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Fetal Hypoxemia Causes Abnormal Myocardial Development In A Preterm *Ex Utero* Fetal Ovine Model: Implications For Adult Cardiovascular Disease and Novel Fetal Therapy

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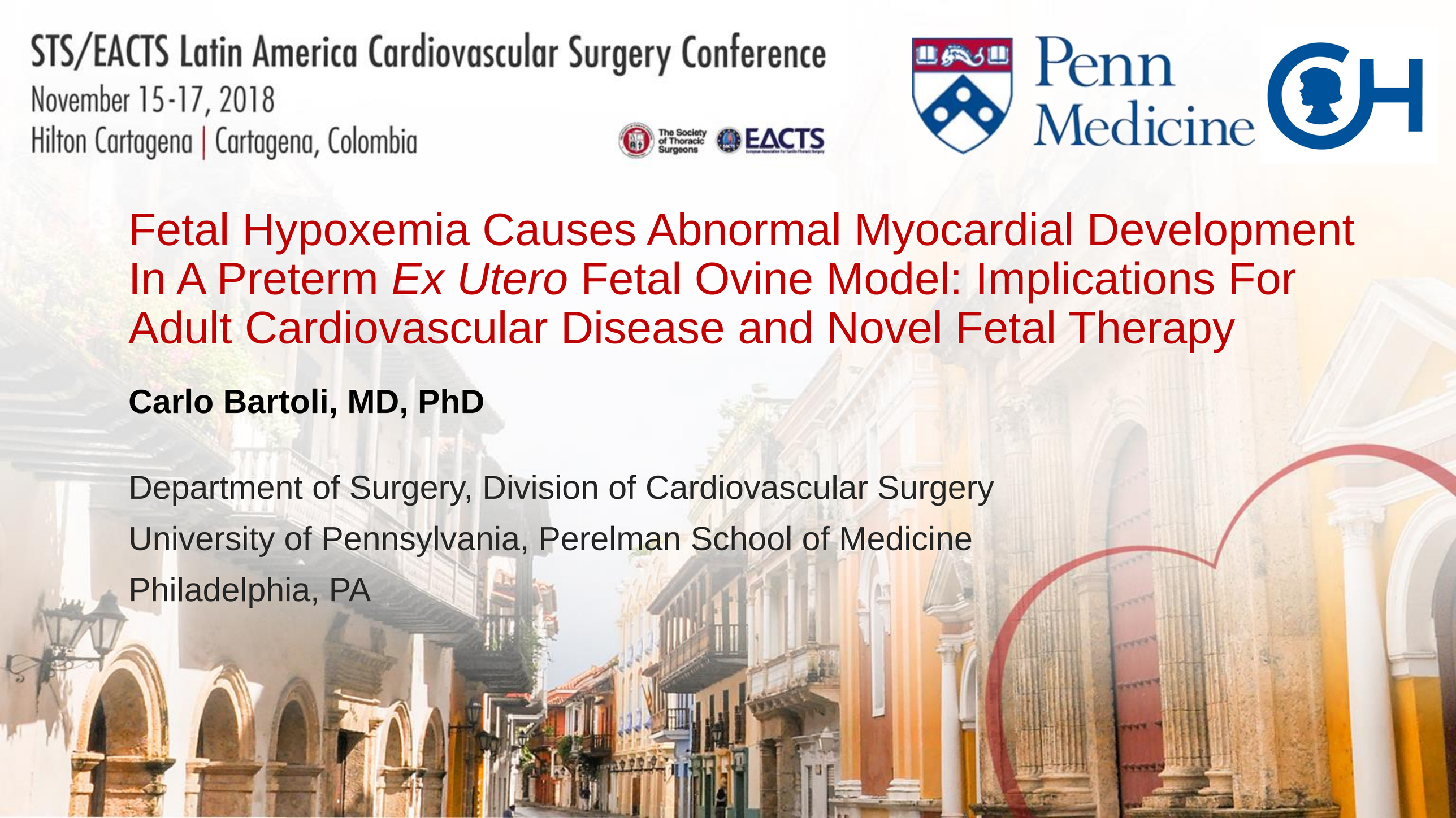
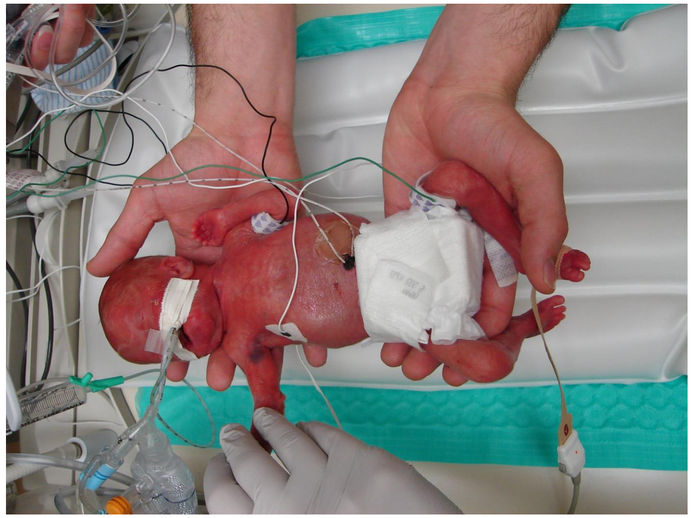


