Body-on-a-chip: Multi-Organ *In Vitro* TOX models for preclinical and clinical drug testing, among other applications

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Body-on-a-chip
Body-on-a-chip
Drug development industry

Phases of the Pipeline

- Preclinical
- Clinical Trials
- Post-Approval

- Discovery and Validation
- Phase I
- Phase II
- Phase III
- Phase IV

# Molecules
Drug development industry

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Novel in vitro assays:
Reduce animal experimentation
Achieve results that may predict human outcome
Mission: Engineering the interface between biological and non-biological systems to construct next-generation systems for toxicology, drug discovery, and basic biology research.

Features Topics
- Hickman laboratory to be featured by PBS affiliate
- Jove comes to UCF
- New Staff
- Hickman research featured in Advances in Engineering

Events
- NOV 17-19, 2014
  - Organotypic Culture Models for Toxicology Meeting, Boston, MA
  - J.J. Hickman, "Body-on-a-chip systems for toxicological evaluations"
- Short Course on Microfluidics and Cell Culture Chips
  - J.J. Hickman, "The basics of integrating cells with microfluidic devices for long-term cell survival and function in organ-on-a-chip devices"
Interdisciplinary lab (cell biology, engineering, pharmacy, chemistry,...)
• Biology: cell and milieu development
• Chemistry: surface modifications to mimic cell attachment molecules, thus improve and extend cell anchorage for chronic studies.
• Engineering: developing features to metric cellular functionality.
Towards “Body-on-a-chip”

Classic *in vitro* models (some used nowadays for FDA regulations)
- Lack:
  - Cellular network
  - Quantifiable cellular functionality metrics.

Animal *in vivo* models
- Lack: Human aspect

Next level of *in vitro* model
- Provides:
  - Cellular environment and network
    - with neighboring organs and medium – as in human body.
  - Cellular functionality in real time
    - *Human* cells
Body-on-a-chip qualities

- Help reduce the cost of drug discovery and increase success rates
- Better predict drug efficacy and toxicity effects on humans
- Predict bioavailability
- Studies of drug combinations targeting different organs
- Option to use: non-physiologic versions of the human body
- As PBPK models
- Individualized medicine

Body-on-a-chip & Research involved

- Design & development of the device
- Common cell culture medium (serum-free formulas)
- Cell sources (cell line, primary cultures, iPSc)
- Stable cellular functionality and culture longevity (chronic exposures)
- Commercialization, validation and standardization

Research Projects

- Surface Chemistry
- Reflex Arc
- Cardiac Chip
- Body-On-A-Chip
- Alzheimer's Disease
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40-70% of drug development failures are due to arrhythmogenic properties (Raschi et al. 2009).

Cardiac Functionality

Electrical activity

Contractile Force
Electrical activity
MEA: MicroElectrodeArray

TiN (titanium nitride) electrodes
MEA; MicroElectrodeArray

iPSc derived Cardiomyocytes (8div)
Spontaneous beating of iPSc derived Cardiomyocytes 21div (average beating ~1Hz)
Paced iPSc derived Cardiomyocytes 21div (average beating ~5Hz)
Electrical activity - QT interval

QT-interval (ms) of spontaneous iPSc cardiomyocytes averaged from active electrode.
Sotalol: class III antiarrhythmic drug, K+ channel blocker and beta blocker.

Pattern iPSc derived Cardiomyocytes attached to fibronectin on ablated PEG (7div)
Electrical activity - Conduction velocity

Conduction velocity (m/s) of spontaneous cardiomyocytes, from active concatenated electrode.
Custom MEA

Advantage

- Custom
- Smaller (1x1cm)
- Cheaper
Contractile force
Cantilever Chip
Laser reflected off silicon cantilevers with adhered CMs to monitor contractile force and beat frequency.
HSL Integrated Cardiac Module

MEA Recording

Cantilever Recording
Spontaneous and paced beating of cardiac cells on cMEA maintained in 2-chamber housing.
Spontaneous cantilever deflection measurement of cardiac cells plated on cantilevers maintained in 2-chamber housing for more than 1 week.
Body-on-a-Chip
Liver

Pre-drug

Metabolite

Drug metabolism
Gluconeogenesis
Albumin production
Urea production

UCF
Biotechnol Prog. 2015 Morphological and functional characterization of human induced pluripotent stem cell-derived neurons (iCell Neurons) in defined culture systems.
Berry BJ, Akanda N, Smith AS, Long CJ, Schnepper MT, Guo X, Hickman JJ.
Skin

Lung

HICKMAN’S HYBRID SYSTEM LAB

[Image of a group of people]