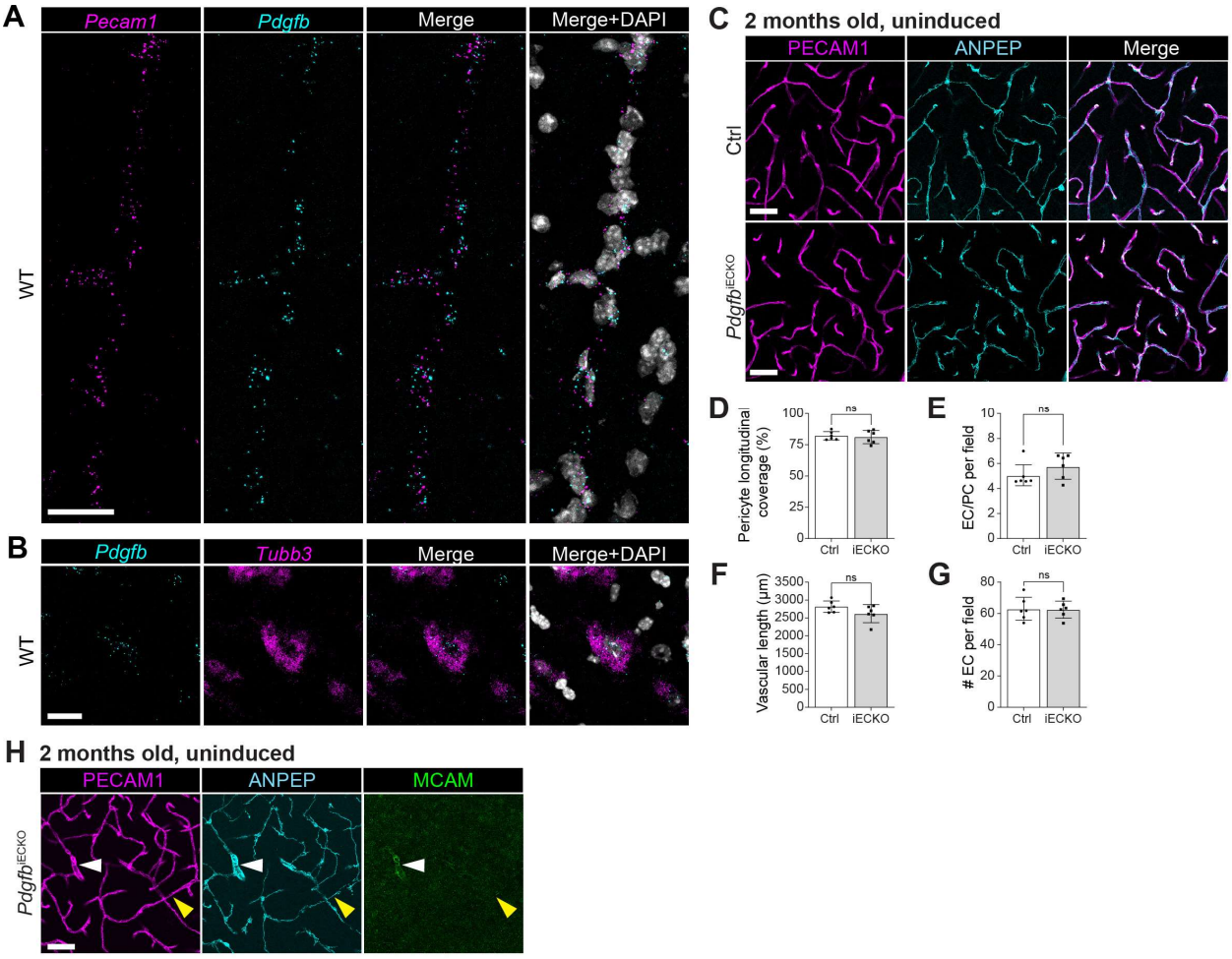
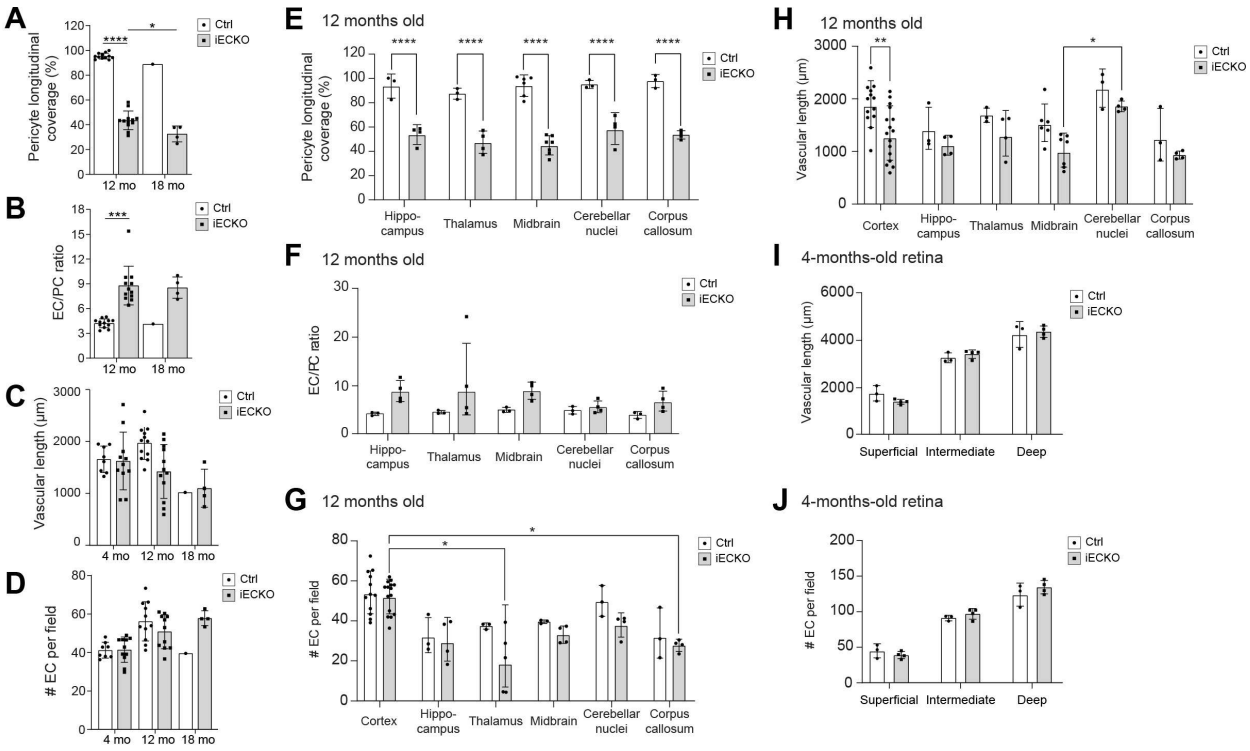
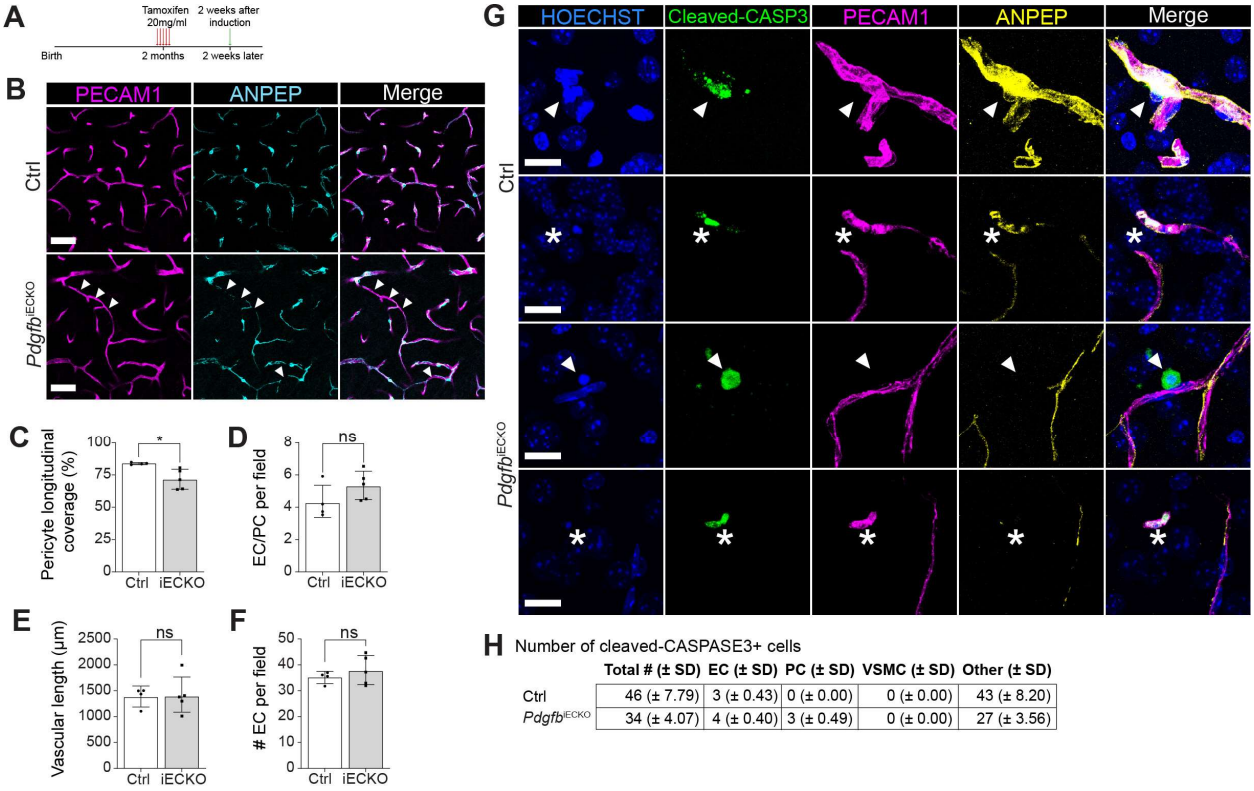


Supplementary figure 1. (A, B) RNA in situ hybridization on 3-months-old C57BL6 mouse cerebral cortex (n=3). *Pdgfb* (cyan) expression colocalizes with *Pecam1* (magenta) positive endothelium **(A)** and *Tubb3* (magenta) positive neurons **(B)**. Cell nuclei are stained with DAPI (white). Scale bars 25 µm and 50 µm. **(C)** Representative overview images from the cortex of uninduced 2-months-old mice. Two litters were analyzed (n=6). Co-immunolabeling of PECAM1 (magenta) and ANPEP (cyan). Scale bars 50 µm. **(D)** Pericyte longitudinal coverage in uninduced *Pdgfb*^{iECKO} and controls (two litters, n=6). **(E)** Quantification of the endothelial cell (ERG+) to pericyte (ANPEP+, DAPI+) ratio per field (two litters, n=6). **(F)** The skeletal length of PECAM1 positive capillaries was quantified and considered as the vascular length per field (two litters, n=6). **(G)** The total number of endothelial cells (ERG+) detected per field (two litters, n=6). **(H)** Representative images from the cortex of uninduced 2-months-old mice. One litter was analyzed (n=3). Co-immunolabeling of PECAM1 (magenta), ANPEP (cyan) and MCAM (green). The white arrowhead marks an MCAM-expressing aaVSMC and the yellow arrowhead marks a faint MCAM-expressing pericyte. Scale bar 50 µm. **E**, Normality tests revealed that the data was unevenly distributed so nonparametric Mann-Whitney U test was used to evaluate significance. **D**, **F** and **G**, The significance of evenly distributed data was evaluated using unpaired 2-tailed t test with Welch correction. ns= not significant. Data is presented as geometric mean with geometric SD.

