Precise Manufacturing of Multi-Lineage Tissues by Integrating Synthetic Cell Receptors, Patterned Biomaterials, and Organoids

Megan L. McCain, PhD

Associate Professor and Chonette Early Career Chair
Alfred E. Mann Department of Biomedical Engineering
Department of Stem Cell Biology and Regenerative Medicine
University of Southern California

Laboratory for Living Systems Engineering
https://livingsystemsengineering.usc.edu
@mccainlab

Laboratory for Living Systems Engineering

USC Viterbi School of Engineering

Children's Hospital Los Angeles
THE SABAN RESEARCH INSTITUTE

wise

ALS ASSOCIATION

TheRoseHills FOUNDATION

American Heart Association.

16SDG29950005 (PI)

NIH

R01 HL130172 (co-I)
R21 EB025534 (co-PI)
R01 HL153286 (PI)

ADDITIONAL VENTURES

the eli and edythe broad foundation

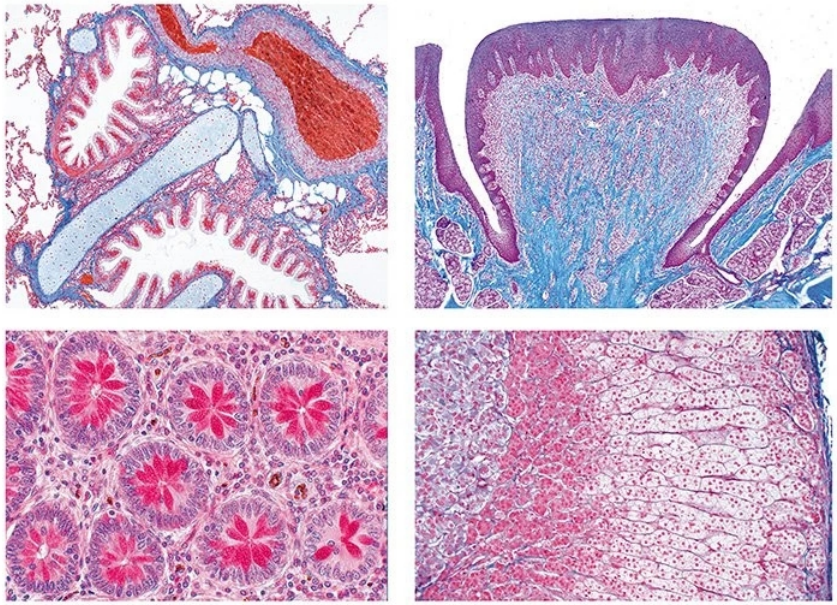
NSF

CMMI CAREER 1944734 (PI)

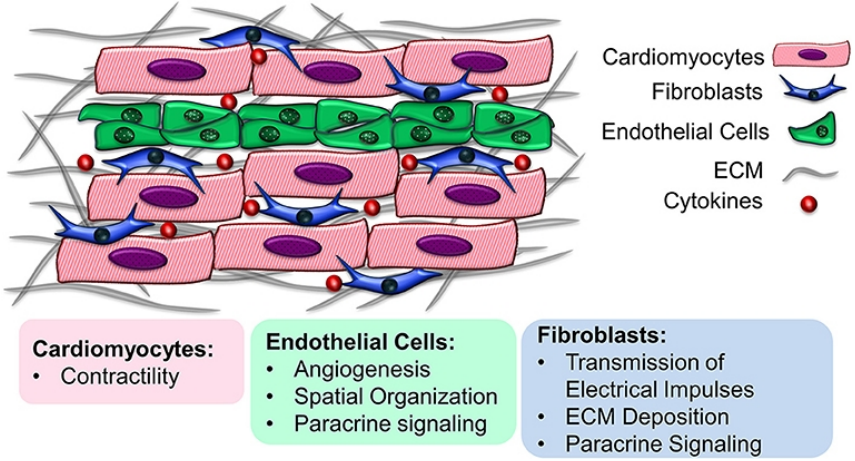
CBET RECODE 2034495 (co-PI)

