ABSTRACT SUBMISSION FORM

LET'S TALK ABOUT

SEX + GENDER

Exploring the role of sex and gender on health research

CHILD HEALTH RESEARCH DAYS

CHRD 2020: Abstract Submission Form

Submitter Name
Jeffery Osagie

Email
osagiej3@myumanitoba.ca

Title
Development of A 3D Bio-printed Model of Airway Smooth Muscle — A Novel Paradigm for Studying Airway Mechanics in Asthma

Background
Asthma is the most common respiratory disease and the leading cause of hospitalization in Canadian children. It is characterized by exaggerated contraction of airway smooth muscle (ASM) and airway remodeling, which alters lung tissue stiffness.

Objective
To elucidate the consequences of airway stiffening on ASM contractile phenotype and function, we used 3D bioprinting technology to produce a physiologically-relevant 3D structure, explicitly designed to model airway narrowing in vitro.

Methods
Human ASM were resuspended at 2.5x107cells/mL in a bio-ink consisting of RGD-coupled-alginate (0.375%w/v), fibrinogen (5mg/mL) and collagen-I (1mg/mL). Cells were then printed as a ring-shaped bundle of muscle, either free-floating or constrained within a stiffness-modifiable acellular framework (0.75 – 1.25% w/v alginate). After printing, constructs were thrombin treated (1.25U/mL, 30min) to polymerize fibrinogen, and maintained in standard ASM culture conditions. We examined contractile phenotype with qPCR, and measured reduction in lumen area to represent muscle contraction.

Results
Free-floating ASM rings shortened excessively and rapidly lost structural integrity. Comparatively, 0.75%, 1% and 1.25% ASM tissues exhibited physical stability and compacted without stimulation to 72.27 ±2.61%, 78.42% ±1.76% and 74.01% ± 4.4% of initial lumen areas respectively at 6 days after printing. Crucially, we observed distinctive contractile responses to maximal doses of acetylcholine, potassium chloride, and cytochalasin-D (2-ANOVA drug response $p < 0.0001$, stiffness $p = 0.0438$) in framed tissues. Finally, acellular stiffness had no statistically significant impact on the genes trialed, however MHC was

elevated in 0.75% and SM22α in 1.25% ASM tissues compared with free-floating rings.

Conclusion
Consistent with previous studies, the observed differential responses in ASM fabricated across a stiffness range, support that mechanical factors alter tissue formation and cellular function. Moving forward, signal transduction pathways through which mechanical cues contribute to asthmatic ASM dysfunction will be characterized, potentially unmasking novel therapeutic strategies for managing disease progression.

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?
All the above

Authors

Name	Email	Role	Profession
Jeffery Osagie	osagiej3@myumanitoba.ca	Presenting Author	Graduate Student
Alexander Krueger	kruegera@myumanitoba.ca	Co Author	Undergraduate Student
Sanjana Syeda	ssyeda@chrim.ca	Co Author	Graduate Student
Emily Turner-Brannen	eturner-brannen@chrim.ca	Co Author	Research Technician
Adrian West	adrian.west@umanitoba.ca	Co Author	Assistant Professor