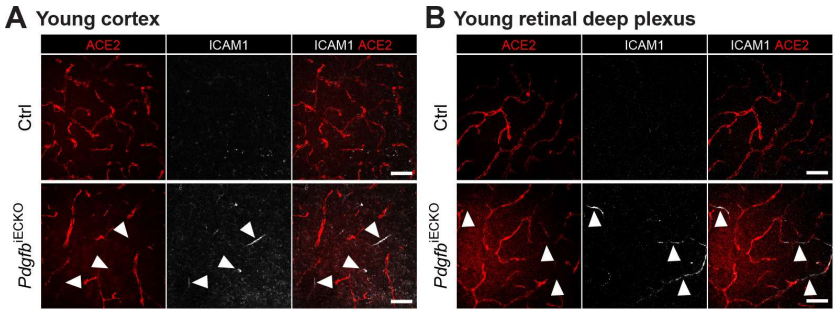


Supplementary figure 2. (A-D) Comparison between 12- and 18-months-old mice. 4 litters of 12-moths-old mice (*Pdgfb*^{iECKO} n=12, Ctrl n=12), 1 litter of 18-months-old mice (*Pdgfb*^{iECKO} n=4, Ctrl n=1). Not significant data is not labeled. **(A)** Pericyte longitudinal coverage of the vasculature per field in cerebral cortex. **(B)** Endothelial cell to pericyte ratio per field in cerebral cortex. **(C)** Vascular longitudinal length per field in cerebral cortex. **(D)** Endothelial cell numbers per field in cerebral cortex. **(E)** Pericyte longitudinal coverage per field in hippocampus, thalamus, midbrain, cerebellar nuclei and corpus callosum of 12-months-old mice. Two litters of 12-months-old mice (*Pdgfb*^{iECKO} n=4, Ctrl n=3). In midbrain, four litters of 12-months-old mice (*Pdgfb*^{iECKO} n=11, Ctrl n=7). **(F)** Endothelial cell to pericyte ratio per field in hippocampus, thalamus, midbrain, cerebellar nuclei and corpus callosum of 12-months-old mice. Two litters of 12-months-old mice (*Pdgfb*^{iECKO} n=4, Ctrl n=3). **(G)** Endothelial cell numbers per field in cerebral cortex, hippocampus, thalamus, midbrain, cerebellar nuclei and corpus callosum of 12-months-old mice. Two litters of 12-months-old mice (*Pdgfb*^{iECKO} n=4, Ctrl n=3). In cerebral cortex, five litters of 12-months-old mice (*Pdgfb*^{iECKO} n=16, Ctrl n=13). In midbrain, four litters of 2-months-old mice (*Pdgfb*^{iECKO} n=11, Ctrl n=7). **(H)** Vascular longitudinal length per field in cerebral cortex, hippocampus, thalamus, midbrain, cerebellar nuclei and corpus callosum of 12-months-old mice (two litters, *Pdgfb*^{iECKO} n=4, Ctrl n=3). In the cerebral cortex, five litters of 2-months-old mice (*Pdgfb*^{iECKO} n=16, Ctrl n=13). In midbrain, four litters of 12-months-old mice (*Pdgfb*^{iECKO} n=11, Ctrl n=7). **(I)** Vascular longitudinal length per field in Superficial, intermediate and deep retinal plexuses of 4-months-old mice (one litter, *Pdgfb*^{iECKO} n=4, Ctrl n=3). **(J)** Endothelial cell numbers per field in Superficial, intermediate and deep retinal plexuses of 4-months-old mice (one litter, *Pdgfb*^{iECKO} n=4, Ctrl n=3). **(K)** Representative images of 18-months-old retinal superficial, intermediate and deep plexuses. One litter was analyzed (*Pdgfb*^{iECKO} n=2, Ctrl n=1). Co-immunolabeling of PECAM1 (magenta) and CSPG4 (cyan). Scale bars 50 µm. **A** and **B**, Normality tests revealed that the data was unevenly distributed so nonparametric Kruskal-Wallis multiple comparison test was used to evaluate significance. **C** and **D**, The significance of evenly distributed data was evaluated using Tukey's multiple comparison test. **G and I Intermediate**, Normality tests revealed that the data was unevenly distributed so nonparametric Mann-Whitney U test was used to evaluate significance. **E**, **F**, **H**, **I Superficial** and **Deep** and **J**, The significance of evenly distributed data was evaluated using unpaired 2-tailed t test with Welch correction. Data is presented as geometric mean with geometric SD. *p<0.05, **p<0.01, ***p=0.001, ****p<0.0001, ns=not significant.

