NCATS Improving Health Through Smarter Science

Tissue Chips Program Update

NTP Board of Scientific Counselors meeting
December 7-8, 2017

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Office of the Director, NCATS, NIH

NIH National Center for Advancing Translational Sciences

Outline

- Background
- Tissue Chips Program Goals
- Current Tissue Chips Consortium
  - Tissue Chips Testing Centers
  - Tissue Chips in Space
  - Tissue Chips 2.0

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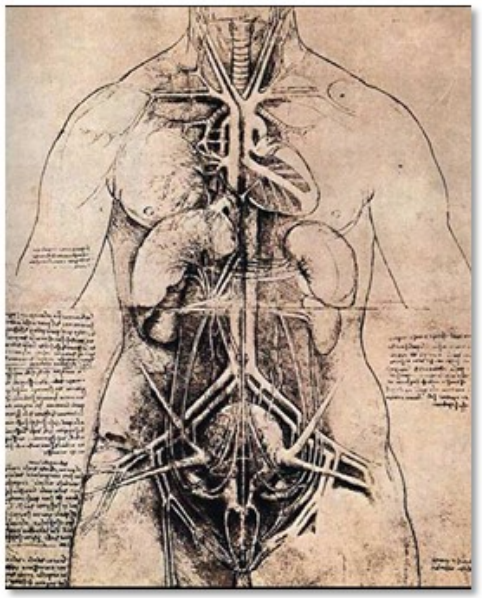
Advancing Regulatory Science
2010-2012

- 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 <u>human</u> 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**

2012-13 | 2013-14 | 2014-15 | 2015-16 | 2016-17

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

****FDA provides insight and expertise throughout the program**

Industry Partners:

- **Astrazeneca**
- **GSK**
- **Pfizer**
- **IQ Consortium**
- **ThermoFisher**

Background

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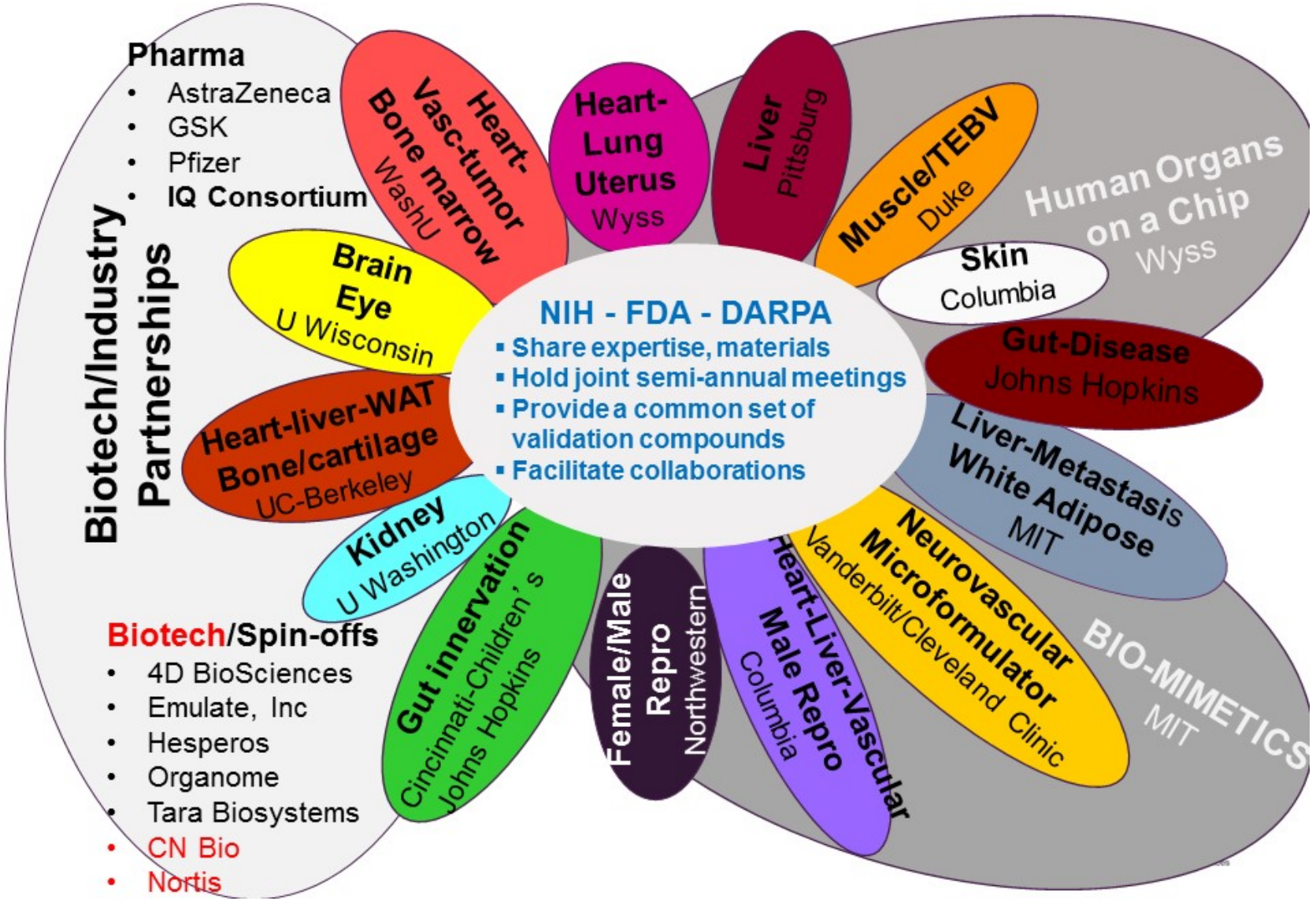
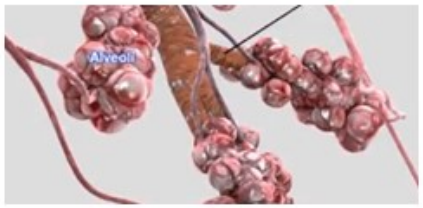
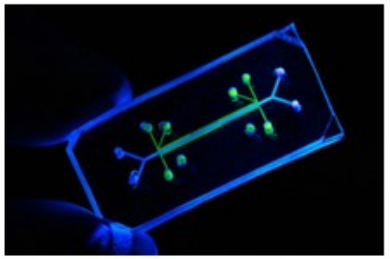
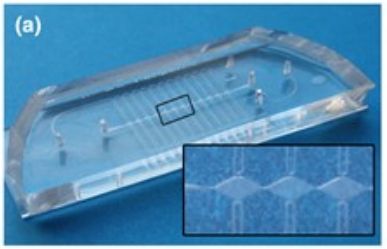
Microphysiological Systems Consortium

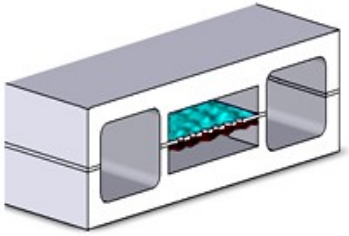


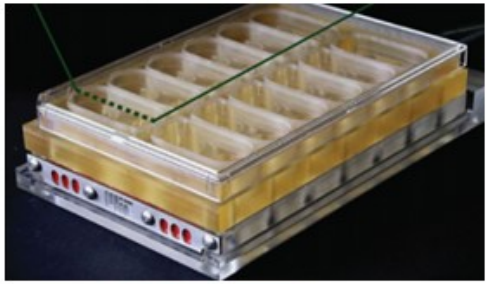
Microphysiological Systems: *In Vitro* Mimics of Human Organ Function

