pathological reports. Analysis was performed for mean of all brain regions and separated for each brain region. Sample size: n=14 for AD, n=5 for MCI, n=1 for CN. Statistical significance *P* is < 0.05 indicated in bold red color. Pearson's *r* correlations analysis was applied to determine relationships; PV – primary visual; VA – visual association; Ctx – cortex.

Table S4. Multiple correlation analysis between % retinal A β_{40} area in vessels and neuropathological parameters

		Neuritic Plaques	Immature Plaques	Diffuse Plaques	NFTs (Silver)	Neuropil Threads
All Brain	<i>r</i>	0.55	0.44	0.16	0.24	0.58
	<i>P</i>	0.0492	0.1292	0.6122	0.4278	0.0375
Hippocampus	<i>r</i>	0.41	0.22	0.08	0.37	0.48
	<i>P</i>	0.1649	0.4702	0.7984	0.211	0.0967
Entorhinal Cortex	<i>r</i>	0.77	0.47	0.2	0.33	0.31
	<i>P</i>	0.0023	0.1012	0.505	0.2755	0.3018
Frontal Cortex	<i>r</i>	0.05	0.53	-0.06	0.40	0.53
	<i>P</i>	0.8747	0.0638	0.8475	0.1777	0.0616
Temporal Cortex	<i>r</i>	0.00	0.23	0.02	0.06	0.57
	<i>P</i>	0.9878	0.4551	0.9574	0.8534	0.0507
Parietal Cortex	<i>r</i>	0.02	-0.09	0.15	0.14	0.38
	<i>P</i>	0.941	0.7627	0.6274	0.6522	0.2022
PV. Ctx. A-17	<i>r</i>	0.18	0.6	0.21	-0.19	0.64
	<i>P</i>	0.5929	0.0373	0.5179	0.5798	0.0347
VA. Ctx. A-18	<i>r</i>	0.54	0.53	-0.09	-0.03	0.84
	<i>P</i>	0.1377	0.1137	0.8081	0.93	0.0042

Correlations between retinal % area of A β_{40} in vessels and the corresponding neuropathological measurements: neuritic plaques, immature plaques, diffuse plaques, neurofibrillary tangles (NFTs; by Gallyas Silver stain), neuropil threads by silver stain. Scores are given as: 0 = None, 1 = Sparse (-5), 3 = Moderate (6-20), 5 = Frequent (21-30 or above) based on pathological reports. Analysis was performed for mean of all brain regions and separated for each brain region. Sample size: n=8 for AD, n=3 for MCI, n=1 for CN patients. Statistical significance *P* is < 0.05 indicated in bold red color. Pearson's *r* correlations analysis was applied to determine relationships; PV – primary visual; VA – visual association; Ctx – cortex.

Table S5. Correlation between % PDGFR β immunoreactive area per retinal subregions and MMSE scores.

Retinal Regions	Total	ST	TI	IN	NS	Superior	Inferior	Nasal	Temporal
<i>r</i>	0.77	0.89	0.82	0.71	0.92	0.92	0.71	0.73	0.89
<i>P</i>	0.0156	0.016	0.1825	0.0499	0.0271	0.0036	0.0486	0.0411	0.0171
N	9	6	4	8	5	7	8	8	6

Total; total retinal average; ST, superiortemporal; TI, temporalinferior; IN, inferioirnasal; NS, nasalsuperior; Superior, mean of ST and NS values; Inferior, mean of TI and IN values; Nasal, mean of IN and NS values; Temporal, mean of ST and TI values. N, number of pairs. Statistical significance *P* is < 0.05. Pearson's *r* correlations analysis was applied to determine relationships.

Table S6. Correlation between A β ₄₀ burden per retinal subregions and MMSE cognitive scores.

Retinal Regions	Total	ST	TI	IN	NS	Superior	Inferior	Nasal	Temporal
<i>r</i>	-0.57	-0.71	N/A	-0.65	N/A	-0.73	-0.67	-0.66	-0.75
<i>P</i>	0.0827	0.0737	N/A	0.1107	N/A	0.0625	0.099	0.1062	0.0539
<i>n</i>	10	7	N/A	7	N/A	7	7	7	7

Total; total retinal average; ST, superiortemporal; TI, temporalinferior; IN, inferioirnasal; NS, nasalsuperior; Superior, mean of ST and NS values; Inferior, mean of TI and IN values; Nasal, mean of IN and NS values; Temporal, mean of ST and TI values. N, number of pairs. N/A, not applicable. Statistical significance *P* is < 0.05. Pearson's *r* correlations analysis was applied to determine relationships.