The NIH Microphysiological Systems Program: Tissue Chips for Drug Safety and Efficacy Studies

Scientific Advisory Committee on Alternative Toxicological Methods Meeting
Sept 20th 2019

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Outline:

• National Center for Advancing Translational Sciences (NCATS), NIH
• Microphysiological Systems/Tissue Chips
• NIH Tissue Chips Consortium
• Building confidence and evolving MPS technology
• Building Partnerships
• Future Initiatives and Summary
National Center for Advancing Translational Sciences

Mission: To catalyze the generation of innovative methods and technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.

- NCATS focuses on the scientific and organizational problems in translation, e.g. tools for predictive safety and efficacy.

NCATS is all about getting more treatments to more patients more quickly.
Current Challenges in Drug Development

- Average time to develop (and bring it to market) a drug 10-15 years

- Average cost to develop a drug to market, including cost of failures, $2.6 billion
  (phRMA, Biopharmaceutical Research Industry Profile, 2016)

- The current drug discovery paradigm has a failure rate of 90%:
  - 55% due to lack of efficacy
  - 28% due to toxic effects in humans

- Clinical trials of homogenous and small sample sizes are used to predict the outcomes on diverse populations

The highest rates of true positives (36%) in animal-human translation is observed for dogs (cardiac & GI) and rats (renal & respiratory)

Arrowsmith and Miller, Nature Reviews Drug Discovery, Volume 12, 569 (2013)
Cook et al., Nature Reviews Drug Discovery, Volume 13, 419 (2014)
Clark and Steger-Hartmann, Regulatory Toxicology and Pharmacology, Volume 96, 94 (2018)

Most animal models are poor predictors of human response

3,290 approved drugs
1,637,449 adverse events
70 years
Therapeutic Modalities are Increasingly Human-specific and Personalized

- SMALL MOLECULES
- ANTIBODIES
- CELL THERAPIES
- PROTEIN THERAPIES
- GENE THERAPIES
- ANTISENSE
Microphysiological Systems Program: Tissue Chips for Drug Screening

GOAL: Develop an *in vitro* platform that uses human cells and tissues, and combine with advances in stem cell biology, microfluidics and bioengineering to evaluate the efficacy, safety and toxicity of promising therapies.

- All 10 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
- Collaboration between NIH, FDA and DARPA and other stakeholders
Tissue Chips

- a multi-channel 3-D microfluidic cell culture chip that simulates the activities, mechanics and physiological response of entire organs and organ systems

Representing relevant biology on bioengineered chips

Scaffold

- purified ECM, synthetic polymers, composites

Cells

- human-derived primary or iPSCs;
- porosity, topography, stiffness

Structure

- controlled release of cytokine and hormone gradients

Spatial and Temporal Patterning

- microfluidic cell culture devices, vasculature

Perfusion

- biomechanical properties

Bioreactor

- signal propagation, coordinated response

Innervation

- generalized inflammation, specific immunity

Host Response

- real-time, label-free, non-destructive sensing, imaging

Functional Readout

- systems integration multi-scale modeling

Computational Design
Microphysiological Systems Program: Tissue Chips 1.0 for Safety and Toxicity Testing

Platform and cell resources development → Physiological Validation, training set of compounds, multi-organ integration


GOALS:
- Develop single organ and Multi-organ chips
- Functional and physiological validation
- Compound testing
- Partnerships

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

$75 M over 5 years - development of 10-organ platforms

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

Phased award and milestone-driven
Microphysiological Systems: *In Vitro* Mimics of Human Organ Function