NSF GRFPs: Jeffrey Santoso, Natalie Khalil, Nina Maxey

All Tissues Comprise Multiple Cell Lineages



https://www.flinnsci.ca/normal-human-histology-slide-set/ml1460/

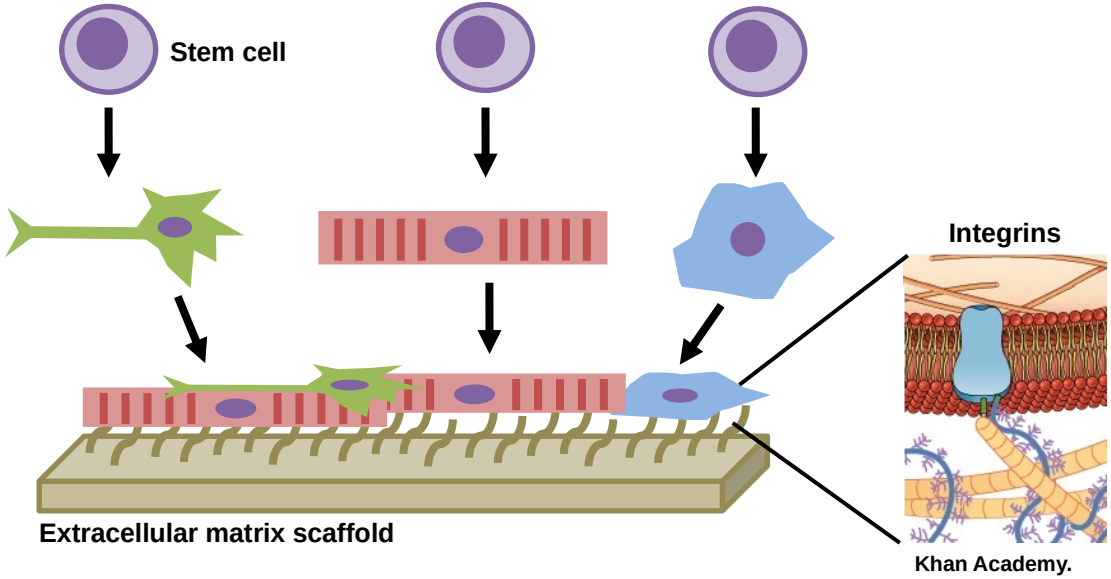


Zamani et al, Frontiers in CV Medicine, 2018.

- During human development, adjacent cell types co-develop into stereotypic tissues
- Cell/tissue structure is critical for cell/tissue maturation and function

Existing Approaches for Engineering Tissues

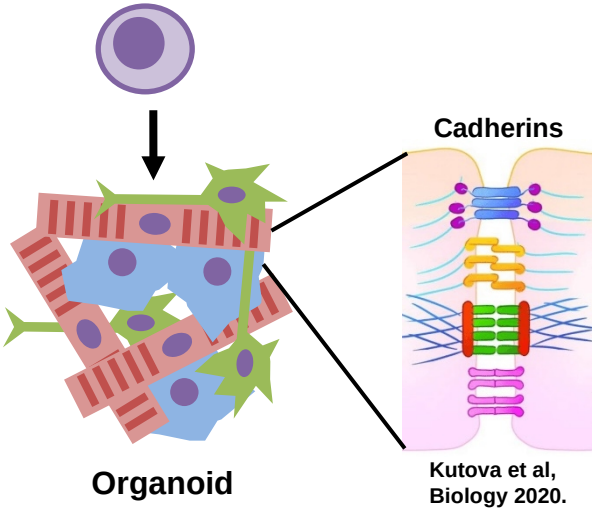
Scaffold-Based Tissue Engineering



Khan Academy.

