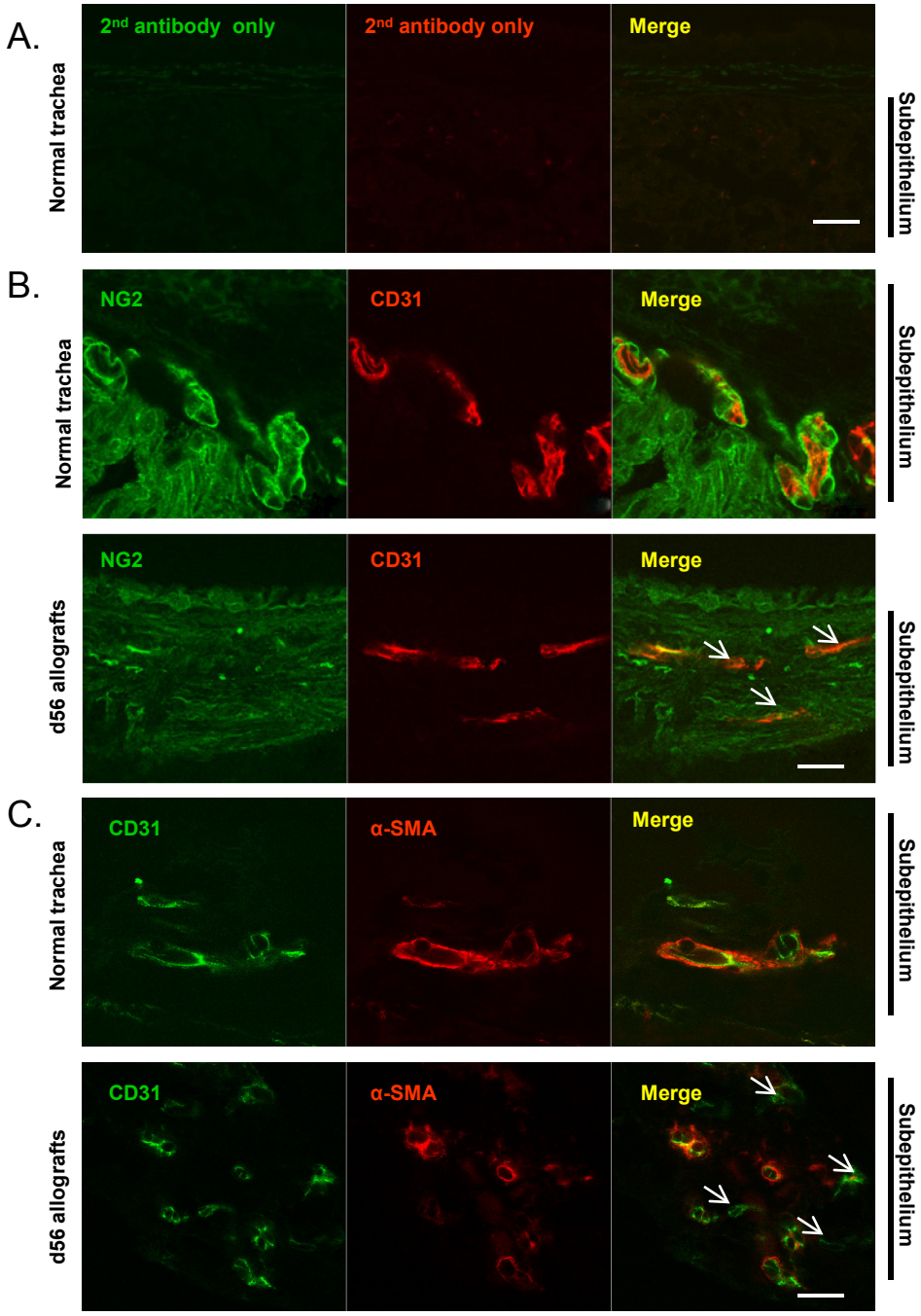
Supplemental Figure 1

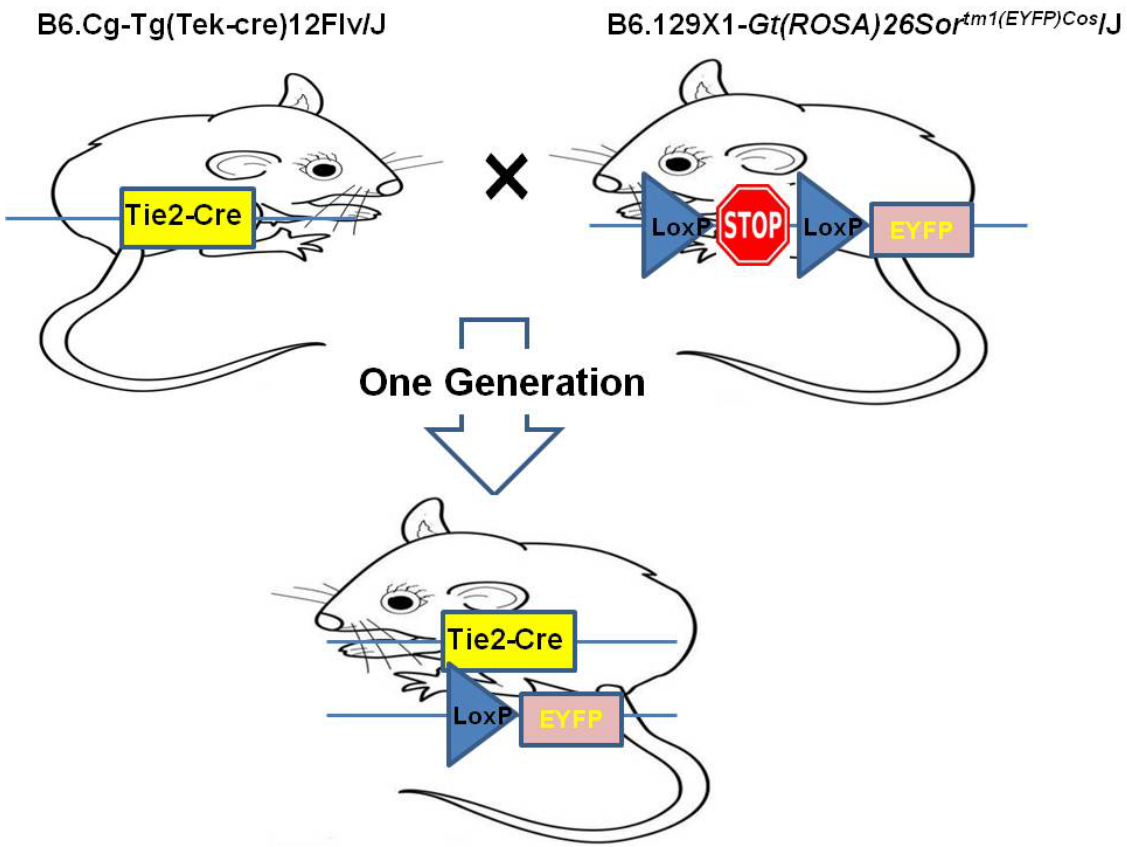


Supplemental Figure 1

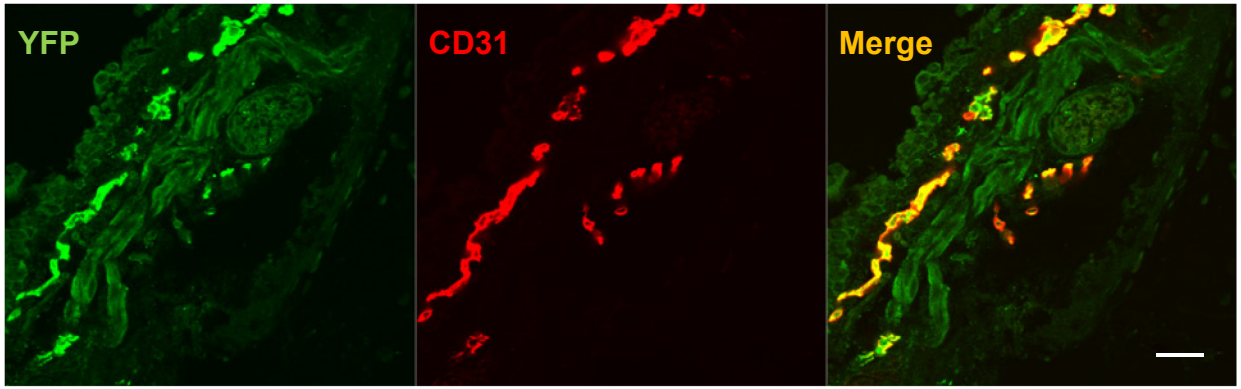
Decreased pericytes coverage in remodeled capillaries of chronically-rejected airway allografts. NG2 and α-SMA were used as pericyte markers. (**A**) Negative control stained with 2nd antibody only. (**B** and **C**) IF staining shows that remodeled, small caliber vessels in chronically-rejected day 56 allografts have more CD31^{+}NG2^{-} (red; arrow) (**B**) and CD31^{+}α-SMA^{-} (green; arrow) vessels (**C**). Scale bar: 20μM.

