Transforming Research, Transforming the Future: The New Role of Organ-on-a-Chip in Herbal and Pharmaceutical Sciences

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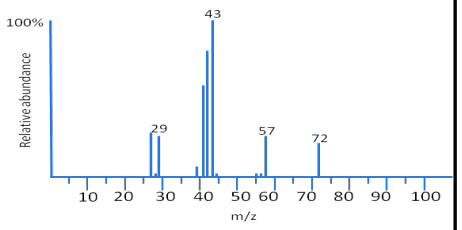
Oct 1st, 2025

Chakri Naruebodindra Medical Institute (CNMI)

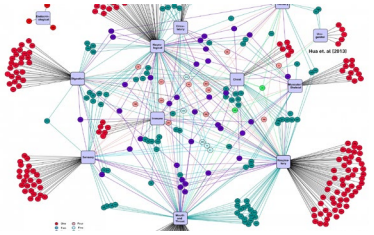
- Interactions b/t preclinical scientists and clinicians
- Biomedical research facilities
- Stem Cell & Cellular Therapy Center

Well equipped molecular and cellular biology lab

Advanced Microscopy Capability



Mass spec/analytical



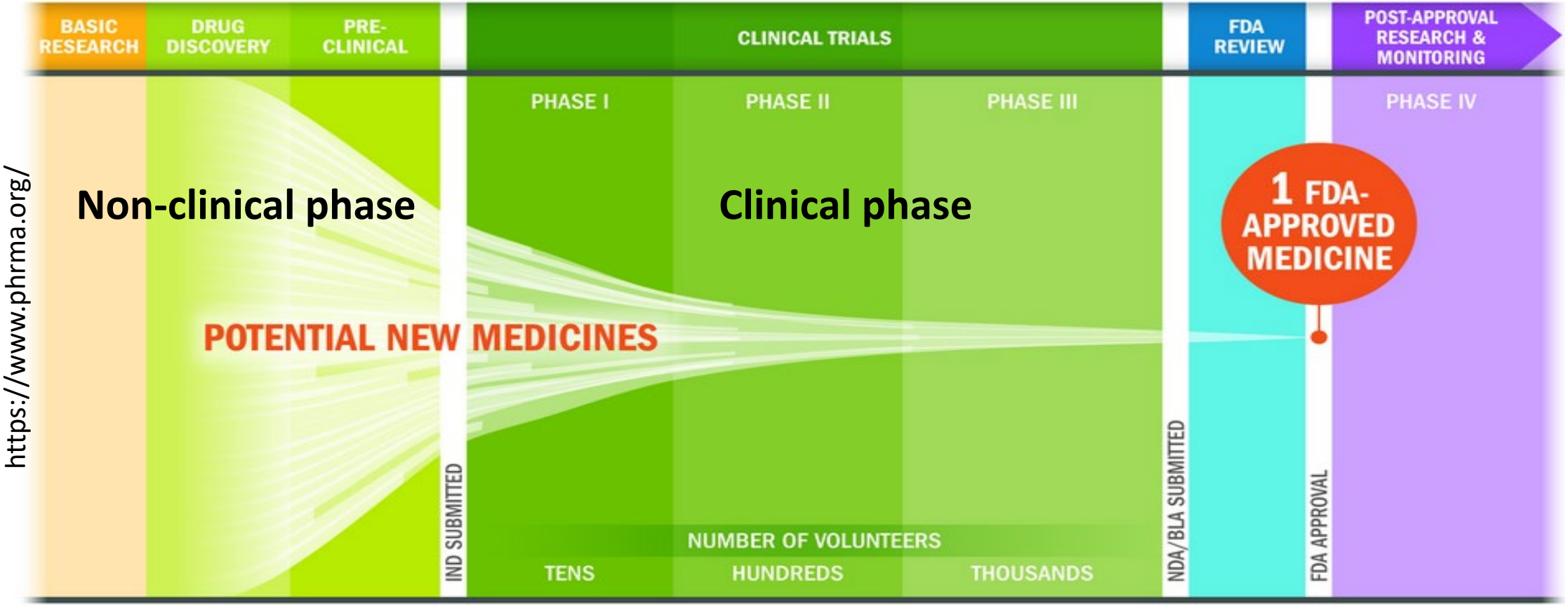
Bioinformatics/ System biology

Outlines

1. Introduction/objective/Significance
2. What's an organ-on-a-chip? Why is it important?
3. US FDA Modernization Act 2.0/ 3.0
4. An organ-on-a-chip technology and its application
5. Success cases for IND filing using an organ-on-a-chip
6. Perspective within the Thai context: Nutraceutical/herbal product development
7. An-organ-on-a-chip models available in our lab

Dilemma in Drug Development Process

https://www.phrma.org/



- The current drug development is a costly and very long process.
- The failure rate could be as high as 100%.

How bad drugs fail in clinical trials and why?

Examples:

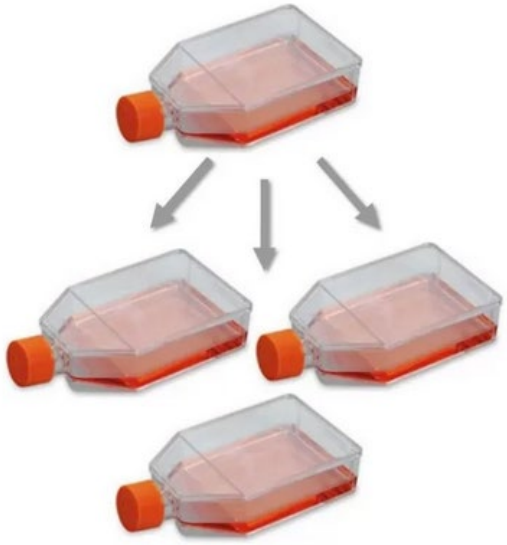
- 97% for cancer drug
- 99% for Alzheimer's disease

Critical problems:

- Approximately 60% of failures are due to unacceptable toxicity and insufficient efficacy.
- Limited predictability of conventional 2D cell cultures and animal models.

