A Biomimetic Microfluidic Platform for Anti-tumor Drug Evaluation

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Introduction

- Chemotherapy drugs are vital for treating and eliminating cancer in patients. Developing new and effective cancer drugs is difficult, because *in vitro* preclinical testing of drug candidates often yields inaccurate results which suggest the drug is more effective than it actually is. Thus, a drug evaluation platform that accurately mimics an *in vivo* tumor environment is imperative to the development of new anti-tumor drugs.
- Traditional 2D cell monolayer drug screening models do not accurately mimic an *in vivo* drug delivery environment. This presents a crucial limitation for accurately estimating the efficacy of a tumor drug in the human body.
- 3D models using tumor cell spheroids more accurately mimic the complex *in vivo* microenvironment in which a tumor is found.
- Here, microfluidic devices are designed to be biomimetic of a blood vessel by coating the device channel with endothelial cells.
- Paclitaxel, a chemotherapy drug, is administered through this "blood vessel" and interacts with tumor spheroids in the device.
- This allows for a drug evaluation model that accurately mimics drug transportation in an *in vivo* blood vessel environment.

Methods

- Microfluidic devices were constructed from glass and PDMS. A schematic of the microfluidic device is shown in Figure 1.

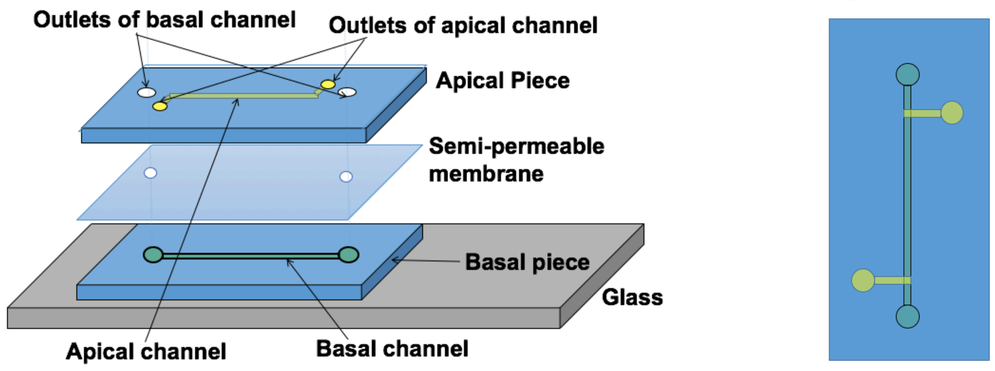

Figure 1: *Schematic of the microfluidic device*

- Endothelial cells (EC) were seeded into the apical channel to coat the semi-permeable membrane with an endothelial layer.
- HCT-116 tumor spheroids were seeded into the device's basal channel in a 1:1 ratio of Matrigel and spheroid-EC media solution, and was cured. A schematic of this is shown in Figure 2.

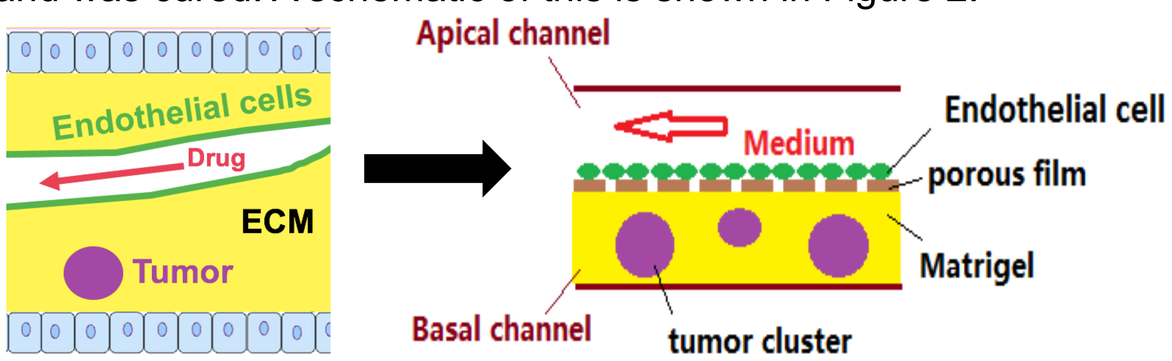

Figure 2: *EC-loaded devices mimic the in vivo tumor environment*

- 8 different concentrations of Paclitaxel-doped media were administered daily for 3 days to 8 devices' apical channels:
  - 0M (control), 1nM, 3 nM, 10nM, 30nM, 100nM, 300nM, 1μM

Results

- Optical Coherence Tomography images of spheroids in the EC-devices generated 3D images[1] of the spheroids in the channel which were used for volume calculation. A 3D image is displayed in Figure 3.

