

NCATS

COLLABORATE. INNOVATE. ACCELERATE.

Tissue Chips for Drug Screening Program

*Interagency Coordinating Committee on the Validation
of Alternative Methods
Public Forum
May 18-19, 2023*

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Director, Office of Special Initiatives
NCATS, NIH

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NIH National Center
for Advancing
Translational Sciences

Re-engineering the Translational Pipeline

NCATS addresses long-standing bottlenecks in the translational research pipeline so that new treatments reach people faster.



Translational Problems:

- 90% of clinical drug development fails
- Average time to develop a drug takes 10-15 years
- Average to develop a drug to market, including cost of failures cost is \$2.6 billion
- Insufficient tools and technologies to predict toxicity and efficacy of new drugs

NCATS Solutions:

- Better predictive tools and human-based model systems
- Models that mimic the structure and function of human tissues
- Models that meet the needs for new therapeutic modalities that are human-specific and personalized



NCATS Tissue Chips for Drug Screening Program

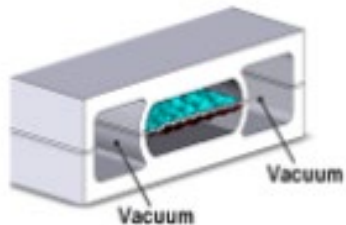
- Program Goal:

- Develop an *in vitro* 3-D culture system (**tissue chips/microphysiological systems**) that emulates organ physiology and function **using human cells and tissues** through advances in stem cell biology, microfluidics and bioengineering for risk assessment to accurately evaluate the efficacy, safety and toxicity of promising therapies

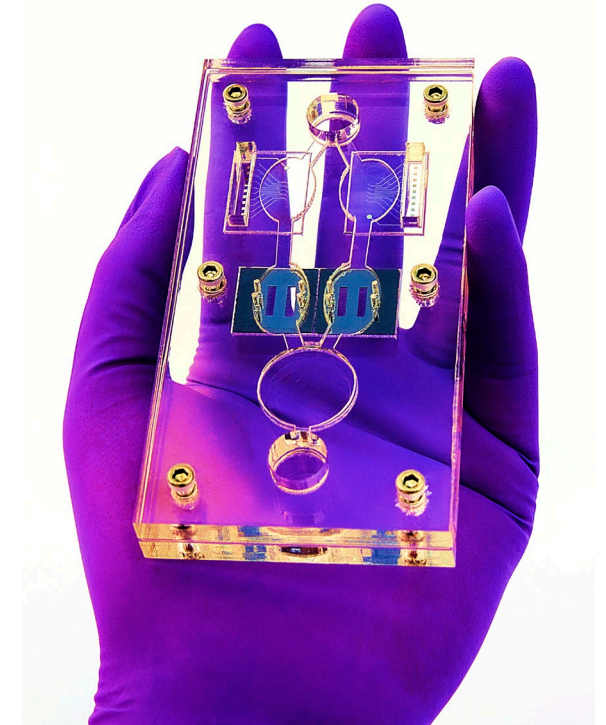
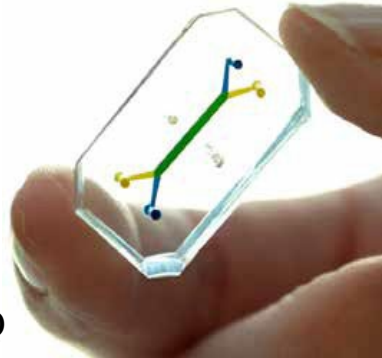


- Represents 10 Major Organ Systems

- Circulatory
- Endocrine
- Gastrointestinal
- Immune
- Skin
- Musculoskeletal
- Nervous
- Reproductive
- Respiratory
- Urinary



Emulate
Single organ chip



Hesperos 5-organ chip

Tissue Chips Consortium 1.0 to Predict Drug Safety

- 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

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

- 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 osteocondral 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 Microphysiological

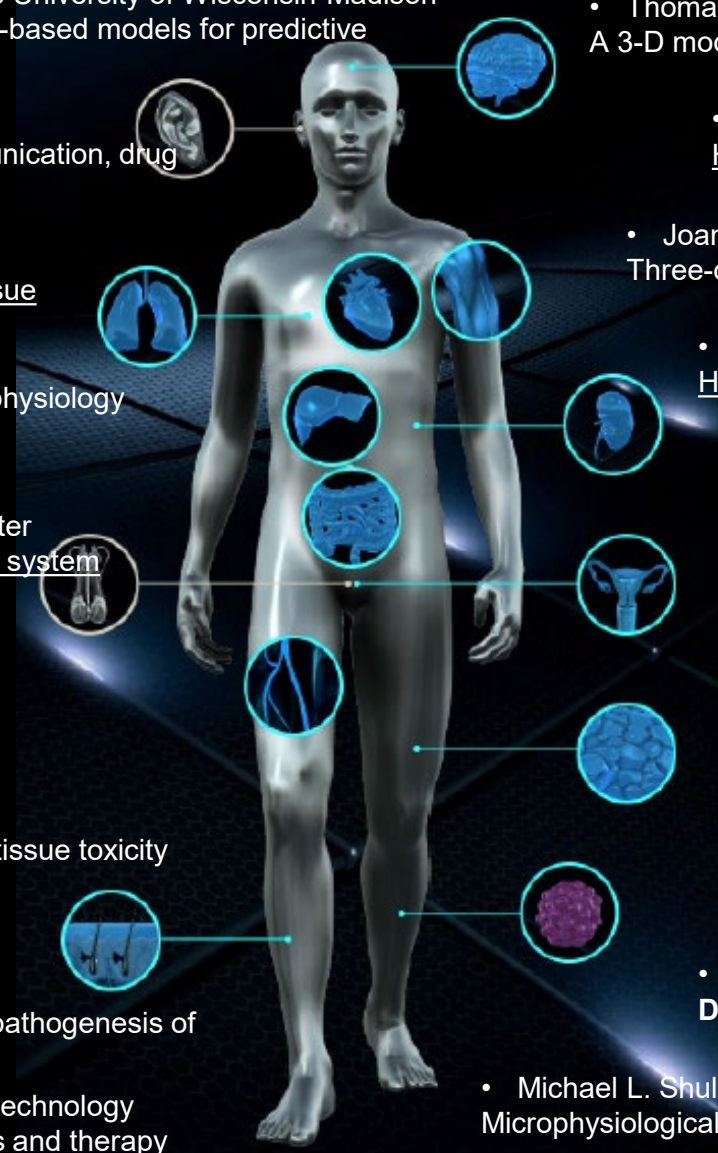
- Jonathan Himmelfarb; University of Washington, Seattle
A tissue-engineered human kidney microphysiological system