Supplemental Figure 2

A.



B.

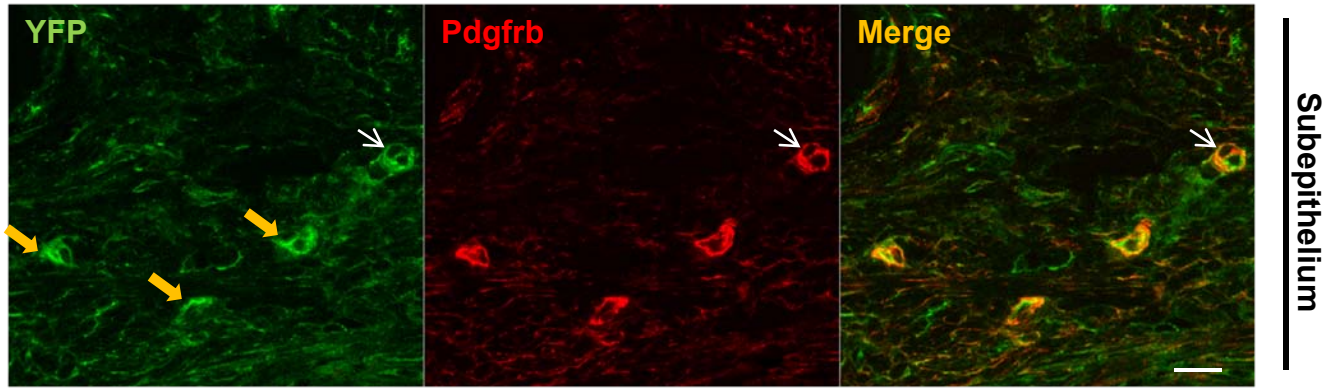


Supplemental Figure 2

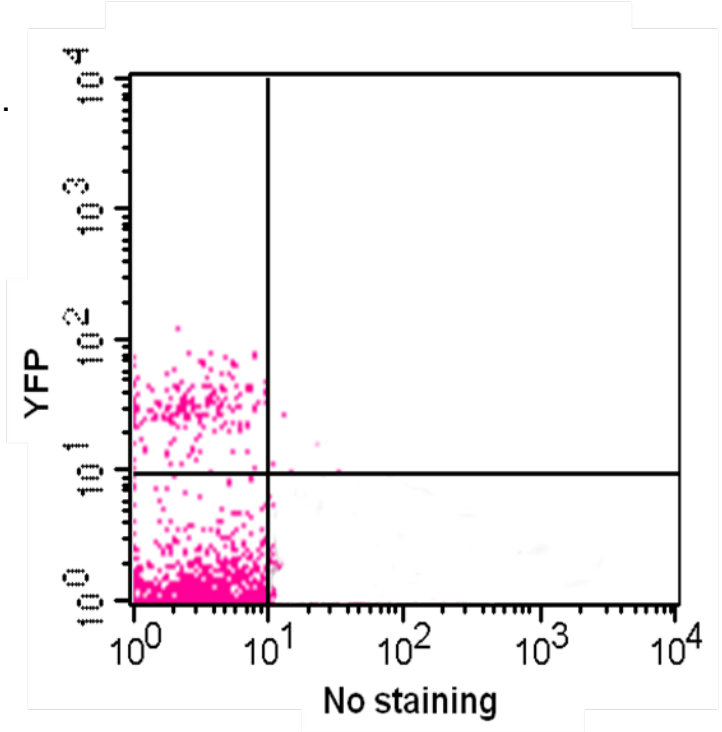
Generation of lineage tracing model for $Tie2^+$ cells. (**A**) Hemizygote mice expressing Tie2-Cre were crossed with homozygote mice expressing ROSA26EYFP to obtain (Tie2-Cre; ROSA26EYFP) double transgenic mice. (**B**) IF staining of the trachea from double transgenic mice show YFP^+ cells express CD31, which is consistent with the majority of $Tie2^+$ cells in a normal trachea being endothelial cells. Scale bar: 20μM.