- Each cell type is differentiated in isolation, limiting maturity
- Scaffolds are used to present matrix ligands for integrins, which can be promiscuous and unpredictable
- Tissues have relatively predictable architecture, but micro-scale spatial patterning of multiple cell lineages remains challenging

Organoids



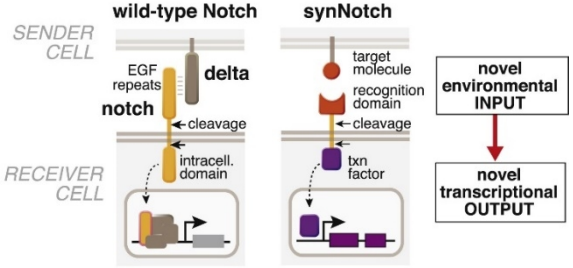
Kutova et al, Biology 2020.

- Cells types are co-differentiated, enhancing maturity
- Tissues have highly unpredictable architecture
- No extracellular matrix

SynNotch Receptors Enable Orthogonal Inputs and Outputs to Mammalian Cells

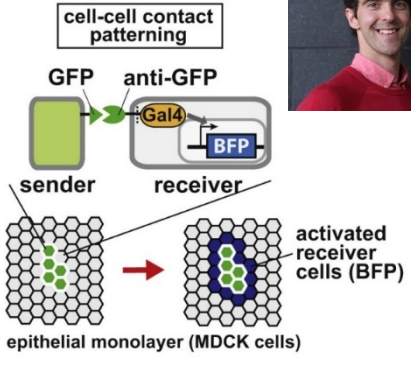
USC

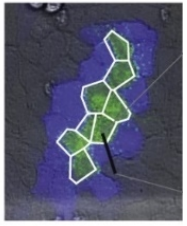
Activating SynNotch with Ligands Presented by Cells



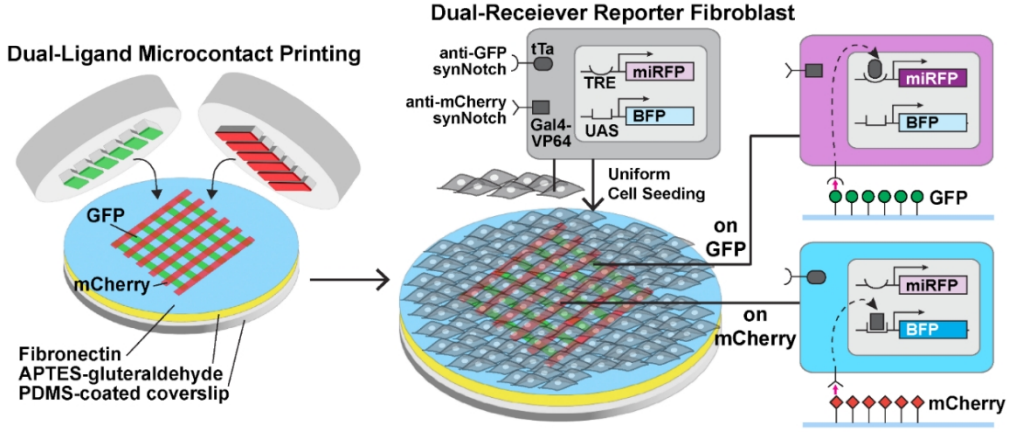
Morsut et al, Cell 2016.

Leonardo Morsut, Asst. Prof. of Stem Cell Biology & Regenerative Medicine





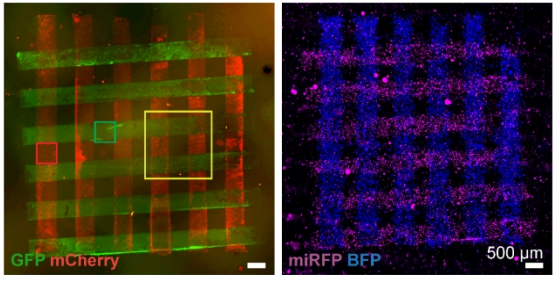
Our New Approach: Activating SynNotch with Ligands Presented by Patterned Materials



