Evolution of Organ-on-a-Chip Technology: A Developer's Journey

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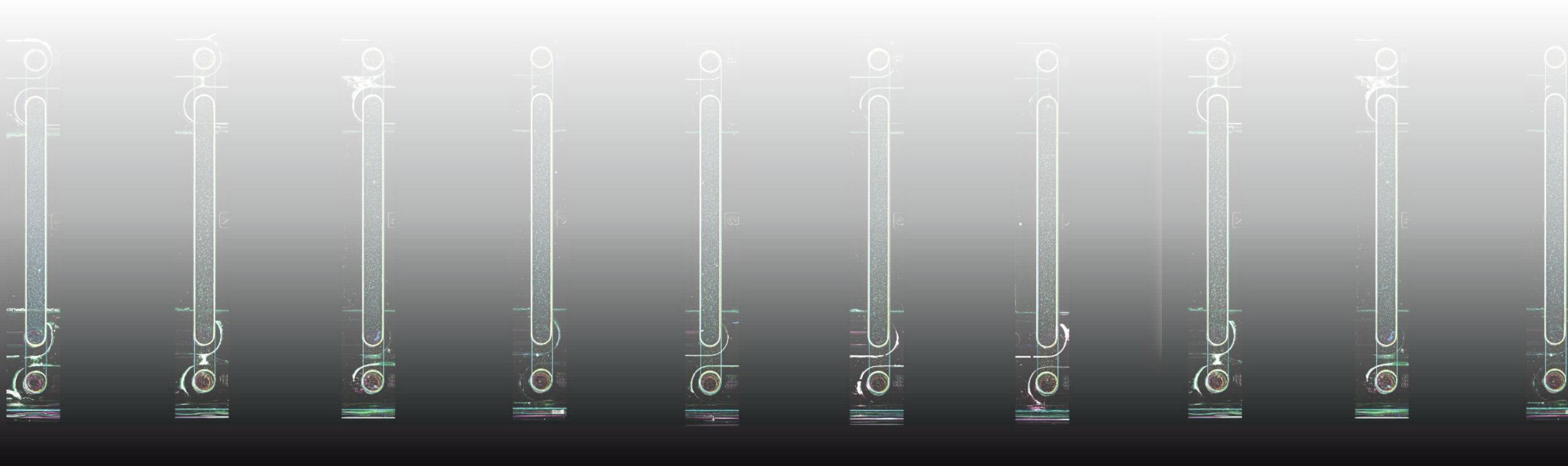
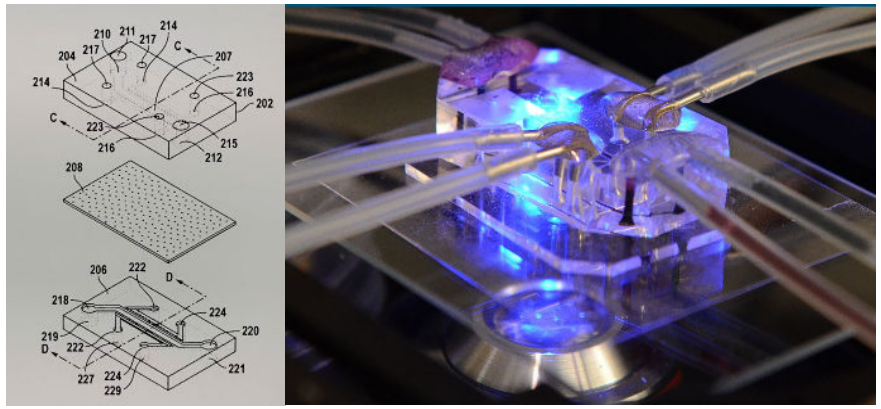
05 March 2026



Transition From Academia to Tangible Industrial Application

Over 30 Organ-Chip models developed with human relevance

WYSS INSTITUTE



Huh et al., 2010 doi: 10.1126/science.1188302

- Syringe pump within incubator
- Separate vacuum module
- Custom tubing setup for each experiment
- Supports small-scale studies, typically 6 Chips

