Physiological Flow Cell Adapted for Monitoring Cardiac Tissue Damage Under High Pressures

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Artificial replicas of physiological systems can be used by investigators to provide extensive *in vitro* evidence to avoid unnecessary and potentially unsafe testing *in vivo*. Significant advances in laboratory-based tissue research have been enabled through three-dimensional growth methods such as scaffold-based techniques (physical supports and hydrogels) that allow mimicry of the extracellular matrix. We present a physiological flow cell that incorporates 3D tissue growth on electrospun, nanofiber polymer scaffolds (Figure 1) with the added capacity to incorporate fluid flow and/or physiological pressures to address specific scientific aims (Figure 2). One attractive use of such a flow cell is mimicry of the pressures and flow on tissues present in the interior of the heart.

Blood pressure is a result of lifestyle, sociodemographic conditions, and heredity. High blood pressure levels can result in cardiovascular tissue damage and dramatically increase the risk of chronic cardiovascular disease. Traditional methods to mimic heart function include the use of pumps that cost tens of thousands of dollars. In this work, a low-cost flow cell that can be sterilized, placed in a CO_2 environment, and externally monitored by flow sensors was developed (Figure 3). In preliminary testing, cell health of 3D tissues grown on electrospun scaffolds was monitored after a 5 hr test and revealed no diminishment of metabolic activity.

The evolution of hypertension can be described by systolic and diastolic blood pressure readings: normal 120/80 mmHg, prehypertension 120-140/80-90 mmHg, stage 1 hypertension 140-160/90-99 mmHg, and stage 2 hypertension or hypertensive crisis >160/>100 mmHg. The cardiac flow cell is undergoing preliminary tests to determine if tissue damage at elevated blood pressure levels can be replicated. Metabolic assays will be used to evaluate tissue health on electrospun scaffolds post-exposure to normal, prehypertension, hypertension, and hypertensive crisis pressure levels in the flow cell, and 3D tissue growth will be monitored by confocal microscopy. Accurate representation of cardiac tissue damage in the model could provide evidence for use of the flow cell as a low-cost laboratory method to predict *in vivo* efficacy of therapeutics meant to prevent tissue damage under pressure. In addition, tissues containing specific mutations could be evaluated for susceptibility to specific pressures and flows in a physiological system.

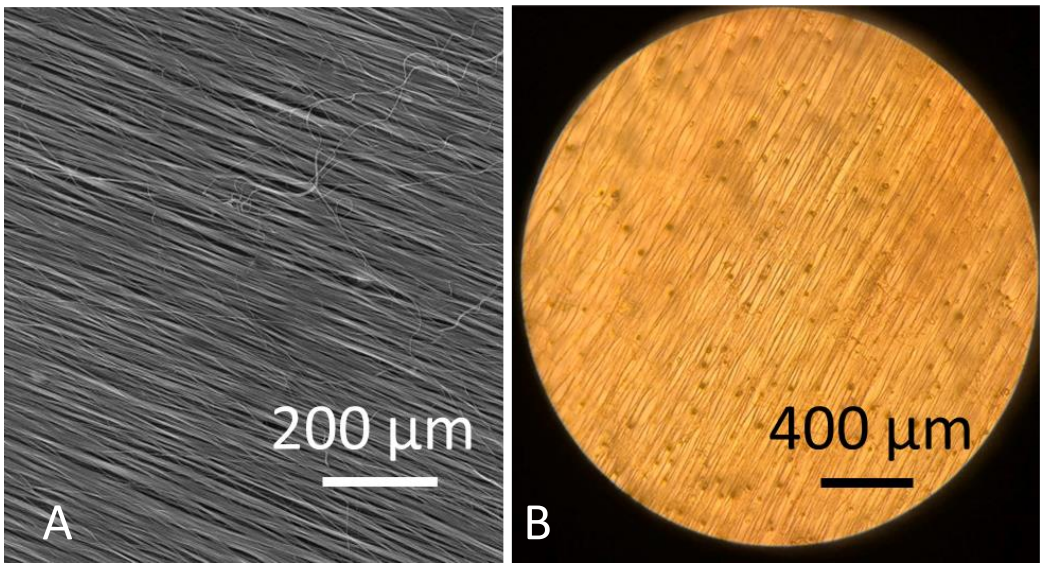

Figure 1: Micrographs of scaffolds used for growing tissues placed in physiological flow cell. A) Electrospun polycaprolactone fibers aligned using elevated parallel gap electrodes. B) Kidney epithelial (Vero) tissue grown on aligned electrospun scaffold.

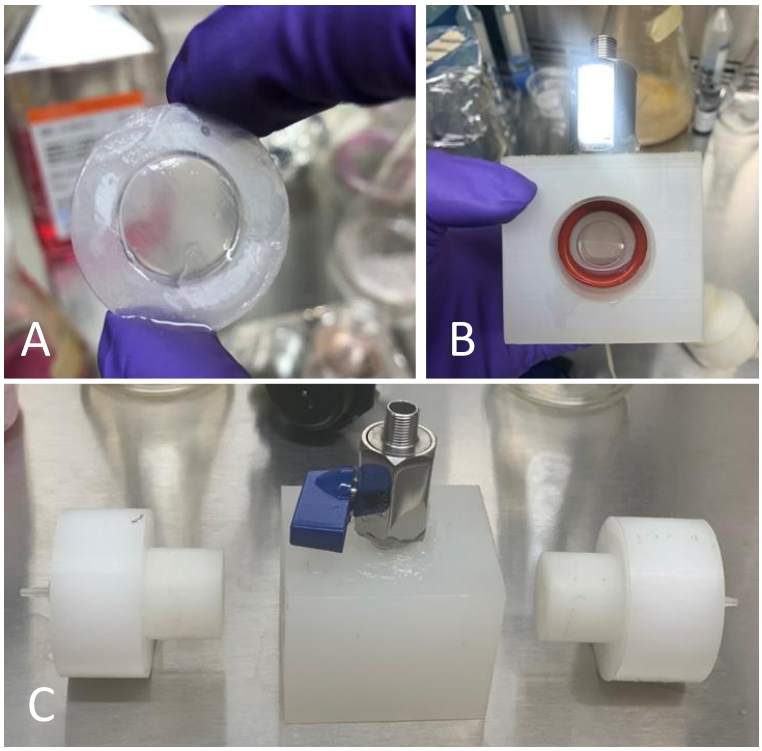

Figure 2: Macroscale images showing components of the physiological flow cell. A) Electrospun scaffold containing kidney epithelial tissue. B) Electrospun scaffold containing tissue placed in the physiological model. C) Image of flow cell showing inlet and outlets and a sample collection port.