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

Thi-Tina Nguyen¹, Caitlin Lewis¹, Daniel Colon Hidalgo¹, Janelle Posey¹, Mariah Jordan¹, Maya Grayck², Clyde Wright², Cassidy Delaney¹, Eva Nozik¹
¹Department of Pediatrics and Cardiovascular Pulmonary Research Laboratories, University of Colorado Anschutz Medical Campus, Aurora, CO 80045,
²Section of Neonatology, Department of Pediatrics, University of Colorado Anschutz Medical Campus, Aurora, CO 80045.

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

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

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 altered 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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ACKNOWLEDGEMENTS
- The Nozik Lab
- The Delaney Lab
- The Integumentary Physiology Program
- NIH/NHLBI R35HL139726 (EN)
- NIH/NHLBI R35HL139726 S1