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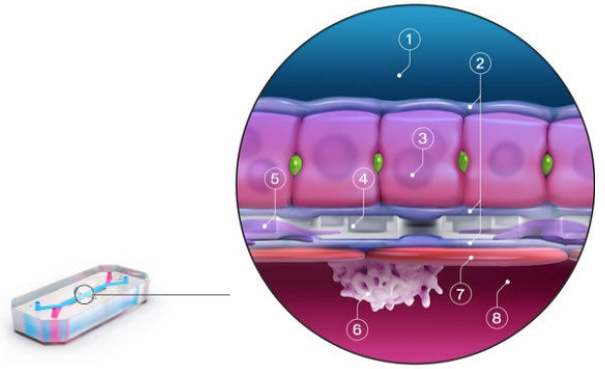
- Integrated instrumentation within incubator
- No tubing required
- Supports up to 12 Chips per instrument
- >600 instruments in labs across the globe

Demonstration of Biological Performance at Scale

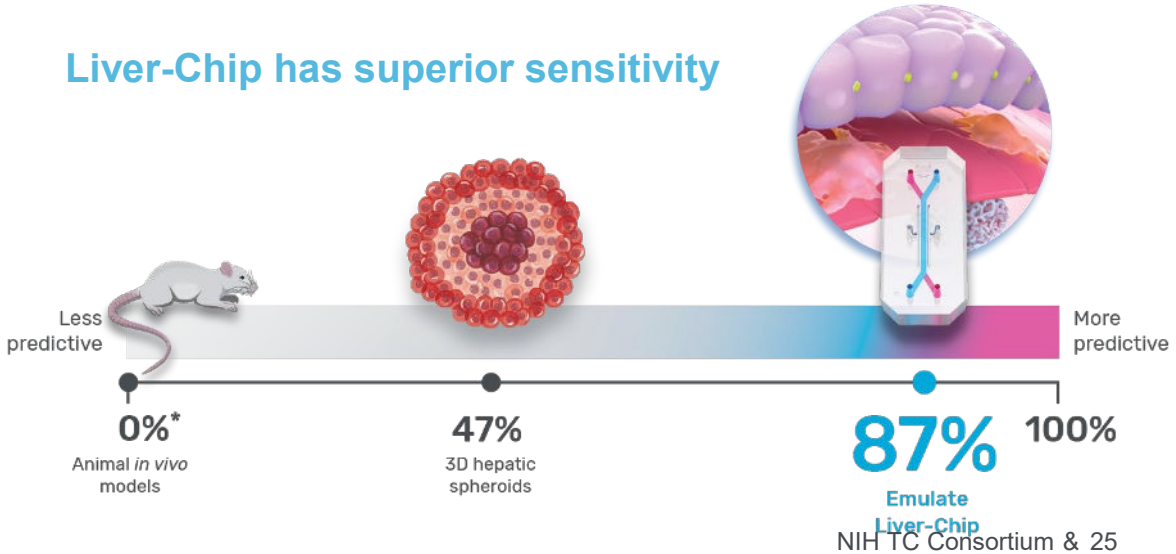
Liver-Chip as a predictive model for Drug Induced Liver Injury (DILI)

- Performance of 870 Liver-Chips[1] evaluated against industry guidelines[2]
- 22 small molecules (including structural analogs) with known clinical DILI tested at six concentrations
- Hepatotoxicity confirmed in three primary hepatocyte donors across multiple biochemical and imaging readouts
- Hepatotoxicity contextualized[3] against industry scale[4]
- Data facilitated acceptance of first organ-chip into FDA ISTAND qualification program



1. Epithelial channel
2. Extracellular matrix
3. Hepatocytes
4. Porous membrane
5. Stellate cells
6. Kupffer cells
7. Liver sinusoidal endothelial cells
8. Endothelial channel

Liver-Chip has superior sensitivity



[1]Ewart et al., 2022; [2]Baudy et al., 2020;[3]Levner & Ewart, 2023; [4]Garside et al., 2014)

