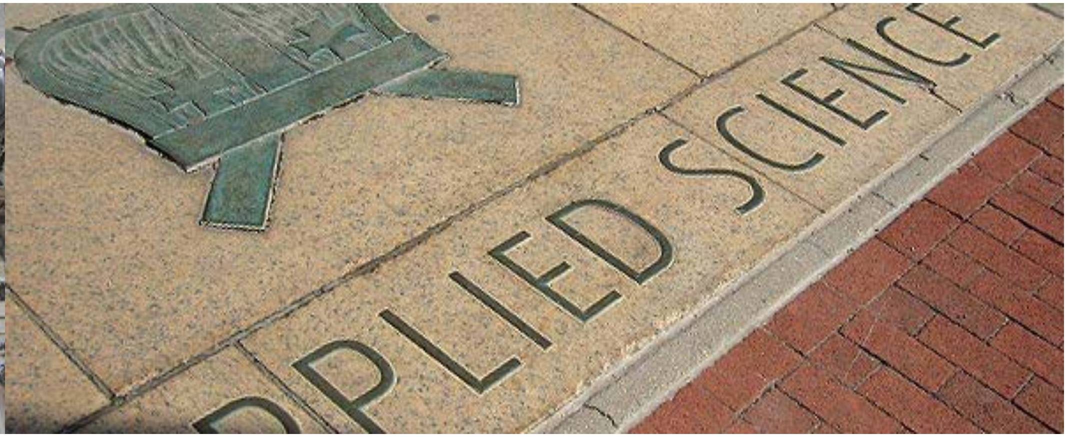
Integrated human multi-organ platforms



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NAS Roundtable
Microphysiological Systems: Bridging Human and Animal Research
January 19-20, 2021

Introduction:

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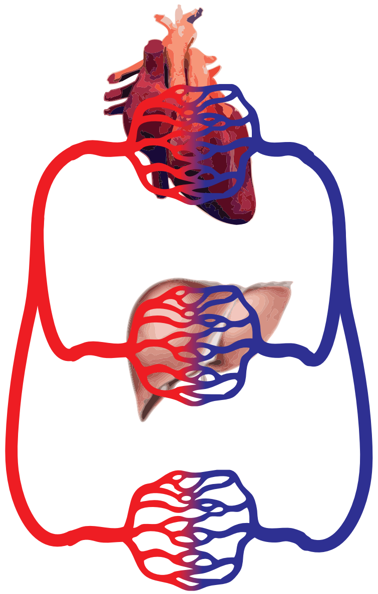
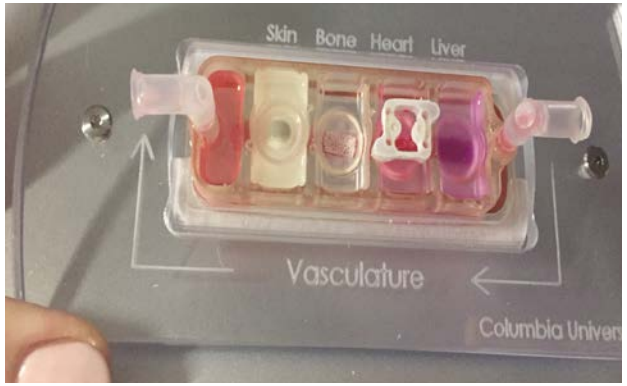
Research

Tissue engineering approaches to improving human health:

- **Regenerative medicine**: engineering functional human tissues/organs including heart, lung, joints and vasculature
- **"Organs-on-a-chip"**: human tissue models for biological research, study of disease and development of therapies

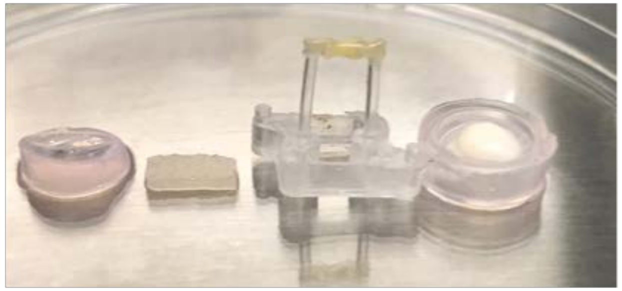
Key requirements:

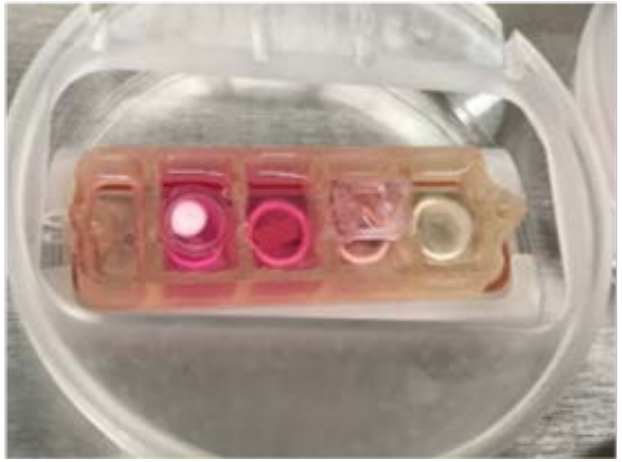


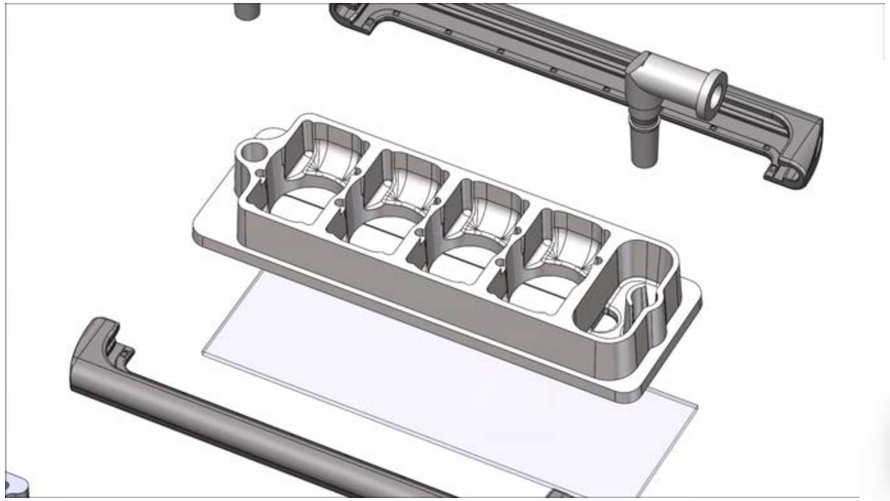


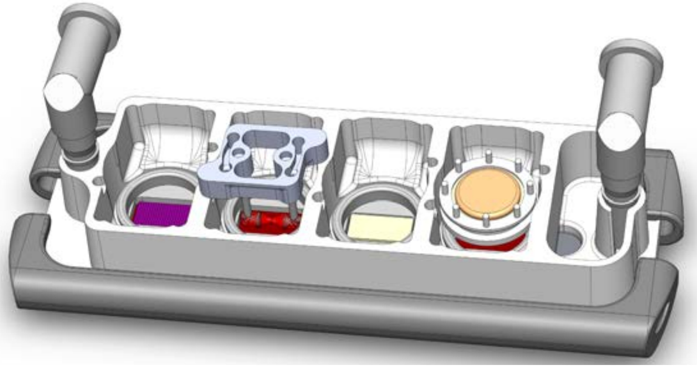
- **Modular, configurable**
  - To form physiological units; vary tissue scaling and order
- **Biological specificity**
  - Individualized settings, defined genetics (iPSCs)
- **Stable tissue phenotypes**
  - Weeks to months
- **Tissue connectivity**
  - Individual control, links by vascular perfusion
- **Functional readouts in real time**
  - On-line, longitudinal studies
- **Building complexity**
  - Co-culture, vascularization, innervation, immune cells