- 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

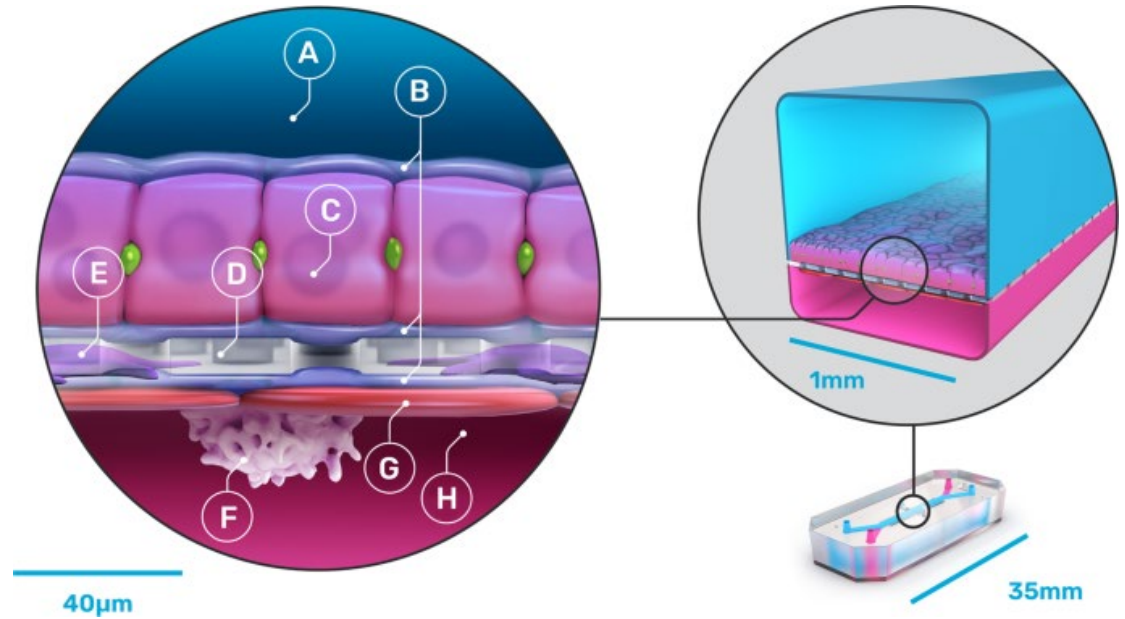
- **Kevin E. Healy; University of California, Berkeley**
Disease-specific integrated microphysiological human tissue models

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



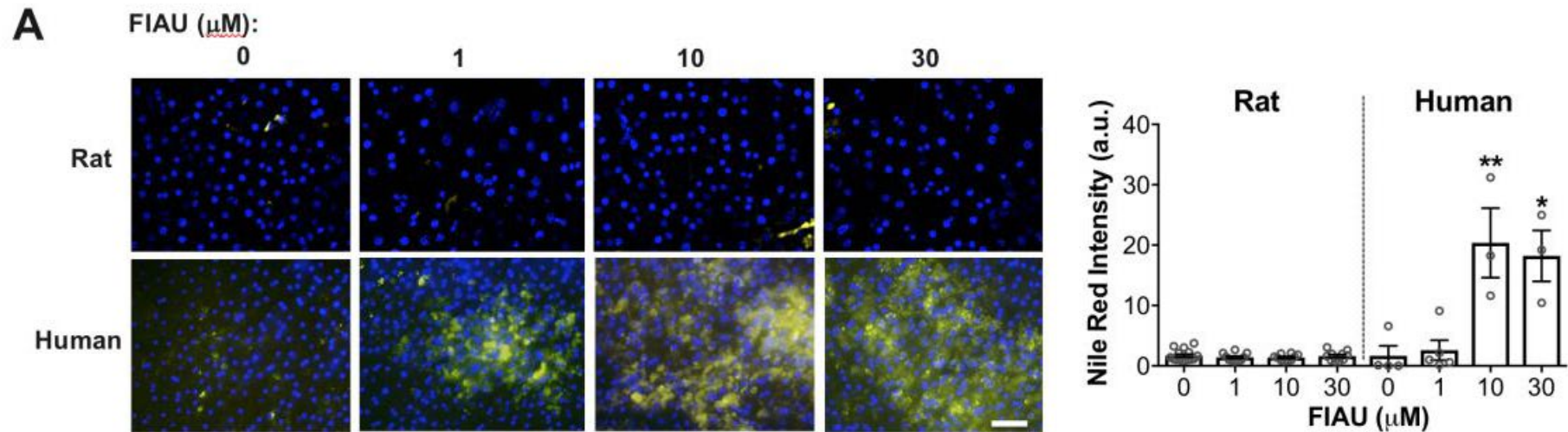
Are Tissue Chips Better Predictors of Human Physiological Response

- Liver is responsible for concentrating and metabolizing a majority of medications
- Drug-induced liver injury (DILI) is the most common cause of acute liver failure (15-20 per 100,000)
- Adverse drug reactions are an important cause of liver injury that may require discontinuation of the drug, hospitalization, or even liver transplantation



- A - parenchymal channel
- B - extracellular matrix
- C - human hepatocytes
- D - porous PDMS membrane
- E - stellate cells
- F - Kupffer cells
- G - endothelial cells
- H - vascular channel

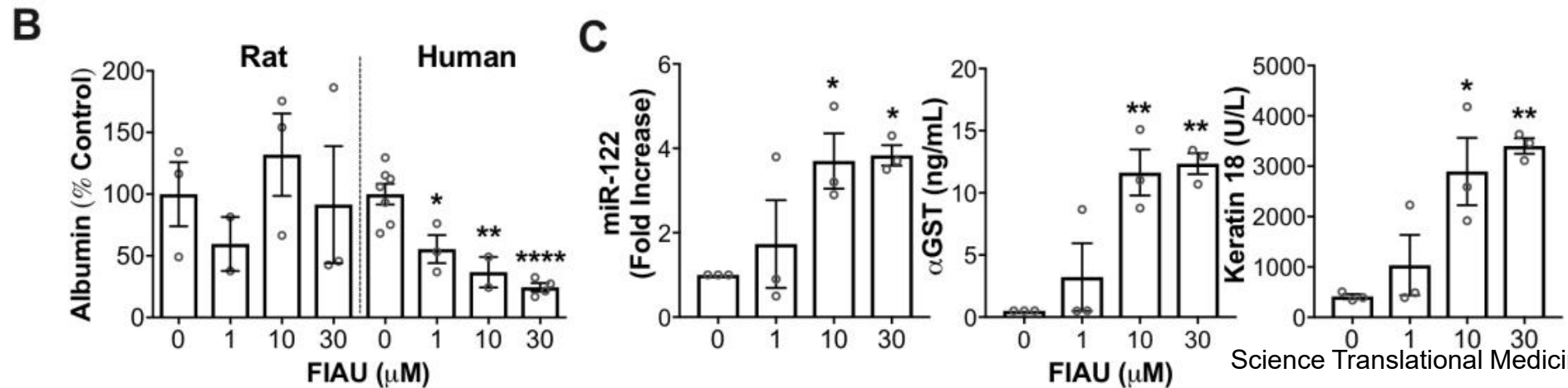
Differences in Steatosis (Fat Deposits) in Rat and Human Liver Chips following Fialuridine (FIAU) Treatment



