Tissue Chips Program Update
NTP Board of Scientific Counselors meeting
December 7-8, 2017

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Outline

• Background
• Tissue Chips Program Goals
• Current Tissue Chips Consortium
  • Tissue Chips Testing Centers
  • Tissue Chips in Space
  • Tissue Chips 2.0
Advancing Regulatory Science
2010-2012

- NIH–FDA Joint Leadership Council
- MOU between NIH and FDA; $7M over 3 years (NIH Common Fund)
- RFA-RM-10-006 Advancing Regulatory Science through Novel Research and Science-Based Technologies (U01)
- 4 awards were made that address four distinct, high priority areas of regulatory science which include:
  - Heart-Lung Micromachine for Safety and Efficacy Testing
  - Accelerating Drug and Device Evaluation through Innovative Clinical Trial Design
  - Replacement Ocular Battery
  - Characterization/Bioinformatics-modeling of Nanoparticle: Complement Interactions
- Microphysiological Systems Workshop in 2011 (DARPA, FDA and NIH)
Microphysiological Systems Program
“Tissue Chips for Drug Screening”
2012-2016

GOAL: Develop an *in vitro* platform that uses human tissues to evaluate the efficacy, safety and toxicity of promising therapies.

- All ten human physiological systems will be functionally represented by human tissue constructs:
  - Circulatory
  - Endocrine
  - Gastrointestinal
  - Immune
  - Skin
  - Musculoskeletal
  - Nervous
  - Reproductive
  - Respiratory
  - Urinary

- Physiologically relevant, genetically diverse, and pathologically meaningful.
- Modular, reconfigurable platform.
- Tissue viability for at least 4 weeks.
- Community-wide access.
Microphysiological Systems Program
“Tissue Chips for Drug Screening”
2012-2016

NIH
National Institutes of Health

Platform and Cell Resources Development
Functional Validation, Training set of Compounds, multi--organ integration

NIH
National Institutes of Health

$75 M over 5 years – cell source, platform development, validation and integration (NCATS, CF, NIBIB, NIEHS, NICHD, ORWH, NCI)

DARPA
$75 M over 5 years - development of 10-organ Platform

**FDA provides insight and expertise throughout the program

Industry Partners:
• AstraZeneca
• GSK
• Pfizer
• IQ Consortium
• ThermoFisher

Background
Microphysiological Systems Consortium

NIH - FDA - DARPA
- Share expertise, materials
- Hold joint semi-annual meetings
- Provide a common set of validation compounds
- Facilitate collaborations

Pharma
- AstraZeneca
- GSK
- Pfizer
- IQ Consortium

Biotech/Industry Partnerships
- Brain
  - Eye
  - U Wisconsin
- Heart-liver-WAT
  - Bone/cartilage
  - UC-Berkeley
- Kidney
  - U Washington
- Gut innervation
  - Cincinnati-Children’s
  - Johns Hopkins
- Female/Male Repro
  - Northwestern
- Male Repro
  - Columbia
- Male-Vascular
  - Cleveland Clinic

Gut Disease
- Johns Hopkins
- Gut-Metastasis
- White Adipose
  - MIT
- White-Metastasis
  - MIT
- Neurovascular
- Microformulator
- Vascular
  - Vanderbilt
  - Cleveland Clinic

BIO-MIMETICS
- MIT

Human Organs on a Chip
- Wyss
- Skin
  - Columbia
- Muscle/TEBV
  - Duke

Liver
- Pittsburg

Liver-Lung
- Uterus
- Wyss

Heart-Lung
- Uterus
- Wyss

Heart
- Vasc-tumor
- Bone Marrow
- WashU

Heart-liver-WAT
- Bone/cartilage
- UC-Berkeley

Biotech/Spin-offs
- 4D BioSciences
- Emulate, Inc
- Hesperos
- Organome
- Tara Biosystems
- CN Bio
- Nortis
Microphysiological Systems: *In Vitro* Mimics of Human Organ Function

Diversity of Bioengineered Platforms
Tissue Chip Testing Centers: Validating Microphysiological Systems

- Resource Centers (U24)
- **GOAL:** Independent analytical validation of tissue chip platforms
  - Portability, reproducibility, sensitivity, specificity, dosing paradigm, cellular vs. organ toxicity, toxicity readouts, etc.
  - Reference set of validation compounds, assays, biomarkers with input from IQ consortium and FDA based on technical specifications of each platform from MPS developers

Partnerships among NCATS, FDA and IQ Consortium
- NCATS support: $12 M over two years; awarded 9/28/16
- FDA and IQ provide expert guidance on reference set of validation compounds, assays, biomarkers

**Testing Centers:**
- MIT (Murat Ciril and Alan Grodzinsky)
- TAMU (Ivan Rusyn)

**MPS Database:** [https://mps.csb.pitt.edu/](https://mps.csb.pitt.edu/)
- U Pittsburgh (Mark Schurdak)

Platforms tested and/or currently being tested:
- Kidney on chip
- BBB on chip
- Brain on chip
- Bone/tumor on chip
- Heart on chip
- Gut on chip
- Skeletal muscle on chip
- Microvasculature on chip
- White adipose tissue on chip
- Liver on chip
- Skin on chip
NIH-CASIS Coordinated Program in Tissue Chip Systems for Translational Research in Space

- GOALS:
  - Leverage MPS technology with space implementation partners for biomedical research at the International Space Station towards a better understanding of the molecular basis of human disease and develop effective diagnostic markers and therapeutic interventions for use on earth
  - Use space engineering approaches to rapidly evolved tissue chips to be automated, turn-key and much reduced footprint
  - 4-year Partnership between NCATS ($12M), NASA ($3.4M) and CASIS for 2 flight opportunities per project (in-kind)
  - 5 Awarded projects from academia, biotech and space industry
Cartilage-Bone-Synovium MPS: Musculoskeletal Disease Biology in Space
Alan Grodzinsky, Ph.D., and Mural Cirit, Ph.D.