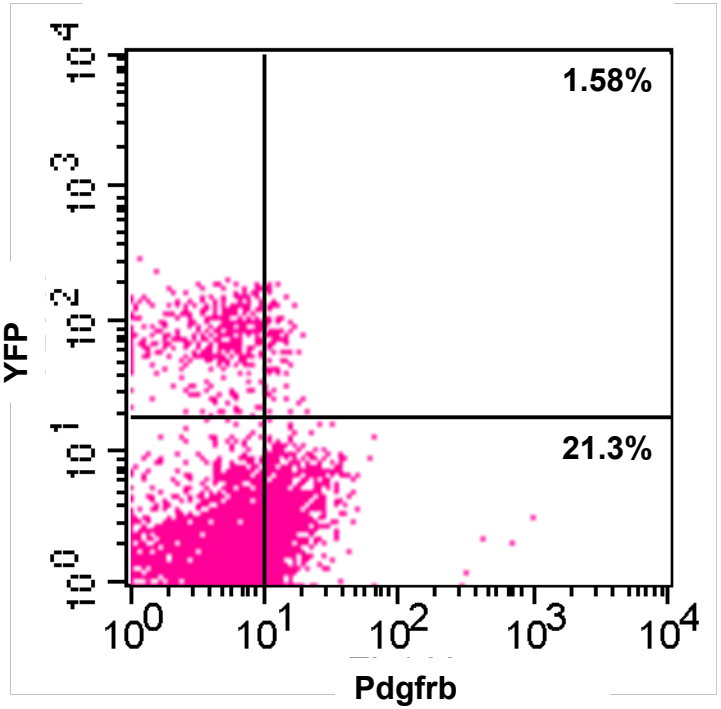
Supplemental Figure 3

A.



B.