Fetal Hypoxia and Severe Prematurity

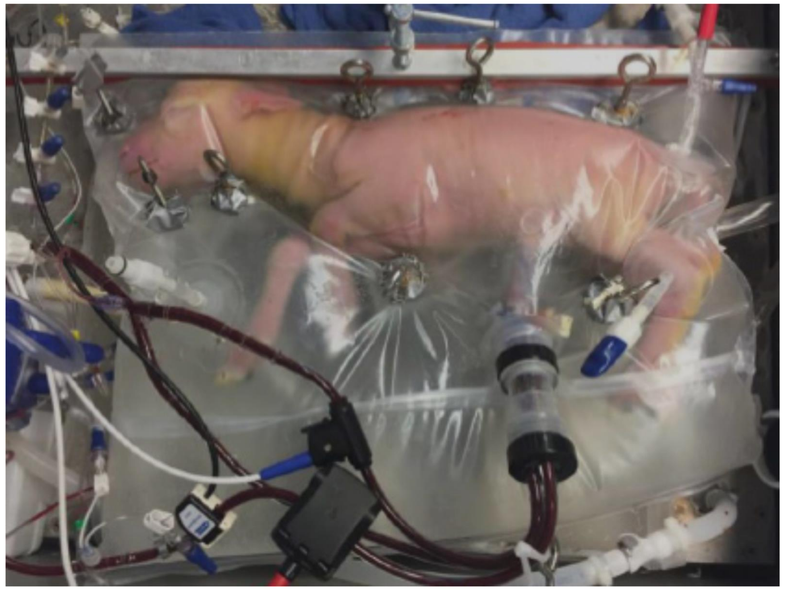
- Fetal hypoxia is a leading cause of extreme prematurity
- Fetal viability of 22 to 23 weeks is possible



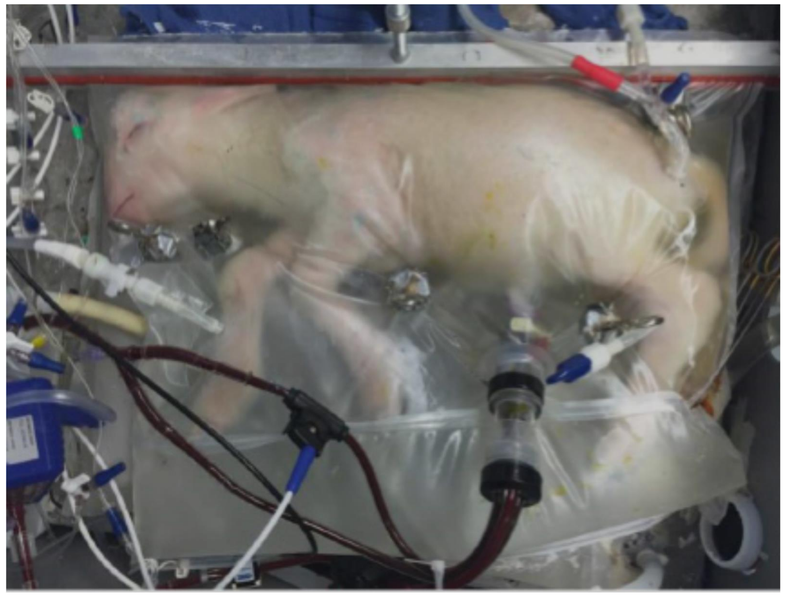
- Chronic lung disease
- Immature end-organ development
- Delayed neurocognitive development
- **Overall poor prognosis**

Ex Utero Fetal Support System

- Novel rescue therapy



Gestational age: 111 Days



Gestational age: 135 Days

6 Months

- Supported *ex utero* for up to 28 days
  - Stable hemodynamics
  - Normal blood gas
  - Somatic growth
- Long-term survival with normal postnatal function

Partridge et al. Nature Communications. 2017.

