

Expanded View Figures

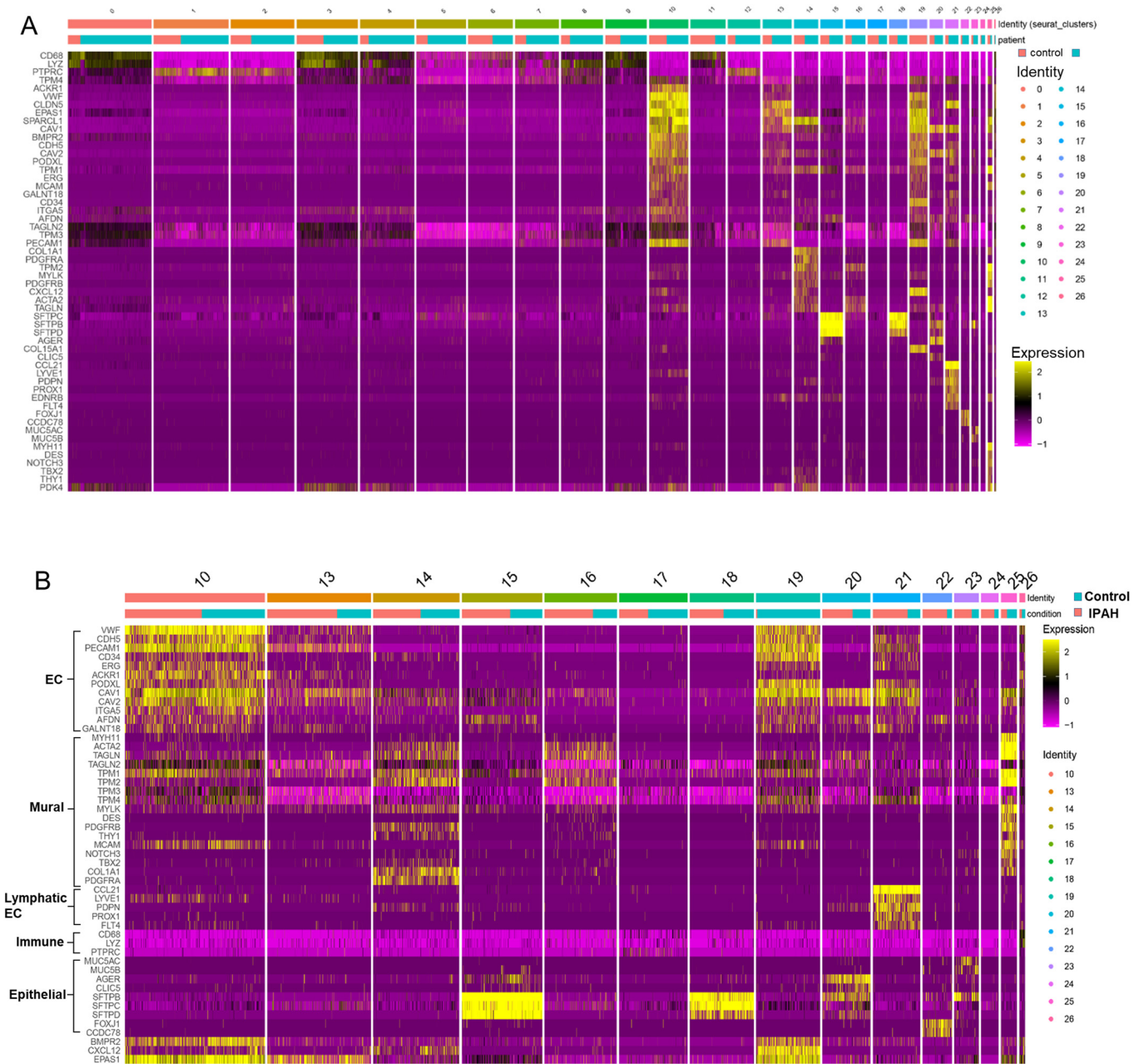


Figure EV1. 27 clusters are identified using human IPAH lung single-cell RNAseq.

(A) 27 distinct cell clusters were generated by Uniform Manifold Approximation and Projection (UMAP) plot from both human control and IPAH lungs by single-cell RNA-sequencing analysis. (B) The heatmap of expressed genes in clusters 10 and 13–26 was determined by the top gene expressions.

