



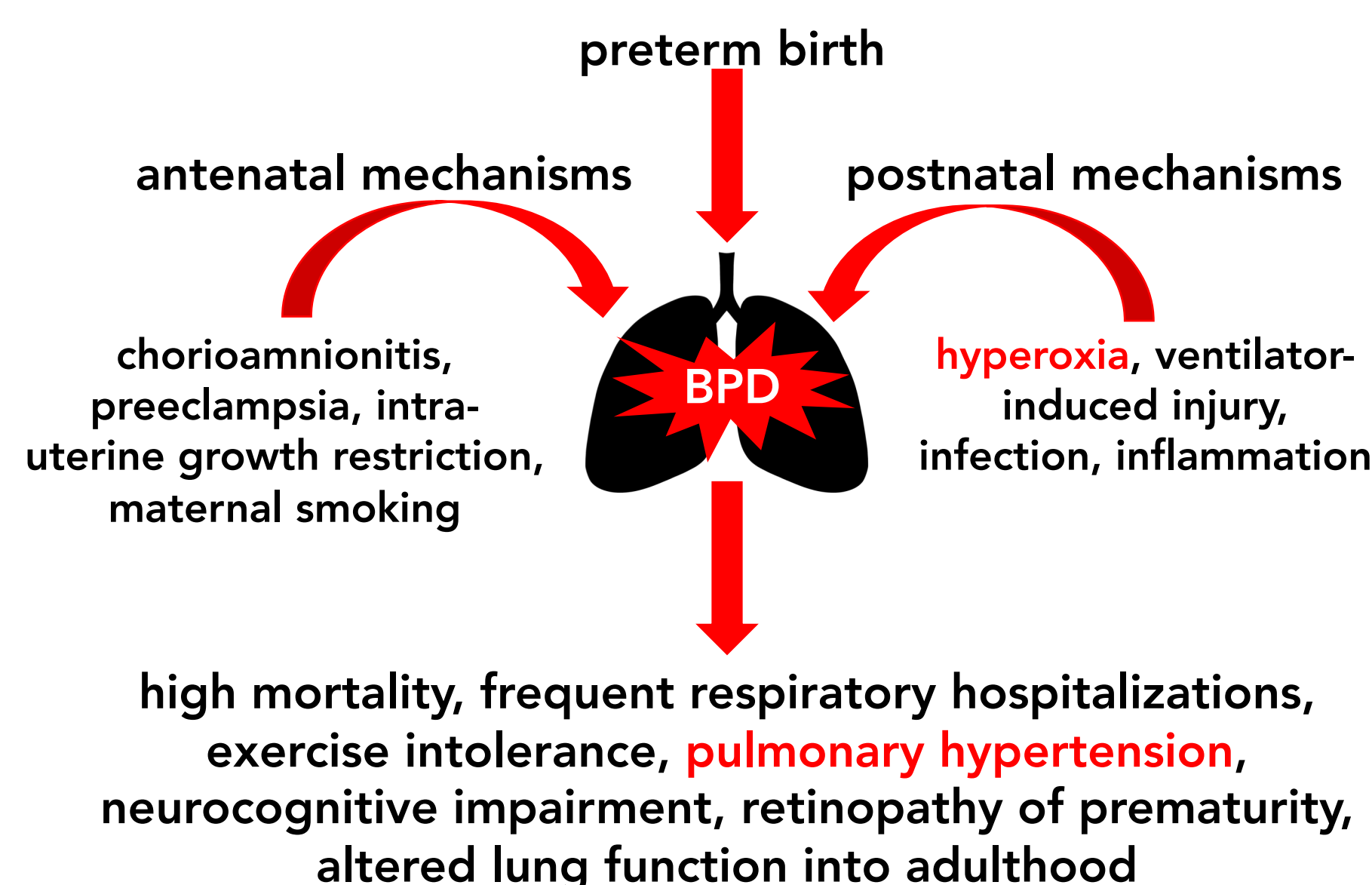
Prostacyclin Analog Treprostinil Enhances Neonatal Rat Lung Endothelial Cell Growth And Angiogenesis *In Vitro*

Kisha G. Thayapran, Gregory Seedorf, Steven H. Abman

Pediatric Heart Lung Center, Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO



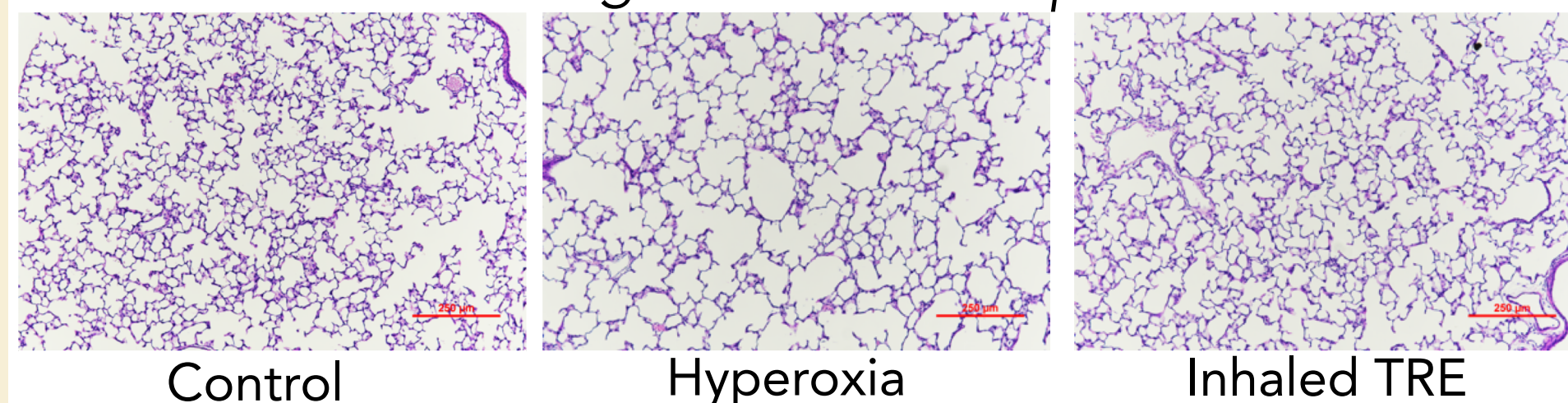
Background



Bronchopulmonary Dysplasia (BPD) is a chronic lung disease of premature newborns associated with mechanisms such as **postnatal hyperoxia** and the risk of significant co-morbidities such as **pulmonary hypertension (PH)**.

Treprostinil (TRE), a synthetic prostacyclin analog, is recommended for treating pulmonary hypertension in older children and adults. However, the **effect of TRE on lung structure is uncertain**.

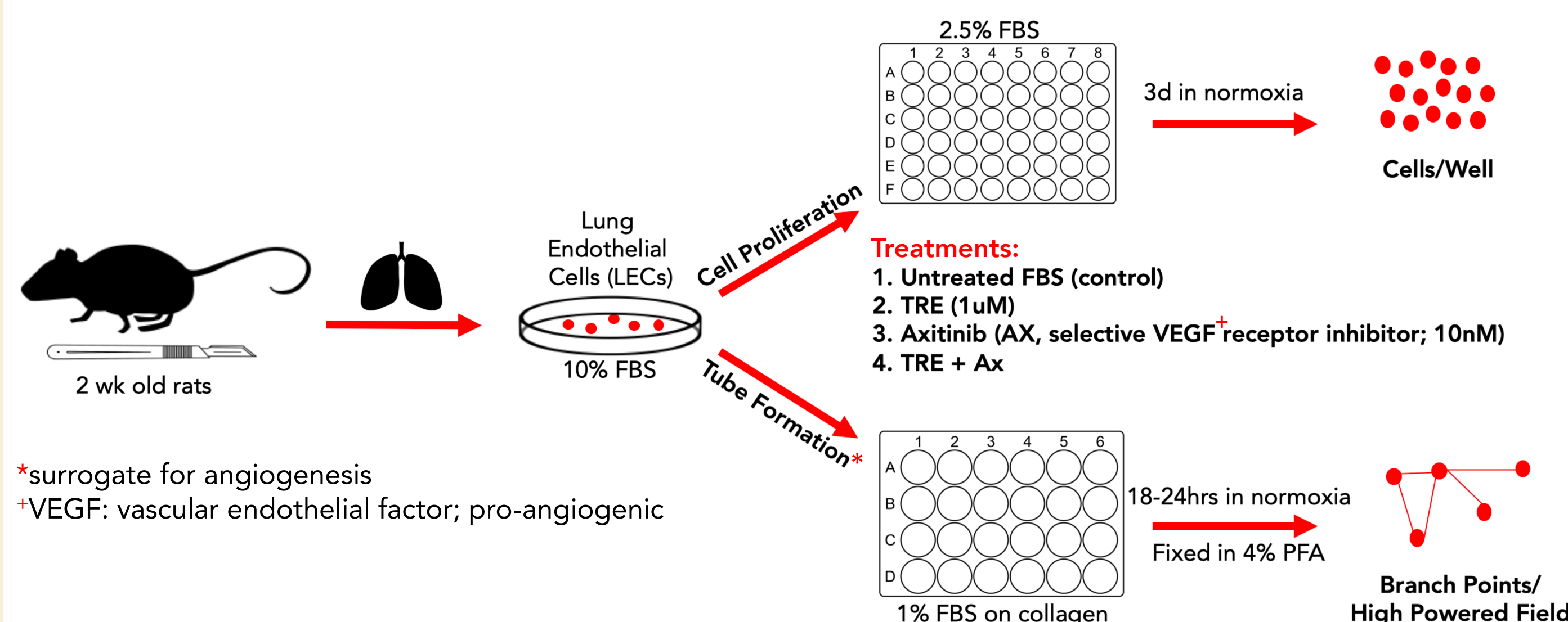
TRE Preserves Lung Structure in Experimental BPD