Patrick NG, et al. Curr Opin Toxicol. 2019

Non-Clinical Studies with 2D Cell Cultures and Animal Models



2D Cultures

Animal Models

Limitations of Current Non-Clinical Models

2D conventional cell cultures	Animal models
-Lack the physiological contexts: ➢ Tissue architecture ➢ Exposure to shear stress ➢ Interactions between cells and cells with the extracellular matrix -Fail to adequately emulate responses to a drug.	-Time-consuming; high cost -Do not adequately represent human disease -Often fail to predict the results in human -Ethical concerns

New ways to improve the drug development process

Modernizing Non-Clinical Drug Screening

Congress passed the FDA Modernization Act 2.0 in Dec 2022, removing the requirement to use animal testing in drug development. This will allow drug companies the option to use alternative safety-testing models when making new drug submissions

Initiatives for Phasing Out Animal Use

U.S. FOOD & DRUG ADMINISTRATION

Home / News & Events / FDA Newsroom / Press Announcements / FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodi

FDA NEWS RELEASE

FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs

FDA

Roadmap to Reducing Animal Testing in Preclinical Safety Studies

NIH National Institutes of Health
Turning Discovery Into Health

Health Information | Grants & Funding | News & Events | Research & Training

Home » News & Events » News Releases

NEWS RELEASES

Tuesday, April 29, 2025

NIH to prioritize human-based research technologies

New initiative aims to reduce use of animals in NIH-funded research.

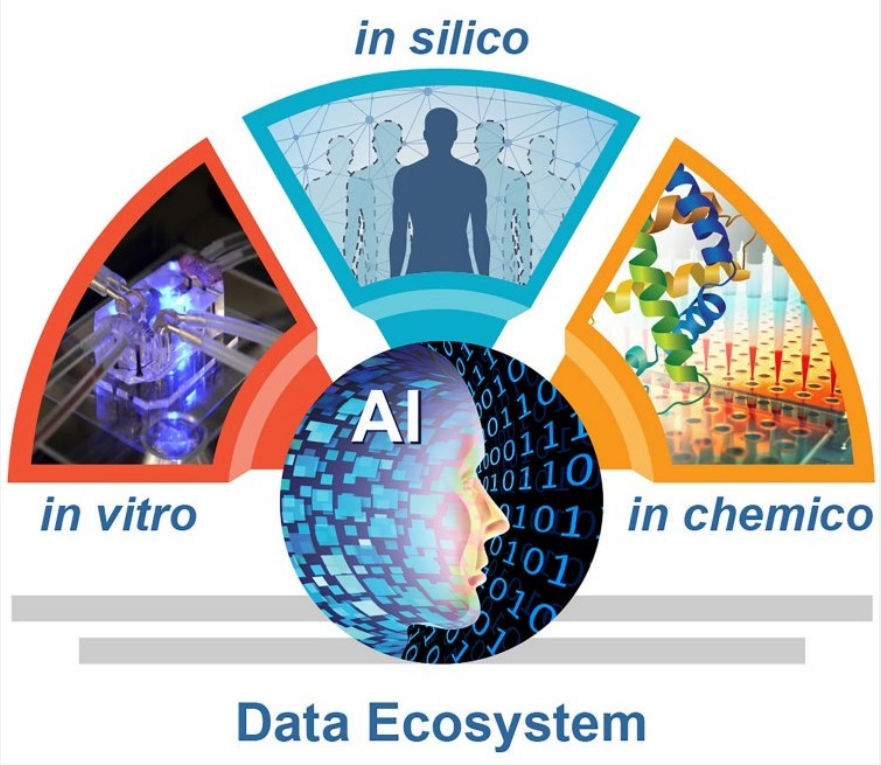
EU roadmap for phasing out animal testing for chemical safety assessments: Recommendations from a multi-stakeholder roundtable

ALTEX, Mar 26, 2025

Examples of Tools to Improve Non-clinical Testing

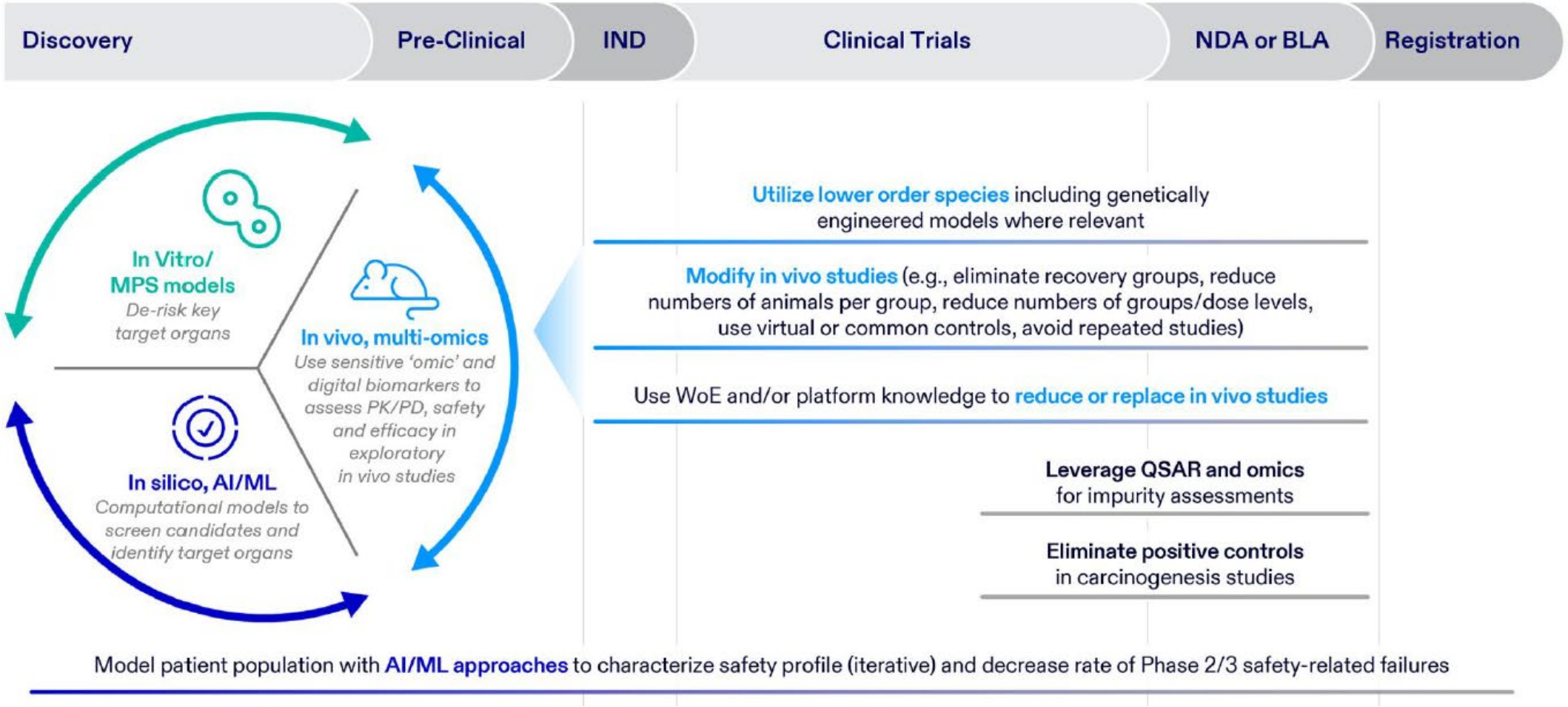
New approach methodologies (NAMs)