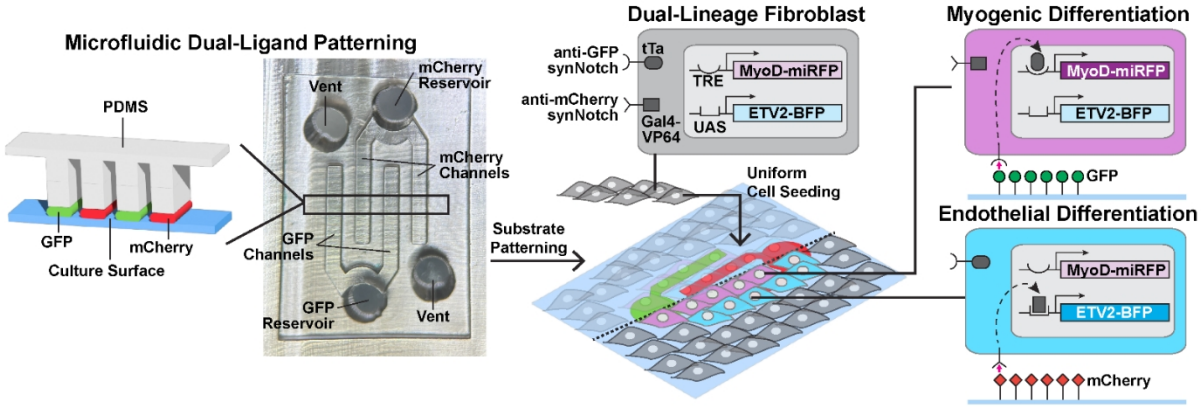
Mher Garibyan Tyler Hoffman

PhD Candidates

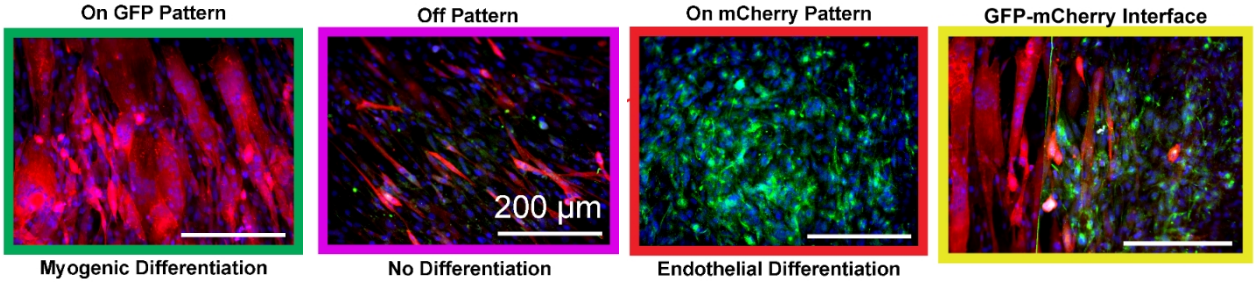
https://www.biorxiv.org/content/10.1101/2023.05.19.541497v1