Diversity of Bioengineered Platforms
<table>
<thead>
<tr>
<th>Tissue Chips 1.0 to Predict Drug Safety (2012-2017)</th>
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<tbody>
<tr>
<td><strong>James A. Thomson; Morgridge Institute for Research at the University of Wisconsin-Madison</strong></td>
</tr>
<tr>
<td>Human induced pluripotent stem cell and embryonic stem cell-based models for predictive neural toxicity and teratogenicity</td>
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<tr>
<td>- John P. Wikswo; Vanderbilt University</td>
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<tr>
<td>Neurovascular unit on a chip: Chemical communication, drug and toxin responses</td>
</tr>
<tr>
<td>- Steven C. George; University of California, Irvine</td>
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<tr>
<td>An integrated in vitro model of perfused tumor and cardiac tissue</td>
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<td>- D. Lansing Taylor; University of Pittsburgh</td>
</tr>
<tr>
<td>A 3-D biomimetic liver sinusoid construct for predicting physiology and toxicity</td>
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<td>- James M. Wells; Cincinnati Children’s Hospital Medical Center</td>
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<tr>
<td>Generating human intestinal organoids with an enteric nervous system</td>
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<tr>
<td>- John P. Lynch; University of Pennsylvania</td>
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<tr>
<td>Modeling oxidative stress and DNA damage using a gastrointestinal organotypic culture system</td>
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<tr>
<td>- George A. Truskey; Duke University</td>
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<tr>
<td>Circulatory system and integrated muscle tissue for drug and tissue toxicity</td>
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<tr>
<td>- Rocky S. Tuan; University of Pittsburgh</td>
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<td>Three-dimensional osteochondral micro-tissue to model pathogenesis of osteoarthritis</td>
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<tr>
<td>- Linda Griffith; Massachusetts Institute of Technology</td>
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<tr>
<td>All-human microphysiological model of metastasis and therapy</td>
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<td>- Thomas Hartung; Johns Hopkins University</td>
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<tr>
<td>A 3-D model of human brain development for studying gene/environment interactions</td>
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<tr>
<td>- Kevin K. Parker; Harvard University</td>
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<tr>
<td>Human cardio-pulmonary system on a chip</td>
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<tr>
<td>- Joan E. Nichols; The University of Texas Medical Branch at Galveston</td>
</tr>
<tr>
<td>Three-dimensional human lung model to study lung disease and formation of fibrosis</td>
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<tr>
<td>- Mark Donowitz; Johns Hopkins University, Baltimore</td>
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<tr>
<td>Human intestinal organoids: Pre-clinical models of non-inflammatory diarrhea</td>
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<tr>
<td>- Teresa Woodruff; Northwestern University</td>
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<tr>
<td>Ex Vivo Female Reproductive Tract Integration in a 3-D Microphysiologic</td>
</tr>
<tr>
<td>- Jonathan Himmelfarb; University of Washington, Seattle</td>
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<tr>
<td>A tissue-engineered human kidney microphysiological system</td>
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<tr>
<td>- Gordana Vunjak-Novakovic; Columbia University Health Sciences</td>
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<tr>
<td>Integrated Heart-Liver-Vascular Systems for Drug Testing in Human Health and Disease</td>
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<tr>
<td>- Angela Christiano; Columbia University Health Sciences</td>
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<td>Modeling complex disease using induced pluripotent stem cell-derived skin constructs</td>
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<tr>
<td>- Kevin E. Healy; University of California, Berkeley</td>
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<td>Disease-specific integrated microphysiological human tissue models</td>
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<tr>
<td>- Michael L. Shuler; Cornell University</td>
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<tr>
<td>Microphysiological systems and low cost microfluidic platform with analytics</td>
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</tbody>
</table>
Commercial Activities around Organ-on-chip Technologies

**Body on-a-Chip**

- **Hesperos**
  - Michael Shuler
  - James Hickman
  - Multi-Organ Chip (2, 4 organs) (6-16 organs)

- **TISSUSE Emulating Human Biology**
  - Uwe Marx
  - 2-Organ-Chip (2-OC)
  - 4-Organ-Chip (4-OC)
  - Human-on-a-chip (HOC)

- **emulate**
  - Donald Inberger
  - Lung on-a-Chip
  - Airway-on-a-Chip
  - Gut on-a-Chip
  - Kidney on-a-Chip
  - Bone Marrow on-a-Chip

- **Alveoix**
  - Olivier Guenat
  - Lung-on-a-chip array

- **Quantum**
  - Thomas Neumann
  - Kidney on-a-Chip
  - Vessel-on-a-Chip

- **AimBiotech**
  - Axel Guenther
  - Artery on-a-Chip

**Parenchymal tissue on-a-Chip**

- **Hepregen**
  - Sangeeta Bhatia
  - HepatoPac®
  - HepatoMune™

- **organovo**
  - Gabor Forgacs
  - Keith Murphy
  - ExVive3D® Liver
  - ExVive3D® Kidney

- **Aspect Biosystems**
  - Tamer Mohamed
  - Konrad Walus
  - Sam Wadsworth
  - Simon Beyer
  - Lab-on-a-Printer™
  - 3DBioRing™ Airway

- **3D Biomatrix**
  - Jan Lichtenberg
  - Jens M. Klem
  - Wolfgang Moritz
  - 3D Insight™ Liver
  - 3D Insight™ Tumor

- **Hirel Corporation**
  - Nicholas Kotov
  - PERFECTA3D®
  - HANGING DROP PLATES

