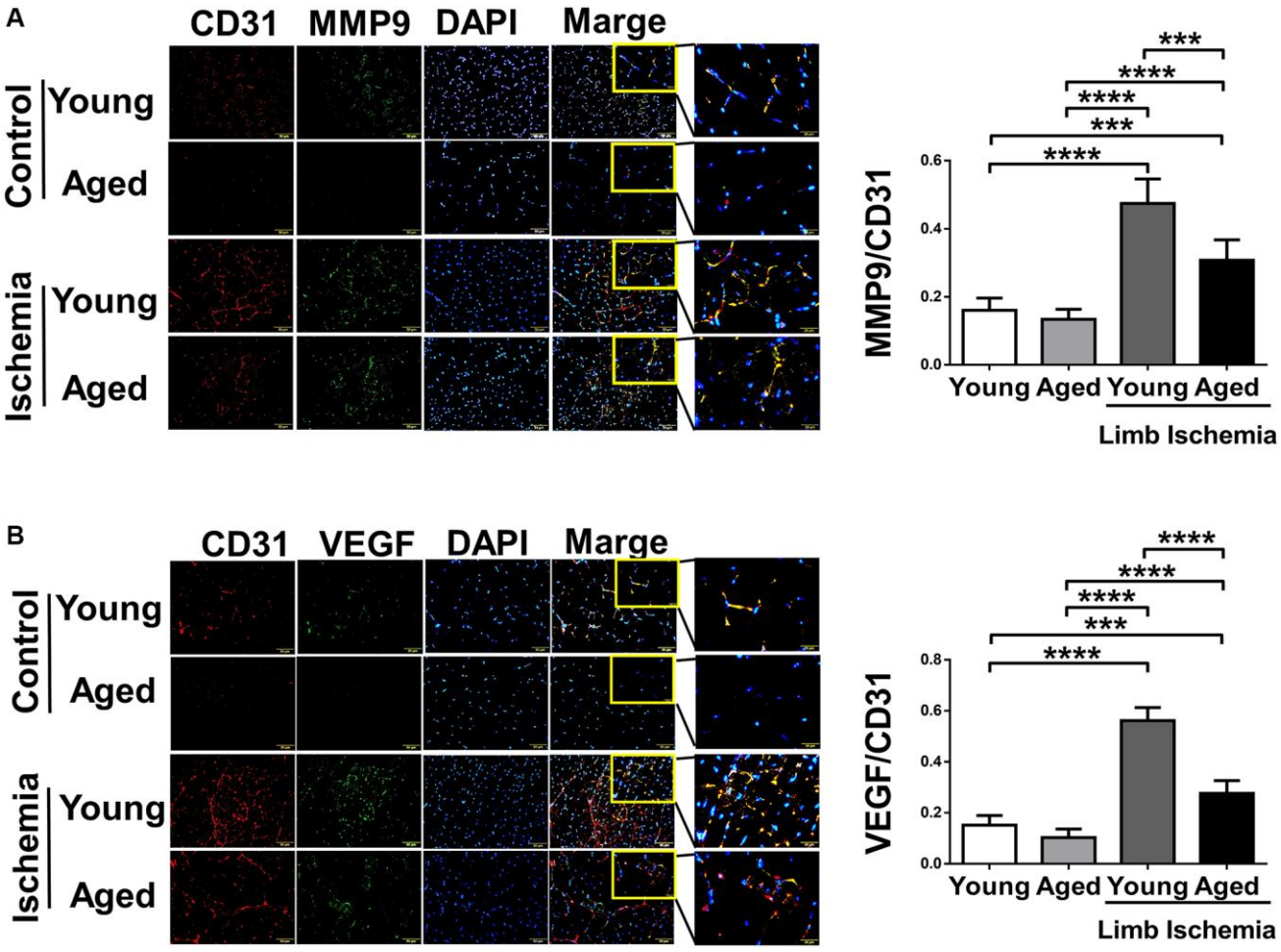
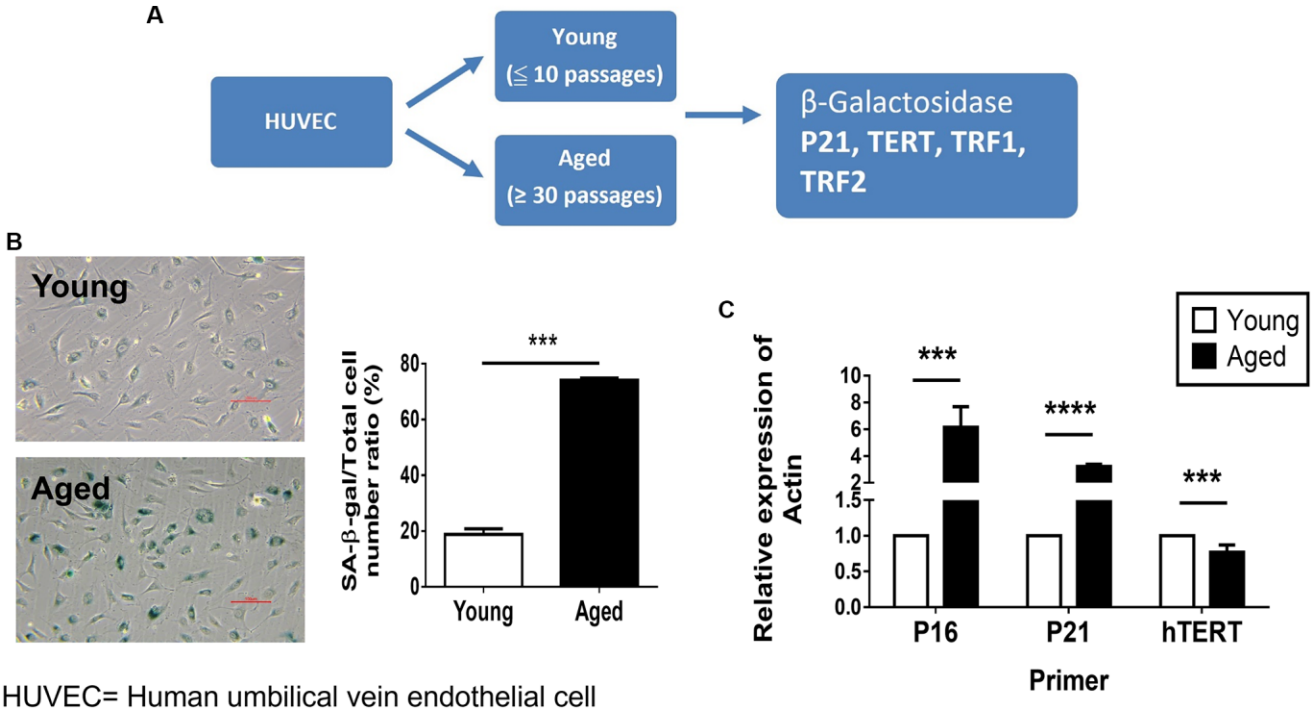
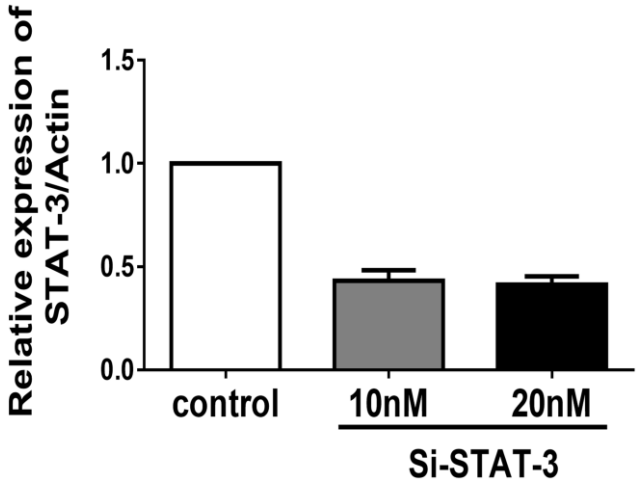
## SUPPLEMENTARY FIGURES