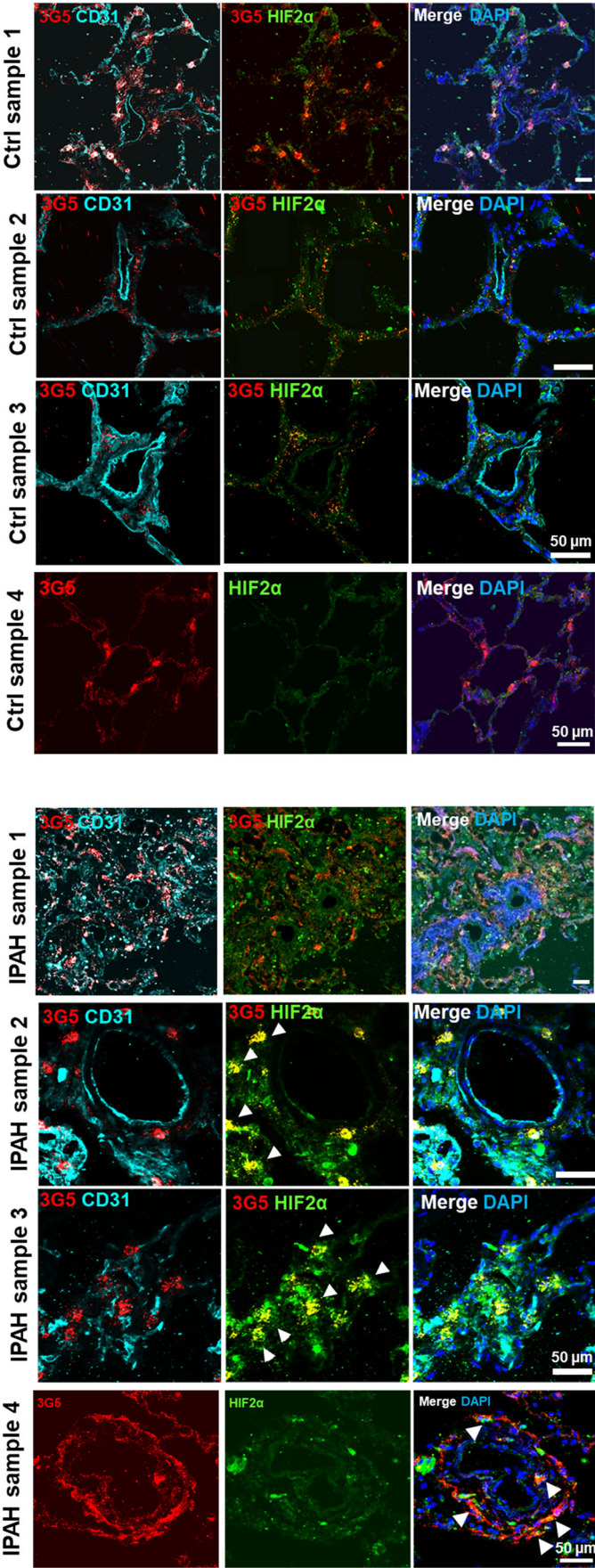




Figure EV2. Four more control and Four more IPAH patient lung tissues were immunofluorescence stained using HIF2 α (Green), 3G5 (Red), CD31 (Cyan), and nuclei were stained by DAPI (blue).

3G5 colocalized by HIF2 α was indicated by arrows. The higher magnification images are on the bottom two rows. Scale bar = 50 μ m.

