Acute Kidney Injury Decreases VEGF-eNOS Signaling and Impairs Alveolar Development in Rat Pups

**Background**
- Neonatal acute kidney injury (AKI) is common and associated with increased mortality, longer duration of hospital stay, and adverse pulmonary outcomes.
- There is evidence of "organ crosstalk," in which the injured kidney affects distant organ function.
- Gaps exist in the understanding of how AKI affects the developing lung.
- Bronchopulmonary dysplasia (BPD), the chronic lung disease of prematurity, is characterized by arrest in alveolar development and impaired vascular growth.
- Animal models have implicated endothelial growth factor (VEGF) and angiogenic signaling involving vascular endothelial nitric oxide synthase (eNOS) in the development of BPD.

**Hypothesis**
AKI in neonatal rat pups induces a systemic inflammatory response that impairs lung structure and function through altered angiogenic signaling.

**Study Questions**
1. Can an animal surgical model of neonatal AKI be developed?
2. Does AKI affect the developing lung?
3. What are the underlying mechanisms of the effect of AKI on the developing lung?

**Methods:** bilateral ischemia-reperfusion-injury (bIRI)
- Sprague-Dawley rat pups
- Creating the model: surgery with 40 min warm ischemia time
- Investigating underlying mechanisms: bIRI with 40 min warm ischemia time
- Day 0, 5, 6, 14
- Sham, Surgical
- Surgical rat pups had a 30% and 17% decrease in eNOS activity compared to controls.

**Results**
- Lung MPO activity was increased acutely in surgical rat pups compared to shams, but not different at 24 hr.
- VEGF activity decreased by 60%, eNOS activity decreased by 55%, and phospho eNOS activity decreased by 22% in surgical rat pups compared to controls.

**Conclusion**
AKI induced by bIRI in neonatal rat pups results in altered VEGF-eNOS signaling and impaired alveolar growth. We speculate that interventions geared towards the restoration of angiogenic signaling will improve pulmonary outcomes in neonates who experience AKI.