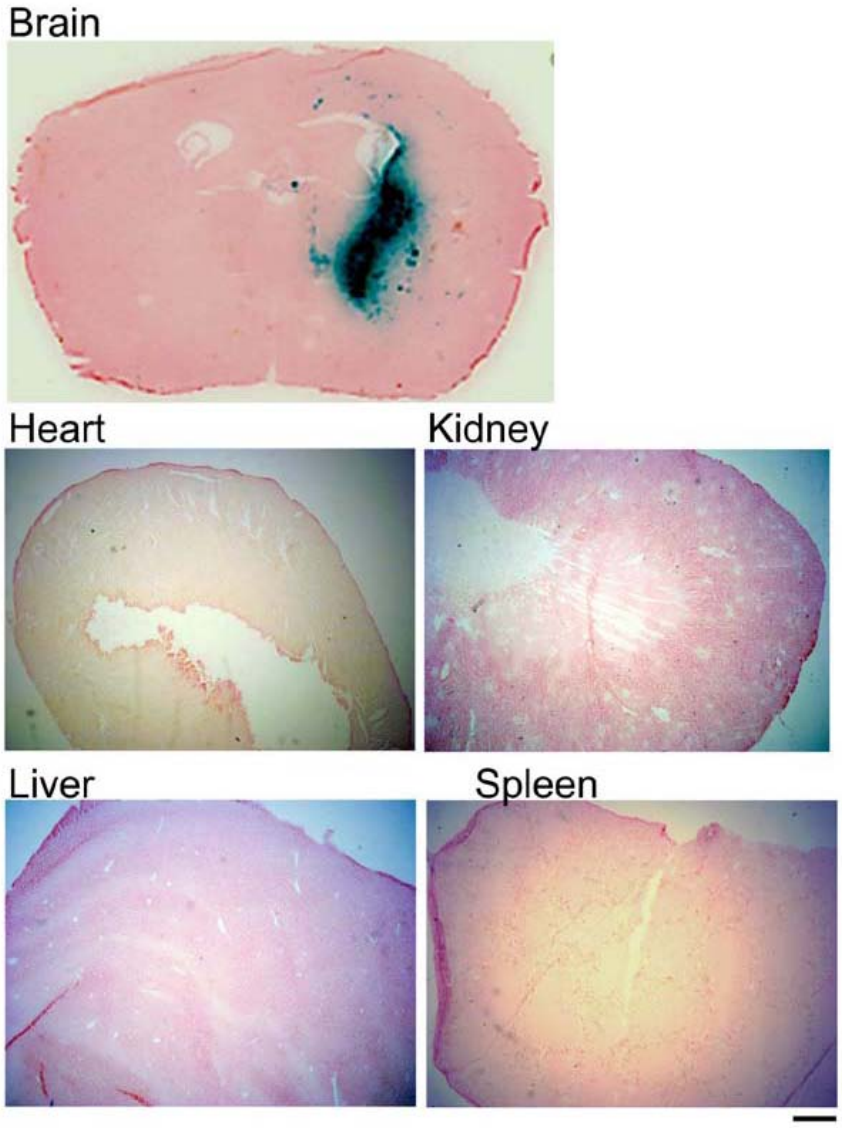
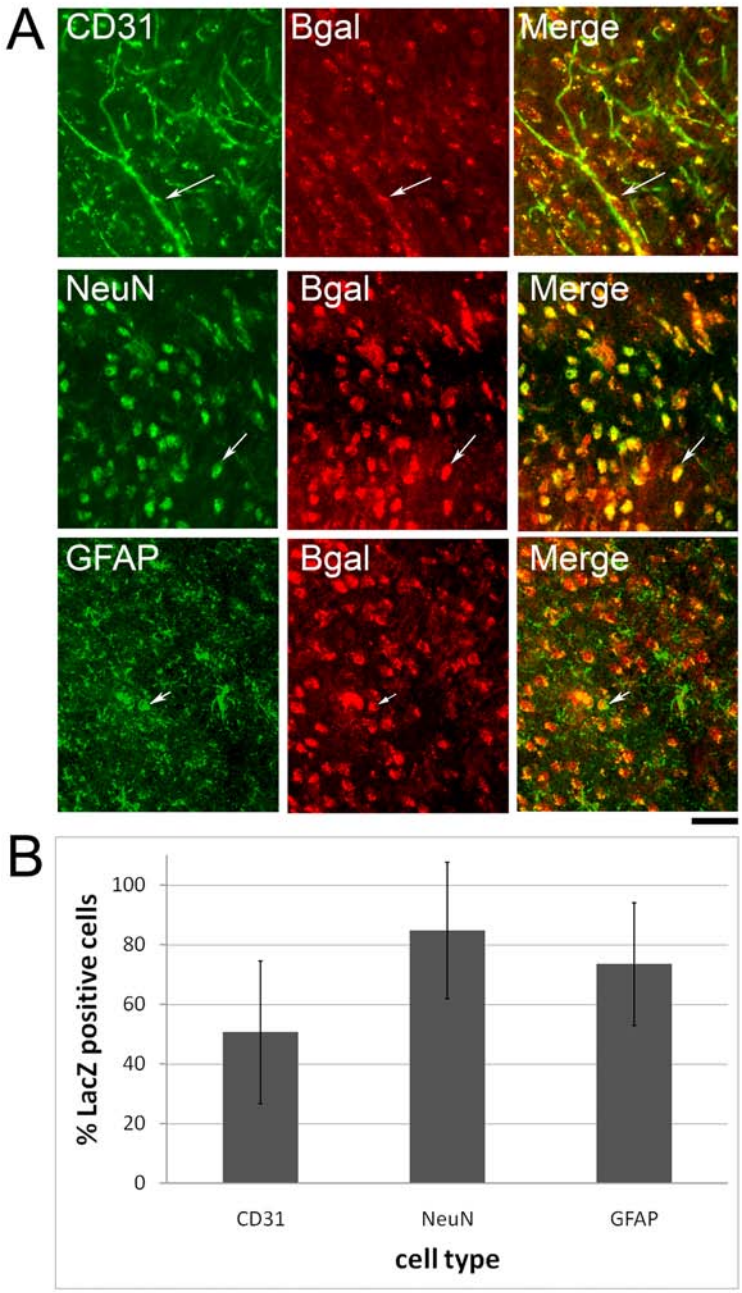
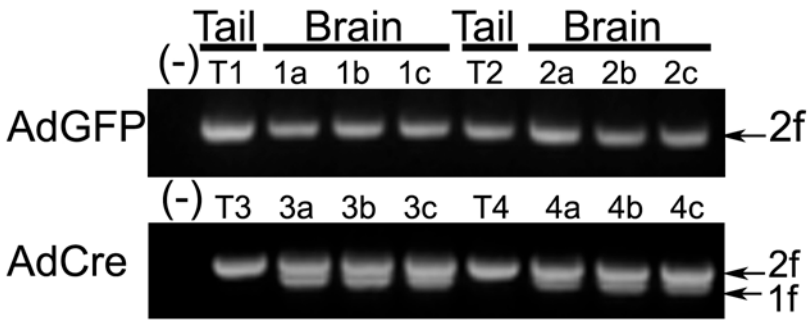


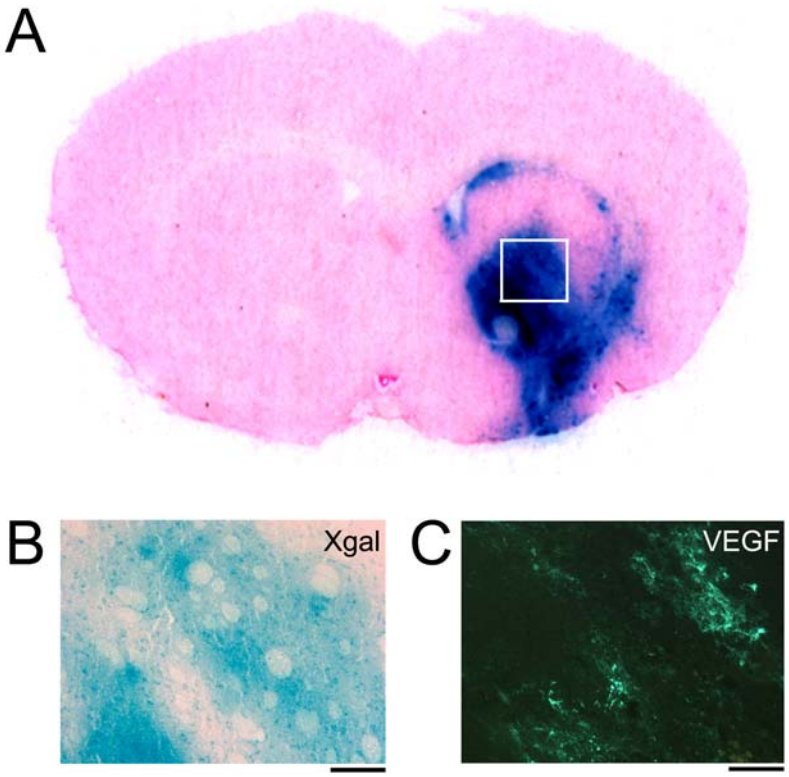
Supplemental Figure 1: **Ad-Cre mediated effective regional deletion of floxed sequence.**
Stereotactic injection of Ad-Cre into the basal ganglia of R26R mice resulted in LacZ gene expression (blue) restricted to the vector injection