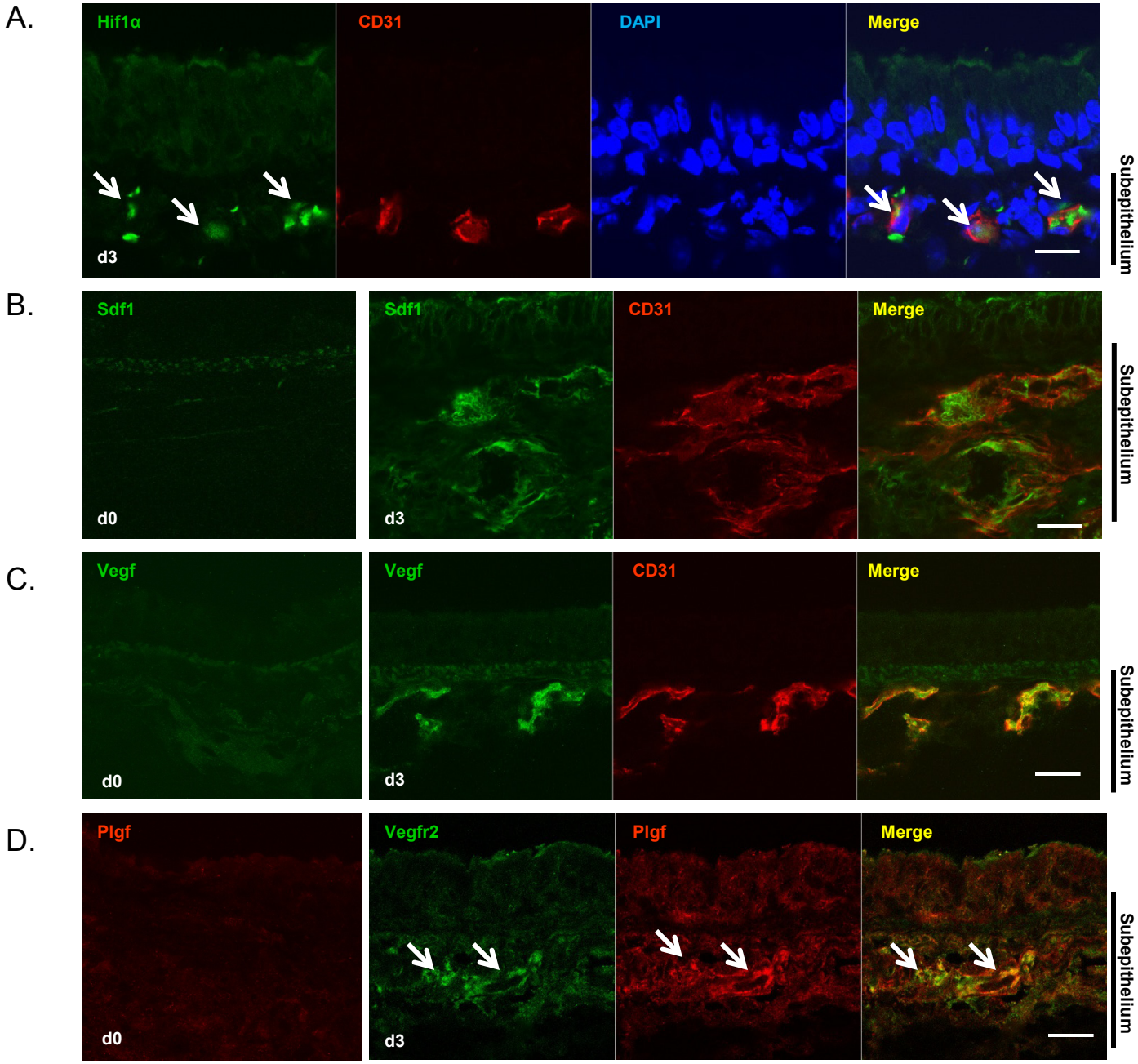




Supplemental Figure 3

Recipient Tie2$^+$ cells migrating into the rejecting allograft can become donor Pdgfrb$^+$ pericytes. (**A**) IF staining of day 56 chronically-rejected airway allograft shows that YFP$^+$ cell (green; arrow) expresses Pdgfrb(red; arrow). (**B**) Flow cytometry analysis of collagenase digested day 56 allografts confirms that YFP$^+$ cells contain a population of Pdgfrb$^+$ cells (left panel, no staining control; right panel, Pdgfrb staining). Scale bar: 20μM.