- **Kiyatec**
  - Greg Baxter
  - Robert Freedman
  - Hurellhuman™
  - HurellBoy™
  - HurellTox™
  - HurellFlow™

- **VaxDBdesign**
  - Matthew R. Gevaert
  - 3DKUBE™

- **MIMiC® Technology**

**Tissue interface on-a-Chip**

- **CNBio Innovations**
  - Linda G Griffith
  - LiverChip®
  - LiverChip® 36

- **Draper**
  - Joseph Charest
  - Microphysiological Systems

- **Emulate**
  - Jos Joore
  - Paul Vulto
  - Thomas Hankemeier
  - OrganoPlates®
  - SynTumor
  - SynBBB
  - SynRAM
  - SynTox

- **MircoBiorev**, **Bio**
  - Kapil Pant
  - B. Prabhakar Pandian
  - G. Wesley Hatfield
  - Christopher Hughes
  - Steven George
  - Abraham Lee
  - Roger Kann
  - 3D cell culture chips

- **Bio-Revolution Biosciences**
  - Milica Radisic
  - Gordana Vunjak-Novakovic
  - Cardiac Biowire™
  - CardioChip™

- **μOrgano**
  - Kevin Healy
  - Thomas Eschenhagen
  - Engineered Heart Tissue (EHT)

- **EHT Technologies**
  - Wolfram-Hubertus Zimmermann
  - 3D Cardiac Systems

- **AxoSim**
  - Michael Moore
  - Nerve-on-a-Chip™

- **Xona**
  - Noon Li Jeon
  - Carl W. Cotman
  - Anne Taylor
  - Standard / Triple Chamber Neuron Device

- **MicroBrain BT**
  - Bernadette Bung
  - Neural Diode

- **Jananda**
  - Margaret Magdesian
  - Neuro Device
Working with Pharma: IQ Microphysiological Systems Affiliate

Mission
To serve as a unified voice, advisory body and thought leader for both developers and stakeholder organizations in industry implementation and qualification of MPS models

AbbVie BMS GSK Novartis Theravance
Amgen Celgene Jansen Pfizer Vertex
Astellas Eisai Merck Sanofi
AstraZeneca Eli Lilly Merck KgA Seattle Genetics
Biogen Genentech Mitsubishi Tanabe Takeda

- Multi-disciplinary team of pharmaceutical scientists representing expertise and interests in drug metabolism and distribution, safety, and the 3Rs of animal use for research
- Ability to leverage existing legal framework and data sharing agreements between IQ member companies
- Provide a venue for cross-pharma collaboration and data sharing that facilitates expeditious uptake and impact of MPS
- Provide a focus of engagement with government (regulatory and non-regulatory) and academic stakeholders with interests and investment in MPS
Building Confidence: Tissue Chip Validation Framework

1) Physiological
• Organ function and structure
• Training set of reference compounds
• TC 1.0 developers

2) Analytical
• Independent: testing for robustness, reproducibility, reliability, relevance
• Validation set of compounds, biomarkers, assays
• TC Testing Centers

3) Industrial
• Use by industry and regulatory agencies
• Proprietary set of compounds?
• CRO-type environment

Publications: (as of Oct 2017)
A total of 506 original and review articles (cited over 5600 times) published in top tier journals, including Nature Medicine, Nature Communications, Nature Materials, PNAS, Science, Science Translational Medicine, etc.

Javelin Biotech
• Murat Cirit

Texas A&M Tissue Chip Testing Consortium
• Ivan Rusyn

MPS Database: https://mps.csb.pitt.edu/
• U Pittsburgh (Mark Schurdak)

Tissue Chip Testing Centers:
• MIT (Murat Cirit and Alan Grodzinsky)
• TAMU (Ivan Rusyn)

MPS Database: https://mps.csb.pitt.edu/
• U Pittsburgh (Mark Schurdak)
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; adherence to OECD guidelines

- NCATS support: Initially awarded in 2016 for two years and renewed in 2018 for two more years

- FDA and IQ Consortium 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/](https://mps.csb.pitt.edu/)
  - U Pittsburgh (Mark Schurdak)

- **Platforms tested during first two years:**
  - 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