Modularity: “plug and play”



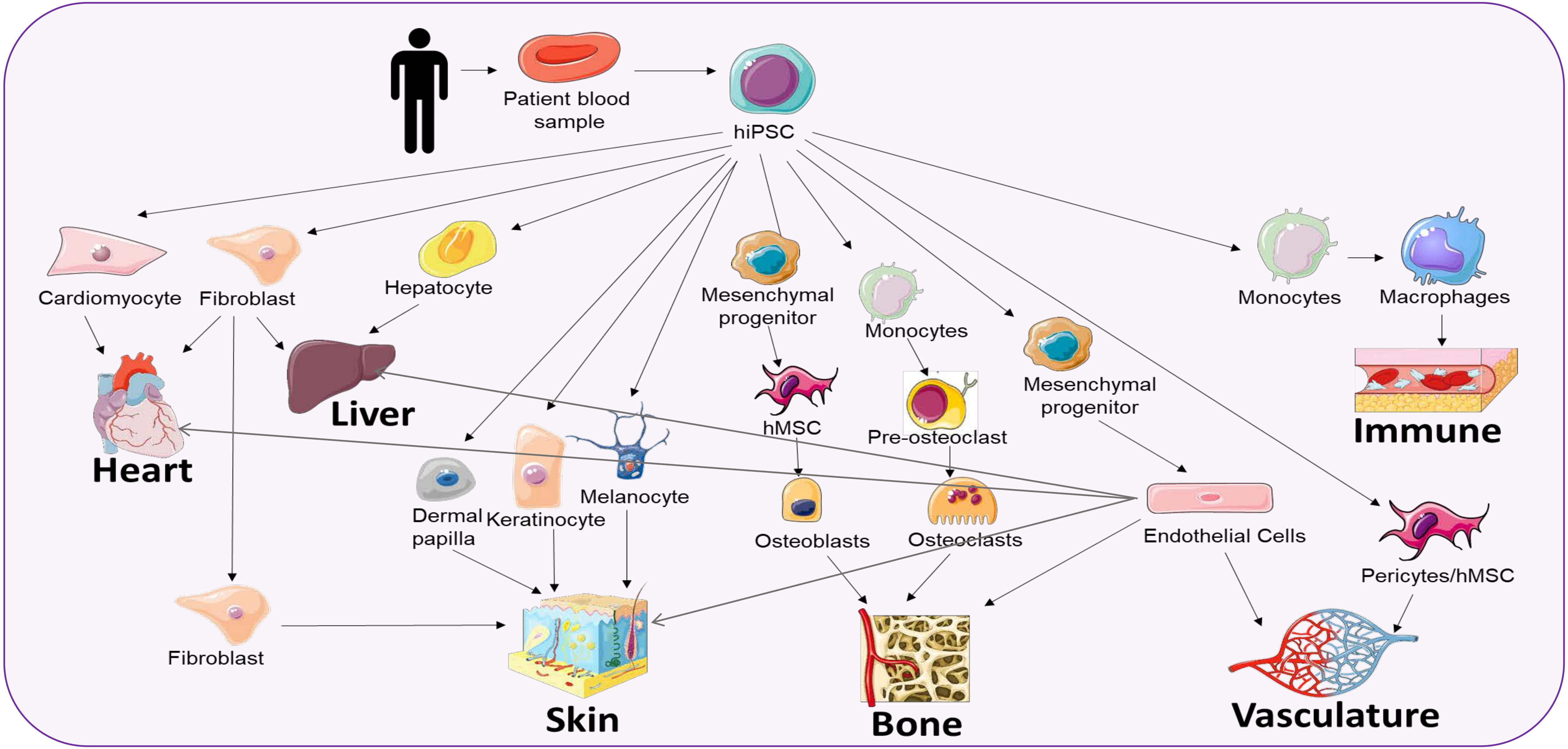




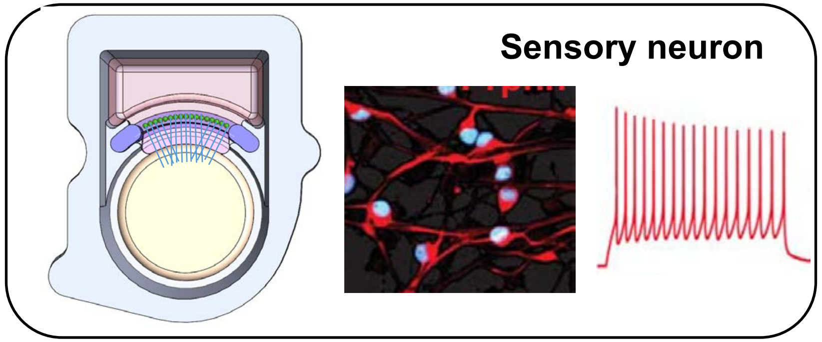


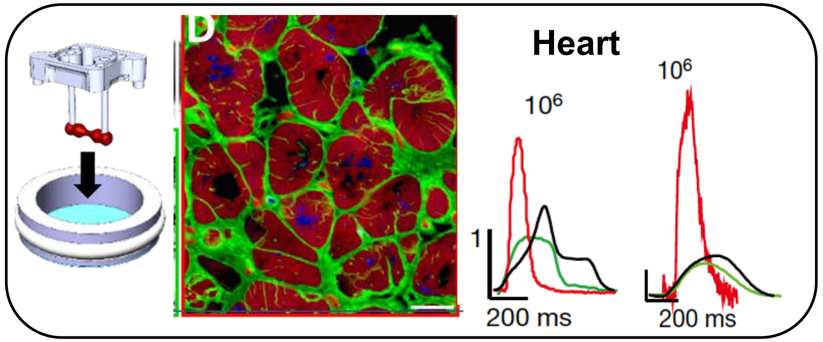
Ronaldson-Bouchard et al (in revision)

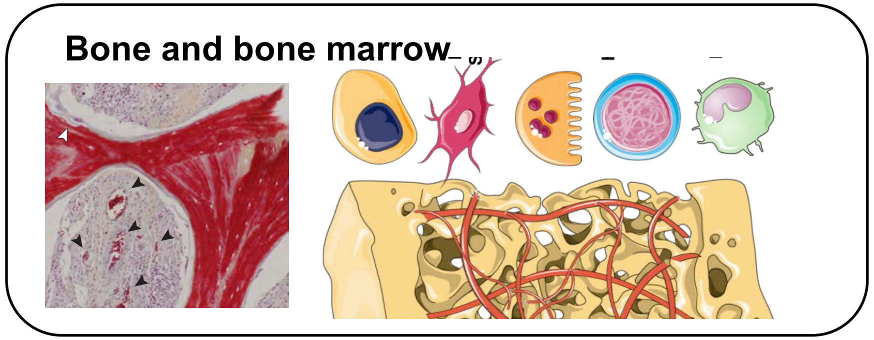
Biologic specificity using iPS cells:

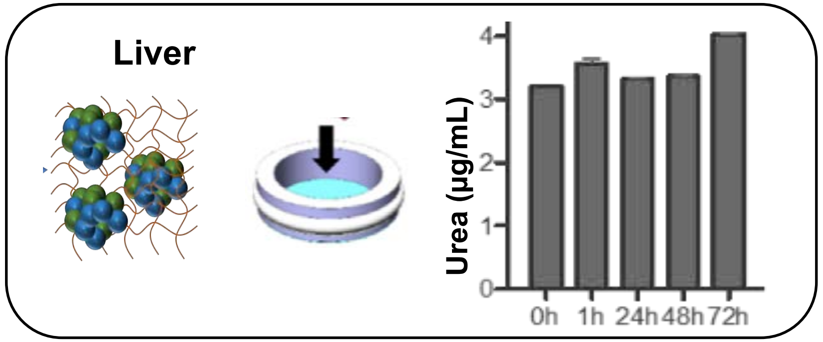


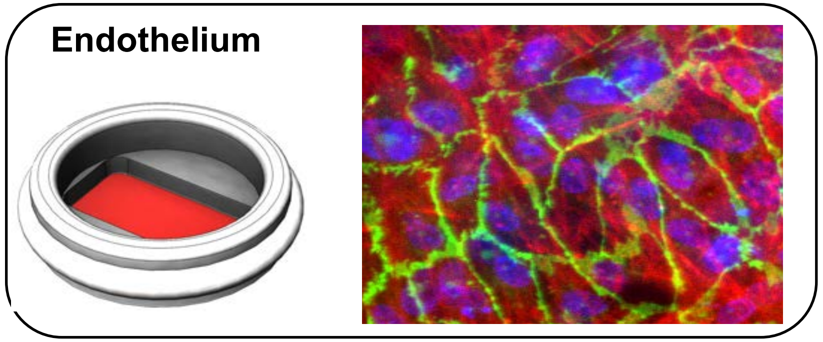
A menu of matured, functional human tissues:

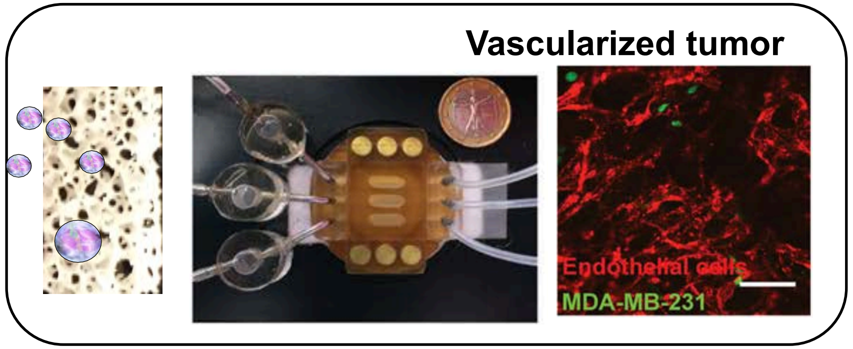


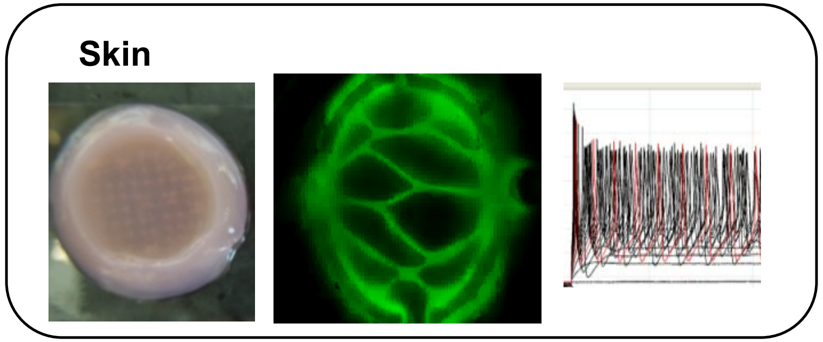


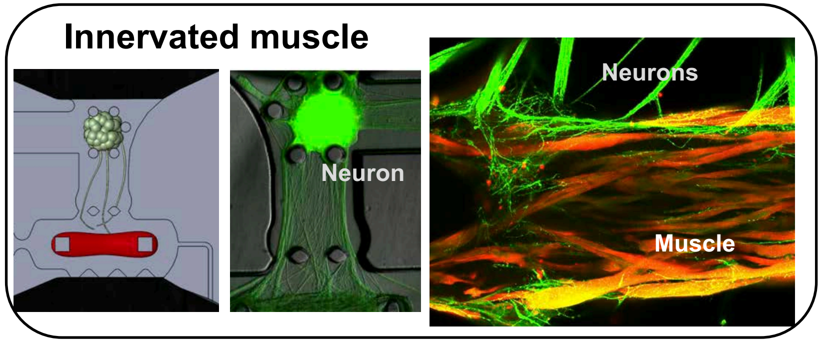


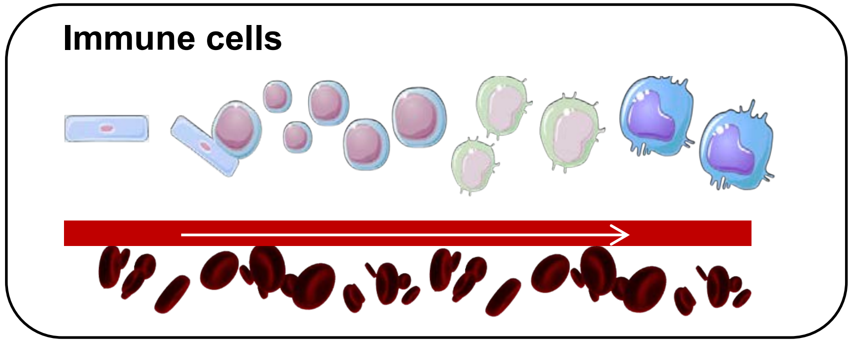




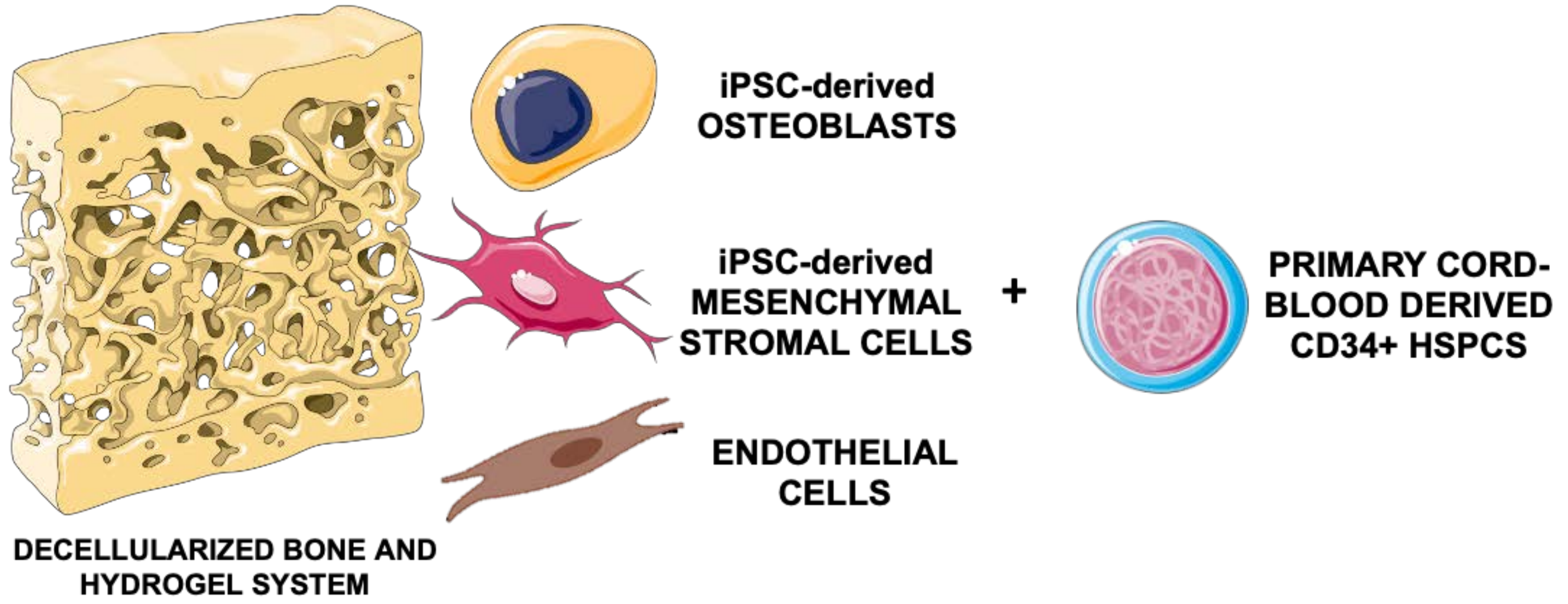


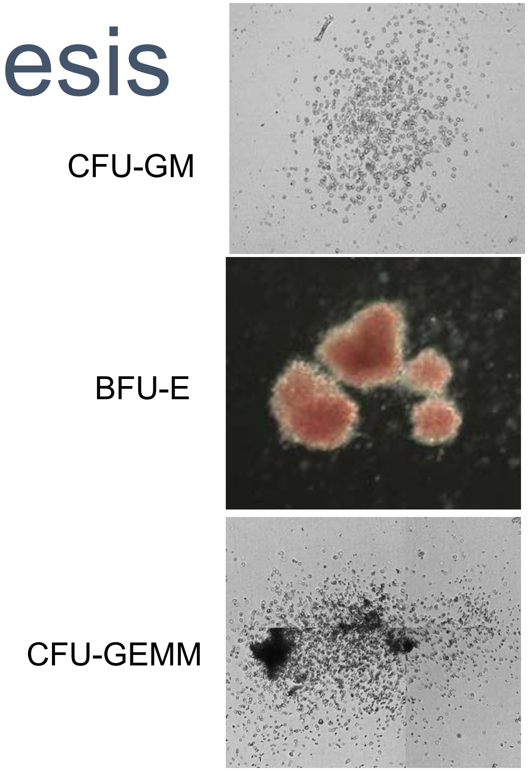


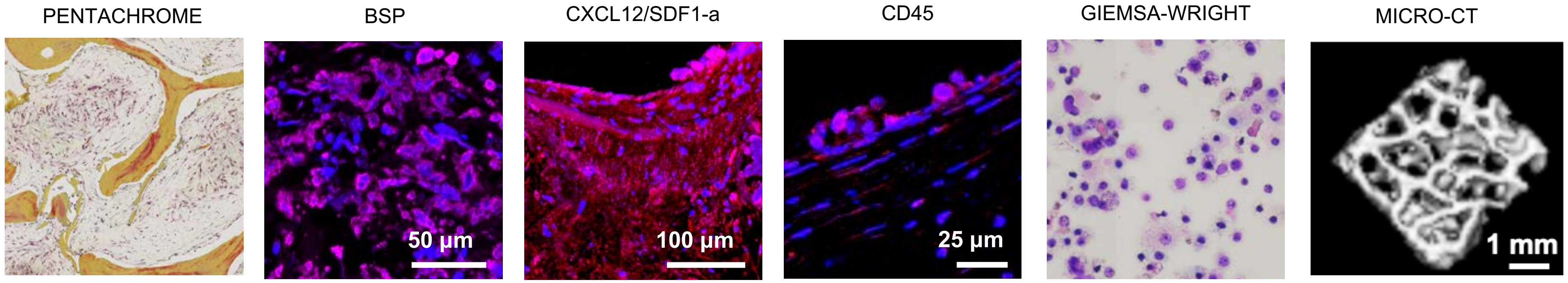