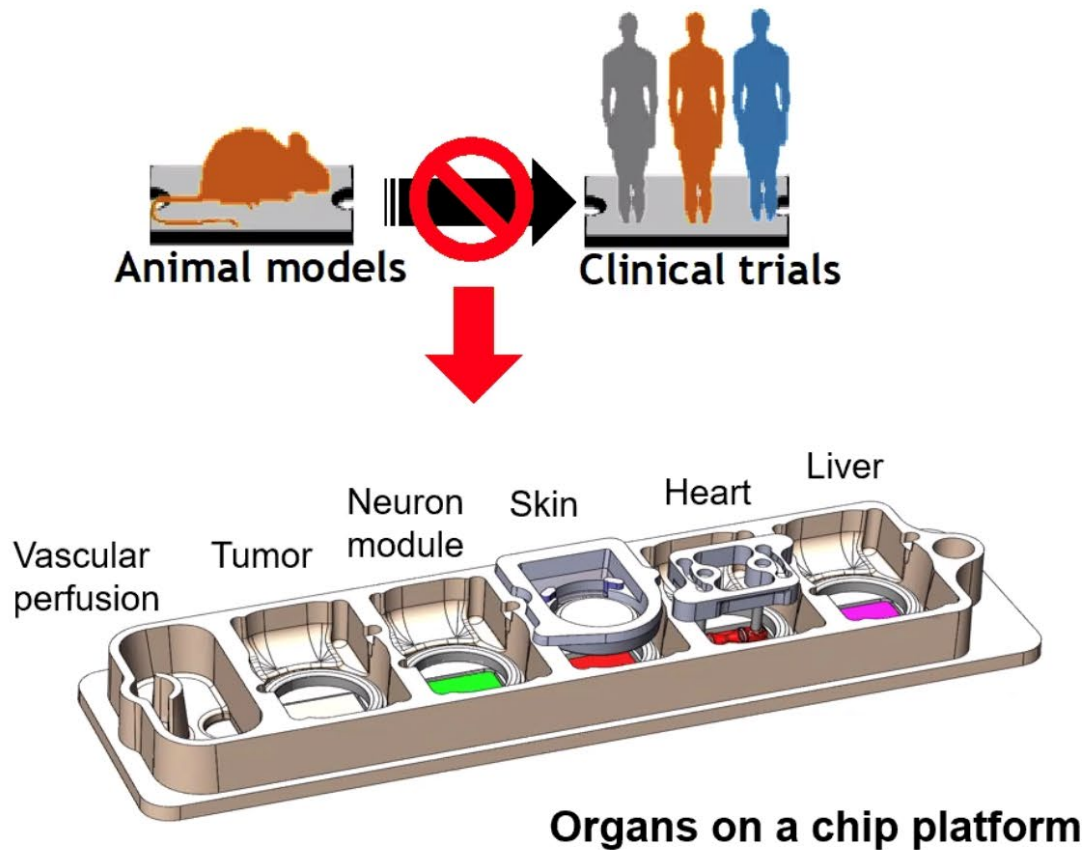
Follow up blinded study to predict DILI caused by 22 compounds with known hepatotoxic (was advanced to human use based on previous preclinical data but was withdrawn due to toxicities which collectively are responsible for more than 200 patient deaths and 10 liver transplants, and (5) non-hepatotoxic compounds – liver chips showed an 87% sensitivity and 100% specificity in predicting drug toxicity, far outperforming liver spheroids (a common preclinical model) which showed a sensitivity of only 47%.

BioRxiv 2022, doi: <https://doi.org/10.1101/2021.12.14.472674>

Nature Commun Med 2022: 2; 154- 170.



Tissue Chips 2.0 for Disease Modeling and Efficacy Testing



Translational Needs:

- Able to recapitulate in vivo functions and responses in both normal and disease states
- Capture the pathophysiology, mutation spectrum and phenotypic diversity of human diseases
- Stable tissue phenotype over weeks and months
- Reflect the multi-organ pathology and organ crosstalk
- Real-time functional readout and surrogate markers

Ronaldson-Bouchard et al, Cell Stem Cell (2018); Tavakol et al Cell Stem Cell (2021);



Tissue Chips for Disease Modeling and Efficacy Testing

Li-Huei Tsai, MIT

Alzheimer's Disease and related dementias

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

Hang Lin, U Pittsburgh

Osteoarthritis, inflammatory arthritis, adipose-mediated diabetic joint complications

Clive Svendsen, Cedars-Sinai

ALS; Parkinson's Disease

Aaron Bowman, Kevin Ess, John Wikswa, 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

Julie Kim, Northwestern U **Polycystic Ovarian Syndrome**

George Truskey, Duke U

rheumatoid arthritis, atherosclerosis

Type-2 Diabetes Mellitus

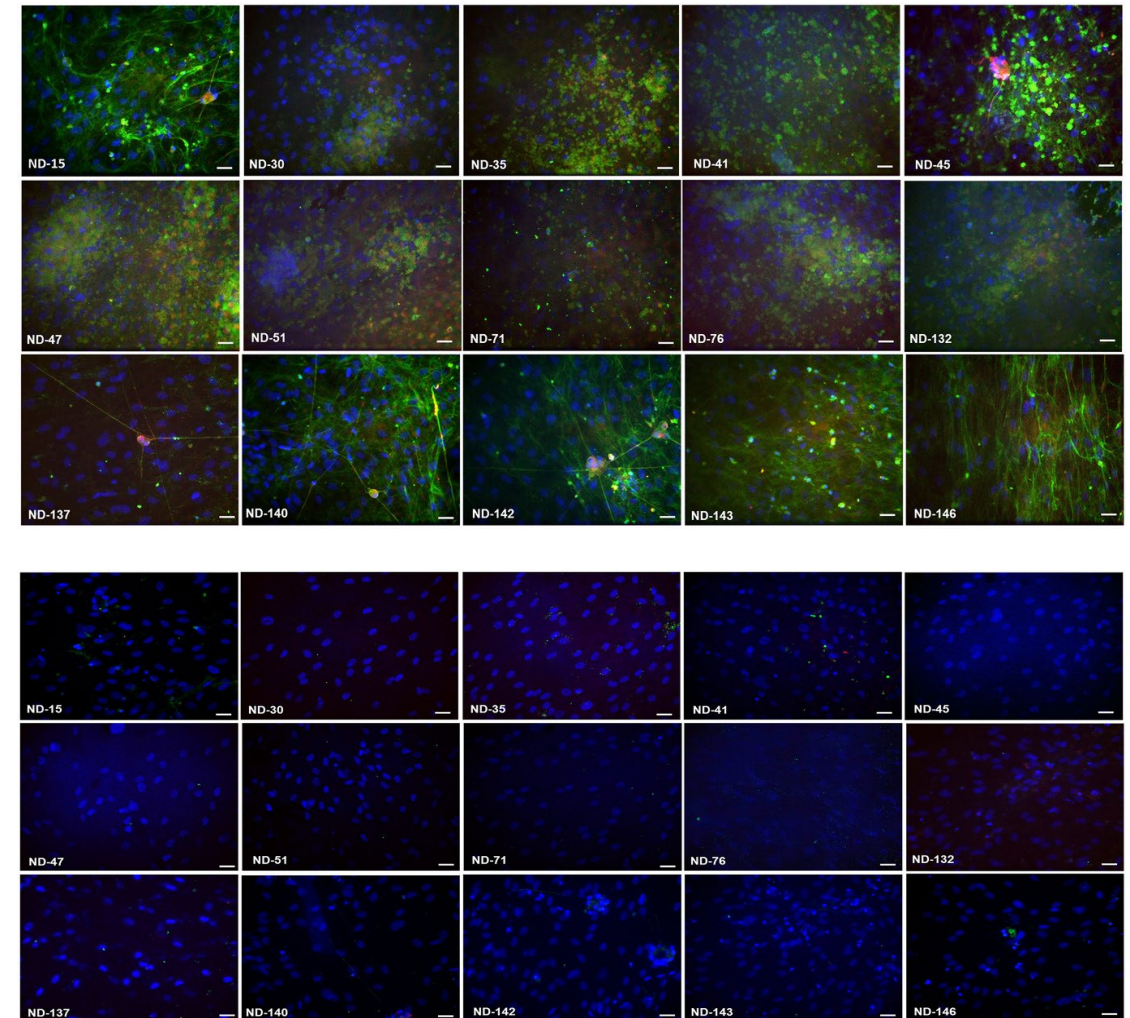
- Andreas Stahl, Kevin Healy, Matthias Hebrok, Edward Hsiao, Holger Willenbring, UC Berkeley - Pancreatic islet, liver, adipose
- Lansing Taylor, U Pittsburgh - Vascularized liver and pancreatic islets
- James Wells, Moo-Yeal Lee, Cincinnati Children's Hospital - Liver, pancreatic islet and intestine