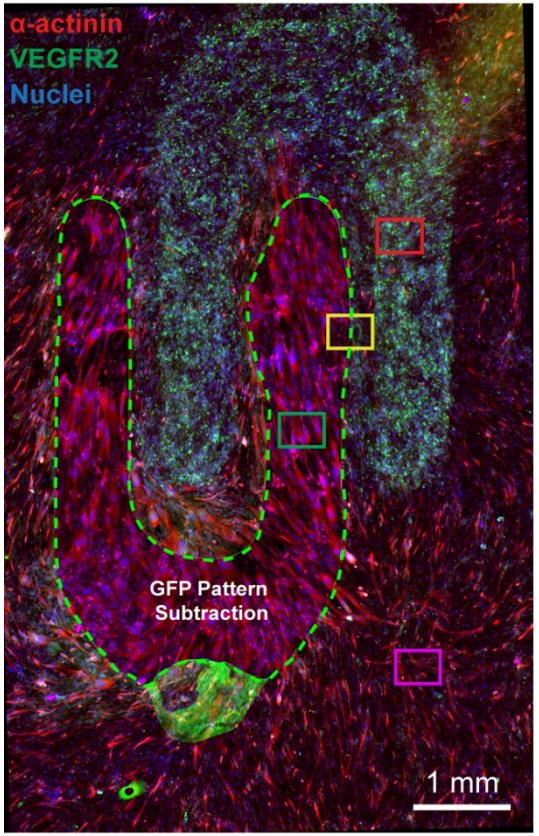


Engineering Multi-Lineage Tissues with Microscale Spatial Control

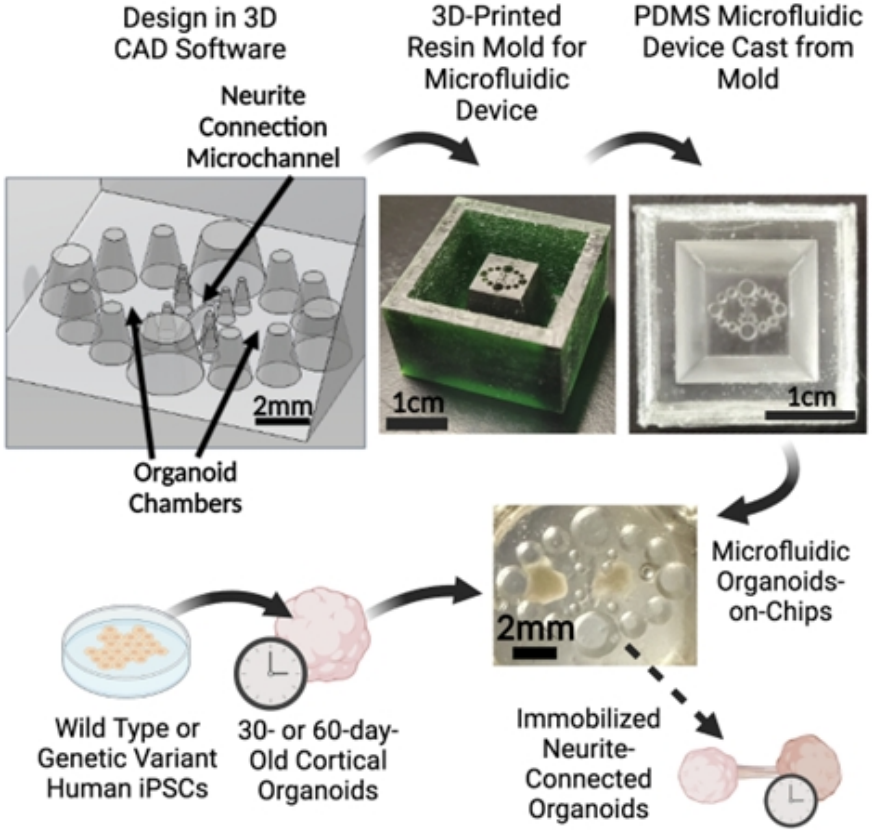


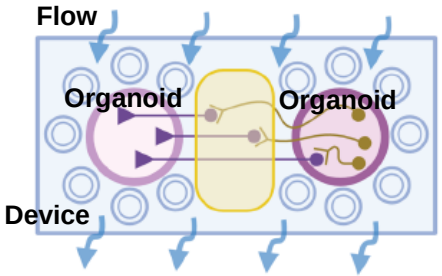
Garibyan, Hoffman et al, bioRxiv
https://www.biorxiv.org/content/10.1101/2023.05.19.541497v1

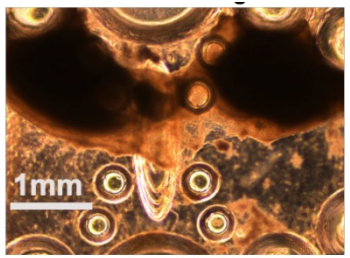




Engineering Devices and Materials to Culture and Connect Brain Region-Specific Organoids







Giorgia Quadrato, Asst. Prof. of Stem Cell Biology & Regenerative Medicine

James Eichenbaum

JP Urenda

PhD Candidates

- Fluidic device enables organoid survival in static culture
- In static culture, organoids representing different brain regions can extend axons and form synaptic connections, likely to enhance maturity
- Integrating synthetic receptors/ligands in the future will endow further control over tissue morphogenesis