Project Goal

JCI insight

Fetal hypoxemia causes abnormal myocardial development in a preterm ex utero fetal ovine model

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Hypothesis

Hypoxemic mechanical circulatory support of the fetus impairs myocardial development, whereas **normoxic** support allows normal myocardial development.

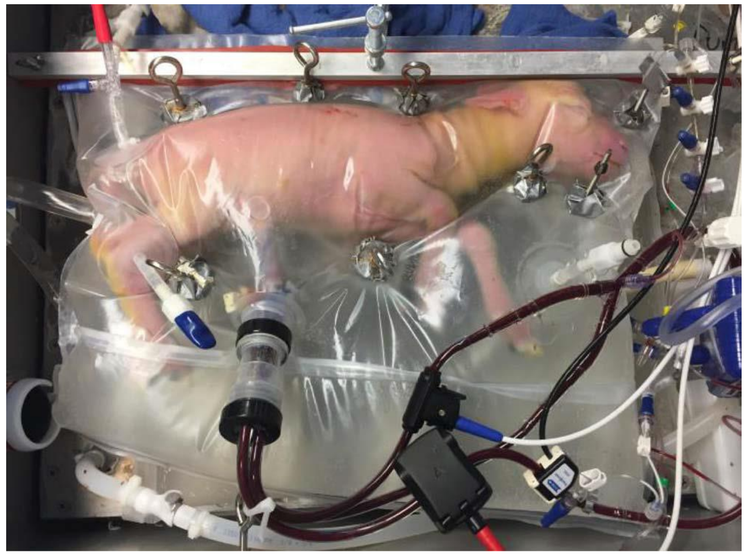