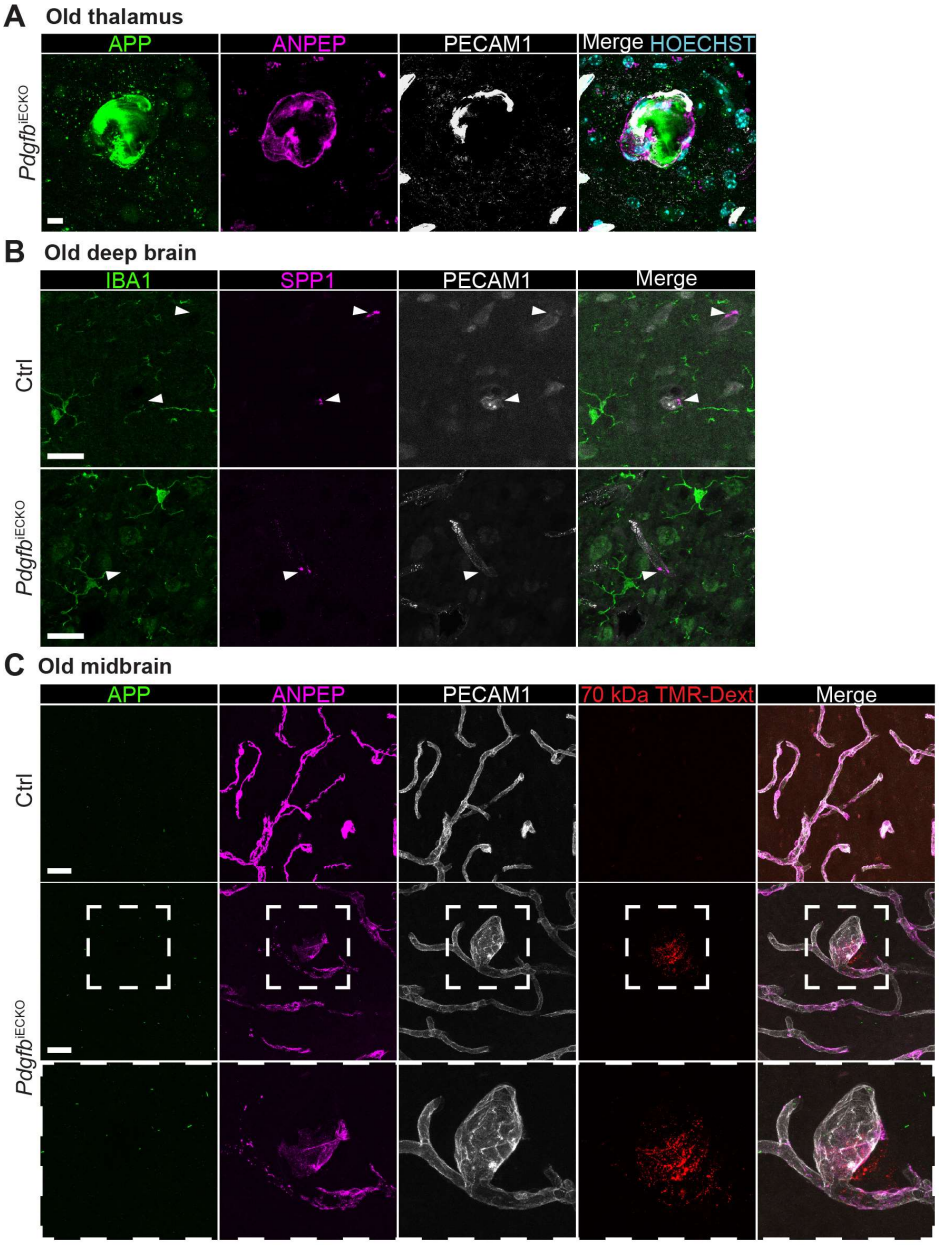


	Total # (± SD)	EC (± SD)	PC (± SD)	VSMC (± SD)	Other (± SD)
Ctrl	46 (± 7.79)	3 (± 0.43)	0 (± 0.00)	0 (± 0.00)	43 (± 8.20)
Pdgfb^{iECKO}	34 (± 4.07)	4 (± 0.40)	3 (± 0.49)	0 (± 0.00)	27 (± 3.56)

Supplementary figure 3. (A) Endothelial specific *Pdgfb* deletion was induced via 5 doses of Tamoxifen administration at 2 months of age. Two weeks after the mice were analyzed. **(B)** Representative overview images from the cortex of mice analyzed 2 weeks after induction. Co-immunolabeling of PECAM1 (magenta) and ANPEP (cyan). Arrowheads mark places where the expression of ANPEP is lacking. One litter was analyzed (Ctrl n=4, *Pdgfb*^{iECKO} n=5). Scale bars 50 µm. **(C)** The pericyte longitudinal coverage in *Pdgfb*^{iECKO} and controls (one litter, Ctrl n=4, *Pdgfb*^{iECKO} n=5). **(D)** Quantification of the endothelial cell (ERG+) to pericyte (ANPEP+, HOECHST+) ratio (one litter, Ctrl n=4, *Pdgfb*^{iECKO} n=5). **(E)** The skeletal length of PECAM1 positive capillaries was quantified and considered as the vascular length per field (one litter, Ctrl n=4, *Pdgfb*^{iECKO} n=5). **(F)** The total number of endothelial cells (ERG+) detected per field (one litter, Ctrl n=4, *Pdgfb*^{iECKO} n=5). **(G)** Representative images from the cortex of *Pdgfb*^{iECKO} and littermate control mice analyzed 2 weeks after induction. Hoechst (white), Cleaved-CASPASE3 (green), PECAM1 (magenta), ANPEP (yellow). Arrowheads show cells undergoing apoptosis and asterisks show potential endothelial cells undergoing apoptosis. One litter was analyzed (Ctrl n=4, *Pdgfb*^{iECKO} n=5). Scale bars 25 µm. **(H)** Quantification of total number of cleaved-CASPASE3 positive cells per two 50 µm-thick sections. Breakdown of the total number of apoptotic cells into endothelial cells, pericytes, VSMCs and other cell types (one litter, Ctrl n=4, *Pdgfb*^{iECKO} n=5). Total