Modeling common and rare diseases; Mendelian and complex, multifactorial diseases



Efficacy: Tissue Chips Model of Rare Autoimmune Demyelinating Neuropathies

- Chronic autoimmune demyelinating neuropathies are a group of rare neuromuscular disorders including **chronic inflammatory demyelinating polyneuropathy (CIDP)** and **multifocal motor neuropathy (MMN)**
- Tissue chip model consisting of co-culture of human primary Schwann cells (SC) and induced pluripotent stem cell-derived motoneurons (MNs)
- CIDP and MMN patient sera contains anti-GM1 IgM and IgG antibodies which is sufficient to activate the classical complement pathway in SC-MN tissue chips, resulting in detection of **C3b** and **C5b-9**
- Efficacy of **TNT005**, a monoclonal antibody that **inhibits C1s protease** rescued the serum-induced complement deposition and functional deficits while treatment with an isotype control antibody has no rescue effect
- **Efficacy data included in an investigational new drug application**



Responding to National Health Emergencies

- **Opioid crisis**

- **HEAL** awards issued in 2019 for program 'Tissue Chips to Model Nociception, Addiction and Overdose'

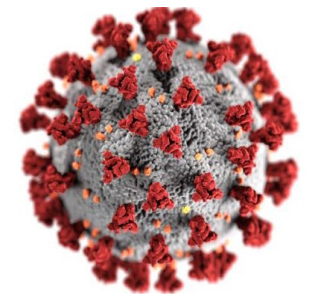
- Sensory/pain circuitry; reward pathways
- Blood-brain barrier (BBB) and respiratory control for overdose studies
- Develop novel drug screening platforms for pain, opioid use disorder (OUD) and/or overdose



- **COVID-19** pandemic

- Through **CARES Act Congressional supplemental funding**, Emergency Awards issued in 2020 for administrative supplements and competitive revisions to:

- Develop tissue chip models for COVID-19
- Understand multiple tissue/organ pathologies
- Model infection
- Test candidate drugs and vaccines
- Understand immune responses
- Model complications from vulnerable and at-risk patient groups





Tissue Chips in Space- A Partnership Involving NCATS, NASA, CASIS and ISS-NL

Goal: Model age-related diseases under microgravity and to translate that understanding to improve human health on Earth

Immunosenescence

emulate UCSF
BIO SERVE SPACE TECHNOLOGIES

PI: Sonja Schrepfer

Drugs across blood-brain barrier

emulate
Space Tango

PI: Christopher Hinojosa

Lung infection

Penn UNIVERSITY OF PENNSYLVANIA
STARS
BIO SERVE SPACE TECHNOLOGIES
Space Tango

PI: Scott Worthen

Post-traumatic osteoarthritis

MIT
techshot

PI: Al Grodzinsky

Proteinuria and kidney stones formation

W SCHOOL OF PHARMACY UNIVERSITY OF WASHINGTON
BIO SERVE SPACE TECHNOLOGIES

PI: Jonathan Himmelfarb

Cardiac dysfunction & engineered heart tissues

JOHNS HOPKINS UNIVERSITY
W UNIVERSITY OF WASHINGTON
THE OHIO STATE UNIVERSITY
UCSB
BIO SERVE SPACE TECHNOLOGIES

PI: Deok-Ho Kim
PI: Joseph Wu

Muscle wasting (sarcopenia)

UF UNIVERSITY OF FLORIDA
Space Tango
SPACEPHARMA

PI: Siobhan Malany

Gut inflammation & Microbiome

emulate
Space Tango

PI: Christopher Hinojosa

Aim: study human biology and disease that otherwise would be difficult or take longer on Earth

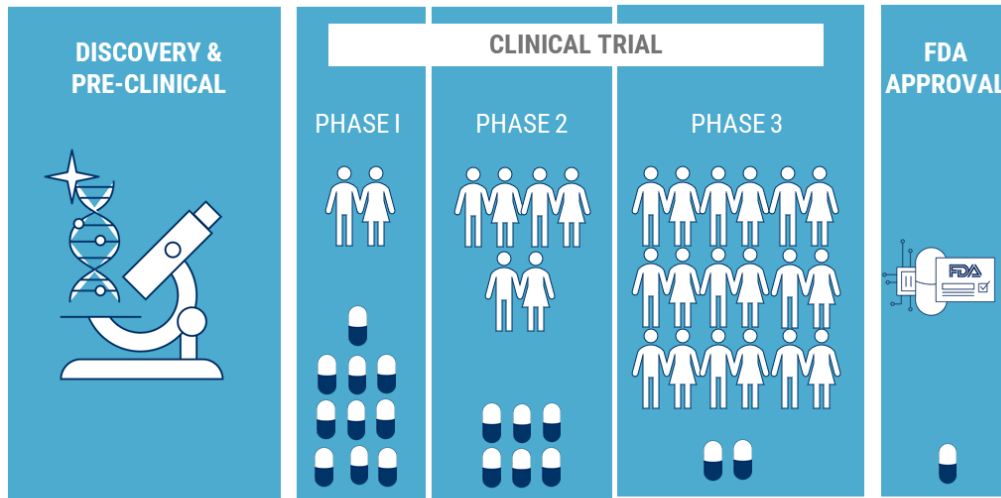
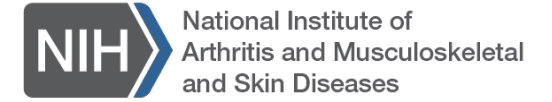
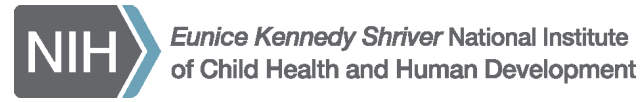
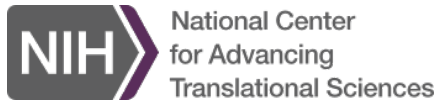


