Establishing a late gestational hypoxia model to study the effects of maternal hypoxia on offspring lung outcomes

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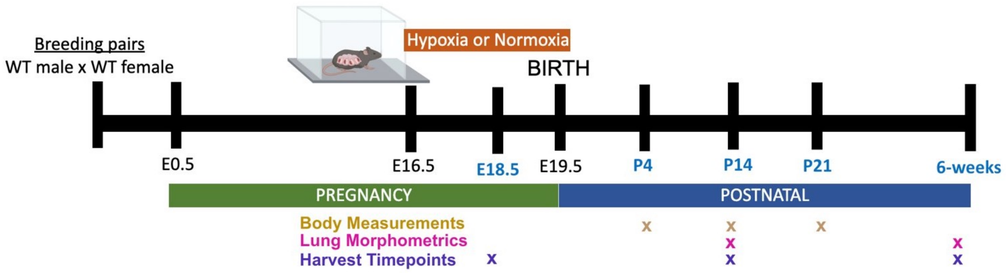
BACKGROUND

- Maternal wellness
  - Critical in fetal and newborn development
  - Health status of mother could determine fetal and into adulthood outcomes
  - Examples of maternal stress: placental insufficiency, lung disease, depression, obesity
- Examples of the impact of maternal stress on lung outcomes in offspring
  - Preterm birth increases risk of chronic lung disease
  - Maternal smoking increases risk of pediatric asthma
  - Residence at high altitude associated with poor lung function
- Animal models of prenatal hypoxia on fetal outcomes
  - Decrease in body weight, lung volume, and pulmonary blood flow
  - Risk of pulmonary hypertension
- **GOAL**: ***Prenatal*** hypoxia model that evaluates ***newborn and adult outcomes***

***Hypothesis*: Late gestational hypoxia, beginning at E16.5, will impair lung and pulmonary vascular development in offspring.**

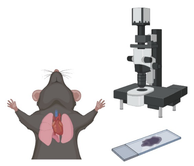
LATE GESTATIONAL HYPOXIA MOUSE-MODEL



•Hypobaric hypoxia (505 torr; 11,500 ft; 13% FiO2)
•Normoxia (626 torr; 5,280 ft; 21% FiO2)

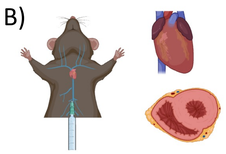
METHODOLOGY

A)



1. Agarose-inflated lungs
2. Paraffin-embedded lung sections
3. H&E for radial alveolar count analysis (**RAC**) and mean linear intercept (**MLI**)
4. Quantification and analysis

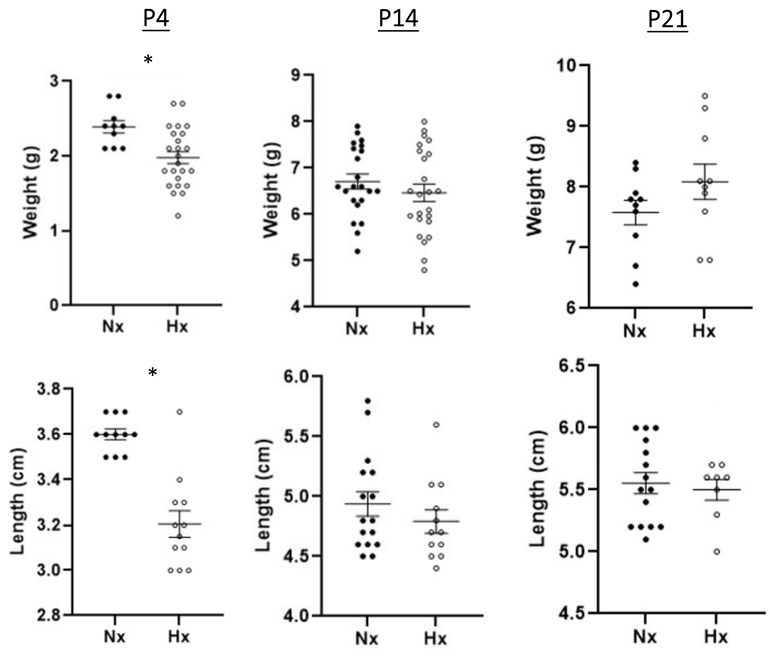
B)



1. Heart H&E cross-section
2. Right heart puncture for right ventricular systolic pressure (**RVSP**)
3. Heart weight measurement for right ventricle hypertrophy (**RVH**)

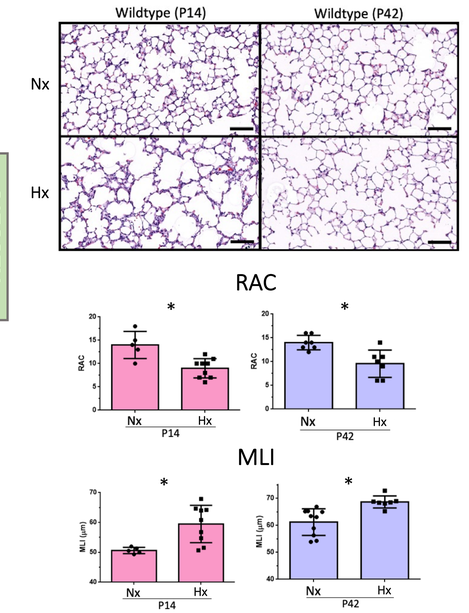
RESULTS

Prenatal hypoxia impairs weight gain and growth in the early postnatal period



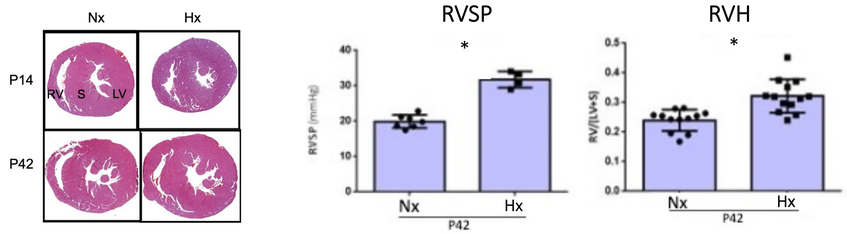
RESULTS

Impaired alveolar development persists to adulthood



RESULTS

Induced pulmonary hypertension at 6 weeks of age



CONCLUSIONS

- Late gestational hypoxia leads to transiently somatic growth and persistent impaired alveolar development.
- This model enables studies of mechanisms for maternal stress on newborn outcomes.

Our future studies will look into the mechanisms responsible for abrupted lung development:

- Extracellular superoxide dismutase:
  - Evidence that EC-SOD is developmentally regulated and contributes to lung development and PH
  - Test whether EC-SOD genotype of mother or offspring impacts lung development and PH in late gestational hypoxia
- Inflammation:
  - Evidence that macrophages may contribute to neonatal outcomes
  - Detect the accumulation of lung macrophage populations

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