- *In vitro*: cell or tissue experiments
- *In silico*: computer simulations and modeling
- *In chemico*: biochemical assays



https://ncats.nih.gov

NAMs to facilitate the FDA Modernization Acts



Sarah A. Carratt, et al. *Toxicological Sciences*, 2025

Why we need better *in vitro* models?

Toxic Concentrations (µM) *in vivo* and *in vitro*

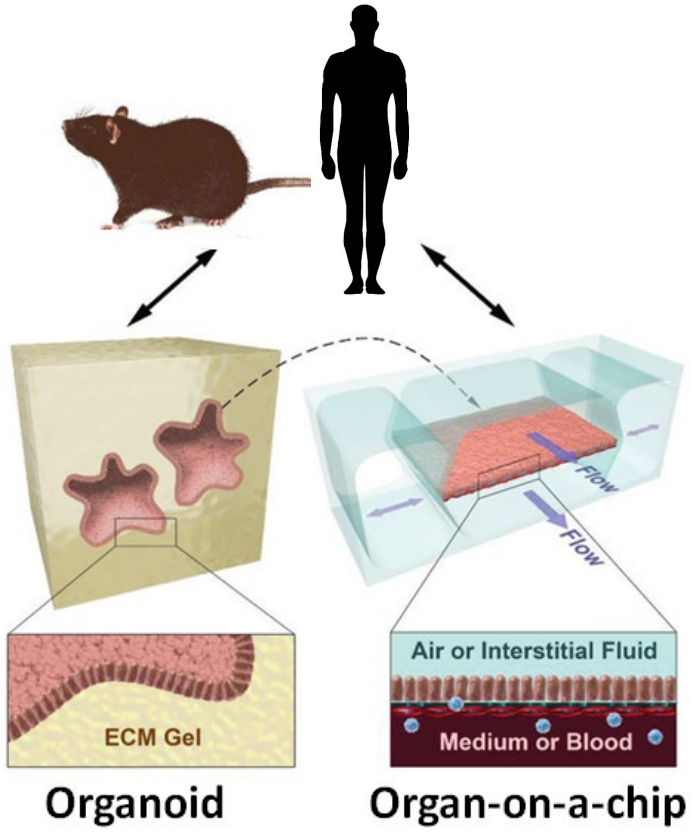
Drug	Plasma Concentration (Rat In Vivo)	2D Hepatocytes	3D Hepatocytes	Reference
Azathioprine	1	1	1	Wu et al., 2006
Chloroquine	2.5	5	2.5	Shen et al., 2008
Clozapine	4	30	5	Lu et al., 2008
Amiodarone	5.4	10	5	Shen et al., 2008
Rifampicin	12	600	12	Shen et al., 2008
Tetracycline	26	100	25	Shen et al., 2008
Isoniazid	30	1100	33	Shen et al., 2006

(Q. Meng ,Zhejiang Zhejiang University CHI)

https://www.ema.europa.eu

Advanced 3D *in vitro* Models for Drug Testing

❖ Complex *in vitro* models (CIVMs): Organoid and Organ-on-a-chip



Modified from Ingber DE. Adv Sci (Weinh). 2020

Organoid

- Self-renewing stem cells
- Self-organized
- Recreating 3D tissue-like structures and functions
- Valuable tools for studying cellular mechanisms of diseases

Limitations:

- Lack tissue-tissue interfaces, vascular flow and circulating immune cells
- Hard to measure nutrient transport and absorption or sampling contents of the internal lumen
- Little control over cell subtypes and location

Ingber DE. Adv Sci (Weinh). 2020; Low LA. Nat Rev Drug Discov. 2021

An Organ-on-a-Chip: Microphysiological system (MPS)

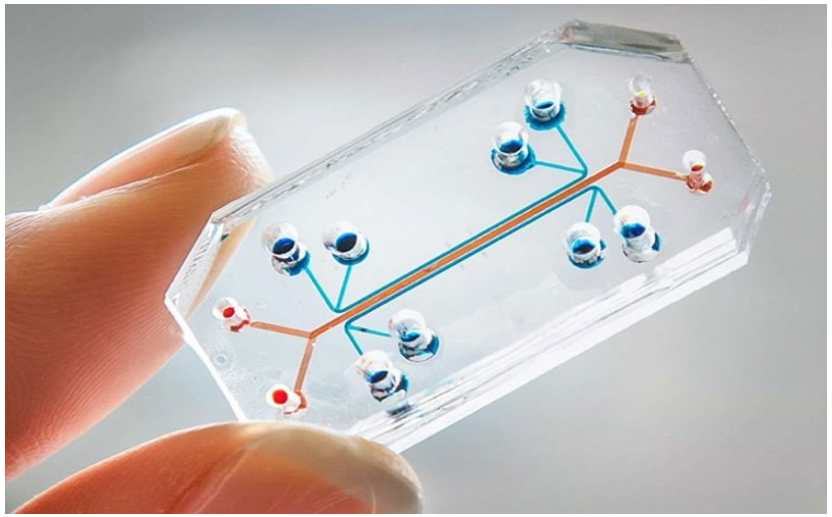
Complex *in vitro* models (CIVMs): Organoid and Organ-on-a-chip