Experimental Methods

Control

In Utero Gestation

- n=8

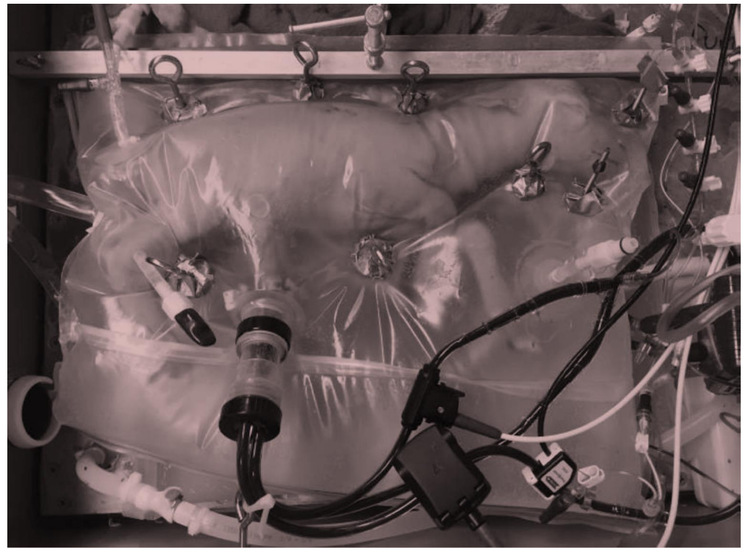
Normoxic



Normal Oxygen Delivery

- 24±2 days in biobag
- n=9

Hypoxic

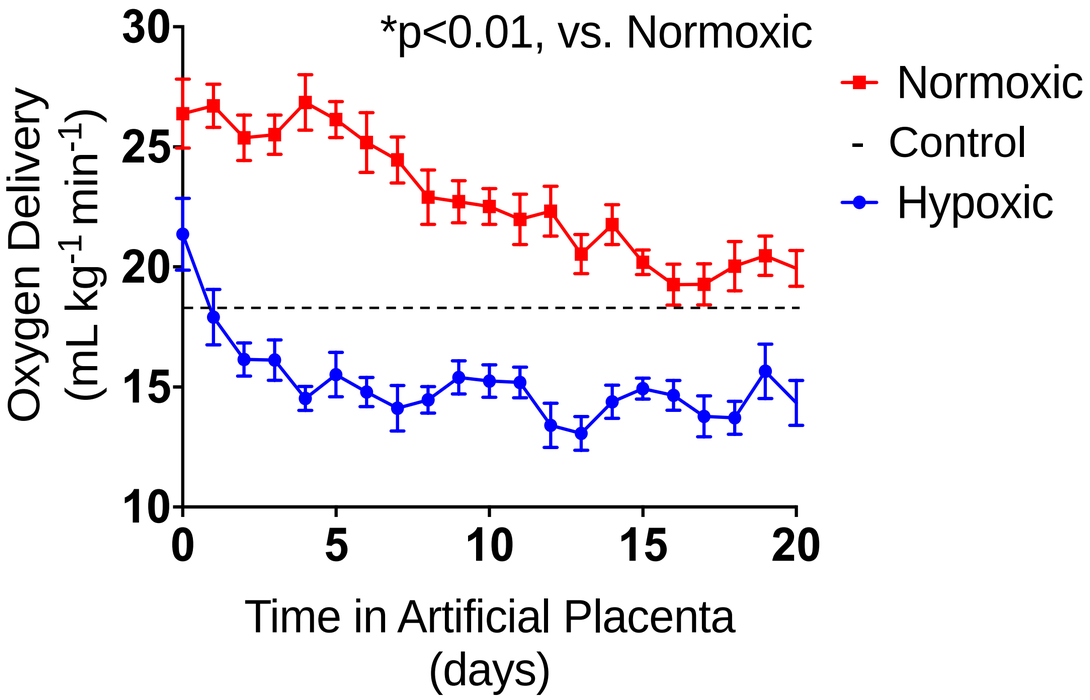


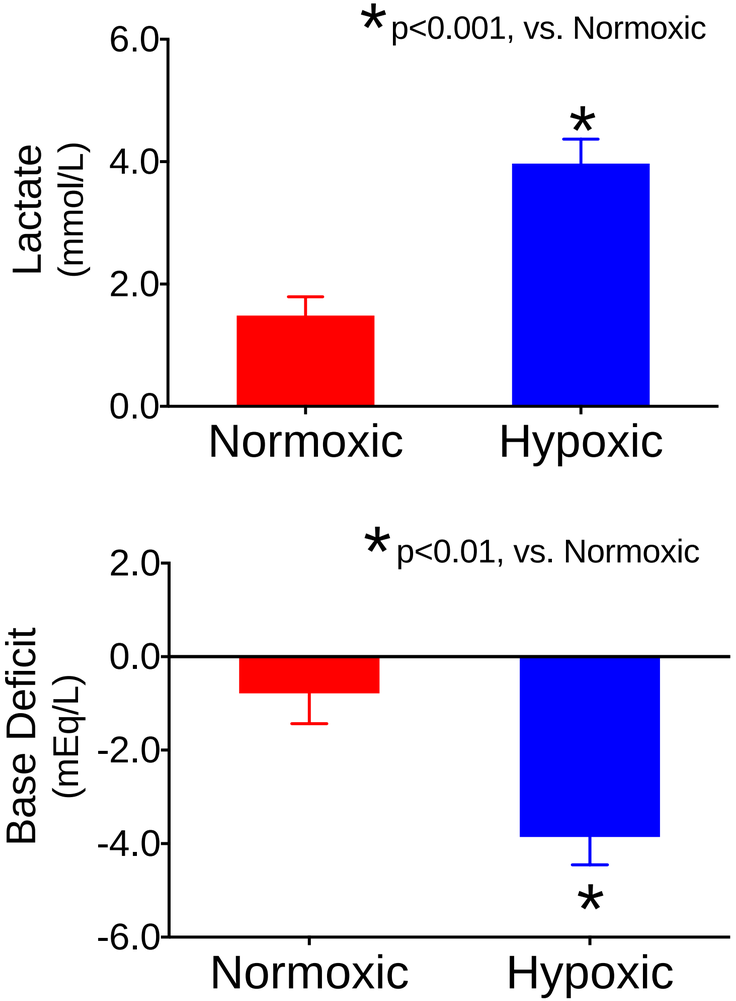
Chronic Hypoxemia

- 22±1 days in biobag
- n=7

Lawrence…Bartoli. Journal of Clinical Investigation - Insight. 2018.