- **Publications thus far:**
  - Kidney on chip
    - CPT Pharmacometrics Syst. Pharmacol. 2019, 8:316
  - Brain on chip
<table>
<thead>
<tr>
<th>MIT transitioned to Javelin Biotech</th>
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<tbody>
<tr>
<td>• CNBio Liver</td>
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<tr>
<td>• CNBio Liver-Tumor</td>
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<tr>
<td>• Nortis Kidney</td>
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<tr>
<td>• TissUse Bone marrow</td>
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<tr>
<td>• TissUse Pancreas-Liver</td>
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<tr>
<td>• Stemonix microBrain</td>
</tr>
<tr>
<td>• Stemonix microHeart</td>
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<tr>
<td>• Mimetas CNS</td>
</tr>
<tr>
<td>• Mimetas Liver</td>
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<table>
<thead>
<tr>
<th>Texas A &amp; M TC Testing Consortium</th>
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<tbody>
<tr>
<td>• Duke Arteriole blood vessel (Truskey)</td>
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<tr>
<td>• UC-Irvine Vascular malformations – Hereditary Hemorrhagic Telangiectasia, Port Wine disease and Sturge-Weber syndrome (Hughes)</td>
</tr>
<tr>
<td>• UC-Berkeley Vasculature with flow, Skeletal Muscle, Pancreatic islet (Healy)</td>
</tr>
<tr>
<td>• U-Pitt Vascularized Liver Acinus (Taylor)</td>
</tr>
<tr>
<td>• U-Pitt Osteochondrial unit and joint chip (Tuan)</td>
</tr>
<tr>
<td>• U-Washington iPSC-derived kidney organoids, vascularized kidney MPS (Himmelfarb)</td>
</tr>
<tr>
<td>• Columbia Cardiomyocyte, Liver, Integrated Heart-Liver-Skin-Bone-Tumor chip (Vunjak-Novakovic)</td>
</tr>
<tr>
<td>• U-Penn Airway and Bone Marrow (Huh)</td>
</tr>
<tr>
<td>• U-Rochester Salivary gland (Benoit)</td>
</tr>
<tr>
<td>• Harvard Stem cell-derived renal organoids (Bonventre)</td>
</tr>
<tr>
<td>• UC-Davis Atria on a chip (George)</td>
</tr>
</tbody>
</table>
The MPS DB Center is Key to Analyze and Model MPS Data Relative to Experimental Animal and Human Data

Preclinical Data

Proprietary Databases and Tools

Clinical Data

Output

Safety and Efficacy

Reproducibility

Computational Models of ADME/Tox & Disease

Mark Schurdak, Director of Operations and Bert Gough, Associate Professor
University of Pittsburgh Drug Discovery Institute
## MPS DB Center Content and Tiered Review for Public Access

### Current MPS-Db Content

**MPS Experimental Models**
- **58** models
- Covering **11** organs
- Developed at **14** Centers

**Data**
- **171** studies
- **133,675** data points
- **10,516** images
- **2,981** videos
- From **8** data providers

<table>
<thead>
<tr>
<th>Data Release Progress</th>
<th>Studies</th>
<th>Data Points</th>
<th>Images</th>
<th>Videos</th>
</tr>
</thead>
<tbody>
<tr>
<td>0. Data provider review</td>
<td>81</td>
<td>74,824</td>
<td>7,754</td>
<td>2,981</td>
</tr>
<tr>
<td>1. Tissue Chip Developer review</td>
<td>28</td>
<td>16,462</td>
<td>230</td>
<td>0</td>
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<tr>
<td>2. NCATS, FDA, IQ Consortium access</td>
<td>43</td>
<td>29,864</td>
<td>1,254</td>
<td>0</td>
</tr>
<tr>
<td>3. Public Access</td>
<td>19</td>
<td>12,525</td>
<td>1,278</td>
<td>0</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>171</strong></td>
<td><strong>133,675</strong></td>
<td><strong>10,516</strong></td>
<td><strong>2,981</strong></td>
</tr>
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</table>

Mark Schurdak, Director of Operations and Bert Gough, Associate Professor, University of Pittsburgh Drug Discovery Institute
NIH Tissue Chips 2.0 for Disease Modeling and Efficacy Testing 2018 to 2022

Kam Leong, Columbia U
Proteus Syndrome and DiGeorge Syndrome

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
tuberculous 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 microangiopaties

Teresa Woodruff, Northwestern U
Polycystic Ovarian Syndrome

George Truskey, Duke U
rheumatoid arthritis, atherosclerosis

Type-2 Diabetes Mellitus
- Andreas Stahl, Kevin Healy, Matthias Hebrok, Edward Hsiao, Holger Willenbring, UC Berkeley - Pancreatic islet, liver, adipose
- Lansing Taylor, U Pittsburgh – Vascularized liver and pancreatic islets
- James Wells, Moo-Yeal Lee, Cincinnati Children’s Hospital - Liver, pancreatic islet and intestine