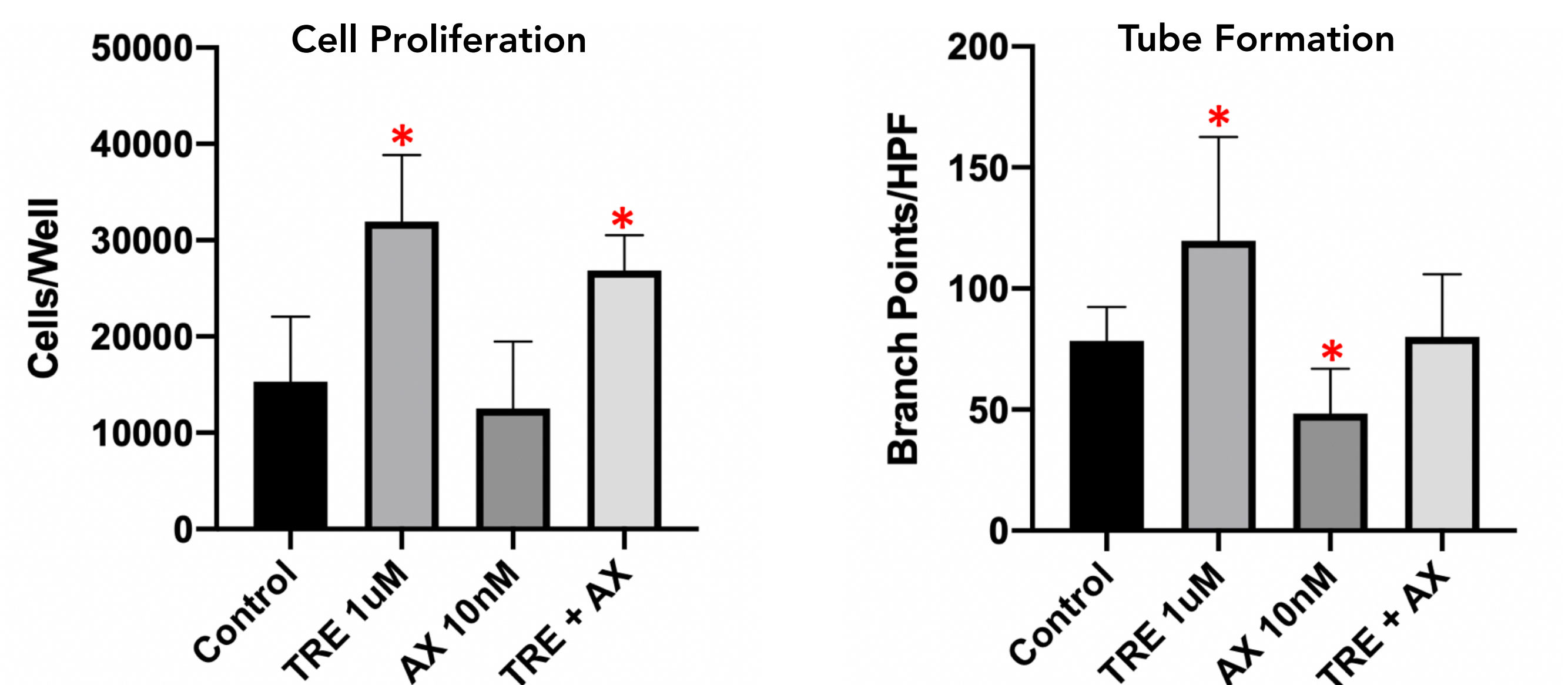
Previously, we found that **TRE preserves lung structure and function, improves vascular growth, and prevents right ventricular hypertrophy** in a hyperoxia-induced neonatal rat BPD model *in vivo*.

Is the effect of Treprostinil on neonatal lung development due in part to stimulation of angiogenesis?

Methods



Results



- TRE increased LEC growth by **109%** (p<0.01)
- AX alone **did not decrease** LEC growth
- TRE administration with AX **did not attenuate** effect of TRE
- TRE increased tube formation by **51%** (p<0.05)
- AX alone decreased tube formation by **38%** (p<0.01)
- TRE administration with AX **restored tube formation** to control

Conclusions

- TRE **enhances both LEC growth and angiogenesis in vitro**.
- VEGF receptor blockade **reduces tube formation but not cell growth**, and this effect can be **reversed by TRE**.

Speculations

- This *in vitro* data **supports our previous findings** that TRE improves lung alveolar and vascular growth *in vivo*.
- We speculate that these **suggests interactions between the VEGF and prostacyclin pathways** that can be targeted to develop novel therapies to prevent BPD and BPD-associated PH.

Future Directions

- Elucidate a further understanding of the signaling pathways at play by performing **Western Blots** on LEC cell homogenates.
- Perform cell proliferation assays, tube formation assays, and Western Blot on LEC cells isolated from animals grown in **hyperoxic conditions** that mimic BPD.

Acknowledgements

- United Therapeutics provided investigational drug Treprostinil
- Steven H. Abman, MD, Gregory Seedorf, BS, and the Pediatric Heart Lung Center
- Allan Prochazka, MD and the CUSOM Medical Research Track