LONGEVITY EXTENSION OF 3D TISSUES AND MICROPHYSIOLOGICAL SYSTEMS FOR MODELING OF ACUTE AND CHRONIC EXPOSURES TO STRESSORS

- Partnerships between **NASA, NIH, BARDA and FDA**
- **GOALS:**
 - To extend the tissue viability and physiological function of tissue chips or microphysiological systems to a **minimum of 6 months**
 - To incorporate automated engineering capabilities for **real-time online readouts** in these complex human in vitro model systems
 - To understand the influence of multiple types of **long-lasting or chronic stressors** on tissue or organ systems and facilitate the translation of results to humans
 - To better understand 1) disease pathomechanisms, 2) drug development, 3) clinical trial design, 4) chemical and environmental exposures and countermeasures, and 5) physiological changes due to the prolonged spaceflight environment

<https://science.nasa.gov/science-news/biological-physical/miniature-avatars-take-on-nasas-biggest-challenge>

"Clinical Trials" on a Chip to Inform Clinical Trial Design and Implementation in Precision Medicine (2021 – 2025)

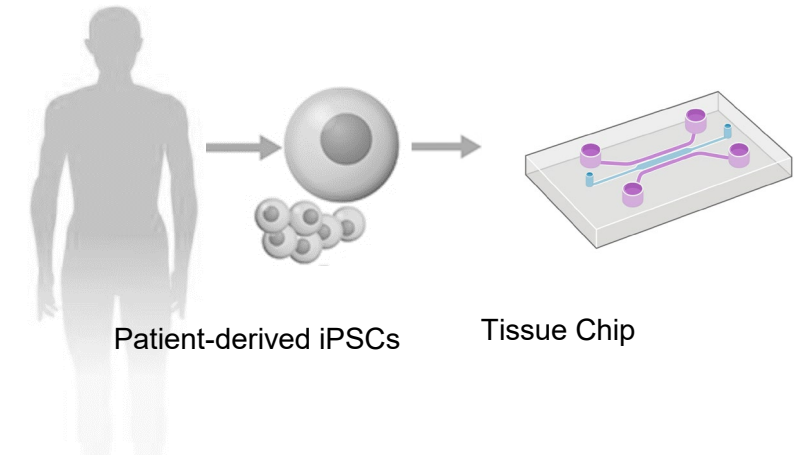


Source: cbinsights.com

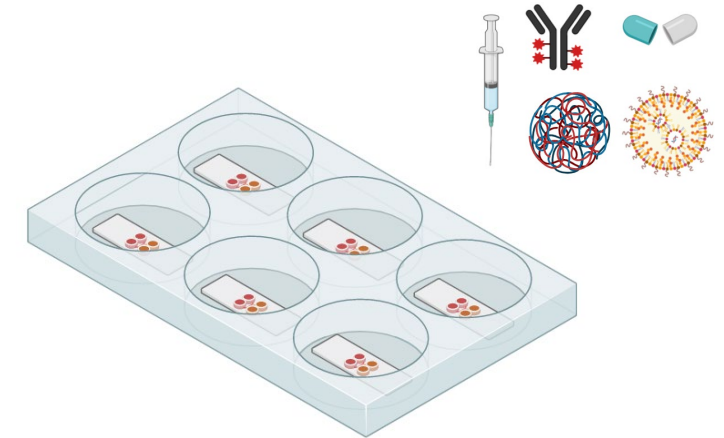
Goal → Inform clinical trial design and execution

1. Establish recruitment criteria
2. Patient stratification
3. Develop clinically relevant biomarkers

Phase 1: Develop and validate rare, pediatric and common disease models containing patient-derived cells representing diversity in patient cohorts



Phase 2: Test potential drugs for efficacy and safety assessments in clinical trials



'Clinical Trials' on-a-Chip Projects



Non-Alcoholic Fatty Liver Disease (NAFLD)  

Lansing D. Taylor, Jaideep Behari, Alejandro Soto-Gutierrez
University of Pittsburgh

Metabolic fatty liver disease

Angela M. Christiano, Columbia University



Atopic Dermatitis



Deok-Ho Kim, David-Alan Kass
Johns Hopkins University

Dystrophin-Deficient Muscular Dystrophy



Yu-Shrike Zhang
Brigham and Women's Hospital

Progeria - Premature Vascular Aging-on-a-Chip Model

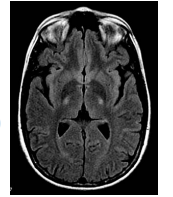
Hani Awad, James Mcgrath, Benjamin Miller
University of Rochester



Tendon inflammation and fibrosis

Clive Svendsen
Cedars-Sinai

Dementia ; Amyotrophic lateral sclerosis (ALS)



William Pu & Kevin Kit Parker
Harvard University

CPVT Heart diseases



Jonathan Himmelfarb & Matthias Kretzler
University of Washington

Polycystic Kidney diseases

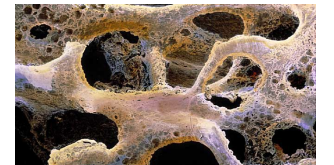


Arum Han & Ramkumar Menon
Texas Engineering Experiment Station
Pre-term birth - Maternal-fetal interface on a chip



David Beebe & Joshua Michael Lang
University of Wisconsin

Prostate cancer bone marrow metastasis



Building Confidence Towards Technology Adoption: Tissue Chip Validation Framework

Comput Struct Biotechnol J. (2016) 14: 207–210

3) Industrial (2019...)

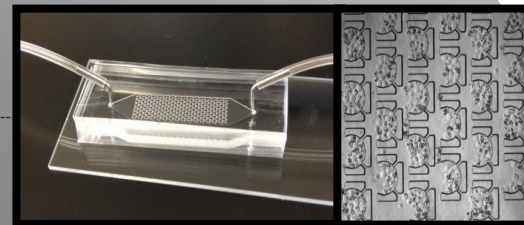
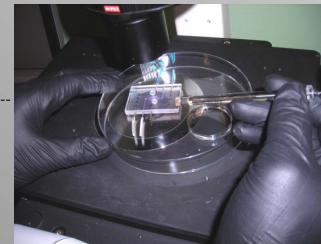
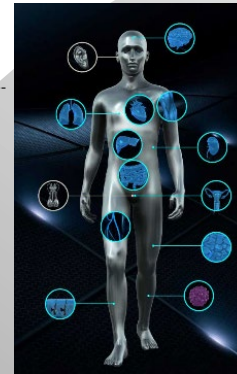
- Use by industry and regulatory agencies
- Proprietary set of compounds
- **CRO-type environment**

2) Analytical (2017...)

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

1) Physiological (2012...)