NCATS, NHLBI, NIAMS, NIBIB, NICHD, NIDCR, NIDDK, NIEHS, NINDS, ORWH
Physiological Changes under Prolonged Microgravity

- **Early response (<3 weeks)**
  - Upper body fluid shift
  - Neurovestibular disturbances
  - Sleep disturbances
  - Bone demineralization

- **Intermediate (3 weeks to 6 months)**
  - Bone resorption
  - Muscle atrophy
  - Cardiovascular deconditioning
  - GI disturbances
  - Hematological changes

**Long Duration (greater than 6 months)**

- Muscle atrophy
- Cardiovascular deconditioning
- GI disturbances
- Hematological changes
- Declining immunity
- Renal stone formation

- Reverts to normal on return to Earth

Opportunities to advance Organ on chips biology and technology
Why send Tissue Chips to the ISS National Laboratory?

- The Chips in Space initiative seeks to better understand the role of microgravity on human health and disease and to translate that understanding to improved human health on Earth.

- Many of the changes in the human body caused by spaceflight resemble the onset and progression of diseases associated with aging on Earth, such as bone loss, muscle wasting, and immune dysfunction. But the space-related changes occur much faster. This means that scientists may be able to use tissue chips in space to model changes that might take months, years or decades to happen on Earth.

- The automation and miniaturization required for spaceflight has contributed to the commercialization opportunities of tissue chip technology, which advances validation and allows broader adoption of the technology on Earth.
NIH and ISS-NL Coordinated Program in Tissue Chip Systems Translational Research in Space

**Immunosenescence**
PI: Sonja Schrepfer

**Post-traumatic osteoarthritis**
PI: Al Grodzinsky

**Drugs across blood-brain barrier**
PI: Christopher Hinojosa

**Lung infection**
PI: Scott Worthen

**Proteinuria and kidney stones formation**
PI: Jonathan Himmelfarb

**Cardiac dysfunction & engineered heart tissues**
PI: Deok-Ho Kim
PI: Joseph Wu

**Muscle wasting (sarcopenia)**
PI: Siobhan Malany

**Gut inflammation**
PI: Christopher Hinojosa

**Improved biology**: study human biology that otherwise would be difficult or take longer on earth
• **Technological improvements:** Organs on chip control systems are more complex than the chips – need for robust, automated, reduced footprint, turnkey (“astronaut/fighter pilot proof”); standardization, minimize variability

**Ground requirements for 24 Chips**
- 72 samples preparations
- 8 syringe pumps
- 4 incubators (48 cubic feet)
- 216 small petri dishes for effluent
- 24 large petri dishes or 72 smaller for triplex chips
- 216 syringes for media and fixative
- ~216 feet of tubing

**On-orbit operational requirements**
- Support up to 10 days of automated perfusion
- 72 individual media or fixative channels and 72 effluent bags
- Downlink telemetry ISS to monitor operation while on orbit
- Payload development - Fit within **compact volumes**
  - **Stowage Locker – Launch:** (17.34”w x 20.32”L x 9.97”H) – 4 syringe pumps, one power module
  - **SABL – on orbit:** (11.1”w x 16.66”L x 7.75”H) – 2 syringe pumps, 2 SABLs

**Improved Tissue Chip Technology: Automation and miniaturization of control systems**
• SpaceX CRS-16 Launch
  • Kennedy Space Center - December 5, 2018
    1:16 pm
  • Payload included
    Immunosenescence on chip project

• SpaceX CRS-17 Launch
  • Kennedy Space Center – May 4, 2019
    2:48 am
  • Payload included tissue chip projects:
    • Lung infection/bone marrow
    • Proteinuria and kidney stone formation
    • Osteoarthritis
    • BBB permeability
NIH to rocket 3-D tissue chips into space to study diseases in microgravity

- May 6, 2019 7:04 a.m. EDT, ISS crew members captured the Dragon spacecraft
- Berthed to the Harmony module on May 6, 2019 9:33 a.m. EDT
- Dragon capsule returned to Earth June 3, 2019 after approximately four-week stay at the ISS.