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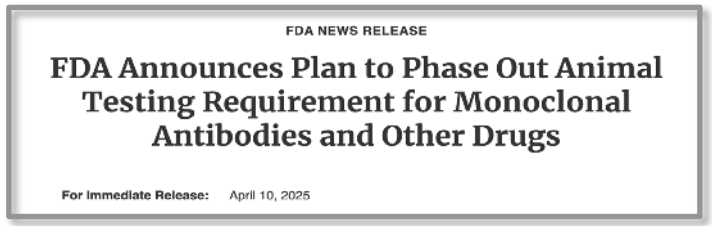
The Time is Now to Implement Routine Use

Unprecedented synchronicity of global regulatory changes in 2025



FDA NEWS RELEASE

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

For Immediate Release: April 10, 2025

NIH Funding Announcements to Align with NIH Initiative to Prioritize Human-based Research

July 10, 2025

On April 29, NIH announced it is prioritizing human-focused research and reducing animal use in research. To further this initiative, all new Notices of Funding Opportunity that relate to animal model systems (NOFOs) must now also support human-focused approaches such as clinical trials, real world data, or new approach methods (NAMs). Examples of NAMs include ex vivo human-based approaches, including perfused human organs and precision-

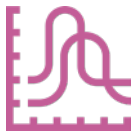
GOV·UK

Home > Business and industry > Science and innovation > Animal research and testing

Press release

Animal testing to be phased out faster as UK unveils roadmap for alternative methods

End-users cite operational obstacles still to be overcome



Reproducibility

- Within and across experiments and laboratories

Reliability

- Instrument, consumable, software and cells

Throughput

- Scale to improve quantity of data generated

Decision Making

- Use data to inform projects and regulatory submissions

Human Relevance at Scale is Achievable

Considerations to demonstrate reliability and reproducibility

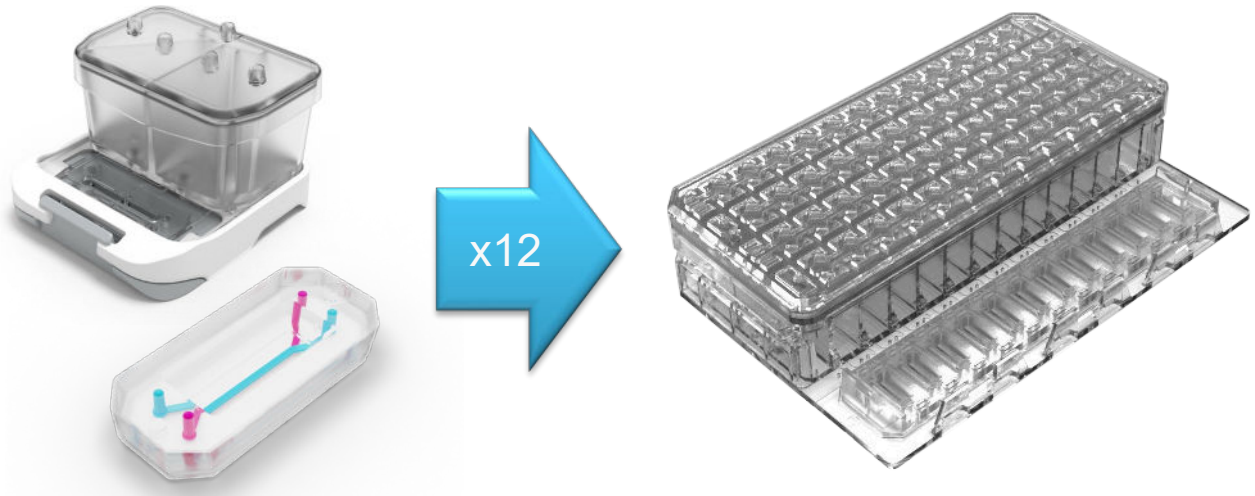
- **Accuracy and Sensitivity**
  - Positive and Negative Controls
  - Assay Limit of Quantification
- **Precision and Reproducibility**
  - Intra-Assay
  - Inter-Assay (different labs, instruments & scientists)
  - Coefficient of Variation
- **Statistical Validation**
  - Power analysis
- **Robustness**
  - Performance equivalent across instruments