Effects of microgravity on the structure and function of proximal and distal tubule MPS
Jonathan Himmelfarb, M.D., Ph.D. and Edward J. Kelley, Ph.D.

Organs-on-Chips as a Platform for Studying Effects of Microgravity on Human Physiology: Blood-Brain Barrier-Chip in Health and Disease
Christopher D. Hinojosa, M.S. and Katia Karalis, M.D., Ph.D.

Microgravity as model for immunological senescence and its impact on tissue stem cells and regeneration
Sonja Schrepfer, M.D., Ph.D., Tobias Deuse, M.D. and Heath J. Mills, Ph.D.

A Microphysiological Model of Lung Host Defense in Microgravity
D. Dan Huh, Ph.D. and G. Scott Worhern, M.D.

Re-issue: RFA TR-18-001
Application Receipt Date: January 16, 2018
Microphysiological Systems (MPS) for Disease Modeling and Efficacy Testing

• **GOAL:**
  • Develop highly reproducible and translatable in vitro models for preclinical efficacy studies using MPS
    • discovery and validation of translatable biomarkers
    • development of standardized methods for preclinical efficacy testing and definitive efficacy testing of candidate therapeutics using best practices and rigorous study design
  • 5-year UG3/UH3 program; $75 M ($25 M from CAN)
    Funding partnerships between NCATS and others ICs (NIAMS, NICHD, NIDCR, NIDDK, NIEHS, NINDS, NIBIB, NHLBI, ORWH)
  • Partnerships between NIH, FDA and IQ Consortium

MPS program is highly collaborative
Tissue Chips 2.0 Disease Models

Danielle Benoit, Lisa Delouise, Catherine Ovitt, U Rochester
**Radiation-induced xerostomia**

Kevin Kit Parker, William Pu, Harvard U
**Barth syndrome, catecholaminergic polymorphic ventricular tachycardia, arrhythmogenic cardiomyopathy**

Steven George, David Curiel, Stacey Rentschler, UC Davis and WashU
**Atrial fibrillation**

Joseph Vincent Bonventre, Luke Lee, Brigham and Women's **autosomal dominant/recessive models of polycystic kidney disease, Focal segmental glomerulosclerosis**

Christopher Hughes, UC Irvine
**Hereditary hemorrhagic telangiectasia, Port Wine stain, Sturge-Weber syndrome**

Rocky Tuan, U Pittsburgh
**Osteoarthritis, inflammatory arthritis, adipose-mediated diabetic joint complications**

Clive Svendsen, Cedars-Sinai
**ALS, Parkinson's Disease**

Aaron Bowman, Kevin Ess, John Wikswo, Vanderbilt U
**Tuberous sclerosis complex (TSC) epilepsy, DEPDC5-associated epilepsy, & associated cardiac dysfunction**

Gordana Vunjak-Novakovic, Columbia U
**Dox induced cardiomyopathy; multi-system pathologies involving heart, liver, skin, bone and vasculature**

Donald Ingber, Harvard U
**Influenza infection, COPD**

Jonathan Himmelfarb, U Washington
**Apolipoprotein L1 mediated kidney disease, drug induced and host-pathogen interaction induced renal thrombotic microangiopathies**

Teresa Woodruff, Northwestern U
**Polycystic Ovarian Syndrome**

George Truskey, Duke U
**Rheumatoid arthritis, atherosclerosis**

UG3 Disease Model development; UH3 Model validation and efficacy testing
Potential Use of Tissue-on-Chips:

- Human Fibroblasts
- Genetic Reprogramming
- iPSCs
- Differentiation/Maturation into All Major Organs

Future Applications:
- Microbiome
- Toxins
- Infectious Diseases
- Countermeasures
- Tools for Clinical Trials

Benefits:
- Personalized Chips:
  - Drug response in individuals
  - Individualized medicine and therapeutics

Physiological Differences Among Diverse Populations:
- Genetic variation
- Examine various demographics
- Gender or age variation

Rare Diseases Research and Therapeutics
Drug Efficacy and Toxicity Screening

Precision Medicine You-on-chip

Clinical Trials-on-chips
Join Us for the 2018 Keystone Symposia conference on:

Organs- and Tissues-on-Chips

April 8–12, 2018
Big Sky, Montana | USA

Scientific Organizers: Christopher P. Austin | Danilo A. Tagle | Christine L. Mummery | Brian R. Berridge

Scholarship/Discounted Abstract Deadline: December 6, 2017
Abstract Deadline: January 9, 2018
Discounted Registration Deadline: February 6, 2018

www.keystonesymposia.org/18D1