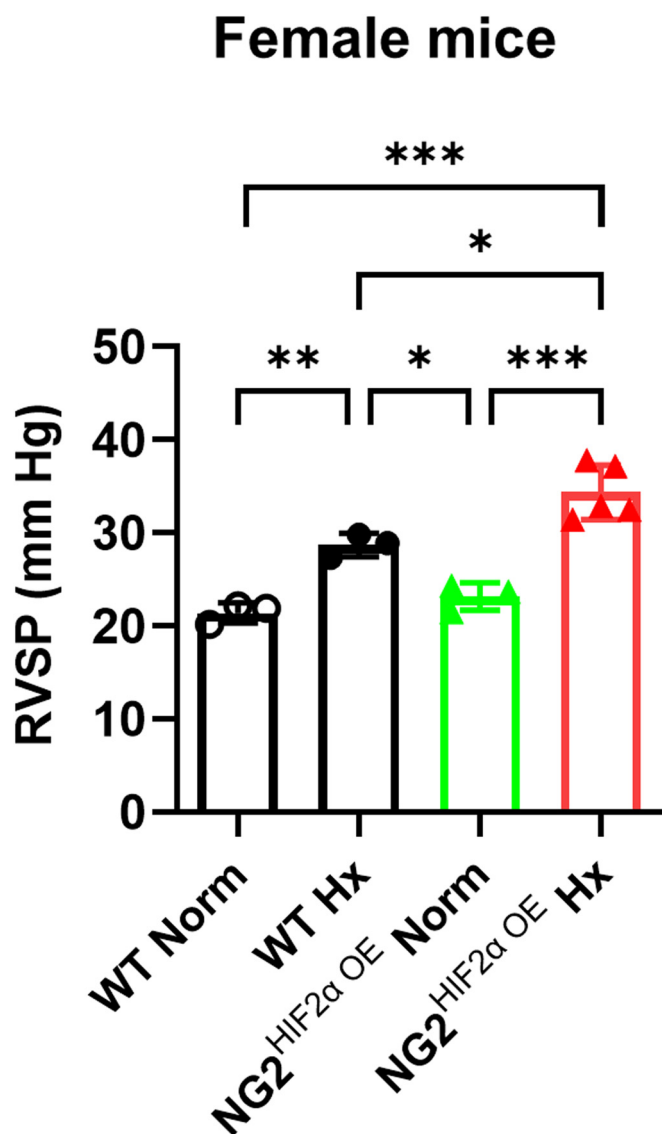
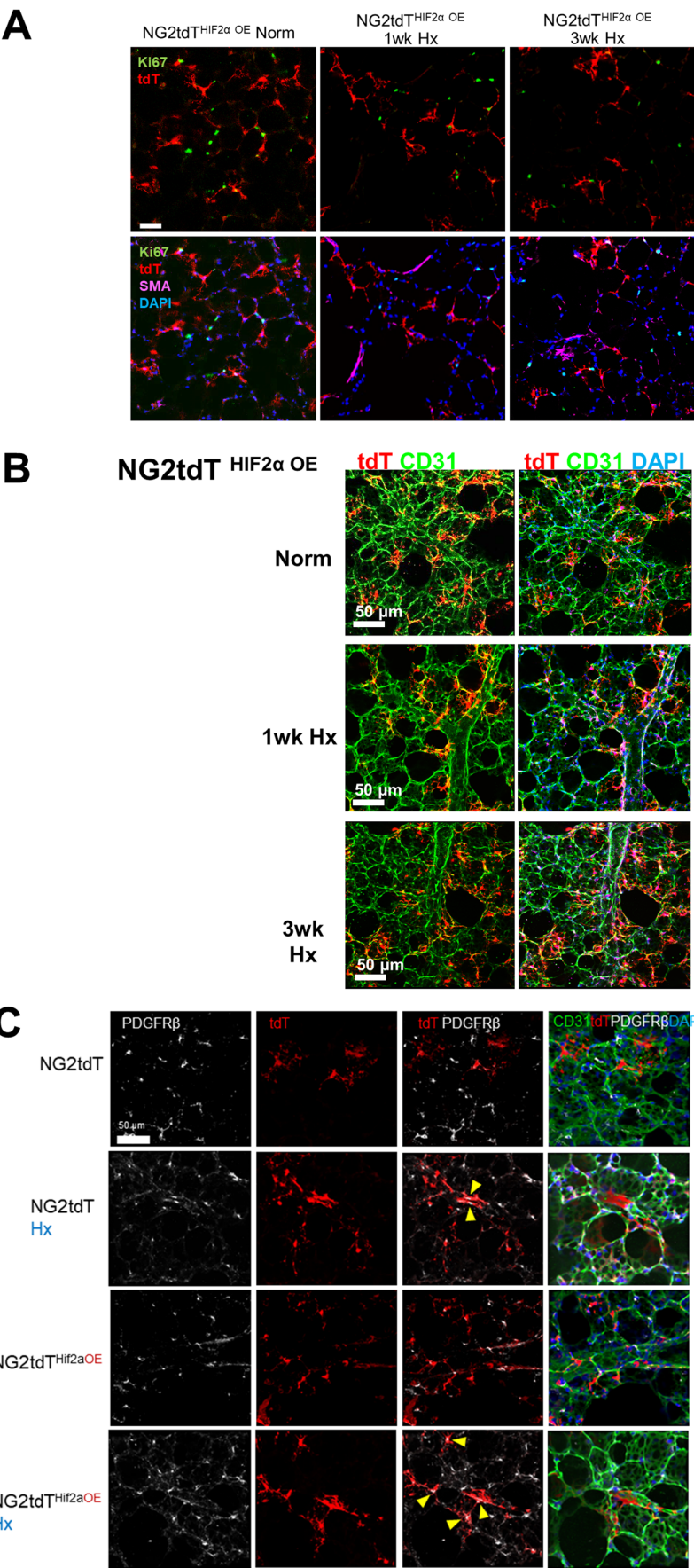


Figure EV3. RVSP measurements were performed on WT and NG2^{HIF2α} OE female mice with or without 3-wk Hx.

*Depicts a statistically significant difference: * $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$ (one-way ANOVA with Turkey's multiple comparisons test).



