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CHRD
CHILD HEALTH RESEARCH DAYS

CHRD 2020: Abstract Submission Form

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Title
Development of a 3D bioprinted Model of Vascular Smooth Muscle To Study Persistent Pulmonary Hypertension of the Newborn

Background
Increased vascular wall stiffness contributes to the pathophysiology of persistent pulmonary hypertension of the newborn (PPHN). Traditional 2D cell culture models fail to accurately replicate the complex microenvironment changes that occur in stiffened tissues, making disease research problematic.

Objective
Using 3D bioprinting, we aimed to fabricate vascular smooth muscle tissue that can mimic the increased wall stiffness associated with PPHN.

Methods
Pulmonary and coronary arterial smooth muscle (PASM and CASM respectively) cells were encapsulated at 2.5x10^7 cells/mL in a bioink comprised of 0.25% - 1.0% w/v sodium alginate, 1 mg/mL collagen and 5 mg/mL fibrinogen. Tissues were bioprinted as an 8-10 mm "bioring" that was free-floating or constrained within a stiff (0.75-1.25% alginate) acellular load-bearing frame. Tissue compaction was assessed by lumen area reduction. Cell organization and viability were determined using filamentous actin and propidium iodide staining respectively. Contractile response was assessed using potassium chloride (KCl) and cytochalasin D.

Results
Free-floating stiff (1% alginate) PASM biorings were mechanically stable, but cells were unable to spread within the structure. Softer (0.25-0.5% alginate) biorings exhibited excessive compaction (>70% lumen area reduction) within 24 hours. Addition of the stiff (1% alginate) load-bearing frame to soft biorings prevented excessive compaction, while promoting high cell viability (>82%) and cellular organization consistent with in vivo tissues. The degree of compaction could be controlled with different frame stiffnesses; soft CASM biorings printed with 0.75% alginate frames had >15% lumen area reduction,

whereas biorings with 1-1.25% alginate frames had <5% lumen area reduction. CASM biorings with stiff frames exhibited physiologically relevant contractile response (>22% lumen area reduction) to KCl.

Conclusion
Our novel stiffness-modifiable bioink and load-bearing frame design promote cell spreading and contraction similar to in vivo vascular smooth muscle tissue. This enables us to replicate increased vascular wall stiffness, making bioprinting a powerful tool to study PPHN.

Theme:
Basic Science

Do you have a table/figure to upload?
No

Are you willing to participate in Goodbear's Den?
Yes

Presenter Status:
Masters Student

What was your role in the project?
Design

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