Scaling Organ-Chips with Reproducible Execution

The AVA™ Emulation System

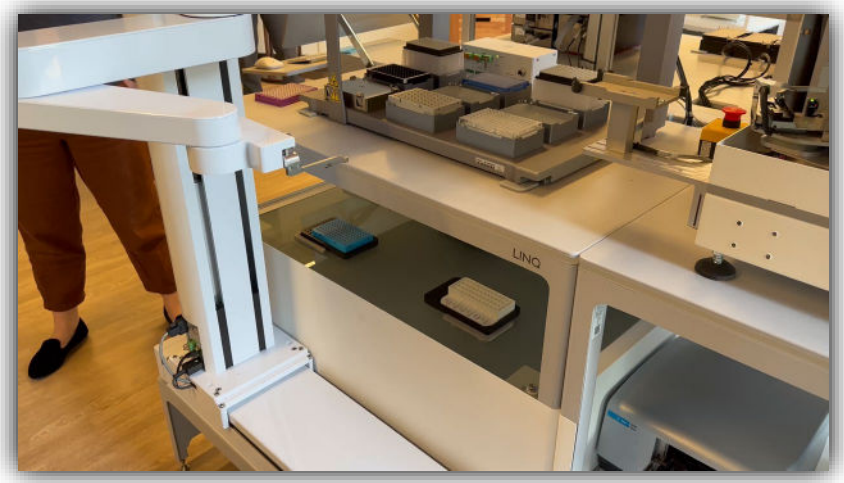
- Supports up to 96 independent Organ-Chip “Emulations” per run
- Benchtop instrument with environmental control
- Automated microscope captures phase contrast and 3-channel fluorescence throughout experiment
- Externally tested in academic and industrial laboratories to ensure instrument robustness and reliability as well as ease of implementation into lab workflows

Chip-Array is Designed for Automation and Data Scale



(Chip-R1 Rigid Chip + Pod) x 12 = Chip-Array

Chip-Array brings the low-drug-absorbing architecture of Chip-R1 Rigid Chip into a 12-Chip parallel configuration to accelerate throughput



Chip-Array consumable is SBS format and can be handled by a standard robotic arms and automated liquid handlers