numbers per group are shown with ± SD. **E**, Normality tests revealed that the data was unevenly distributed so nonparametric Mann-Whitney U test was used to evaluate significance. **C**, **D** and **F**, The significance of evenly distributed data was evaluated using unpaired 2-tailed t test with Welch correction. *p<0.05, ns= not significant. Data is presented as geometric mean with geometric SD.



Supplementary figure 4. (A) Representative images of the cortex of young *Pdgfb*^{iECKO} and littermate controls. Co-immunolabeling of ACE2 (red) and ICAM1 (white). White arrowheads mark capillaries with ICAM1 expression that lack pericyte coverage. Scale bar 50 µm. *Pdgfb*^{iECKO} n=11, Ctrl n=10. **(B)** Representative images of the retinal plexuses of young *Pdgfb*^{iECKO} and littermate controls. Co-immunolabeling of ACE2 (red) and ICAM1 (white). White arrowheads mark capillaries with ICAM1 expression that lack pericyte coverage. Scale bar 50 µm. *Pdgfb*^{iECKO} n=4, Ctrl n=3.



Supplementary figure 5. (A) Calcified nodule in the thalamus of an old *Pdgfb*^{iECKO} mouse. Co-immunolabeling of amyloid precursor protein, APP (green), ANPEP (magenta), PECAM1 (white) and labelling of nuclei with Hoechst (cyan). Scale bar 10 µm. Four independent experiments, *Pdgfb*^{iECKO} n=16, Ctrl n=12. **(B)** Representative images of SPP1 nodules (white arrowheads) on the endothelium of old *Pdgfb*^{iECKO} mice and littermate controls (two litters, *Pdgfb*^{iECKO} n=7, Ctrl n=6). Co-immunolabeling of IBA1 (green), SPP1 (magenta) and PECAM1 (white). Scale bars 25 µm. **(C)** Representative images of the midbrain of old mice. Co-immunolabeling of APP (green), ANPEP (magenta), PECAM1 (white) and 70 kDa TMR-dextran (red). Dashed inset shows a 70 kDa TMR-dextran hotspot on an enlarged capillary without any signs of APP+ calcification. One litter, *Pdgfb*^{iECKO} n=3, Ctrl n=3. Scale bars 25 µm.