- Samples being analyzed
  - Biological – omics marker analysis (transcriptomics, metabolomics, epigenetic), histological, immunohistochemical
  - Technological – structural soundness of chips platform and instrumentation; experimental automation
- Testing of compounds on re-flight

NASA astronaut Christina Koch works inside the Life Sciences Glovebox conducting tissue chips research
NIH - FDA - DARPA

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

Tissue Chip Consortium 2012-2017
“Fundamental learnings from program evolution”
Brian Berridge

- Clearly identify gaps and opportunities
  - Create established supporting partnerships (e.g. government agencies)
  - Involvement of end-users from the start (e.g. FDA, pharma)

- Give researchers what they need to succeed
  - Establish a precompetitive environment
    - Supplemental funding
    - Consortium meetings for updates, group troubleshooting, and networking
    - Access to proprietary resources and/or information
  - Programmatic support and guidance

- Expect setbacks and failures
  - Build in procedures to avoid e.g. milestone-driven phased awards
  - Invite feedback to help guide progress
Current NIH Initiatives for Tissue Chips

• Co-culture of many differentiated iPSC-derived cell types per tissue architecture and composition
• Integration of different tissue chips to form human body on chip
• Genome editing to introduce various polymorphisms on isogenic iPSC lines
• Developmental/pediatric response to drugs/toxins
• Rare diseases

• Clinical Trials-on-chips for Precision Medicine (You-on-chip) RFA-TR-19-014 (October 9, 2019)
• BBB/interface on chip RFA-HL-20-21 (December 2, 2019; October 19, 2020)
• Nociception-on-chip RFA-TR-19-003
• Immune system-on chip PAR-19-138
• ADRD on chip RFA-NS-19-027

To be awarded:
RFA-TR-19-014 "Clinical Trials" on a Chip: Tissue Chips to Inform Clinical Trial Design and Implementation in Precision Medicine

• **RFA Goal:** To demonstrate the utility of tissue chips in informing clinical trial framework and for precision medicine through trial design, establishing recruitment criteria and stratification of patient populations towards identifying the best responders to candidate therapeutics

• **Participating NIH ICs:** NCATS, NCI, NIAMS, NICHD, NIDCR, NINDS

• **Areas of interests:**
  - Use of tissue chip models that have the potential to substantially impact clinical trial design in terms of anticipated key outcomes (e.g., assessment of clinical benefit and risk, safety and tolerability profile, dosing regimen, population stratification to include the best responders, identification of surrogate clinical trial endpoints
  - Studies on mission-relevant diseases and disorders for the participating ICs

• **Application receipt date:** October 9, 2019
Growing Partnerships and Investments in MPS beyond NCATS

Other NIH ICs

- Microphysiological Systems (MPS) for Modeling Diabetes (NIDDK)
- ImmuneChip: Engineering Microphysiological Immune Tissue Platforms (NIBIB)
- Human Three-Dimensional Cell Model Systems for Alzheimer's Disease-Related Dementias (NINDS)
- Trans-agency Blood-Brain Barrier Interface (NHLBI)

Other Countries

Europe
Australia
Asia

Other Interests

- BARDA
- CDC
- Translational Research Institute for Space Health
- NASA Human Research Program
- EPA
- USGS

NASA and HHS

- NCATS-NASA State of the Science Workshop: 3D Tissues and Microphysiological Systems
- NIH ICs, FDA, NASA, BARDA, CDC, ISS-NL
Summary and Future Directions

Partnerships with NCATS

Other NIH Institutes and Centers:
- NHLBI, NIAMS, NIBIB, NICHHD, NCI, NIDCR, NIDDK, NIEHS, NINDS, ORWH

Government agencies:
- DARPA, FDA
- NASA

Pharma:
- AstraZeneca
- GSK
- Pfizer

Non-profits:
- IQ MPS Affiliate
- CASIS/ISS NL

NCATS Tissue Chips For Drug Screening Program

Human body on chip

- Predictive toxicology
- Disease models and efficacy studies
- Microgravity and space radiation effects
- Tools for clinical trials
- Personalized chips and precision medicine
- Microbiome
- Environmental toxins and contaminants
- Infectious agents
- Countermeasures
Tissue Chips Consortium Partners – Lead: Danilo A. Tagle
Program Manager: Lucie Low, Ph.D.

Trans-NIH Microphysiological Systems Working Group

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- Steven Becker (NEI)
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- IQ MPS Affiliate
  - IQ MPS Executive Committee (EC): IQ MPS Chair (Will Proctor, Genentech), Vice Chair (Monicah Otieno, Janssen) and Vice Chair-Elect (Terry van Vleet, AbbVie); IQ-NCATS engagement workstream POC (Jason Ekert GSK)
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Thank you!

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