

Supplementary Figure 1. Schematic view of the culture system as used for model predictions and lid-resistance to oxygen mass transfer. (A) The 3D HUVEC collagen gel culture comprises three individual layers: (i) collagen gel containing HUVECs (bottom layer), (ii) growth medium (middle layer), and (iii) air (top layer). **(B)** Oxygen measurements illustrate the additional resistance of the culture plate lid to the mass transfer of oxygen.

Supplementary Figure 2. Small interfering RNA studies. Real-time RT-PCR analysis of siRNA-transfected HUVECs shows significant suppression of HIF1 α or HIF2 α compared to controls (luciferase-transfected HUVECs). Significance levels were set at * $p < 0.05$, and *** $p < 0.001$, respectively.

Supplementary Figure 3. DPI-treated HUVECs in 3D collagen gel under hypoxic conditions. We observed no tube formation when encapsulated HUVECs in 3D collagen gel were cultured in media containing DPI neither in **(A)** 2% O₂ nor **(B)** followed reoxygenation; image on the left; controlled DO levels mimicking the untreated case on the right. Fluorescence microscope images - phalloidin in green, nuclei in blue. Scale bar= 100 μm .