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Optimization of a 3D bioprinted model to study the effects of increasing airway stiffness on the contractile function of airway smooth muscle in asthma

Jeffery Osagie, Children's Hospital Research Institute of Manitoba, University of Manitoba; **Sanjana Syeda**, Children's Hospital Research Institute of Manitoba, University of Manitoba; **Emily Turner-Brannen**, Children's Hospital Research Institute of Manitoba; **Adrian West**, Children's Hospital Research Institute of Manitoba, University of Manitoba

Background:

Asthma affects over 600,000 Canadian children. It is characterized by airway wall remodeling and stiffening that may modulate the contractile behavior of airway smooth muscle (ASM). However, due to limitations with existing experimental models, the precise effects of airway stiffening are unclear. We have used 3D bioprinting technology to design novel stiffness-modifiable 'biorings' of ASM.

Objective:

We hypothesize that the exact stiffness and composition of biorings can be optimized to elucidate the effects of airway stiffening on ASM contractile function in asthma.

Methods:

A 15 mm diameter bioring structure was printed with human ASM cells ($2.5x10^7$cells/mL) in an alginate based bio-ink. Stiffness was optimized by modifying alginate content (0.25-1% w/v) and biocompatibility was conferred with 100µM RGD-alginate and collagen-I (1-2 mg/mL). Bioring structural integrity, diameter reduction (compaction), cell viability and cell spreading were tracked daily by macroscopic imaging, Hoechst/Propidium Iodide staining and filamentous actin (F-actin) staining respectively.

Results:

Biorings printed with 1% alginate were physically robust for >10days but exhibited no significant compaction. Live/dead staining showed a low cell viability (<50% 72 hours after printing), while F-actin staining revealed a rounded cell morphology. Biorings printed with 0.5% alginate had similar viability, morphology and compaction to 1% alginate, but limited structural integrity (<5 days). Increasing the collagen concentration (2mg/mL) and reducing the total alginate content (0.25%) enhanced bioring compaction and cell spreading.

Conclusion:

Stiff biorings provide excellent structural integrity but limit the compaction and spreading required to create functional ASM. Decreasing stiffness and increasing collagen content provides improved features of a functional muscle at the expense of structural integrity. Moving forward, a lower alginate concentration range and including an acellular structural component to support biorings will provide the combination of features required to recreate a physiological relevant ASM. This will be suitable for evaluating the effects of airway stiffening on ASM function in asthma.