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

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

Danilo A. Tagle, Ph.D.
Associate Director for Special Initiatives
Office of the Director, NCATS, NIH
danilo.tagle@nih.gov

Lucie Low, Ph.D.
Scientific Program Manager
Office of the Director, NCATS, NIH
lucie.low@nih.gov
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
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.
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
  \[ \text{(phRMA, Biopharmaceutical Research Industry Profile, 2016)} \]

- 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)

![Graph showing System Organ Class True Positive Counts]

3,290 approved drugs
1,637,449 adverse events
70 years

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
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 \textit{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
- multi-channel modeling
Microphysiological Systems Program: Tissue Chips 1.0 for Safety and Toxicity Testing

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

$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
Tissue Chips 1.0 to Predict Drug Safety (2012-2017)

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

- D. Lansing Taylor; University of Pittsburgh
  A 3-D biomimetic liver sinusoid construct for predicting physiology and toxicity

- Linda Griffith; Massachusetts Institute of Technology
  All-human microphysical model of metastasis and therapy

- John P. Wikswo; Vanderbilt University
  Neurovascular unit on a chip: Chemical communication, drug and toxin responses

- Angela Christiano; Columbia University Health Sciences
  Modeling complex disease using induced pluripotent stem cell-derived skin constructs

- Michael L. Shuler; Cornell University
  Microphysiological systems and low cost microfluidic platform with analytics

- Kevin K. Parker; Harvard University
  Human cardio-pulmonary system on a chip

- Joan E. Nichols; The University of Texas Medical Branch at Galveston
  Three-dimensional human lung model to study lung disease and formation of fibrosis

- Mark Donowitz; Johns Hopkins University, Baltimore
  Human intestinal organoids: Pre-clinical models of non-inflammatory diarrhea

- Teresa Woodruff; Northwestern University
  Ex Vivo Female Reproductive Tract Integration in a 3-D Microphysiologic System

- Jonathan Himmelfarb; University of Washington, Seattle
  A tissue-engineered human kidney microphysiological system

- Gordana Vunjak-Novakovic; Columbia University Health Sciences
  Integrated Heart-Liver-Vascular Systems for Drug Testing in Human Health and Disease

- Angela Christiano; Columbia University Health Sciences
  Modeling complex disease using induced pluripotent stem cell-derived skin constructs

- Kevin E. Healy; University of California, Berkeley
  Disease-specific integrated microphysiological human tissue models

- Michael L. Shuler; Cornell University
  Microphysiological systems and low cost microfluidic platform with analytics
# Commercial Activities around Organ-on-chip Technologies

## Body on-a-Chip

<table>
<thead>
<tr>
<th>Company</th>
<th>Scientific Founders</th>
<th>Selected Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hesperos</td>
<td>Michael Shuler, James Hickman</td>
<td>Multi-Organ Chip (2, 4 organs) (6-10 organs)</td>
</tr>
<tr>
<td>TISeUSe</td>
<td>Uwe Marx</td>
<td>3-Organ-Chip (3-OC) 4-Organ-Chip (4-OC) Human-on-a-chip (HOC)</td>
</tr>
</tbody>
</table>

## Tissue interface on-a-Chip

<table>
<thead>
<tr>
<th>Company</th>
<th>Scientific Founders</th>
<th>Selected Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>emulate</td>
<td>Donald Ingber, Olivier Guenat, Thomas Neumann, Axel Guenther</td>
<td>Lung-on-a-Chip (Airway-on-a-Chip) Gut-on-a-Chip Kidney-on-a-Chip Bone Marrow-on-a-Chip Lung-on-a-chip array Kidney-on-a-Chip Vessel-on-a-Chip Artery-on-a-Chip</td>
</tr>
</tbody>
</table>

## Parenchymal tissue on-a-Chip

<table>
<thead>
<tr>
<th>Company</th>
<th>Scientific Founders</th>
<th>Selected Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>organovo</td>
<td>Sangeeta Bhatia, Gabor Forgacs, Keith Murphy, Tamer Mohamed, Konrad Walus, Sam Wadsworth, Simon Beyer, Jan Lichtenberg, Jens M. Kelm, Wolfgang Moritz, Nicholas Kotov, Greg Baxter, Robert Freedman, Matthew R. Gevaert, William L. Warren</td>
<td>HepatoPac®, Hepatomuno™ ExVive3D™ Liver ExVive3D™ Kidney Lab-on-a-Printer™ 3D BioRing™ Airway 3D Insight™ Liver 3D Insight™ Islet 3D Insight™ Tumor PERFECTA3D® HANGING DROP PLATES 3DKUBE™ MINIC® Technology</td>
</tr>
<tr>
<td>µOrgano</td>
<td>Milica Radisic, Gordana Vunjak-Novakovic, Kevin Healy, Thomas Eschenhagen, Wolfraam-Hubertus Zimmermann, Michael Moore, Nuo Li Jeon, Carl W. Cotman, Anne Taylor, Bernadette Bung, Margaret Magdesian, Neuron Device</td>
<td>Cardiac Biowire™ II AngioChip™ Engineered Heart Tissue (EHT) 3D Cardiac Systems Nerve-on-a-Chip™ Standard / Triple Chamber Neuron Device Neuronal Diode Neuro Device</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>AbbVie</th>
<th>BMS</th>
<th>GSK</th>
<th>Novartis</th>
<th>Theravance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amgen</td>
<td>Celgene</td>
<td>Jansen</td>
<td>Pfizer</td>
<td>Vertex</td>
</tr>
<tr>
<td>Astellas</td>
<td>Eisai</td>
<td>Merck</td>
<td>Sanofi</td>
<td></td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Eli Lilly</td>
<td>Merck KgA</td>
<td>Seattle Genetics</td>
<td></td>
</tr>
<tr>
<td>Biogen</td>
<td>Genentech</td>
<td>Mitsubishi Tanabe</td>
<td>Takeda</td>
<td></td>
</tr>
</tbody>
</table>