Organ-on-a-chip

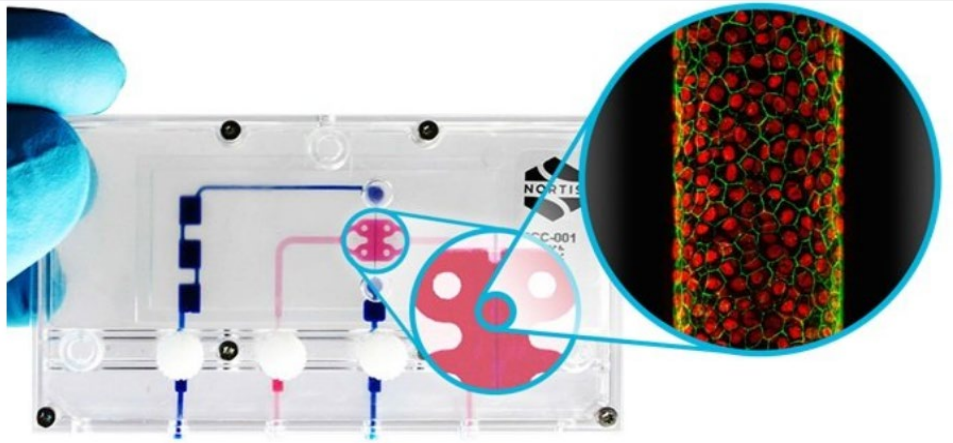
- Engineered 3D tissues with dynamic fluid flow
- Shown to replicate key aspects of human organs physiology and tissue microenvironment
- Allowing high levels of control over cell type and placement
- Allowing integration of circulating immune cells/co-culture with other cell types

Limitations:

- Cannot recapitulate functions of human tissue completely
- Reproducibility
- Difficult to use
- Low-medium throughput



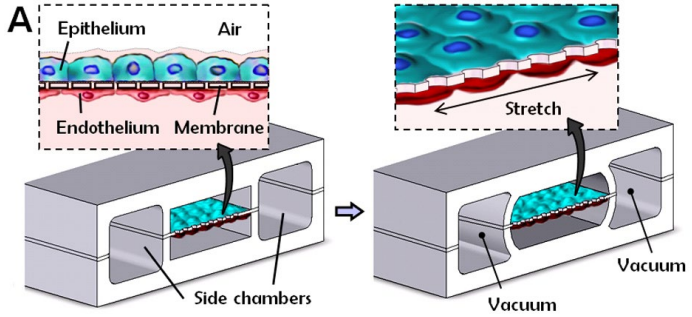
https://wyss.harvard.edu



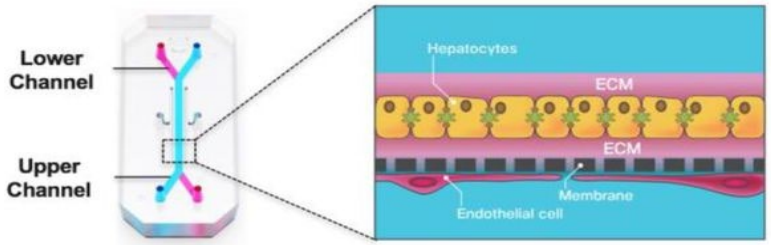
https://nortisbio.com/

Ingber DE. Adv Sci (Weinh). 2020; Low LA. Nat Rev Drug Discov. 2021

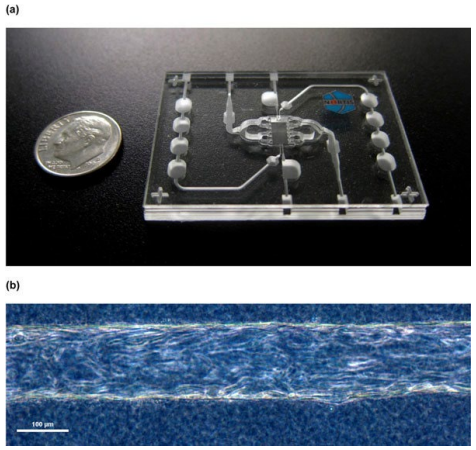
What are organ-on-a-chip models out there?