Oxygen Delivery

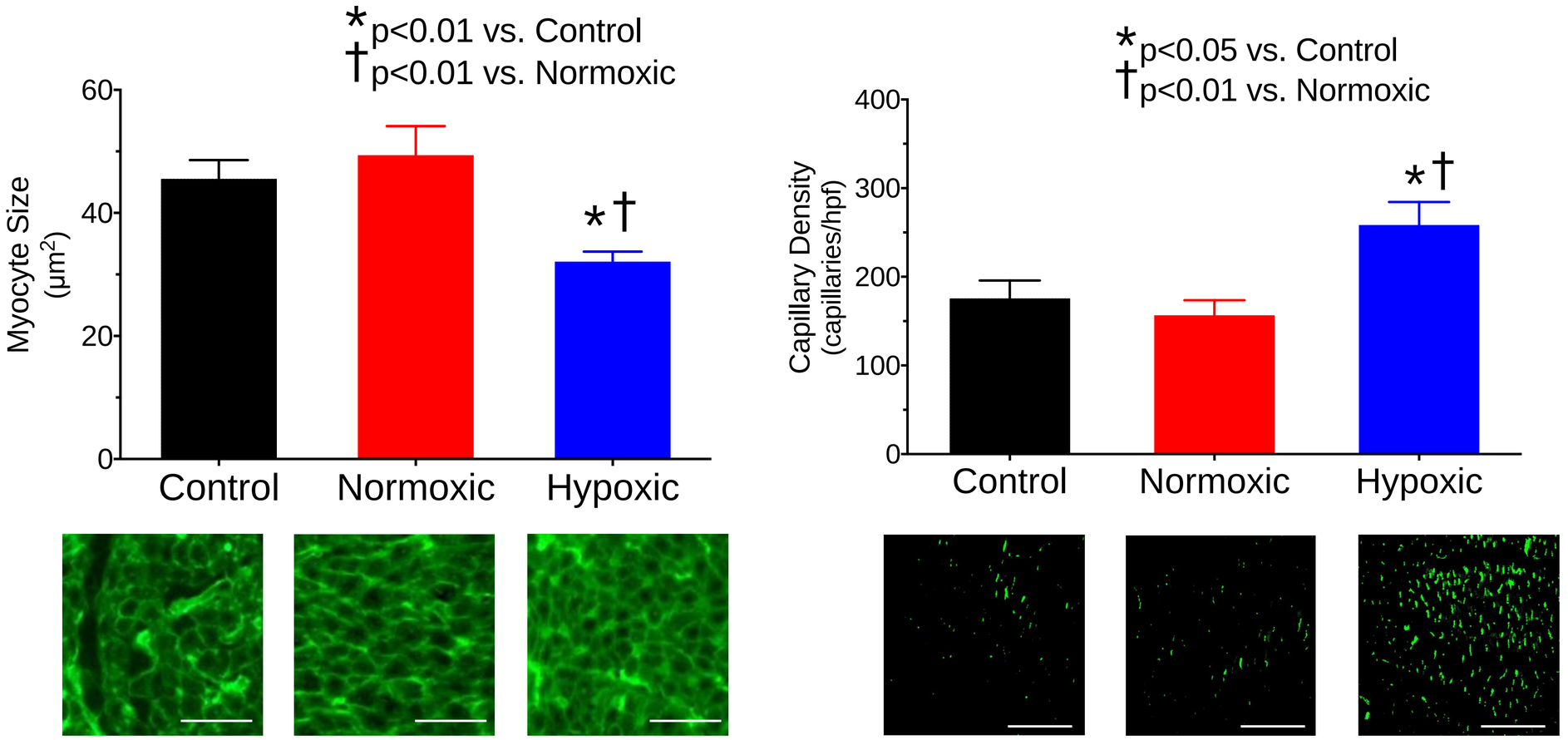




Hypoxic but not normoxic animals developed anaerobic metabolism.

Lawrence…Bartoli. Journal of Clinical Investigation - Insight. 2018.

Myocardial Histology



Hypoxic fetuses exhibited abnormal myocardial architecture.

Normoxic fetuses demonstrated similar architecture to controls.

Lawrence…Bartoli. Journal of Clinical Investigation - Insight. 2018.

Conclusions

1. *Ex utero* fetal support under normoxic conditions resulted in normal myocardial architecture.

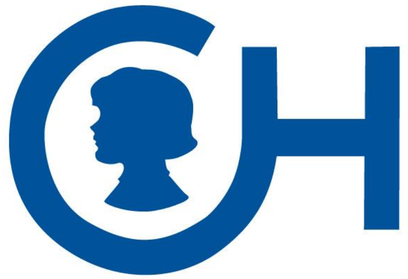
2. Fetal hypoxemia altered myocardial architecture.

Clinical Translation

1. These data will inform the nascent field of **fetal mechanical circulatory support.**

2. Additional studies will help to define the role for an artificial placenta as a rescue therapy for intrauterine pathology.

3. In hypoxic fetuses, myocardial histologic changes in the fetal period that persist into adulthood may contribute to adult heart disease.



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