Developing a Renal Cell Carcinoma Kidney-Tumor-on-a-Chip to Mimic Tumor-Induced Angiogenesis

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Introduction:

Currently, developing cancer drugs are tested in 2D cell cultures and animal xenografts; these have been proven to be poor predictors of drug effectiveness. After success in animal models, just 8% of cancer therapeutics are successful in phase 1 human clinical trails[1].

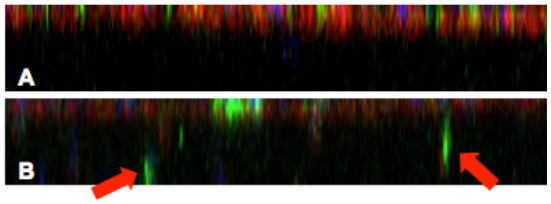
Combining microfluidics and tissue engineering, biomimetic organs-on-chips address the issue of inaccurate physiological models. The Zheng Lab, in conjunction with the Kidney Research Institute, has worked to develop a kidney-tumor-on-a-chip to accurately mimic angiogenesis in renal cell carcinoma, the most prevalent type of kidney cancer.

Materials and Methods:

In order to develop a kidney-tumor-on-a-chip, Human Kidney Microvascular Endothelial Cells (HKMECs) were cultured with primary renal cell carcinoma cells from the University of Washington Medical Center. Initial experiments were conducted by culturing a HKMEC monolayer over a well of cell spheroids suspended in type I collagen. Cell spheroids at a density of 1000 cells/spheroid were made using a standard hanging drop technique. Wells were fluorescently imaged using confocal microscopy, and endothelial sprouts were quantified by a scientist blinded to the experiment conditions.

Results and Discussion:

Nine total experiments were performed with HKMEC monolayers grown above no cells, normal kidney cortex spheroids, or RCC spheroids. On average, there were 11 times more endothelial sprouts in experiments with RCC spheroids compared to ones with normal spheroids or no cells. This suggests the presence of RCC spheroids induced angiogenesis in the HKMEC monolayer.



(A) HKMEC monolayer on normal kidney cell suspended collagen **(B)** HKMEC monolayer on RCC cell suspended collagen. *Blue: Hoechst, Green: CD31, Red: Phalloidin.*

Conclusions:

While simplified, the development of these wells to mimic tumor-induced angiogenesis is the first step toward developing a kidney-tumor-on-a-chip and a key proof-of-concept. After showing tumor-induced angiogenesis can be mimicked *in vitro*, the next step is to implement microfluidics. Key physiological aspects such as the lumen architecture, fluid flow, and shear stress are missing from the previously conducted experiments. By implementing microfluidics, an even better mimic of a vascularized tumor will be created. A more accurate physiologic model could test anti-angiogenesis drugs more effectively and could eventually become a strategy to personalize medicine by culturing patient specific cells for drug testing.

Acknowledgments:

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References:

1. Mak I., Evanview N., Ghert M., Lost in translation: animal models and clinical trials in cancer treatment (2015), 6, 114-118