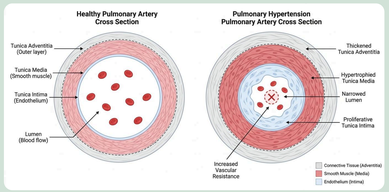
How Oxygen Deprivation Affects Pulmonary Endothelial Cells

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Background

- Pulmonary hypertension (PH) is a chronic disease characterized by thickening of the pulmonary arteries which leads to an increase in pulmonary arterial pressure.



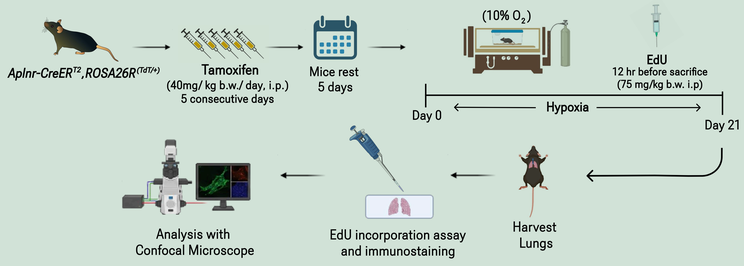
- PH affects approximately 1% of the global population, with ~43,000 new cases reported annually and has no cure.
- Key underlying pathophysiology includes excess proliferation of lung vascular cells (i.e., endothelial cells and smooth muscle cells), resulting in vascular remodeling, increased vascular resistance, and in severe cases, right ventricular failure.

Aim of Study

Investigating the effect of hypoxia (low oxygen) on pulmonary arterial endothelial cell proliferation using both cell culture based (*in vitro*) and animal (*in vivo*) models.

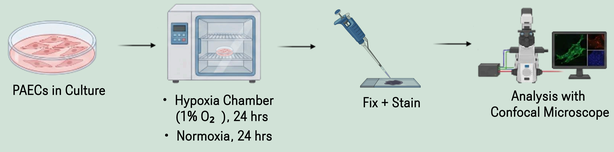
Methodology

In vivo



Aplnr-CreER^{T2},ROSA26$^{TdTf/+}$ mice were induced with tamoxifen and subjected to chronic hypoxia (10% O_2) for 21 days, followed by labelling and detection of proliferating endothelial cells in lung tissue using EdU (5-ethynyl-2'-deoxyuridine) incorporation and immunofluorescence analysis.

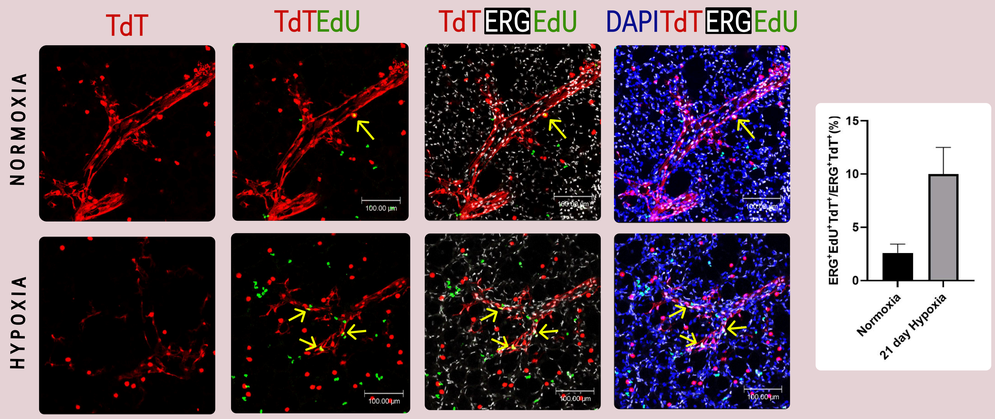
In vitro



Human pulmonary arterial endothelial cells (hPAECs) were exposed to 1% O_2 hypoxia for 24 hours at 37°C. Cellular proliferation was assessed via immunofluorescence staining with a proliferation marker, Ki-67.

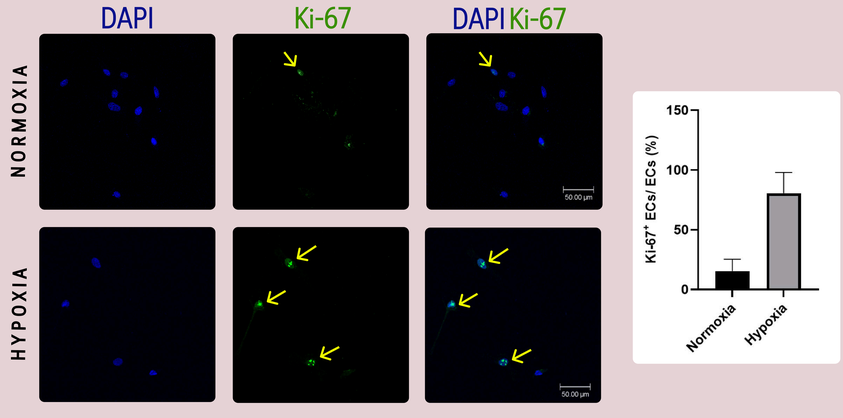
Results

Figure 1



Immunostaining of lung sections from mice exposed to hypoxia for 21 days reveals that hypoxia enhances proliferation of arterial endothelial cells, as indicated by an increase in EdU$^+$ cells from 2.6 ± 0.8% under normoxia to 10.0 ± 2.5%. Yellow arrows indicate EdU$^+$ proliferating cells.

Figure 2



Immunostaining of primary pulmonary arterial endothelial cells exposed to hypoxia for 24 hours reveals that hypoxia enhances EC proliferation, as indicated by an increase in Ki67$^+$ cells from 15.4 ± 9.9% under normoxia to 80.6 ± 17.3%. Yellow arrows indicate Ki67$^+$ proliferating cells.

Summary

- The results indicate that hypoxia is a potent inducer of pulmonary arterial endothelial cell proliferation in both controlled in vitro conditions and physiologically relevant in vivo models.
- The work warrants further investigation to delineate how such proliferative responses of pulmonary arterial endothelial cells contribute to the development and progression of PH.

Future Directions

- Increase sample size in vivo and in vitro to strengthen statistical power and confirm reliability of the proliferative response.
- Investigate gene expression profiles of proliferating endothelial cells to identify genes and pathways driving the hypoxic response.
- Delineate the proliferative response of endothelial cells to determine their contribution to vascular remodeling.

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