**Figure EV4. Characterization of tdT cells in NG2tdT^{HIF2α OE} lungs.**

(A) tdT cells did not colocalize with Ki67 (cell proliferation marker) under normoxia and hypoxia over time (1 wk and 3-wk Hx), by comparing the precision-cut lung slices of NG2tdT^{HIF2α OE} mice. Slices were stained for Ki67 (green), tdTamato (red), SMA (magenta) and DAPI (blue). (B) tdT cells closely contacted with CD31 (Green) endothelial cells under normoxia and hypoxia over time (1 wk and 3-wk Hx). (C) tdT cells from both NG2tdT and NG2tdT^{HIF2α OE} co-expressed PDGFRβ (White) under normoxia and 3-wk Hx. Yellow arrowheads indicate tdT wrapped around arterioles and co-expressed PDGFRβ. Scale bar = 50 μm.

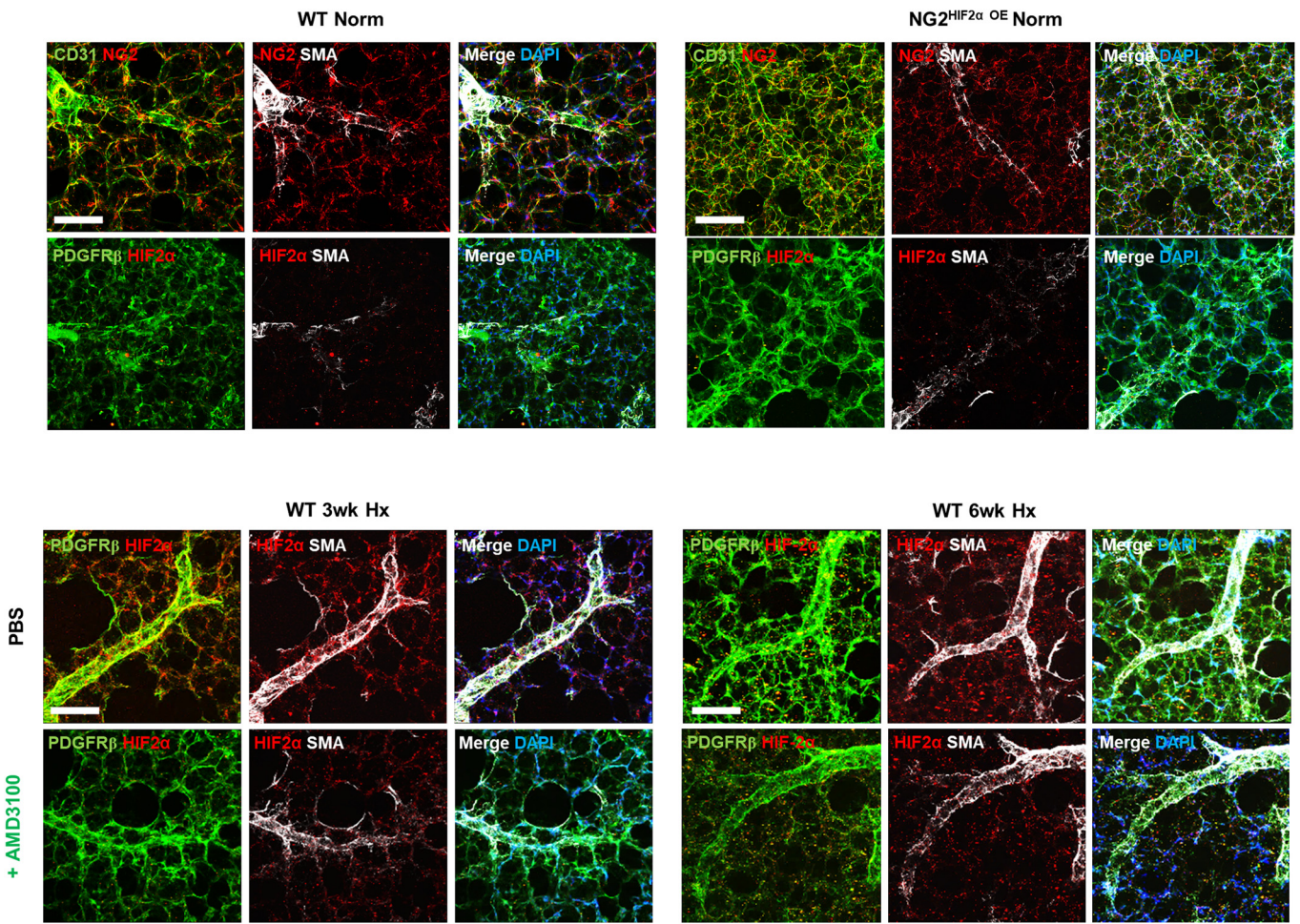


Figure EV5. Treatment of AMD3100 successfully prevents and alleviates vessel muscularization.
The precision-cut lung slices of WT mice in 3-wk (left) and 6-wk (right) hypoxia were stained for PDGFRβ (green), HIF2α (red), and SMA (white) with DAPI (blue) stained for nuclei. Scale bar = 50 μm.