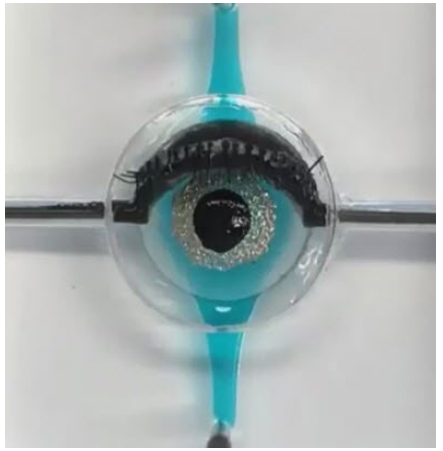
Lung-on-a-chip



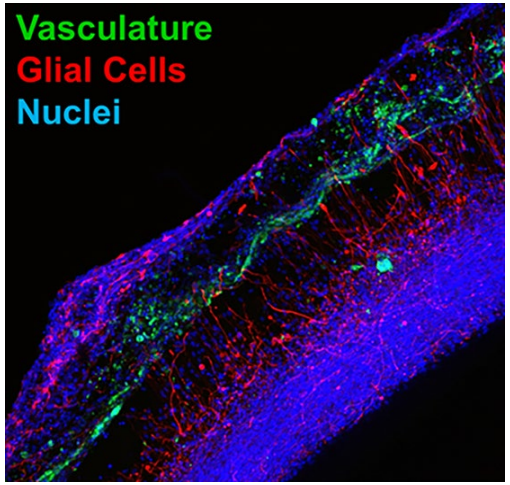
Liver-on-a-chip



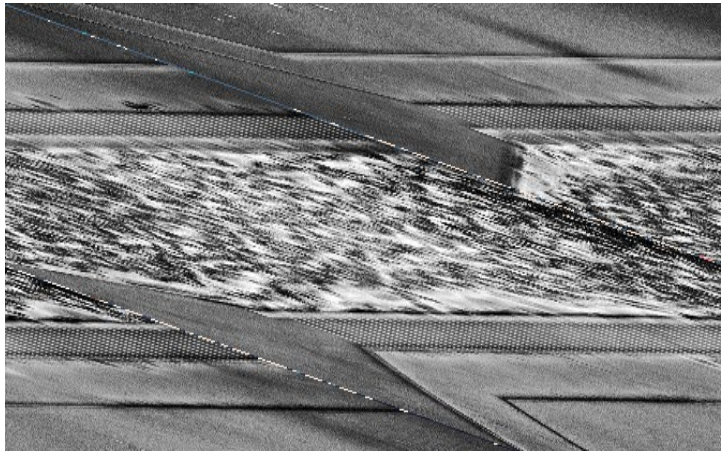
Kidney-on-a-chip



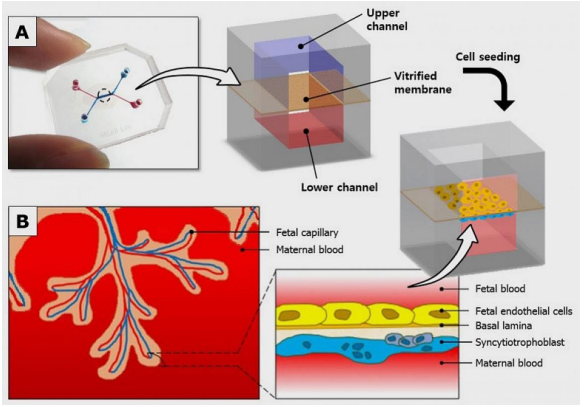
Eye-on-a-chip



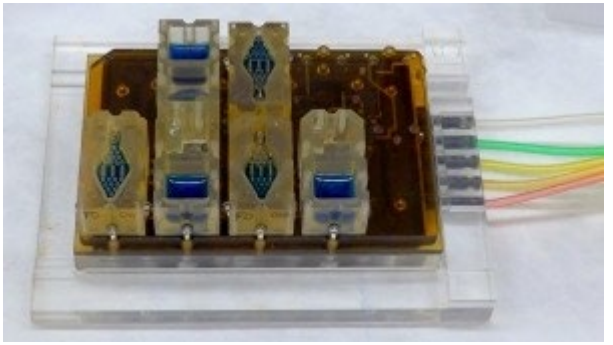
Brain-on-a-chip



Heart-on-a-chip



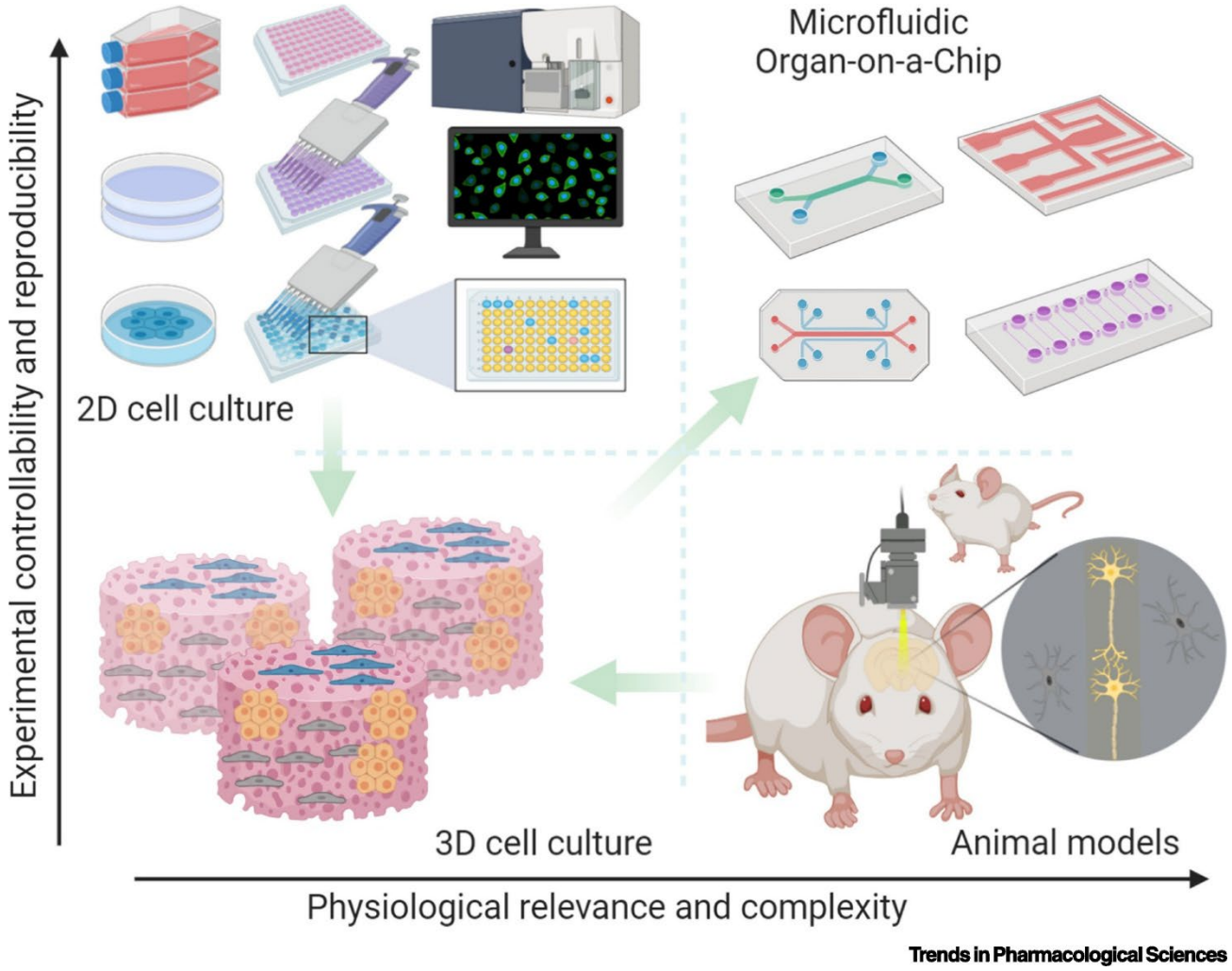
Placenta-on-a-chip



Menstrual cycle-on-a-chip

https://ncats.nih.gov/tissuechip/projects; Ingber DE. Adv Sci (Weinh). 2020; Kelly EJ, et al. Stem Cell Res Ther. 2013; Seo J, et al. Nature Medicine, 2019; Low LA. Nat Rev Drug Discov. 2021; https://www.nih.gov/news-events, Xiao S, et al. Nat Commun 2017.