Chip-Array is Designed for Automation and Data Scale

Experimentation Phase On Instrument

Endpoint Assays & Analysis

Experiment Day

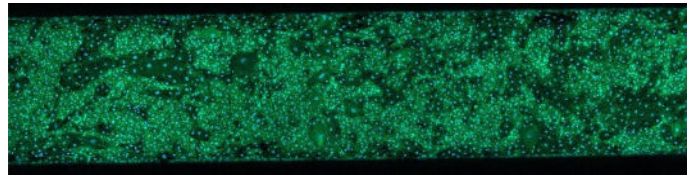
1 2 3 4 5 6 7 8

Post-takedown assays can generate millions of data points

Daily sampling and imaging provide valuable longitudinal data

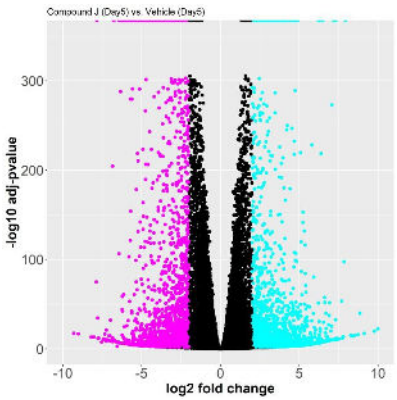
On-Chip

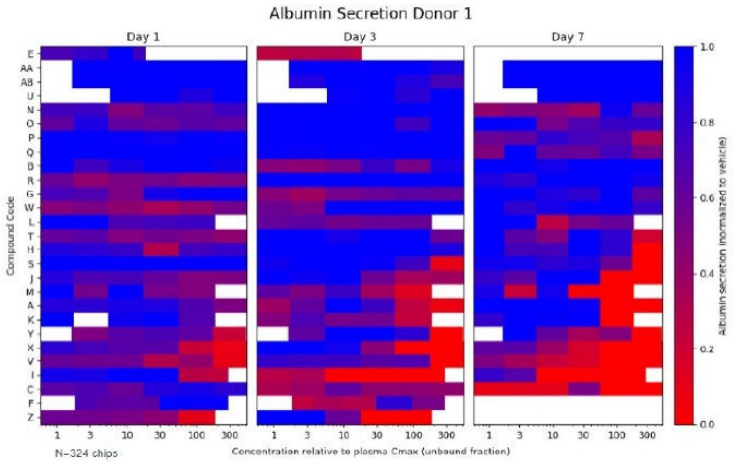
Quantitative Fluorescence Microscopy

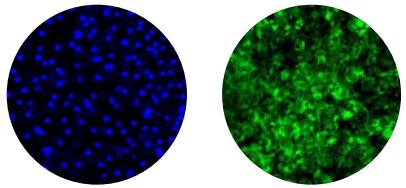


Off-Chip

Transcriptomics
Proteomics
Metabolomics

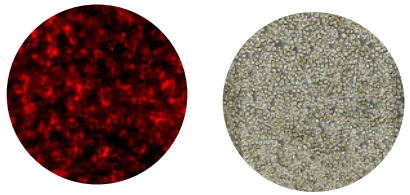






DAPI

FITC



Texas Red

Phase contrast

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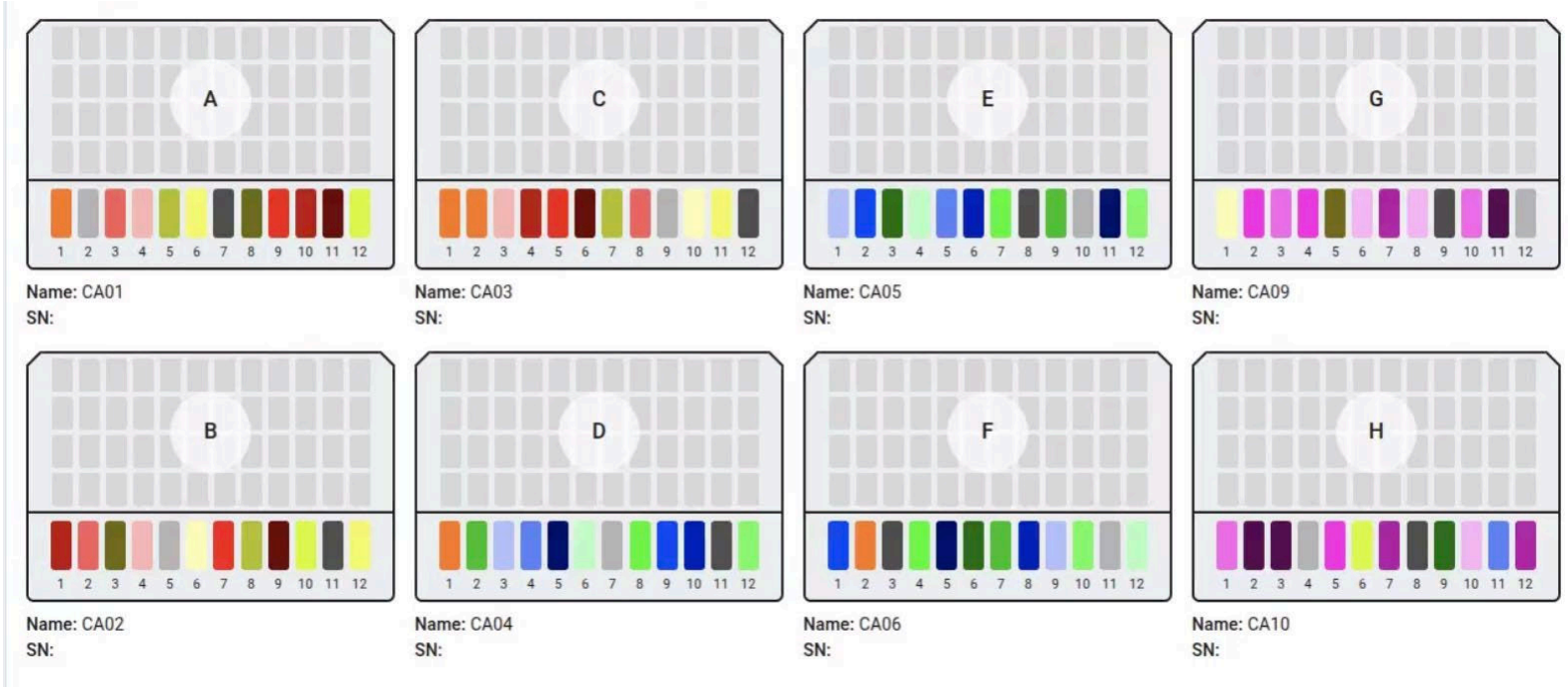
Thousands of daily on-chip data points plus millions of data points via omics endpoints enables multi-model AI training