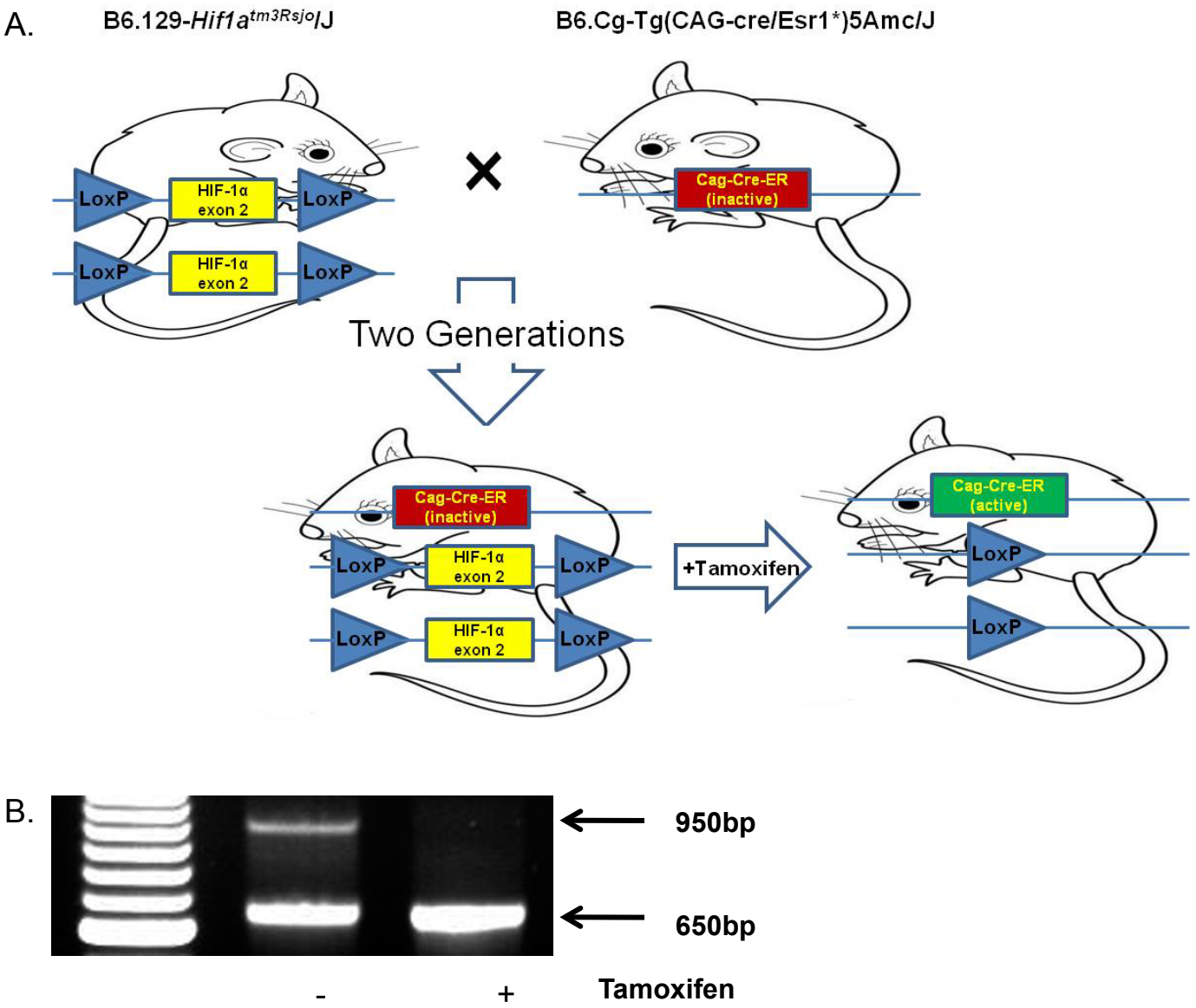
Supplemental Figure 4



Supplemental Figure 4

Endothelial origin of Hif1α and angiogenic growth factors, Sdf1, Vegf and Plgf. (**A**) IF staining of day 3 allografts (Balb/C to B6) shows that cells stained with nucleus-localized Hif1α (green; arrow) express CD31. (**B-D**) IF staining of control day 0 trachea shows negative staining of Sdf1 (**B**), Vegf (**C**) and Plgf (**D**), staining of day 3 allografts shows that Sdf1 (**B**), Vegf (**C**) or Plgf (**D**) positive cells are stained with endothelial marker CD31 or Vegfr2. Scale bar: 20μM.