site. The sections were counterstained with Eosin (pink). No LacZ expression was detected in the heart, kidney, liver, and spleen, indicating that the vectors did not distribute out of the brain. Scale bar 500μm.



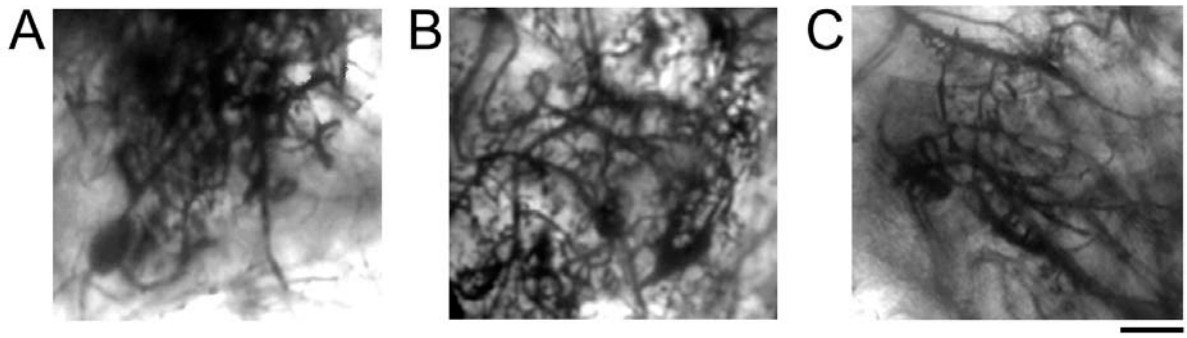
Supplemental Figure 2: **Ad-Cre mediated effective deletion of floxed sequence in endothelial cell, neurons and astrocytes.**
A) Double immunolabeling shows cre mediated activation of LacZ gene expression in brain cells of R26R mice. Antibodies specific to CD31, NeuN and GFAP were used to label endothelial cells, neurons, and astrocytes (green). LacZ expression was detected using βgal specific antibody (red). Scale Bar=50μm. B) Bar graph shows the percentage of endothelial cells (51%), neurons (85%) and astrocytes (74%) that express LacZ.