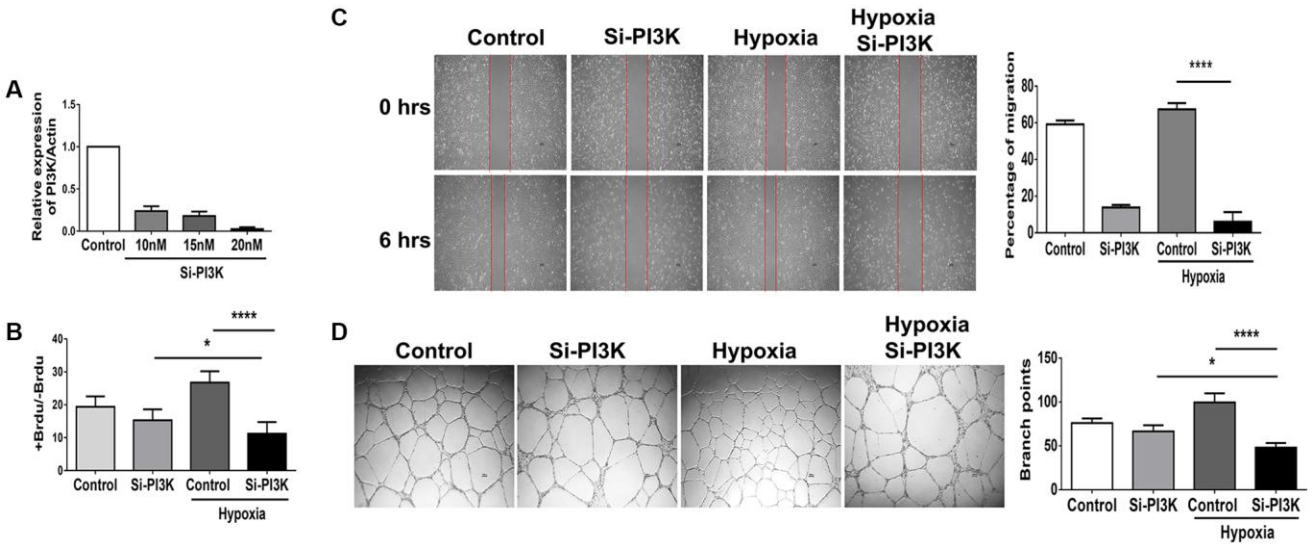

**Supplementary Figure 1. Double immunostaining with endothelial marker CD31 and VEGF or MMP9 in young and aged mice post hindlimb ischemia surgery.** Representative images and quantification of (**A**) VEGF (green) and (**B**) MMP9 (green) expressions in endothelial cells (red; CD 31 positive). Cell nuclei were stained with DAPI (blue). Scale bar: 50 μm. $^{***}P < 0.001$ and $^{****}P < 0.0001$ compared with the indicated groups.



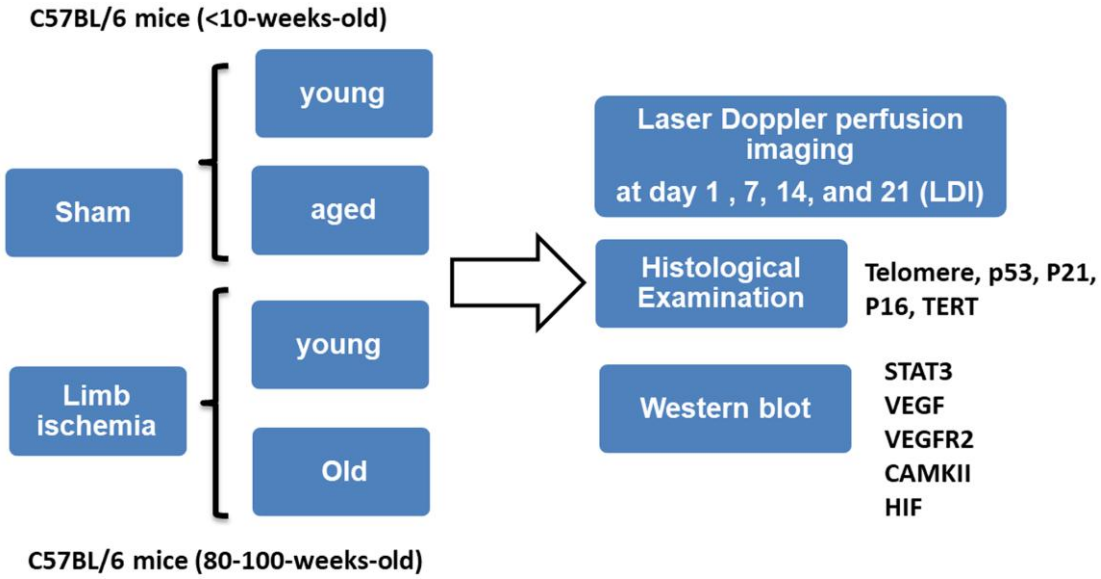

**Supplementary Figure 2. The evaluation of aging in HUVECs.** (**A**) Definitions of young (≤10 passages) and aged (≥30 passages) HUVECs. (**B**) Representative images and quantification of β-galactosidase staining in young and aged HUVECs. (**C**) Quantification PCR of P16INK4a, P21, and hTERT mRNA. $^{***}P < 0.001$ and $^{****}P < 0.0001$ compared with the indicated groups ($N = 3–6$).




**Supplementary Figure 3. The level of STAT3 in HUVECs transfected with STAT3 small interfering RNA (siSTAT3).** HUVECs were transfected with siSTAT3 for 48 hours, and STAT3 mRNA expression was measured by qPCR.




**Supplementary Figure 4. Knocking down PI3K suppresses proliferation, migration and tube formation in human umbilical vein endothelial cells (HUVECs).** (**A**) HUVECs were transfected with PI3K small interfering RNA (si-PI3K) for 48 hours, and PI3K mRNA expression was measured by qPCR. (**B**) Cell proliferation, evaluated by measuring BrdU incorporation into cells, (**C**) cell migration after 24 hours, and (**D**) tube formation, evaluated by the branched points, in HUVECs treated with scramble or si-PI3K under normoxia or hypoxia for 24 hours. The experiment was repeated in triplicate, $^{*}P < 0.05$ and $^{****}P < 0.0001$.




**Supplementary Figure 5. The groups in the animal study.** The study design for investigating the effects of angiogenesis in young (<10-week-old) and aged mice (80–100 week-old) with hindlimb ischemia. The images of laser Doppler perfusion flow and histological and angiogenesis-associated proteins were measured at the end of the experiment.