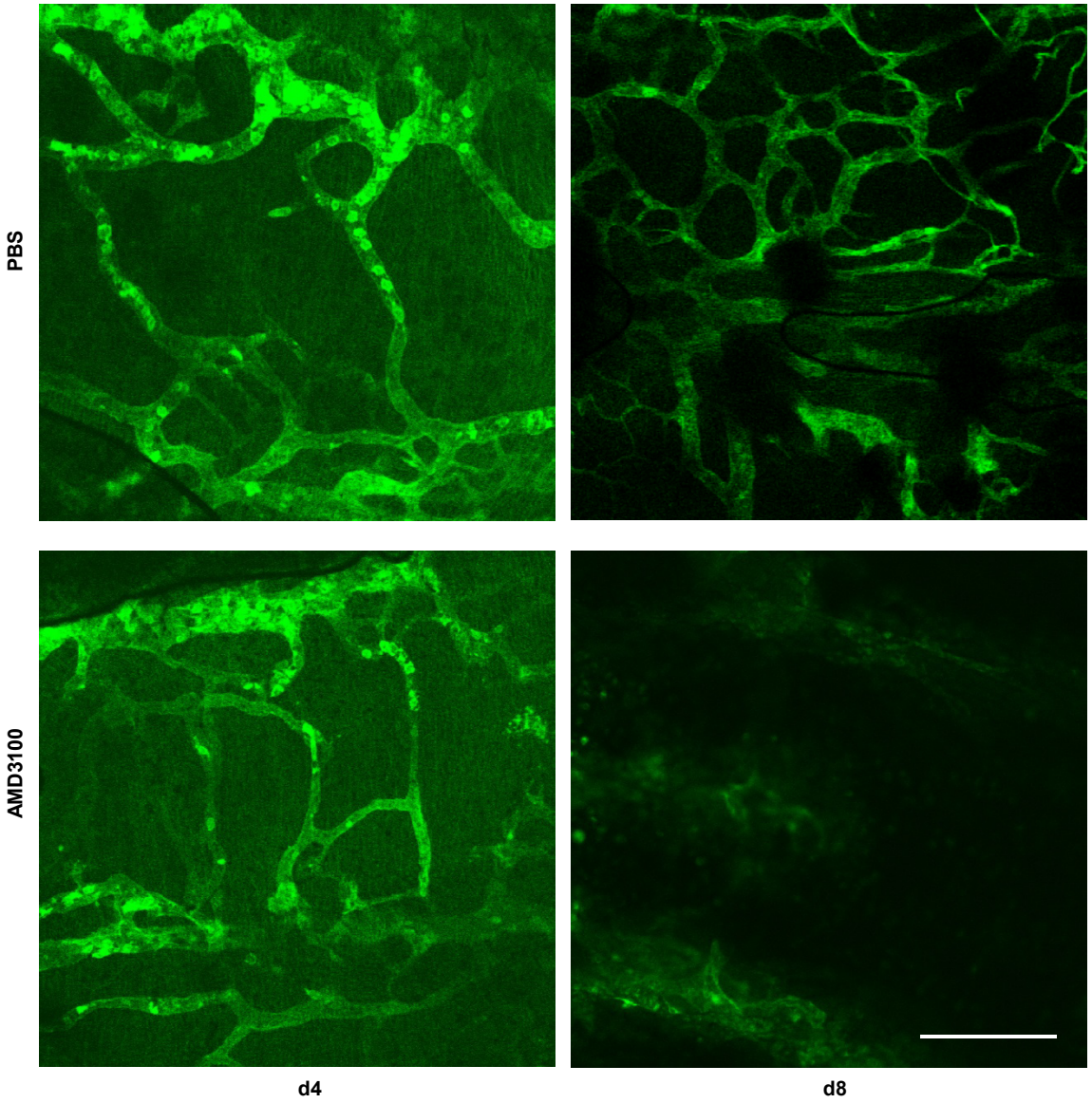
Supplemental Figure 5



Supplemental Figure 5

Generation of Hif1α conditional knockout mice and characterization of HIF-1α deficient airways. (**A**) Breeding strategy. (**B**) Mice carrying Cag-Cre-ER and Floxed Hif1α genes were treated with tamoxifen for 5 consecutive days at a dose of 120mg/kg and waited for at least 2 more days to allow sufficient recombination. Genomic DNA was then extracted from the airways and subjected to PCR analysis. Tamoxifen treatment leads to disappearance of 950 bp product because of the excision of exon 2. Primers used for PCR: 5'-GCA GTT AAG AGC ACT AGT TG-3' and 5'-TGT TAA ATA AAA GCT TGG AC-3' as described in (1).