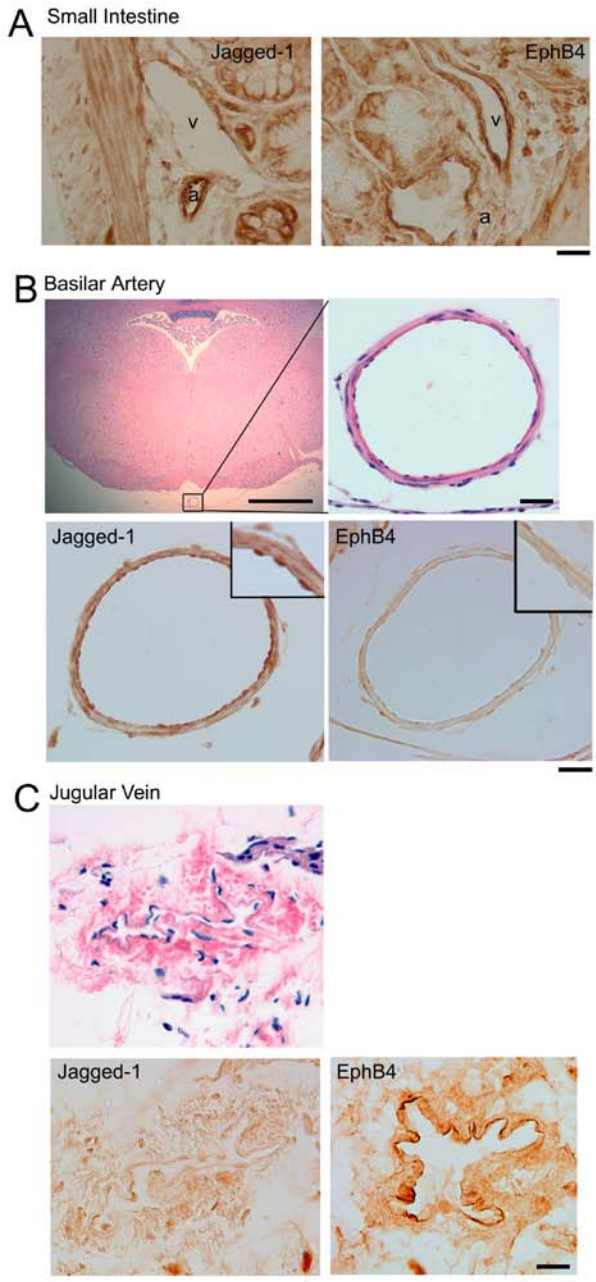
Supplemental Figure 3: Ad-Cre mediated regional Alk1 deletion.
PCR analysis detected the 1f allele only from the genomic DNA isolated from brain tissues around the Ad-Cre-injected region. No 1f allele was detected from genomic DNA isolated from tail and brain tissues collected from the Ad-GFP injected region. (-): negative controls for PCR reactions: no DNA was added in the PCR reactions. T1, T2, T3, and T4 are tail DNA from each animal. a. b. c. are brain DNA from the three brain tissues collected from each animal. 2f: 2f allele (450 bp); 1f: 1f allele (383 bp).



Supplemental Figure 4: **AAV mediated gene expression at the injection sites.** (A) Representative image shows LacZ expression at the AAV-LacZ injected region. (B) Enlarged image of the square region in (A). (C) Representative image shows VEGF expression in AAV-VEGF injection site (green). Scale Bars = 50μm



Supplemental Figure 5: Additional examples of vascular phenotype in three individual *Alk1* floxed mice treated with Ad-Cre and AAV-VEGF.
Similar to the vascular casting shown in Figure 1, these additional samples demonstrate large tangled vessels resembling a bAVM at the injection site of Ad-Cre and AAV-VEGF in the brain of three different *Alk1* floxed mice. Scale bar = 100µm.



Supplemental Figure 6: **Jagged-1 and EphB4 specific antibodies stain arteries and veins, respectively, in small intestine, basilar artery and jugular vein.**
(A) Small intestine. Jagged-1 specific antibody selectively stained the artery (a, left) and EphB4 specific antibody selectively stained the vein (v, right). Scale Bar 20 µm. (B) Basilar artery. H&E staining of a brain coronal section (top left) shows basilar artery indicated in the box. Scale Bar: 1mm. An enlarged image of H&E stained basilar artery is shown in the top right picture. Scale Bar: 20 µm. Jagged-1 positive staining (brown, low left picture) was observed in the endothelial cells of the basilar artery. No EphB4 positive staining was detected (low right). Scale Bar: 20 µm. (C) Jugular vein. Top picture shows H&E staining. EphB4 positive staining was detected in the endothelial cells of the jugular vein (lower right picture). No Jagged-1 staining was observed in the endothelial cells of the jugular vein (lower left picture). Scale Bar: 20 µm.