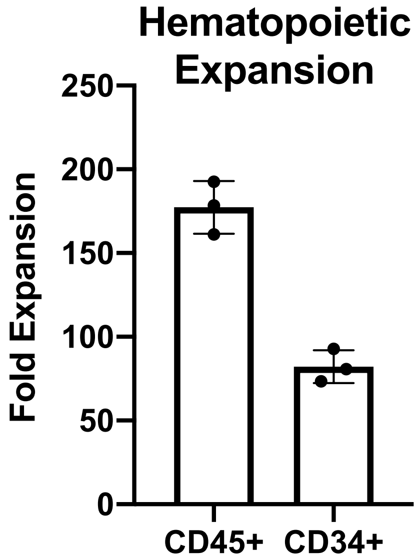


Example: human bone marrow with hematopoiesis



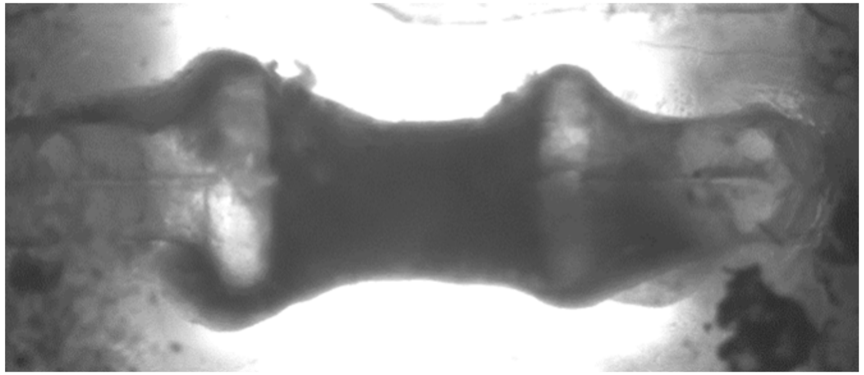


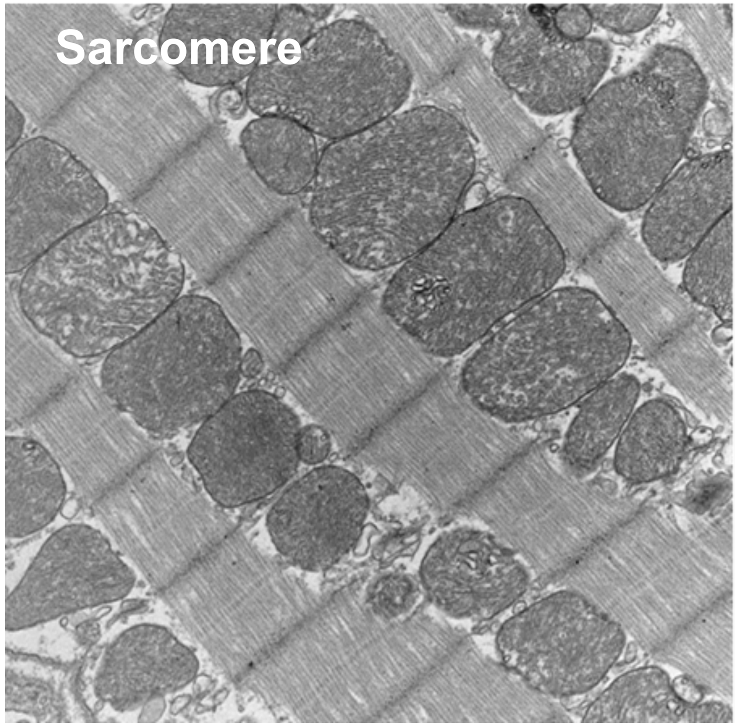


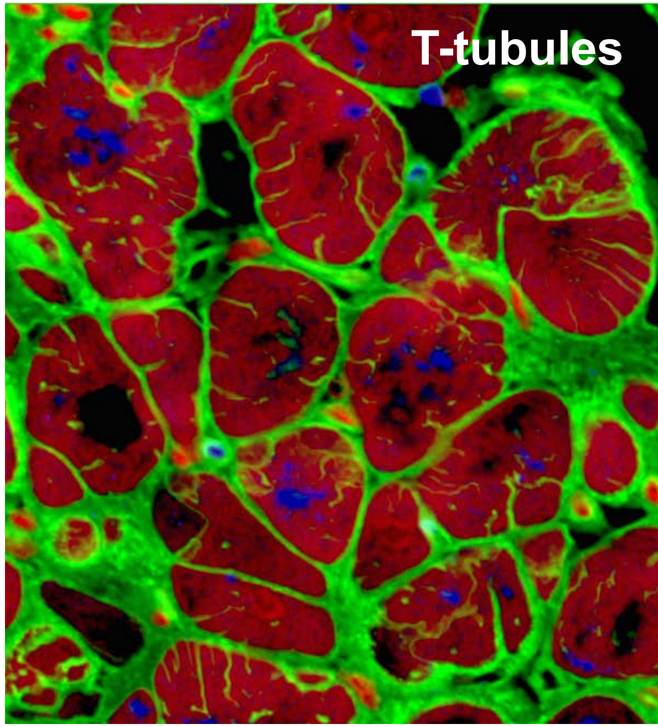


Tavakol et al., in preparation

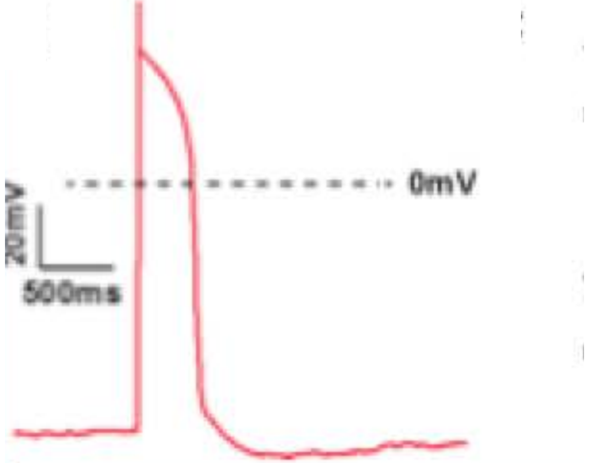
Example: Human heart muscle:



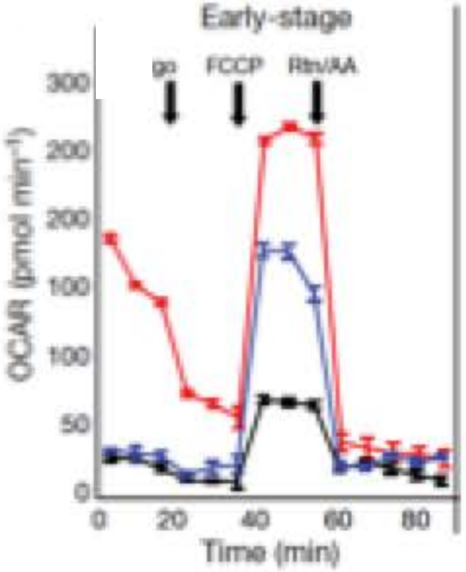




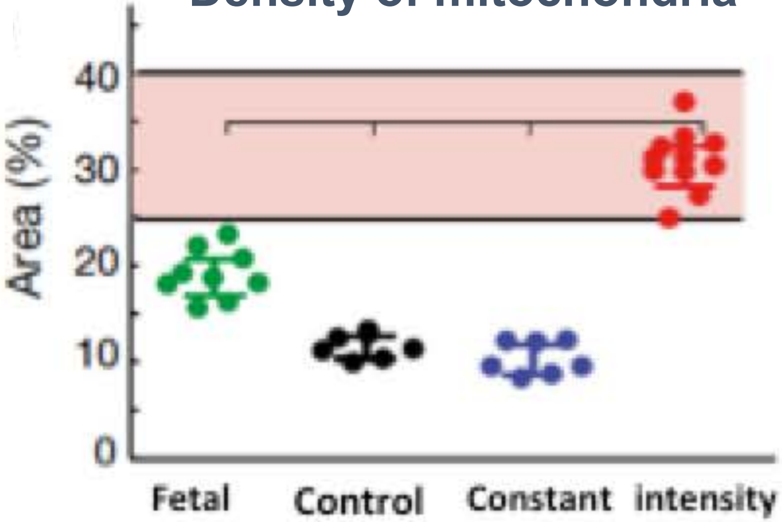
Action potential



Oxidative metabolism

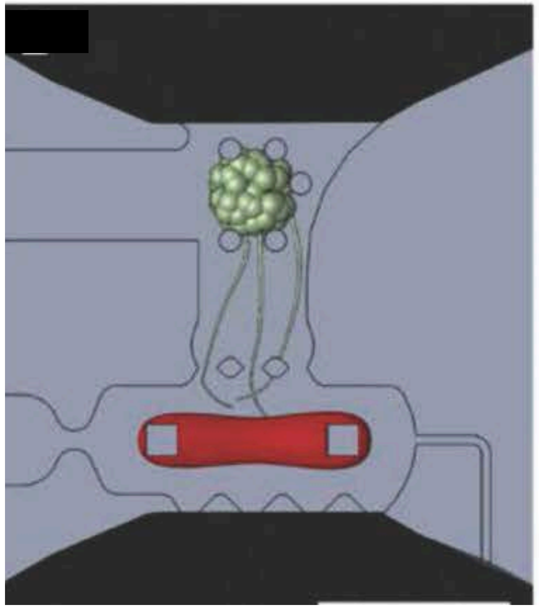


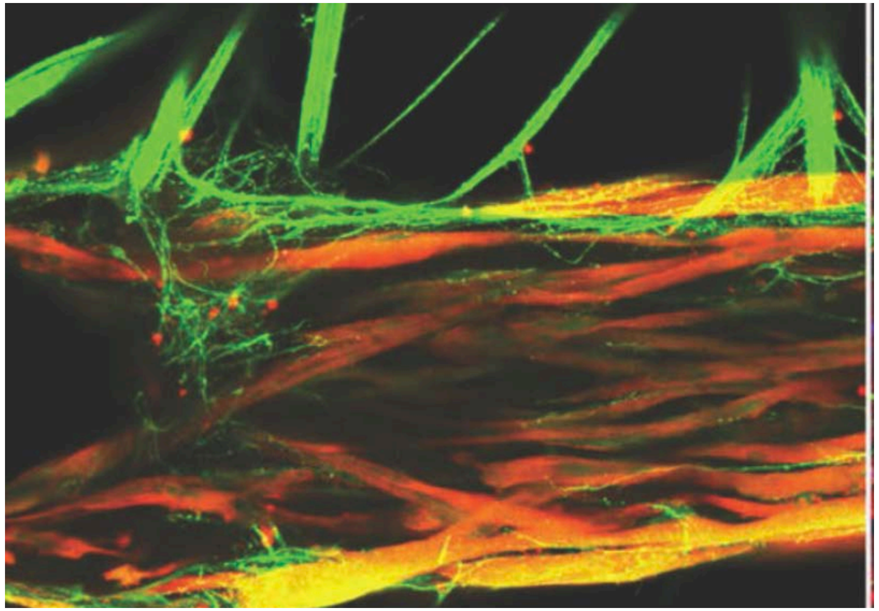
Density of mitochondria

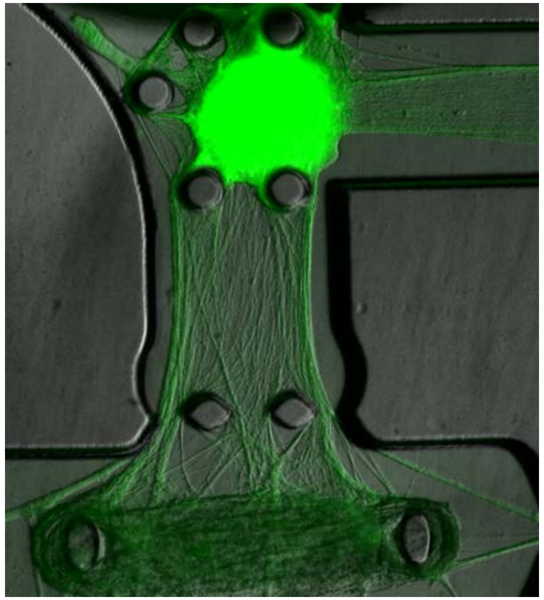


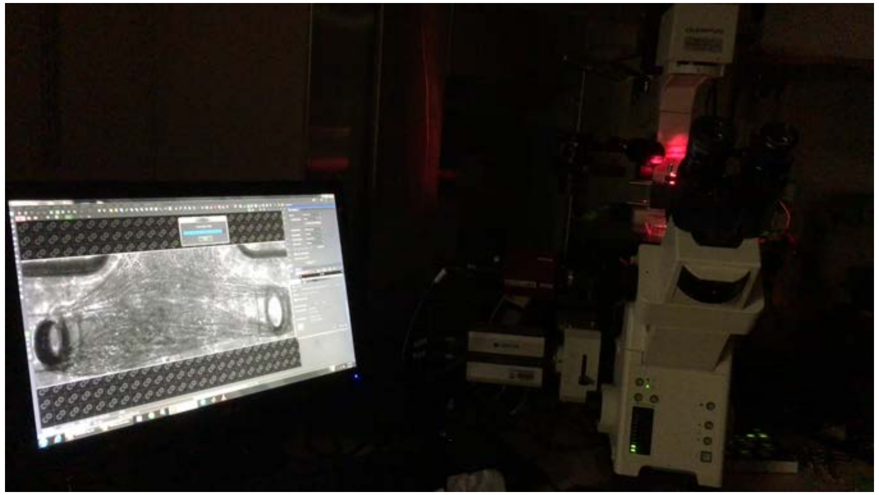
Ronaldson-Bouchard et al, Nature, 2018

Example: Neuromuscular junction



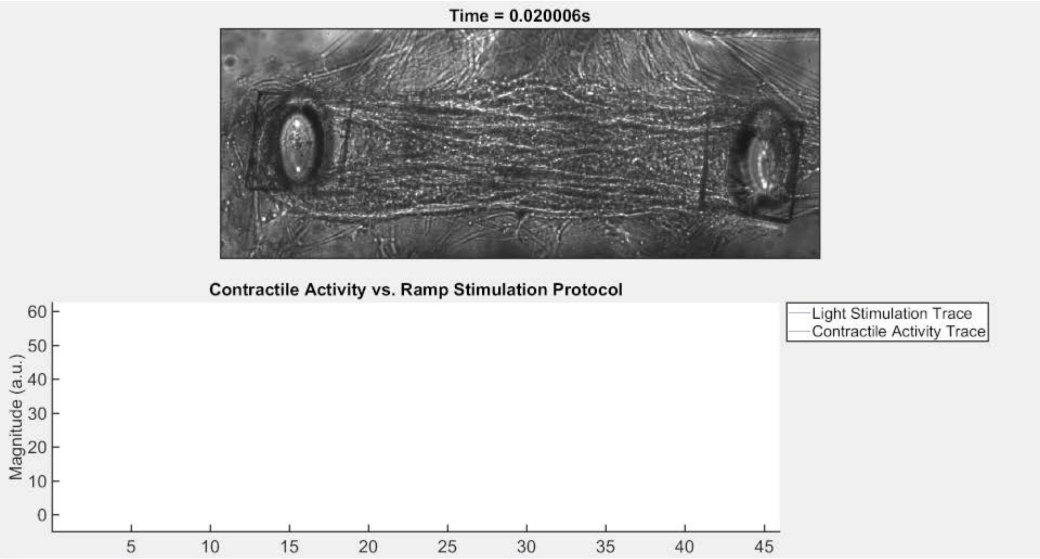




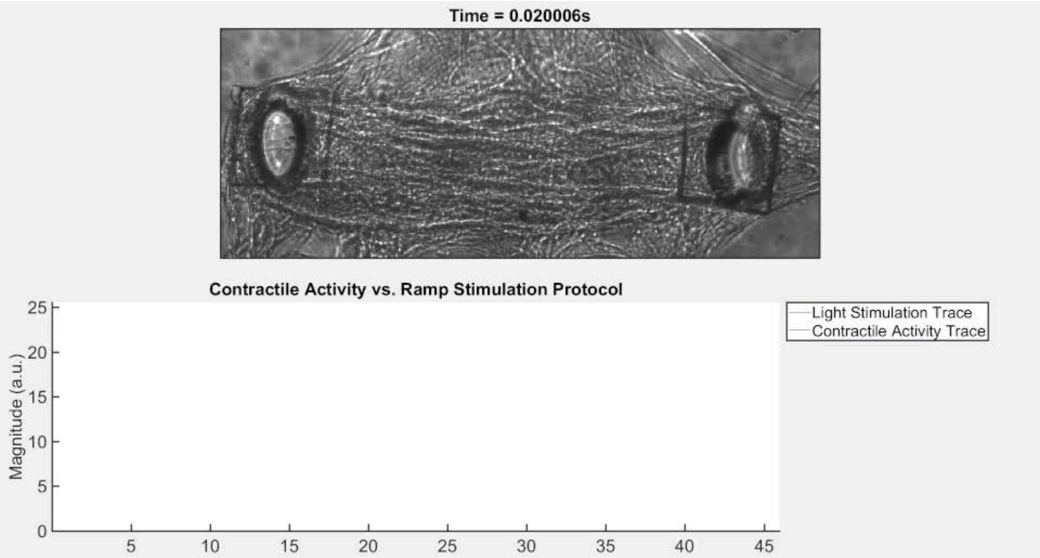


Vila et al, Theranostics (2019)