An Organ-on-a-chip: A New Paradigm for Drug Development



- Enables precise control of cell culture within a physiologically relevant microenvironment
- Offers 3D microarchitecture for systematically interrogating human biology
- Prolonged culture time allows for chronic testing assays

(Chao Ma, et al. Trends in Pharmacological Sciences, 2021)

Success cases for IND filing using an organ-on-a-chip

WYSS INSTITUTE Who We Are Our Work

Fighting viruses is as easy as breathing

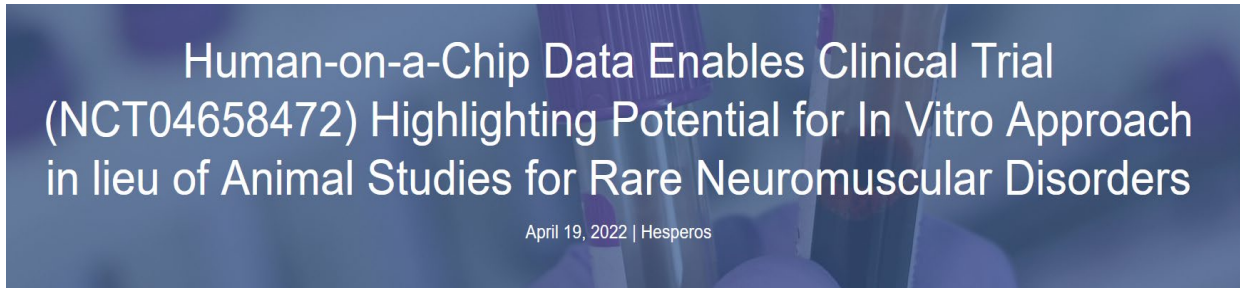
April 8, 2022

Human Lung Chip reveals the effects of breathing motions on lung immune responses and leads to repurposing of potential therapeutics for respiratory diseases, including COVID-19

"the Wyss Institute's Human Alveolus Chip were included in Cantex Pharmaceuticals' Investigational New Drug (IND) application to the FDA to initiate Phase 2 clinical trials"

https://wyss.harvard.edu/technology/human-organs-on-chips/

https://www.mimetas.com/en/news/819/mimetas-contributes-with-human-organ-on-chip-data-to-ind-application-by-argenx.html



https://hesperosinc.com/efficacy-study-for-rare-neuromuscular-disorders/

Other potential applications of an organ-on-a-chip

Drug development

- Target organ toxicity
- Efficacy testing
- Directional transport
- Drug pharmacokinetics and pharmacodynamics across tissues

Herbal/Nutraceutical products

Toxic metabolites in diseases

Pollutants: PM2.5, microplastics

Tools, environmental and biowarfare models

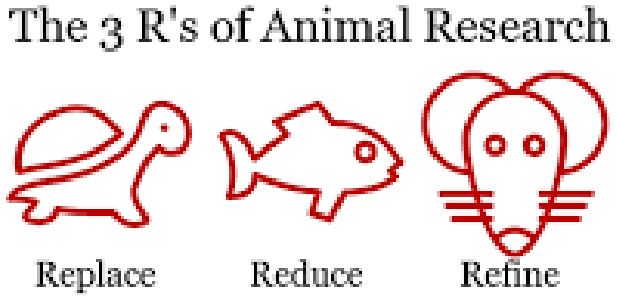
- Diagnostics
- Microgravity
- Bio-weapons/Radiation

https://www.nasa.gov/tissue-chips

NIH National Center for Advancing Translational Sciences

Personalized Medicine

Cosmetics testing



(https://publichealth.jhu.edu)

(Low LA. Nat Rev Drug Discov. 2021)

Roadblocks of an Organ-on-a-Chip dissemination

Technical challenges

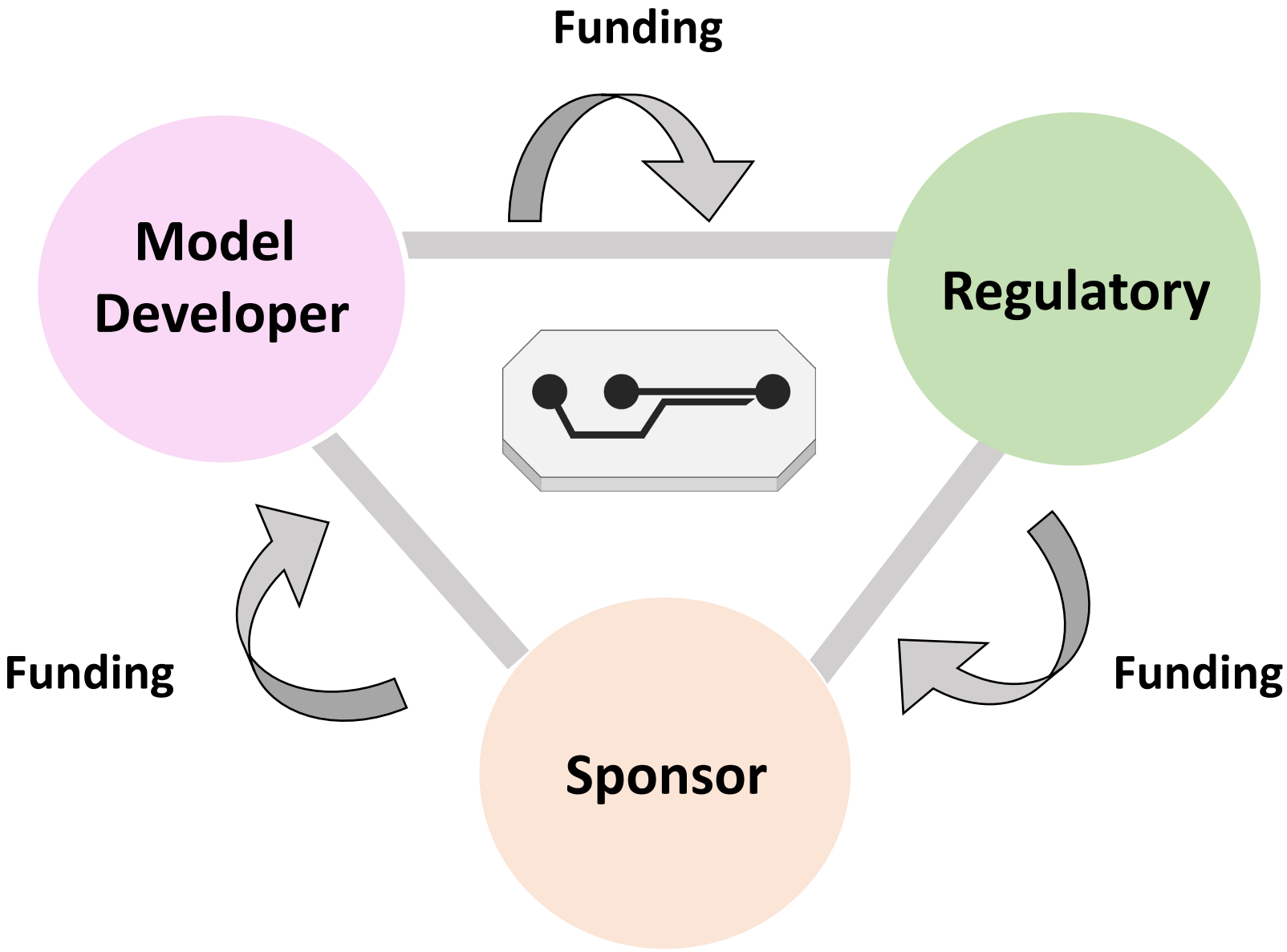
- Cannot recapitulate functions of human tissue completely
- Reproducibility
- Difficult to use
- Lack of model validation