- 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

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

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

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

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.

Path to Adoption and Commercialization

- 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/
  • 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

• Brain on chip

Publications thus far:
• Kidney on chip
  • Nature Scientific Reports (2018) 8:14882
  • CPT Pharmacometrics Syst. Pharmacol. 2019, 8:316
• Brain on chip
# NextGen Testing Centers and Business Models for Self-Sustainability

## MIT transitioned to Javelin Biotech
- CNBio Liver
- CNBio Liver-Tumor
- Nortis Kidney
- TissUse Bone marrow
- TissUse Pancreas-Liver
- Stemonix microBrain
- Stemonix microHeart
- Mimetas CNS
- Mimetas Liver

## Texas A & M TC Testing Consortium
- **Duke** Arteriole blood vessel (Truskey)
- **UC-Irvine** Vascular malformations – Hereditary Hemorrhagic Telangiectasia, Port Wine disease and Sturge-Weber syndrome (Hughes)
- **UC-Berkeley** Vasculature with flow, Skeletal Muscle, Pancreatic islet (Healy)
- **U-Pitt** Vascularized Liver Acinus (Taylor)
- **U-Pitt** Osteochondrial unit and joint chip (Tuan)
- **U-Washington** iPSC-derived kidney organoids, vascularized kidney MPS (Himmelfarb)
- **Columbia** Cardiomyocyte, Liver, Integrated Heart-Liver-Skin-Bone-Tumor chip (Vunjak-Novakovic)
- **U-Penn** Airway and Bone Marrow (Huh)
- **U-Rochester** Salivary gland (Benoit)
- **Harvard** Stem cell-derived renal organoids (Bonventre)
- **UC-Davis** Atria on a chip (George)
The MPS DB Center is Key to Analyze and Model MPS Data Relative to Experimental Animal and Human Data

Preclinical Data
- EMA, CT.gov, Health Canada
- MPS Data
- PubChem
- MPS DB Center
- Output
- Safety and Efficacy
- Reproducibility
- Computational Models of ADME/Tox & Disease

Clinical Data
- Proprietary Databases and Tools
- EMA, CT.gov, Health Canada
- ToxNet, LiverTox
- OpenFDA, NAMCS/NHAMCS
- ChEMBL, Unichem, DrugBank

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

<table>
<thead>
<tr>
<th>MPS Experimental Models</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 58 models</td>
</tr>
<tr>
<td>• Covering 11 organs</td>
</tr>
<tr>
<td>• Developed at 14 Centers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 171 studies</td>
</tr>
<tr>
<td>• 133,675 data points</td>
</tr>
<tr>
<td>• 10,516 images</td>
</tr>
<tr>
<td>• 2,981 videos</td>
</tr>
<tr>
<td>• From 8 data providers</td>
</tr>
</tbody>
</table>

#### Data Release Progress

<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>
</tr>
<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>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>171</td>
<td>133,675</td>
<td>10,516</td>
<td>2,981</td>
</tr>
</tbody>
</table>

Mark Schurdak, Director of Operations and Bert Gough, Associate Professor  
University of Pittsburgh Drug Discovery Institute
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
• 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

Biotech/Industry Partnerships

Heart-Vasc-Tumor
WashU

Heart-Lung
Wyss

Liver
Pittsburgh/IGH

Muscle/TEBV
Duke

Skin
Columbia

Gut-Disease
Johns Hopkins

Liver-Metastasis
MIT

Neurovascular
Vanderbilt/Cleveland Clinic

BIO-MIMETICS
MIT/Draper Labs

Human Organs on a Chip
Wyss

Brain
U Wisconsin

Heart-liver-WAT
UC-Berkley

Kidney
U Washington

Female Repro
Northwestern

Gut innervation
Cincinnati/Children's
Johns Hopkins

Heart-Liver-Vascular
Columbia
“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)

To be awarded:
• Nociception-on-chip RFA-TR-19-003
• Immune system-on-chip PAR-19-138
• ADRD on chip RFA-NS-19-027
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

**NCATS**
- 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 NIH ICs**
- NCI
- NHLBI
- NIDCR
- NINDS
- NIBIB
- NIEHS
- NIAMS
- NIDDK
- NICHD
- OD
- ORWH

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

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

**Other Countries**
- Asia
- Europe
- Australia
Summary and Future Directions

Partnerships with NCATS

**Other NIH Institutes and Centers**
- NHLBI, NIAMS, NIBIB, NICHHD, NCI, NIDSCPR, 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

- 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

Human body on chip
Tissue Chips Consortium Partners – Lead: Danilo A. Tagle
Program Manager: Lucie Low, Ph.D.