Healthy: 78% reponse

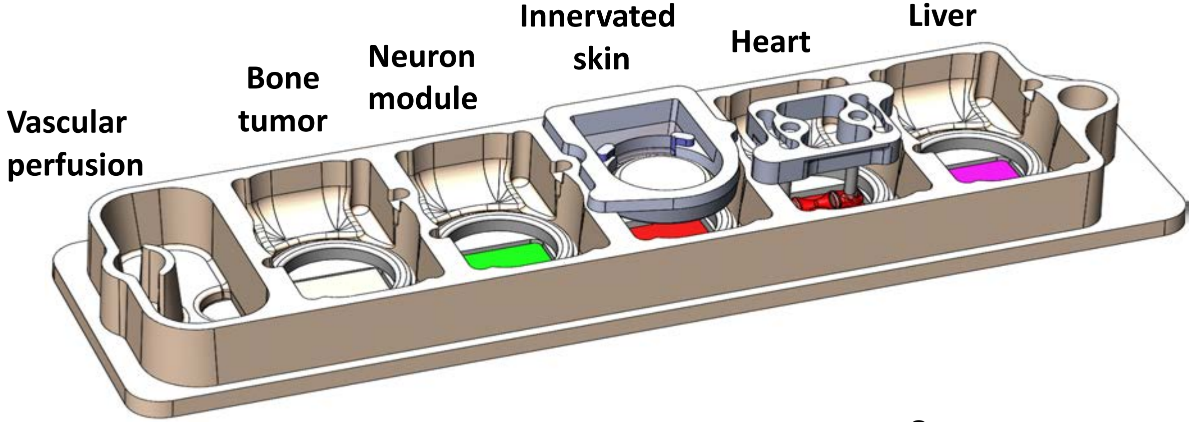


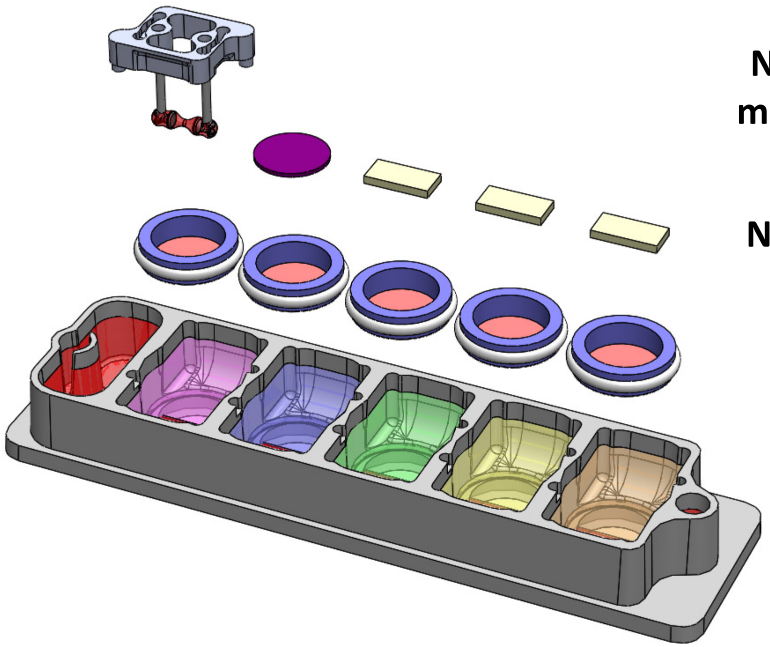
Myasthenia gravis: 0% response



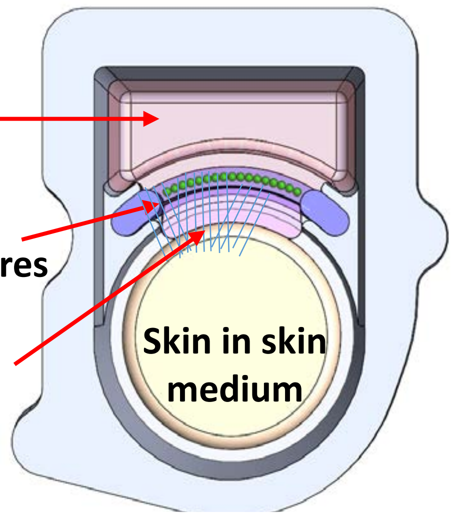
Connecting tissues into physiological units:

Cancer metastasis on a chip

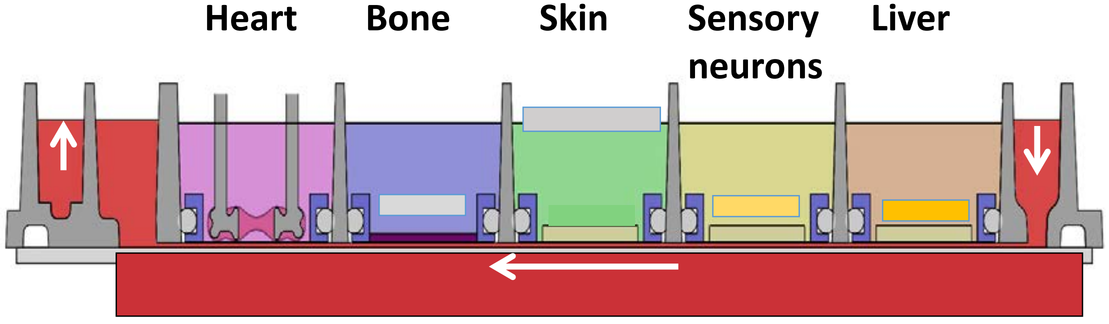




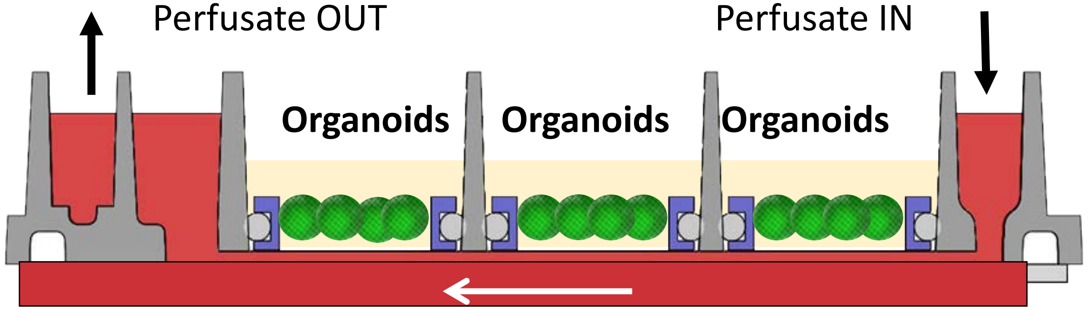
Sensory neuron module



Studies of nociception
(*de Nooij, Bunnett*)