Pathways to adoption

- Translational relevance in comparison to other models
- Define “Context of use”
- Collaboration b/t stakeholders: engineers, biologists, industries, funding agencies, and regulatory bodies

(Alver CG. Nat Commun. 2024)

Interactions between different stakeholders



The Use of OOC in the Thai Context: a Perspective

❖Functional Food, Herbal and Nutraceutical industry

1. Provide safety and pharmacological evidence to support the development of functional food, herbal and nutraceutical products.
2. Enhance translational relevance to human outcomes.
3. Reduce and refine animal studies.

Suggested Applications in Herbal/Nutraceutical Product Development

Kidney OOC

- Nutraceutical-induced nephrotoxicity (e.g. cellular viability and renal biomarkers)
- Renal transport, filtration, and reabsorption

Liver OOC

- Nutraceutical metabolism and hepatotoxicity
- Efficacy (e.g. fatty liver)

Gut OOC

- Gastrointestinal toxicity (e.g. cellular viability, barrier integrity, and inflammation markers)
- Nutraceutical compounds' absorption and bioavailability

BBB OOC

- Neurotoxicity, neurotransmitter release, and neuronal activity
- The impact of nutraceuticals on the integrity and permeability

Farooqi MA, et al. ACS Omega 2023

OOC = an organ-on-a-chip

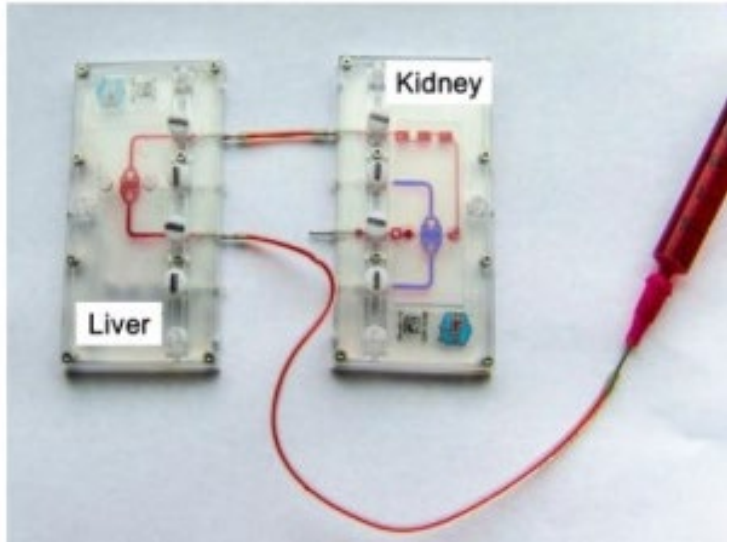
Example Studies

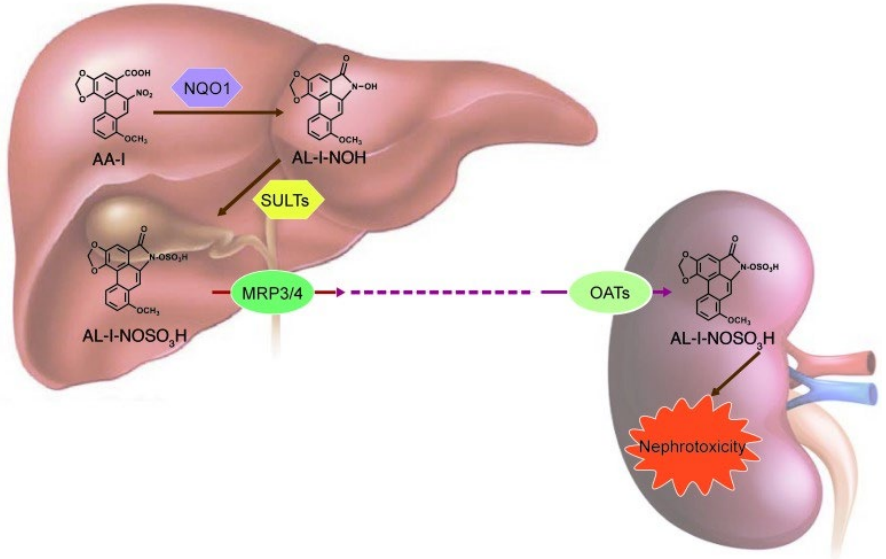
JCI insight

Published by The American Society for Clinical Investigation | Founded 1908

▸ JCI Insight. 2017 Nov 16;2(22):e95978. doi: 10.1172/jci.insight.95978

Human liver-kidney model elucidates the mechanisms of aristolochic acid nephrotoxicity