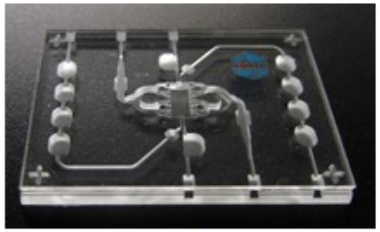


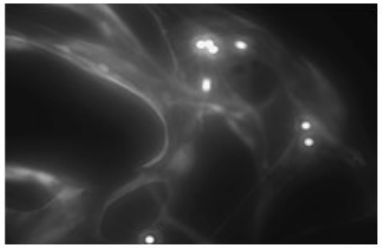


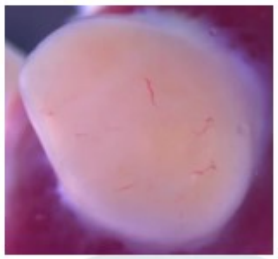


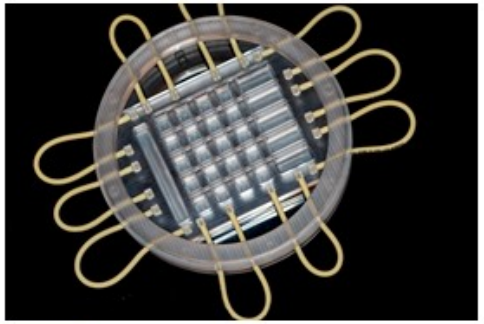












Diversity of Bioengineered Platforms

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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 Cirit and Alan Grodzinsky)
  - TAMU (Ivan Rusyn)
- MPS Database: 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

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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

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Cartilage-Bone-Synovium MPS: Musculoskeletal Disease Biology in Space

Alan Grodzinsky, Ph.D., and Murat 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 Worthern, 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

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Tissue Chips 2.0 Disease Models

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

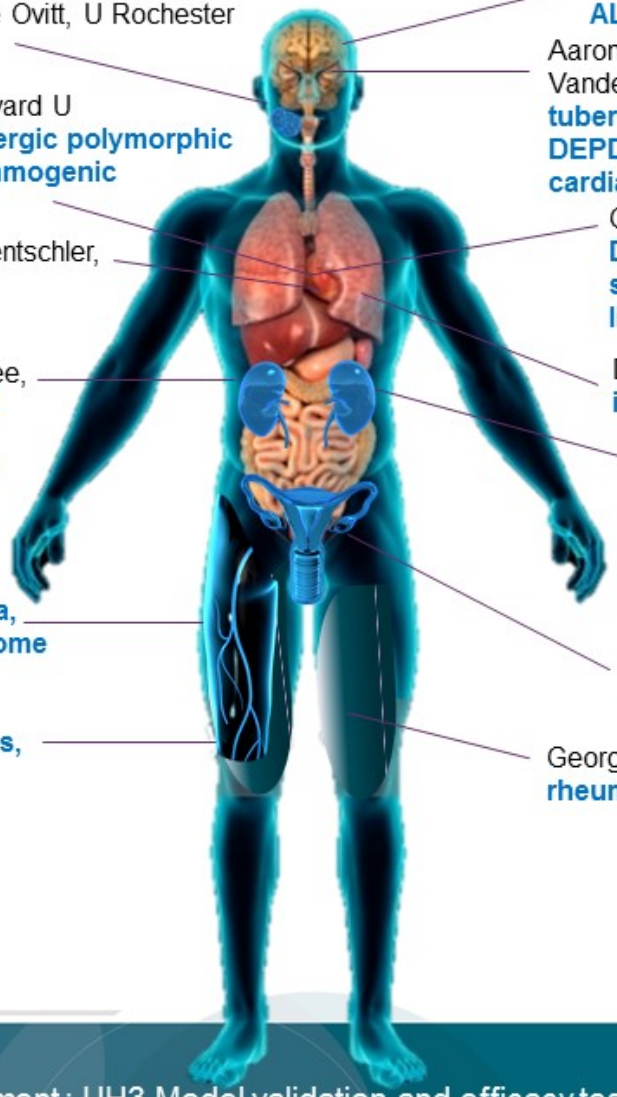
Kevin Kit Parker, William Pu, Harvard U
Barth syndrome, catecholaminergic polymorphic ventricular tachycardia, arrhythmogenic cardiomyopathy

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

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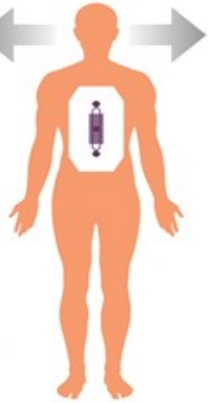
Potential Use of Tissue-on-Chips:

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

Human-on-a-Chip

Clinical Trials-on-chips

Precision Medicine You-on-chip

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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
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