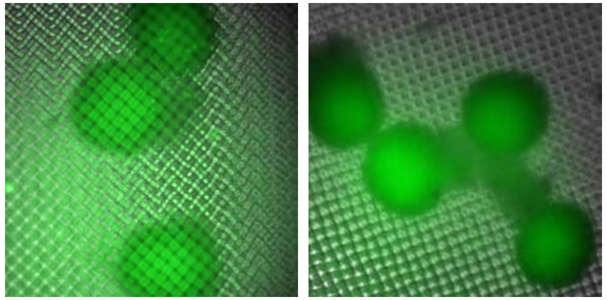


Vascular flow with circulating cells

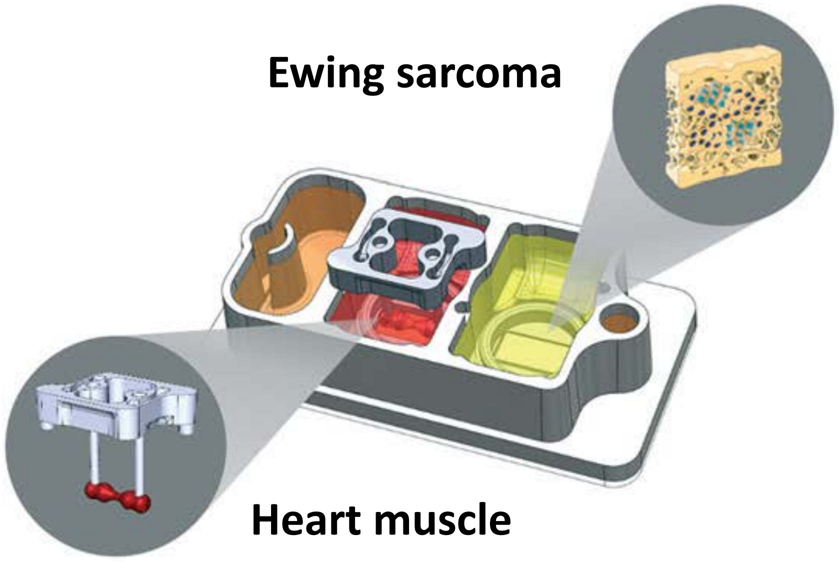


Vascular flow with circulating cells

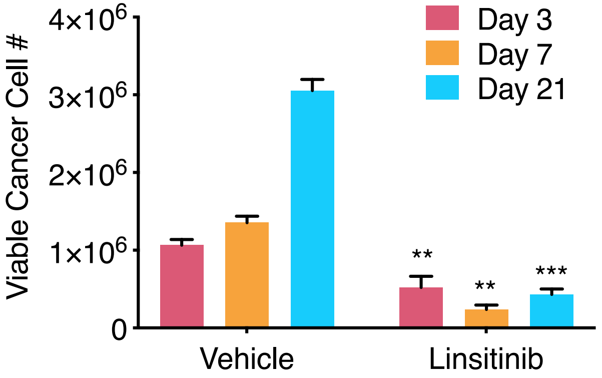
Beta-cell organoids cultured in the platform
(*Egli, Creuset*)

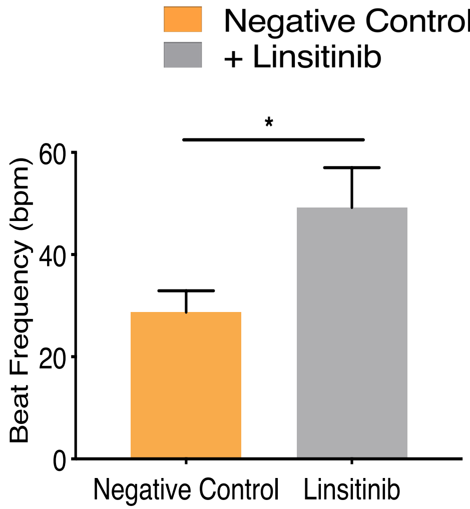


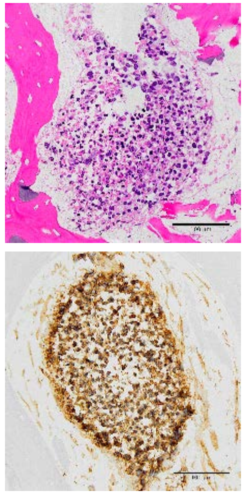
Modeling anticancer drug efficacy and cardiac safety:



Isolated tissues







H&E

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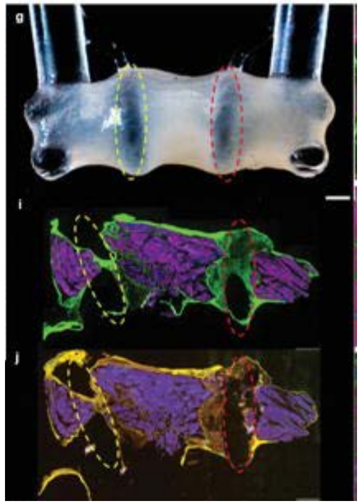
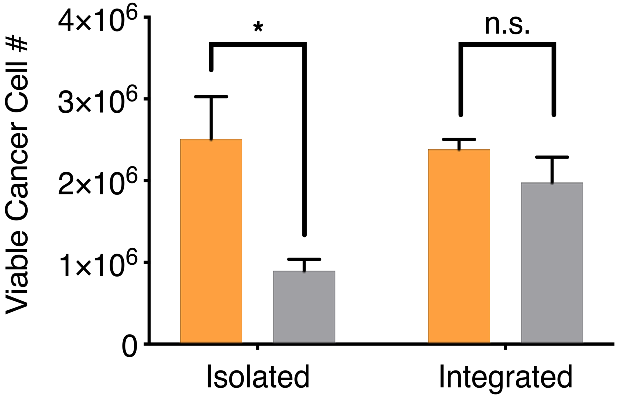
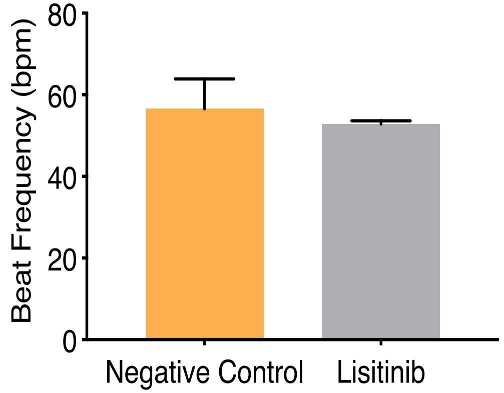


Integrated tissues





Chramiec, Teles et al., Lab on a Chip (2020)

Summary and challenges: Biology

Summary: Multi-tissue platforms can serve as high-fidelity models for studies of development, regeneration, organ specific and systemic diseases. iPS cells allow individualized studies of disease and biological diversity.

Establish and maintain mature tissue phenotypes

- How much is enough?
- Benchmarking and validation

Build complexity

- How simple is complex enough?
- Multiple tissue types, innervation, vascularization, immune system…
- iPS-based cells for biological compatibility
- Integrated multi-tissue models for studying systemic patho/physiology

Enable studies of biological diversity

- Sex, age, race, status of health or disease as experimental variables

Summary and challenges: Engineering

“Biologist-friendly” platforms

- Standardized designs
- Interfaces with imaging and analytics
- Commercial availability

“Plug and play” designs for optimizing tissue scaling and order

- Scaling by volume, metabolism, blood flow…?
- Configurability to support a broad range of experimental needs

Recapitulating tissue and organ functions

- Minimally functional units capturing specific cell/tissue/organ responses
- Real time measurements of biological parameters at cell/tissue levels
- Designing dynamic systems with biological sensing and actuation
- Integration of different types of data, at different scales, over time

The lab team:

EPIBONE grow your own bone

XYLYX

TARA biosystems

IMMUNOPLACATE REVOLUTIONIZING CELL THERAPIES

@GVNlab

Funding:
NIBIB
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