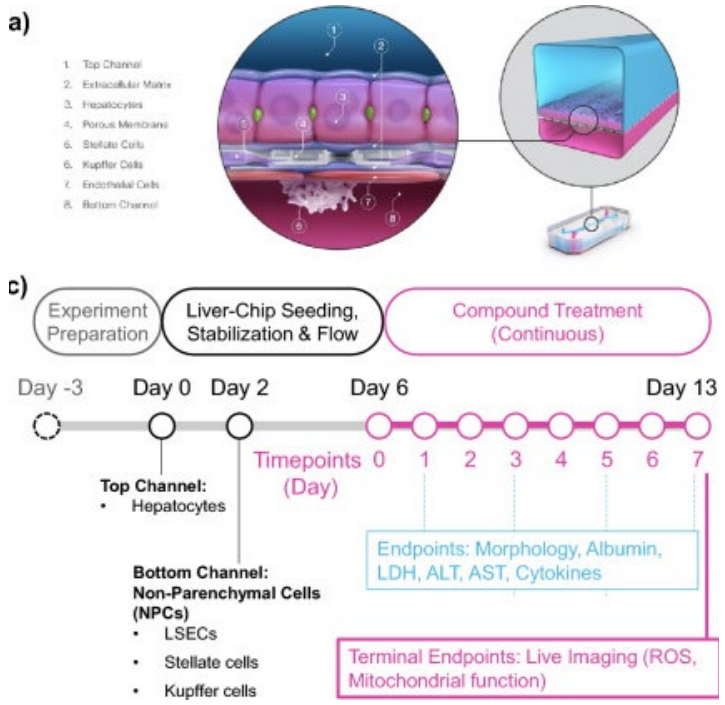


Example Studies

SCIENTIFIC REPORTS
nature research

▸ Sci Rep. 2025 Aug 1;15:28132. doi: 10.1038/s41598-025-12846-2

Hepatotoxicity evaluation of cannabidiol, cannabinol, cannabichromene and cannabigerol using a human quad culture liver chip



Our Research Focus

Establishing 3D organ models using microfluidic devices (an-organ-on-a-chip) aimed to build capabilities of new drug/compound testing platform

Pimonrat, PhD

- **3D human microvessel chip**

Kenjiro, PhD

- **3D Human Liver Chip**

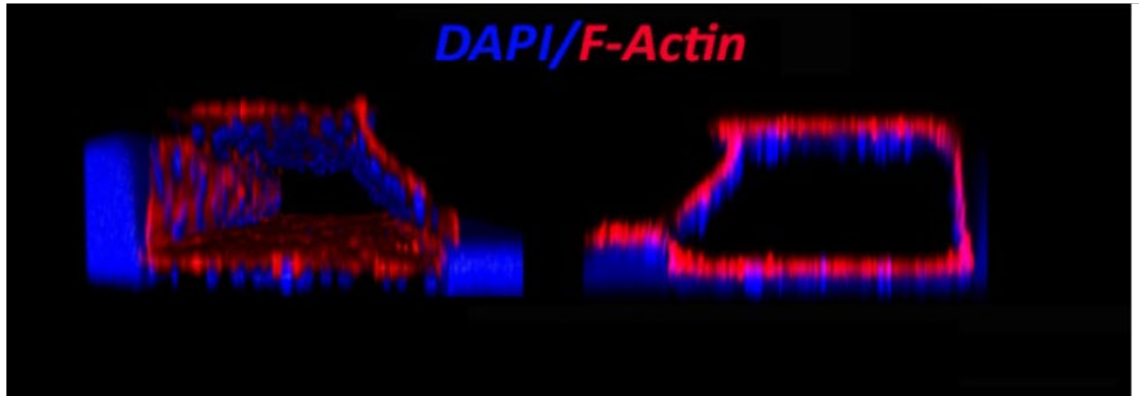
What do we do in our lab?

1. Develop and qualify the human microvessel- and liver-on-a-chip models

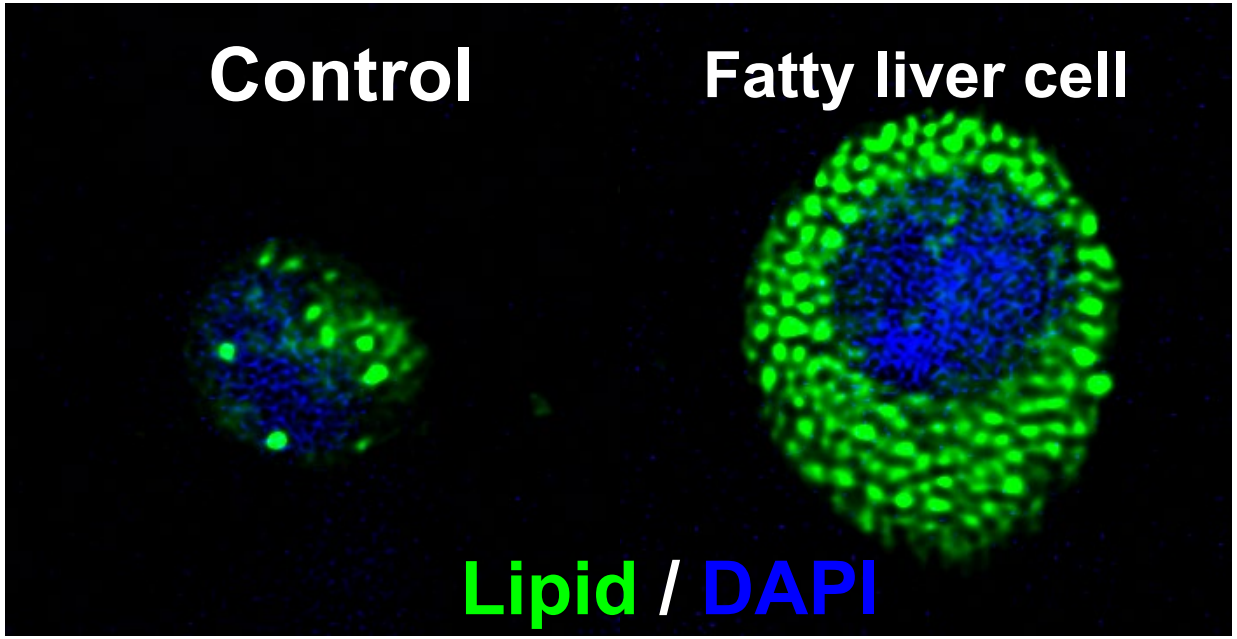
2. Utilize the validated organ-on-a-chip models for drug/compound testing

Our Current Organ-on-a-Chip Models

Human Microvessel



Human Liver



Wiriyakulsit N, et al. Sci Rep. 2023;13(1):17019
Mankhong S, et al. Sci Rep. 2024;14(1):18553
Den-Udom, T, et al. Heliyon 2025; 11(10): e43397

OOC Applications Available in Our Lab

Human Microvessel OOC

- Endothelial viability
- Endothelial toxicity
- Cytokine release
- Vascular Permeability
- Monocyte adhesion

Human Liver OOC

- Hepatocyte viability
- Hepatotoxicity
- Liver function test (i.e. albumin and urea production)
- Fatty liver

Lab members

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Anunyaporn Phungsom
PhD student

Htun Aung Kyaw
Msc student

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Mintra Kwathai
RA

Thank you for your attention

Q&A