- Organ function and structure
- Training set of reference compounds
- **TC developers**



Path to Adoption and Commercialization

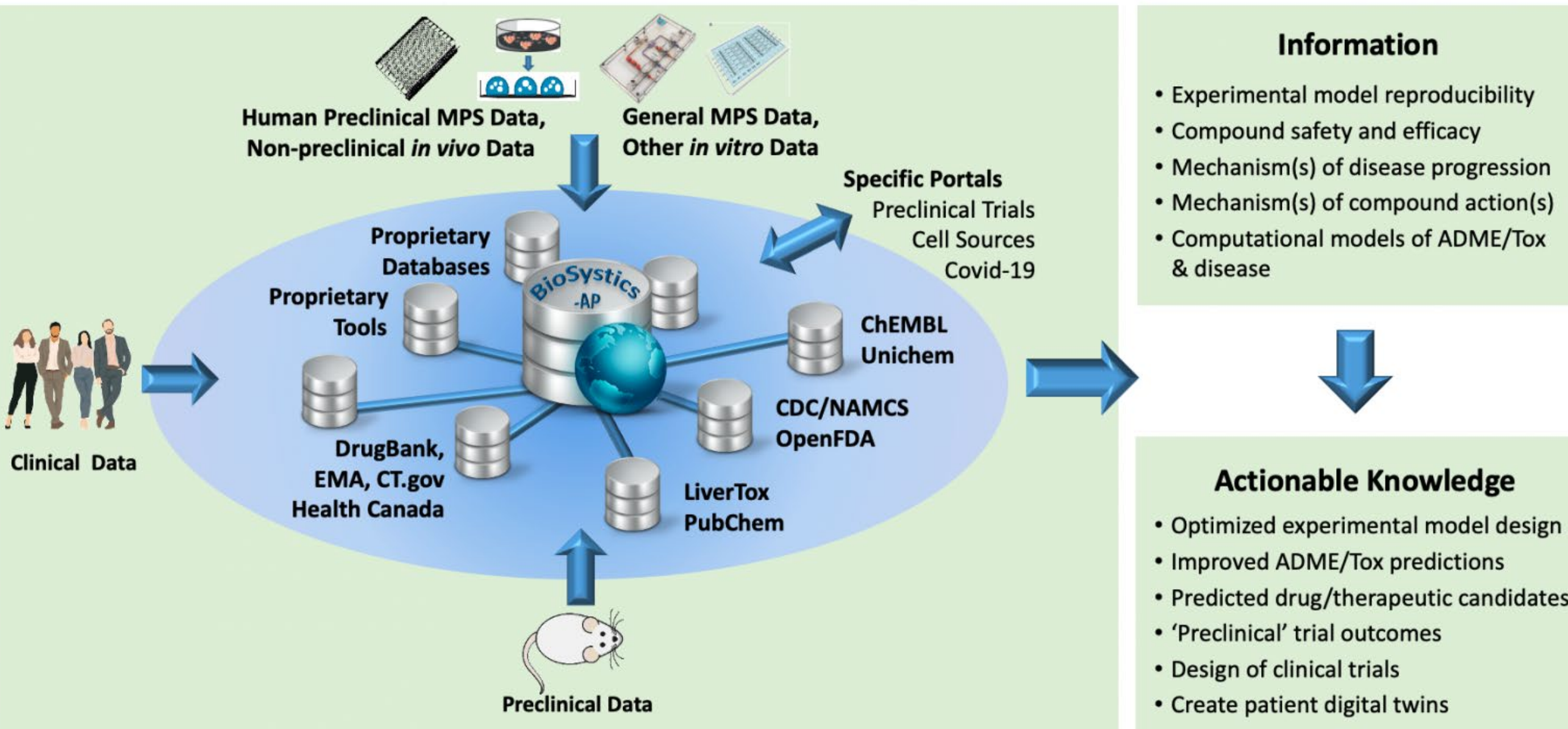
- **Javelin Biotech** (spin off from MIT)
 - CRO business model
- **Texas A&M Tissue Chip Testing Consortium**
 - Play for pay model with academia, government and industry
- **BioSystics Analytic Platform**
 - University of Pittsburgh

- **Tissue Chip Testing Centers:**
 - Massachusetts Institute of Technology
 - Texas A&M University
- **MPS Database:** <https://mps.csb.pitt.edu/>
 - University of Pittsburgh

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.



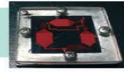
The MPS-Db is designed to aggregate, analyze and model MPS experimental data relative to human and animal exposure data



Commercial Activities around Tissue/Organ-on-chip Technologies

Body on-a-Chip

Hesperos®



Scientific founders
Michael Shuler
James Hickman

Selected products

Multi-Organ Chip
(2, 4 organs)
(5-10 organs)*

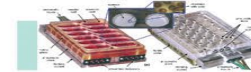
TISSUSE
Emulating Human Biology



Scientific founders
Uwe Marx

2-Organ-Chip (2-OC)
4-Organ-Chip (4-OC)
Human-on-a-Chip
(HoC)*

cnBio
innovations



Scientific founders
Linda G Griffith

Selected products
LiverChip®
LiverChip® 36

DRAPER



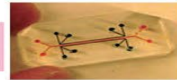
Scientific founders
Joseph Charest

Selected products
Microphysiological
Systems

Tissue interface on-a-Chip



emulate



Scientific founders
Donald Ingber

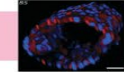
Lung on-a-Chip
Airway on-a-Chip
Gut on-a-Chip
Kidney on-a-Chip
Bone Marrow on-a-Chip

AlveoliX
In-vitro models inspired by nature



Scientific founders
Olivier Guenat

Lung-on-a-chip array



Scientific founders
Thomas Neumann

Kidney on-a-Chip
Vessel on-a-Chip



Quorum



Scientific founders
Axel Guenther

Artery on-a-Chip

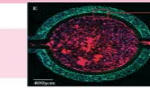
MIMETAS
the organ-on-a-chip company



Scientific founders
Jos Joore
Paul Vulto
Thomas Hankemeier

Selected products
OrganoPlates®

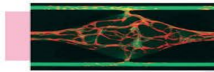
SYNVIVO



Scientific founders
Kapil Pant
B. Prabhakar Pandian

Selected products
SynTumor
SynBBB
SynRAM
SynTox

Bio
4DESIGN BIOSCIENCES



Scientific founders
G. Wesley Hatfield
Christopher Hughes
Steven George
Abraham Lee