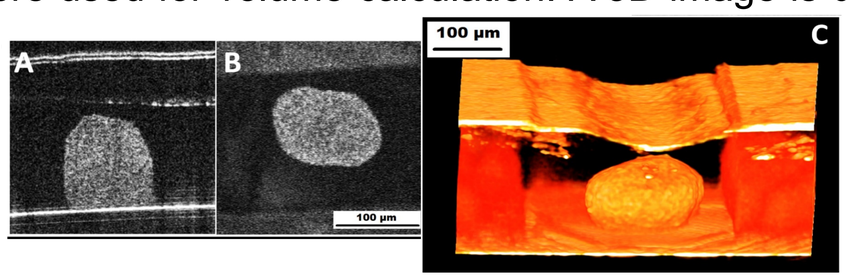

Figure 3: *OCT scans (left) and generated 3D image of a spheroid (right)*

- Cell staining using a dead/live cell staining kit and confocal microscopy showed higher cell viability in the well plate and EC-free device after 3-day drug treatment. This is displayed in Figure 4.

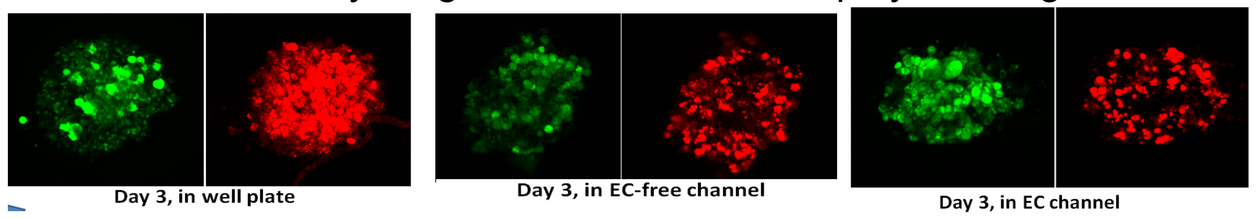

Figure 4: *Dead-live staining for well plate and EC/EC-free devices (100nM)*

- Spheroid volume and cell viability decreased as drug treatment progressed, and the decrease was more rapid for higher drug concentrations. This is shown in Figure 5.

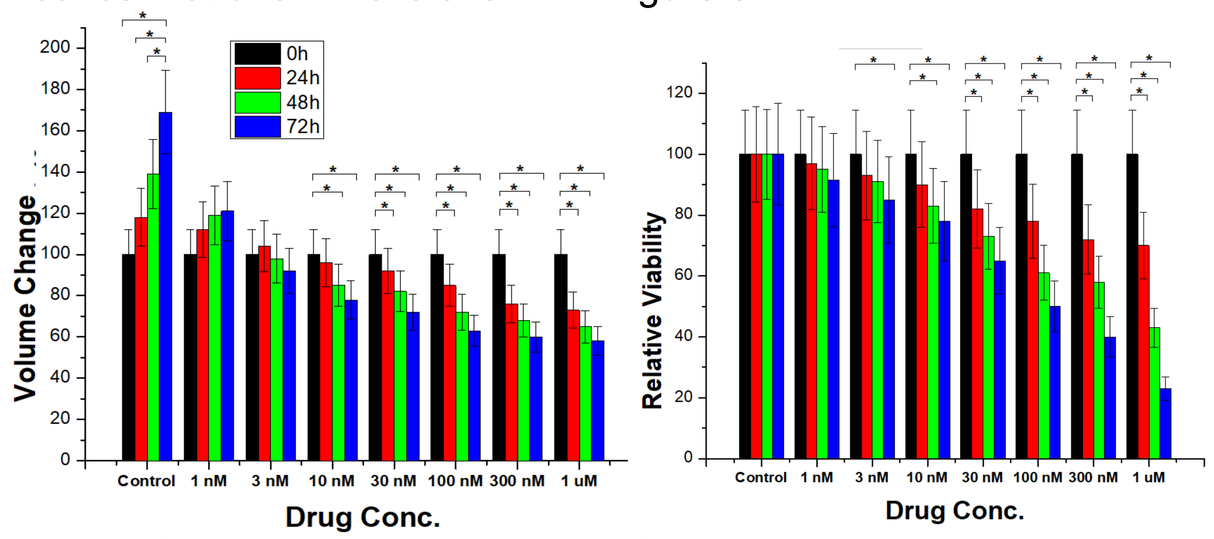

Figure 5: *Spheroid volume and viability in EC-devices decreases with drug treatment*

Discussion and Conclusions

- This biomimetic, 3D microfluidic drug screening platform better mimics the *in vivo* blood vessel microenvironment.
- The EC layer and Matrigel acted as hindrances to drug delivery, dramatically inhibiting drug delivery from the apical channel to the tumor spheroids.
- This research serves as an initial step toward anti-tumor drug evaluation in the form of a "lab-on-a-chip" platform.
- Further steps include a more complex microfluidic system which more closely mimics a blood vessel environment, automation, and testing other chemotherapy drugs with the device.

References

1. Y. Huang, S. Wang, Q. Guo, S. Kessel, I. Rubinoff, L.L.-Y. Chan, P. Li, Y. Liu, J. Qiu, and C. Zhou, Cancer Res. 77, 6011 (2017).

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