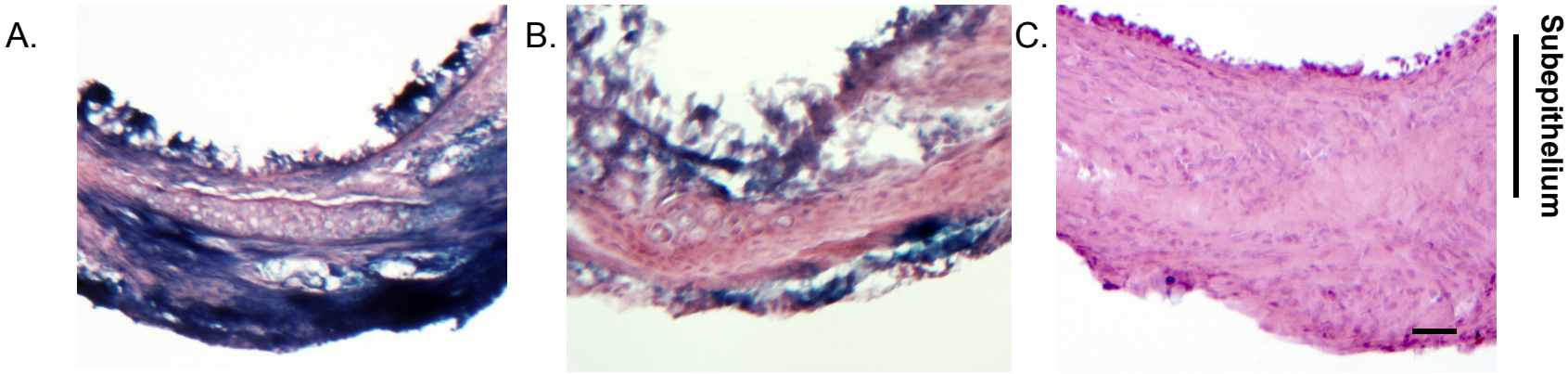
Supplemental Figure 6



Supplemental Figure 6

Inhibition of CXCR4 mediated signaling by AMD3100 accelerated the loss of microvascular perfusion but did not affect the donor and recipient vascular anastomosis formation. AMD3100 treated allografts lost microvascular perfusion at day 8, and it did not affect the day 4 microvascular perfusion, which reflects the microvascular reconnection between the donor and the recipient. Scale Bar: 100μM.

Supplemental Figure 7



Supplemental Figure 7

LacZ expression kinetics of AdLacZ-treated airway allograft. AdLacZ-treated airway allografts were harvest at day 4 (**A**), day 8 (**B**) and day 12 (**C**). After X-gal staining (blue), the allografts were sectioned and subjected to H&E staining. Scale bar: 40μM.

Supplemental Table 1. Sequences of primers for qRT-PCR analysis

Gene	Forward Primer	Reverse Primer
Plgf	GGATGTGCTCTGTGAATGC	CCTCTGAGTGGCTGGTTAC
Vegf	GGCTGCTGTAACGATGAAG	CTCTCTATGTGCTGGCTTTG
Sdf1	GAGAGCCACATCGCCAGAG	TTTCGGGTCAATGCACACTTG
Angpt1	CTACCAACAACAACAGCATCC	CTCCCTTTAGCAAAACACCTTC
Angpt2	CTGTGCGGAAATCTTCAAGTC	TGCCATCTTCTCGGTGTT
MCP-1	GAAGGCCAGCCCAGCACCAG	GTGGATGCTCCAGCCGGCAA
IL-1β	GCCTCGTGCTGTCGGACCCA	TGAGGCCCAAGGCCACAGGT
IL-6	GGTGACAACCACGGCCTTCCC	AAGCCTCCGACTTGTGAAGTGGT
Col1a1	CCAGGCCCTGCCGGAGAAGA	CCAGGCCCTGCCGGAGAAGA
Col3a1	CCAGAACATTACATACCACTGCAAA	GTGTTTAGTACAGCCATCCTCTAGAACTG
Col5a1	GAGGCCACGAGACTAGAAGGAGGAG	CACGGCGCAGGGATCGACTGTG
18S	GAATCGAACCCTGATTCCCCGTC	CGGCGACGACCCATTCGAAC

Supplemental Data Reference:

1. Milosevic, J., Maisel, M., Wegner, F., Leuchtenberger, J., Wenger, R.H., Gerlach, M., Storch, A., and Schwarz, J. 2007. Lack of hypoxia-inducible factor-1 alpha impairs midbrain neural precursor cells involving vascular endothelial growth factor signaling. *J Neurosci* 27:412-421.