

School of Biological and Health Systems Engineering (SBHSE)

Engineering Organotypic Disease On-a-Chip Models; Harnessing Innovations in Microfluidics, Biomaterials and Single-Cell Resolution Analysis

Mehdi Nikkhah, Ph.D.

Associate Professor Biomedical Engineering School of Biological and Health Systems Engineering Biodesign Virginia G. Piper Center for Personalized Diagnostics Arizona State University

18th U.S.-Korea Forum on Nanotechnology

Sept 2024



Silicon Micro-Topographies for Biosensing SBHSE

Virginia Tech , PhD



Nikkhah, et. al., Biomedical Microdevices, 11, 585-595(2009) Nikkhah, et. al., Biomedical Microdevices, 11: 429-441 (2009) Nikkhah, et. al., Biomaterials, 31: 4552-4561 (2010). Biomaterials, 32: 7625-7632 (2011).

Micro/Nanoengineering Biomaterials Biology/Medicine

Engineering Biomimetic and Organotypic Tissue Models















Tumor microenvironment (TME); The need for better tumor on-chip platforms



- A highly complex diseased tissue landscape, ECM
- Multitude of different cell types (cancer, fibroblast, endothelial, immune cells)
- Tissue architecture



SBHSE

Organotypic Microfluidic TME Model



Catteau et al. (2013). 8(3) PLOS ONE.









10 Organotypic Features:

- Organized 2-layer concentric semi-circular region
- Cells in Tumor and Stroma Regions
- Re-configurable tumor and stroma

Ravi et. al., Biomaterials, 2024 A. Swah et. al., Advanced Science, 2022 Truong et. al., Cancer Research, 2019 Saini et. al., Biomaterials, 2020 Nagaraju, Moneharan, et. al., Advanced Health Mater, 2018, 2024 Truong et. al., Scientific Reports, 2016

US patent # 10,017,724 US patent # 10,712,339

Influence of Stromal Fibroblasts

SBHSE



Truong et. al., Cancer Research, 2019

ASU Real time Tumor Invasion into the stroma



Truong et. al., Scientific Reports, 2016

High Resolution Single-cell Imaging

Fluorescent Movie

3D Movie

+ EGF







ASU Gene Expression Profiling of Cancer Cells



- *GPNMB* encodes for a cell surface transmembrane glycoprotein that is highly expressed among many cancers, including breast cancer
- Two clinical datasets (METABRIC and TCGA) demonstrated the alterations of *GPNMB* occur in 10 and 16% of breast cancer patients *Truong et. al. , Cancer Research, 2019*



Microengineering of Glioblastoma (GBM) Model on-a-Chip





- Interrogate the behavior of GSCs in the Perivascular Niche
- Tri-layer microfluidic chip
- Introduced a separate region for vasculature

Sowah et. al., Advanced Science, 2022 Truong et. al. , Biomaterials, 2019 Image: strong stron

Collaborators: Dr. Shwetal Mehta, BNI Dr. Chris Plaisier, ASU

SBHSE

GB3

Modeling the Brain Perivascular Niche



Sowah et. al., Advanced Science, 2022 Truong et. al., Biomaterials, 2019

Identification of novel ligand-receptor pairs using Sc-RNA seq

SBHSE



Vascular region Stroma region Tumor region Matrix plots of receptor and ligand expression in the mono-culture (orange) and triculture (purple) conditions across cell types

• Relative receptor expression per patient across scRNA-seq glioma datasets

Sowah et. al., Advanced Science, 2022

•



Heart on-a-Chip Model; Interface of Nanomaterials with Human tissue



Veldhuizen et. al. , Science Advances, 2022 Veldhuizen et. al. , Biomaterials, 2020 Veldhuizen et. al. , Biomaterials, 2022

Collaborators: Raymond Migrino, MD Phoenix VA Medical Center



Heart on-a-Chip

SBHSE



Veldhuizen et. al., Biomaterials, 2020



Heart on-a-Chip



Veldhuizen et. al. , Biomaterials, 2020 Veldhuizen et. al. , Biomaterials, 2022



Acknowledgments

Current Lab Members:

Kalpana Ravi, PhD Candidate Shaun Wooten, PhD Candidate Lydia Sakala, PhD Candidate Twinkel Monehraran, PhD Candidate Yamini Singh, PhD Candidate Kegan Neff, BS BME Ethan Hurt, BS BME Ronin Komarnisky, Lab Engineer

Graduate/Postdoctoral Alumni:

Dr. Ronald Nelson, Postdoctoral Fellow Dr. Karen D'Souza, Research Scientist Dr. Amrita Pal, Postdoctoral Fellow Hamid Esmaeili, PhD, BME Alejandra Patino, PhD, BME Jaime Veldhuizen, PhD, BME Harpinder Saini, PhD, BME Danh Truong, PhD, BME Ali Navaei, PhD, BME Michelle Jang, MS Candidate Ritvik Srivant, MS Candidate Shivani Mantri, MS Candidate Twinkel Monehraran, MS, BME Ouse Sheblak, MS, BME Emmanuella Sowah, MS, BME Zach Ticktin, MS, BME Yuka Sugamura, MS, BME Supriya Nagaraju, MS, BME John R. Jakoubek, MS, BME Ankita Sripathi Urala, MS, BME Feb S. Sam, MS, BME Harpinder Saini, MS, BME

Funding resources:



National Science Foundation WHERE DISCOVERIES BEGIN

Award # EBMS 2309859 Award # CAREER CBET 1653193 Award # EBMS 1914680 Award # BME 1510700 Award # Nanoscale 2016501



National Institutes of Health

R01 Award # HL172784-01 R01 Award # NS123038 R21 Award # EB028396







ARIZONA DEPARTMENT OF HEALTH SERVICES

ARIZONA BIOMEDICAL RESEARCH COMMISSION



U.S. Department of Veterans Affairs





THE INTERNATIONAL FOUNDATION FOR ETHICAL RESEARCH