Trans-NIH Microphysiological Systems Working Group

- Nathan M. Appel (NIDA)  - Christine Livingston (NCATS)  - Seila Selimovic (NIBIB)
- Guillermo Arreaza-Rubin (NIDDK)  - Lucie Low (NCATS)  - Jose Serrano (NIDDK)
- David Balshaw (NIEHS)  - Nadya Lumelsky (NIDCR)  - Lillian Shum (NIDCR)
- Steven Becker (NEI)  - Martha Lundberg (NHLBI)  - Kentner Singleton (NIAID)
- Lisa Begg (OD)  - Su-Yao Mao (NIAMS)  - Christine Sizemore (NIAID)
- Bonnie Burgess-Beusse (NIDDK)  - Elizabeth Maull (NIEHS)  - Brian Sorg (NCI)
- Warren Casey (NIEHS)  - Glen Mcgugan (NIAID)  - Denise Stedrick (OD)
- Preethi Chander (NIDCR)  - Matthew McMahon (NHLBI)  - Danilo Tagle (NCATS)
- Ricardo Cibotti (NIAMS)  - Leah Miller (OD)  - James Tricoli (NCI)
- Ki-Cha Flash (NCATS)  - Melody Mills (NIAID)  - Hung Tseng (NIAMS)
- Nancy Freeman (NIDCD)  - Lisa Neuhold (NEI)  - Katerina Tsilou (NICHID)
- Daniel Gossett (NIDDK)  - Margaret Ochocinska (NHLBI)  - Dawn Walker (NCATS)
- Halonna Kelly (NIAID)  - David Panchision (NIMH)  - Fei Wang (NIAMS)
- Anthony Kirilusha (NIAMS)  - Aaron Pawlyk (NIDDK)  - David Weinberg (NICHID)
- Lilian Kuo (NIAID)  - Mary Perry (OD)  - Vicky Whittemore (NINDS)
- Timothy Lavaute (NINDS)  - Leslie Reilinib (NIEHS)  - Bradley Wise (NIA)
- Jennie Larkin (NIDDK)  - Dobrila Rudnicki (NCATS)  - Da-Yu Wu (NIDA)
- Sara Lin (NHLBI)  - Sheryl Sato (NIDDK)  - Nastaran Zahir (NCI)

- FDA
  - Khaled Bouri, Ph.D., M.P.H., OC
  - Paul Brown, Ph.D., CDER
  - Tracey Chen, Ph.D., DABT, OC
  - Karen Davis-Bruno, Ph.D., CDER
  - Suzanne Fitzpatrick, Ph.D., CFSAN
  - Timothy McGovern, Ph.D., CDER
  - Donna Mendrick, Ph.D., NCTR
  - Thomas Papolian, Ph.D., DABT, CBER
  - Alexandre Ribeiro, Ph.D., CBER
  - James Weaver, Ph.D., CDER

- ISS-NL (CASIS)
  - Michael Roberts, Ph.D.
  - Marc Giulianotti, Ph.D.
  - Bill McLamb, Ph.D.
  - Melissa Rhodes, Ph.D.

- 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)
  - Szczepan Baran, Ph.D., Novartis
  - Ananthsrinivas Chakilam, Ph.D., Vertex
  - Yvonne Dragan, Ph.D., Takeda
  - David Duignan, Ph.D., AbbVie
  - Jeetendra Eswaraka, DVM, Ph.D., Amgen
  - Jason Ekert, Ph.D., GSK
  - Lorna Ewart, Ph.D., AstraZeneca
  - Jiping Gan, Ph.D., BMS
  - Peggy Guzzie-Peck, Ph.D., DABT, J & J
  - Claire Jeong, Ph.D., GSK
  - Douglas Keller, Ph.D., Sanofi
  - Jonathan Phillips; Ph.D., Boehringer Ingelheim
  - William Proctor, Ph.D., DABT, Genentech
  - Terry Van Vleet, Ph.D., DABT, AbbVie
  - Rahda Sura, Ph.D., AbbVie
  - Matthew Wagoner, Ph.D., Takeda
  - David Watson, Ph.D., Eli Lilly
  - Yvonne Will, Ph.D., Pfizer
Thank you!

danilo.tagle@nih.gov
lucie.low@nih.gov

- Website: https://ncats.nih.gov/tissuechip
- Facebook: facebook.com/ncats.nih.gov
- Twitter: twitter.com/ncats.nih.gov
- YouTube: youtube.com/user/ncatsmedia
- E-Newsletter: https://ncats.nih.gov/enews
- Announce Listserv: https://bit.ly/1sdO15w