Selected products
Vascularized
micro-organ
(VMO) platform

AIM
BIOTECH
ADVANCED - INTEGRATED - MICROFLUIDICS

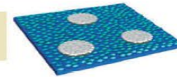


Scientific founders
Roger Kamm

Selected products
3D cell culture chips

Parenchymal tissue on-a-Chip

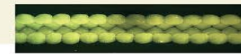
Hepregen



Scientific founders
Sangeeta Bhatia

HepatoPac®
HepatoMune™

organovo™



Scientific founders
Gabor Forgacs
Keith Murphy

ExVive3D™ Liver
ExVive3D™ Kidney*

Aspect
biosystems



Scientific founders
Tamer Mohamed
Konrad Walus
Sam Wadsworth
Simon Beyer

Lab-on-a-Printer™
3DBioRing™ Airway

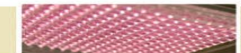
insphero



Scientific founders
Jan Lichtenberg
Jens M. Kelm
Wolfgang Moritz

3D Insight™ Liver
3D Insight™ Islet
3D Insight™ Tumor

3D Biomatrix™
Three-Dimensional Cell Culture



Scientific founders
Nicholas Kotov

PERFECTA3D®
HANGING DROP
PLATES

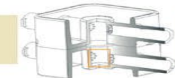
HµREL CORPORATION



Scientific founders
Greg Baxter
Robert Freedman

HµREL human™
HµREL flux™
HµREL Tox™
HµREL flow™

KIYATEC®



Scientific founders
Matthew R. Gevaert

3DKUBE™

VAXDESIGN

Scientific founders
William L. Warren

MIMIC® Technology

TARA



Scientific founders
Milica Radisic
Gordana Vunjak-Novakovic

Selected products
Cardiac Biowire™ II
AngioChip*

µOrgano



Scientific founders
Kevin Healy

Selected products
µOrgano

EHT
Technologies



Scientific founders
Thomas Eschenhagen

Selected products
Engineered Heart
Tissue (EHT)

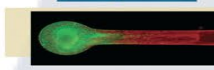
myriamed



Scientific founders
Wolfram-Hubertus
Zimmermann

Selected products
3D Cardiac Systems

AxoSim



Scientific founders
Michael Moore

Selected products
Nerve-on-a-Chip™

xona
MICROFLUIDICS



Scientific founders
Noo Li Jeon
Carl W. Cotman
Anne Taylor

Selected products
Standard /
Triple Chamber
Neuron Device

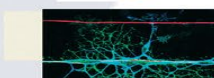
MicroBrain BT



Scientific founders
Bernadette Bung

Selected products
Neuronal Diode

Jananda™



Scientific founders
Margaret Magdesian

Selected products
Neuro Device

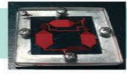


National Center
for Advancing
Translational Sciences

Commercial Activities around Tissue/Organ-on-chip Technologies

Body on-a-Chip

Hesperos®

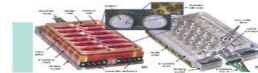


Scientific founders
Michael Shuler
James Hickman

Selected products

Multi-Organ Chip
(2, 4 organs)
(5-10 organs)*

cnBio
innovations



Scientific founders
Linda G Griffith

Selected products

LiverChip®
LiverChip® 36

TISSUSE
Emulating Human Biology



Scientific founders
Uwe Marx

2-Organ-Chip (2-OC)
4-Organ-Chip (4-OC)
Human-on-a-Chip
(HoC)*

DRAPER



Scientific founders
Joseph Charest

Microphysiological
Systems

Tissue interface on-a-Chip

emulate
AlveoliX
In-vitro models inspired by nature



Parenchymal tis

Hepregen

organovo™

Aspect
biosystems

insphero

3D Biomatrix™
Three-Dimensional Cell Culture

Hμ HμREL
CORPORATION

KIYATEC®

VAXDESIGN

- NIH supports a number of spinoff and startup organoid and tissue chip companies
- At least 30 companies providing CRO-like services and/or selling a variety of tissue chip platforms and consumables
- Global Organ On Chip market is projected to reach \$601.6 million by 2028 from an estimated \$80 million in 2022, at a CAGR of 39.9% during 2023 and 2028



Scientific founders
Jens M. Keim
Wolfgang Moritz

3D insight™ Tumor

synGene

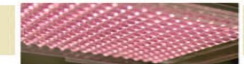
AxoSim



Scientific founders
Zimmermann

Michael Moore

3D Cardiac Systems



Scientific founders
Nicholas Kotov

PERFECTA3D®
HANGING DROP
PLATES

xona
MICROFLUIDICS



Scientific founders
Noo Li Jeon
Carl W. Cotman
Anne Taylor

Nerve-on-a-Chip™



Scientific founders
Greg Baxter
Robert Freedman

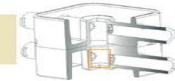
HμRELhuman™
HμRELflux™
HμRELTox™
HμRELflow™

Micr-Brain BT



Scientific founders
Bernadette Bung

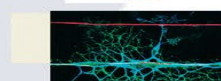
Standard /
Triple Chamber
Neuron Device



Scientific founders
Matthew R. Gevaert

3DKUBE™

Jananda™



Scientific founders
Margaret Magdesian

Neuronal Diode

Neuro Device

Scientific founders
William L. Warren

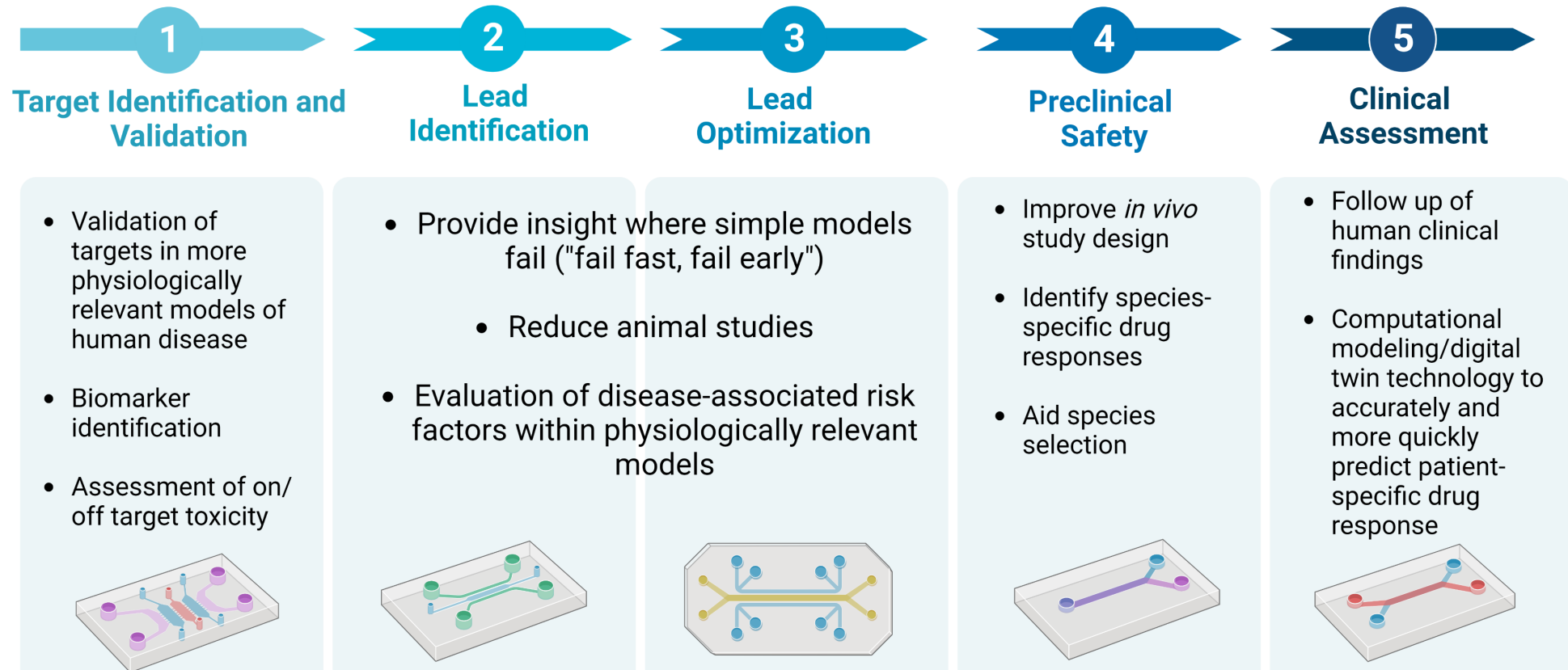
MIMIC® Technology



Tissue Chip Applications and Impact in Pharmaceutical Drug Development

A recent survey of 15 pharmaceutical experts forecast that within 5 years, **tissue chips would save between 10% and 26%** of drug development R&D cost.

Drug Discovery Today
24:1720–1724 (2019)



Adapted from *Nature Reviews Drug Discovery*, Low et al. 2020



NIH National Center for Advancing Translational Sciences

Engaging Next Generation Scientists and Engineers

- ✓ Global harmonization of regulatory use and standardization of platforms – MPS World Summit
- ✓ Train next generation of MPS scientists – International MPS Society



MPS WORLD SUMMIT

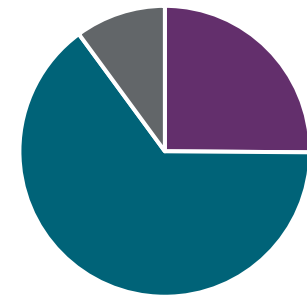
CONNECT, EXCHANGE, EDUCATE

2022 New Orleans, LA, USA
2023 Berlin, Germany (June 26-30)
2024 Seattle, WA USA
2025 ?

<https://mpsworldsummit.com/>

- 22 domestic travel awards for students and postdocs
- 13 International travel awards for students and postdocs
- 8 Best Poster and 7 Oral Awards

Inaugural Attendees
665 Total – 107 Trainees



■ Europe & Africa ■ Americas ■ Austrolasia ■



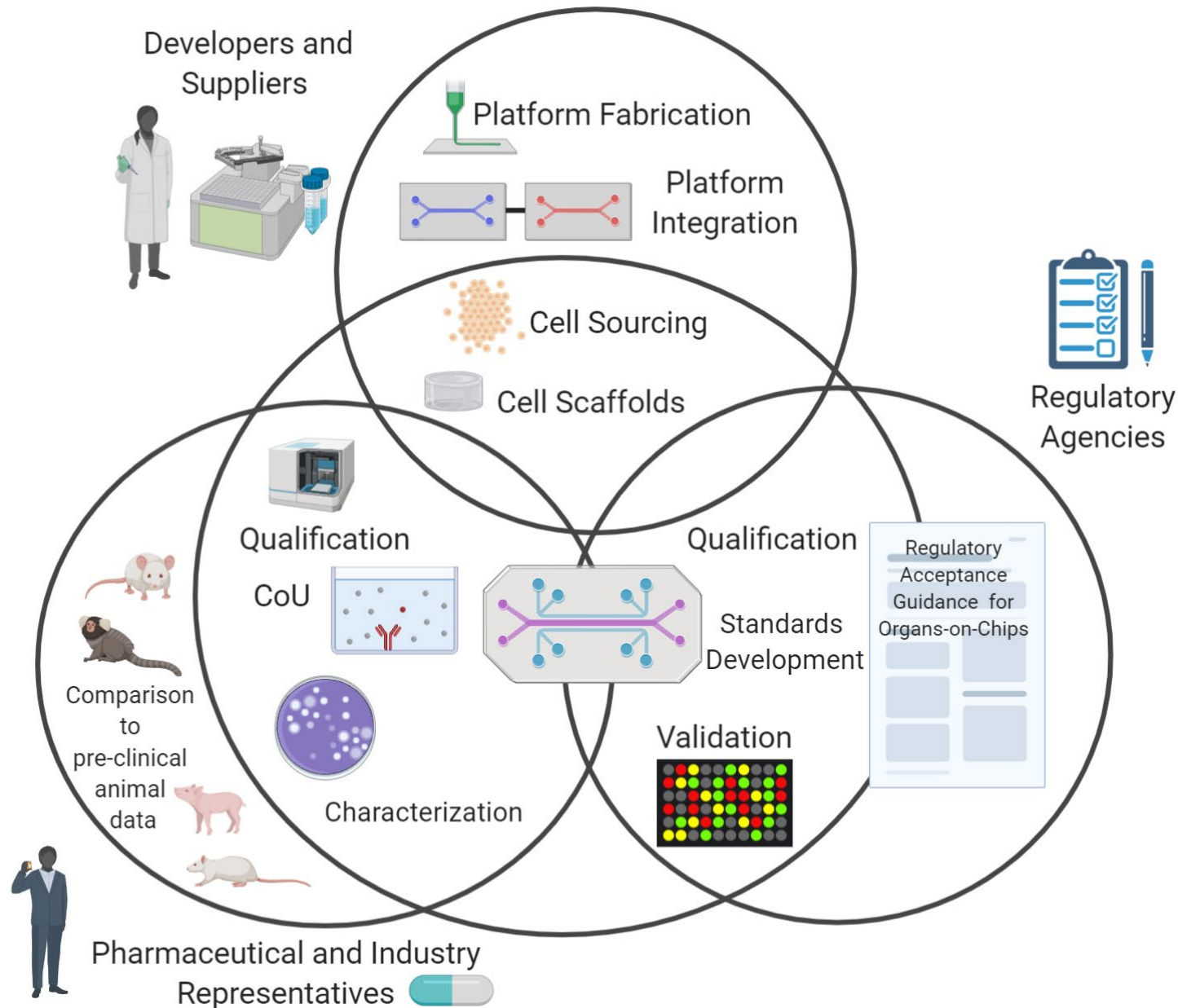
INTERNATIONAL MPS SOCIETY
CONNECT, EXCHANGE, EDUCATE

<https://impss.org/>



National Center
for Advancing
Translational Sciences

Summary of Tissue Chips Program



- ✓ Demonstration and validation for tox & safety studies
- ✓ Establishment of Testing Centers and Database Center
- ✓ Demonstration and validation for rare and common disease modeling and efficacy studies
- ✓ Clinical Trials on Chips
- ✓ Adoption and use by pharma in drug development
- ✓ Global harmonization for regulatory use and standardization of platforms – MPS World Summit
- ✓ Train next generation of MPS scientists – International MPS Society
- Regulatory qualification as drug development tools – Translational Centers for MPS



- FDA
- International Space Station – National Lab
- Center for Advancement of Science in Space
- NASA
- IQ Consortium MPS Affiliate
- BARDA, VA

Tissue Chips Consortium
Program Lead: Danilo A. Tagle

Program Officers:
Passley Hargrove-Grimes
Dmitriy Kripkey
Program Analyst:
Kris Sunderic

Trans-NIH MPS Working Group:

55 Program Officers from NCATS, NCI, NHLBI, NIA, NIAID, NIAMS, NIBIB, NICHD, NIDA, NIDCR, NIDCD, NIDDK, NEI, NIEHS, NIMH, NINDS, ORWH/OD