Reproducing DILI Predictivity at Scale | Chip-Array Map



Chip-Array Key

- Vehicle (0.1% or **0.2%** DMSO) or blank
- Drugs (Acetaminophen, Clozapine, Olanzapine, Nefazadone, Buspirone)
- Concentration (low to high based on color intensity)

Importance of Randomization

- Minimizing systemic bias
  - Edge effects or instrument position
- Reduce experimental variability
  - Pipetting or handling effects
- Ensure statistical rigor
  - True replication and blocking confounding effects
- Improve reproducibility
  - Ensures findings replicated across labs

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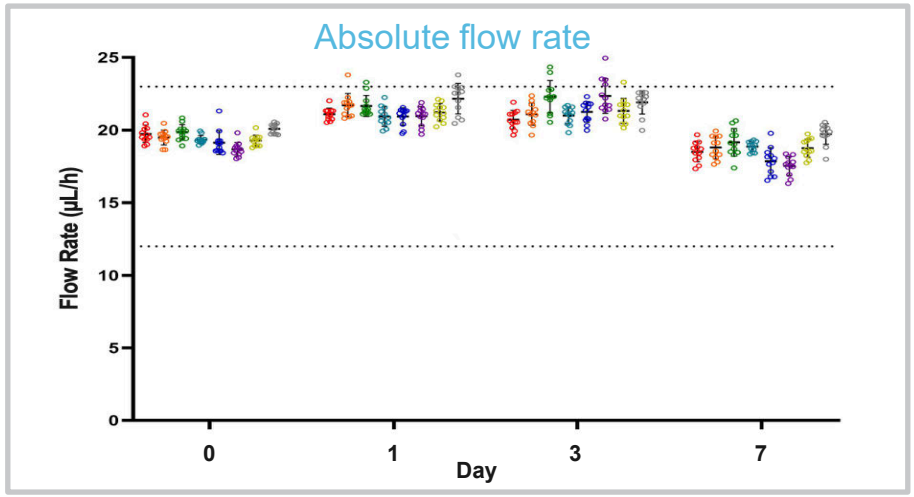
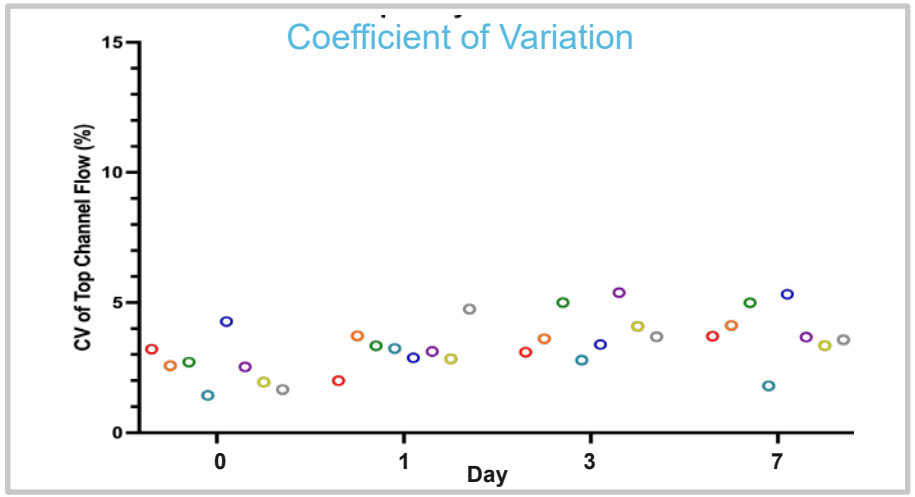
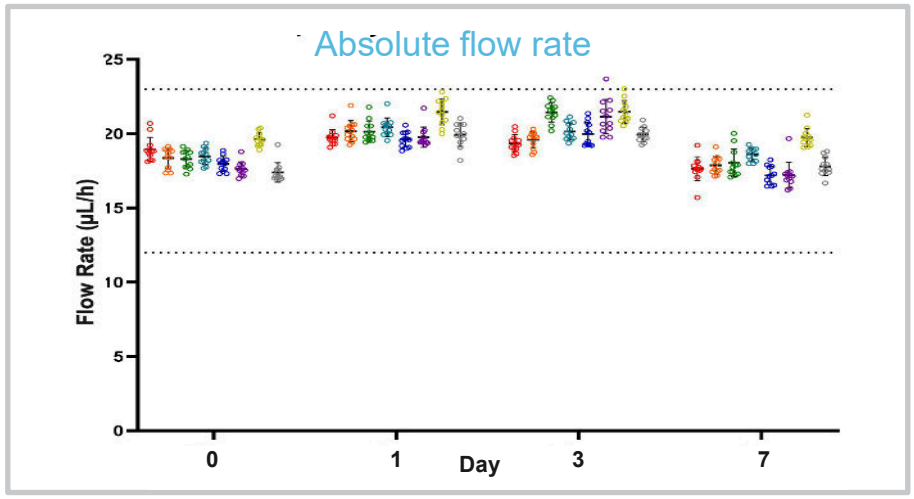
Flow Rate Precision Maintained Throughout Experiment

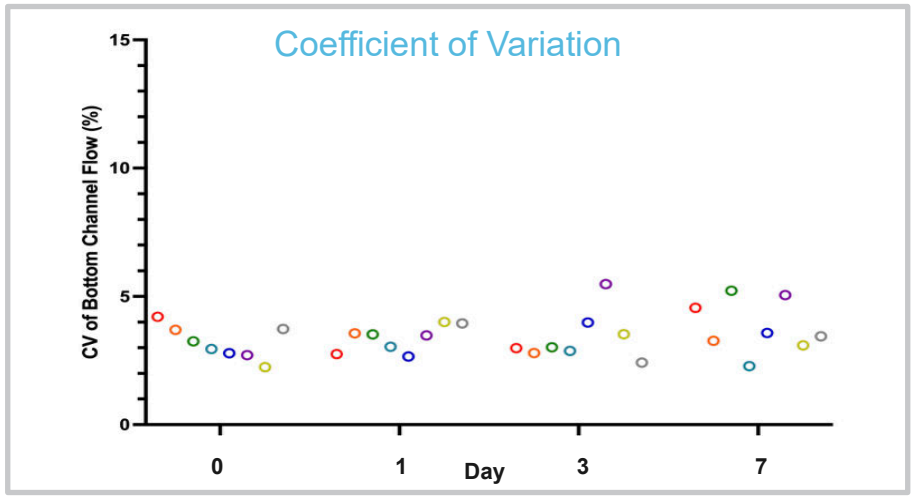
Top Channel





Bottom Channel





Chip-Array 01
Chip-Array 02
Chip-Array 03
Chip-Array 04
Chip-Array 05
Chip-Array 06
Chip-Array 07
Chip-Array 08

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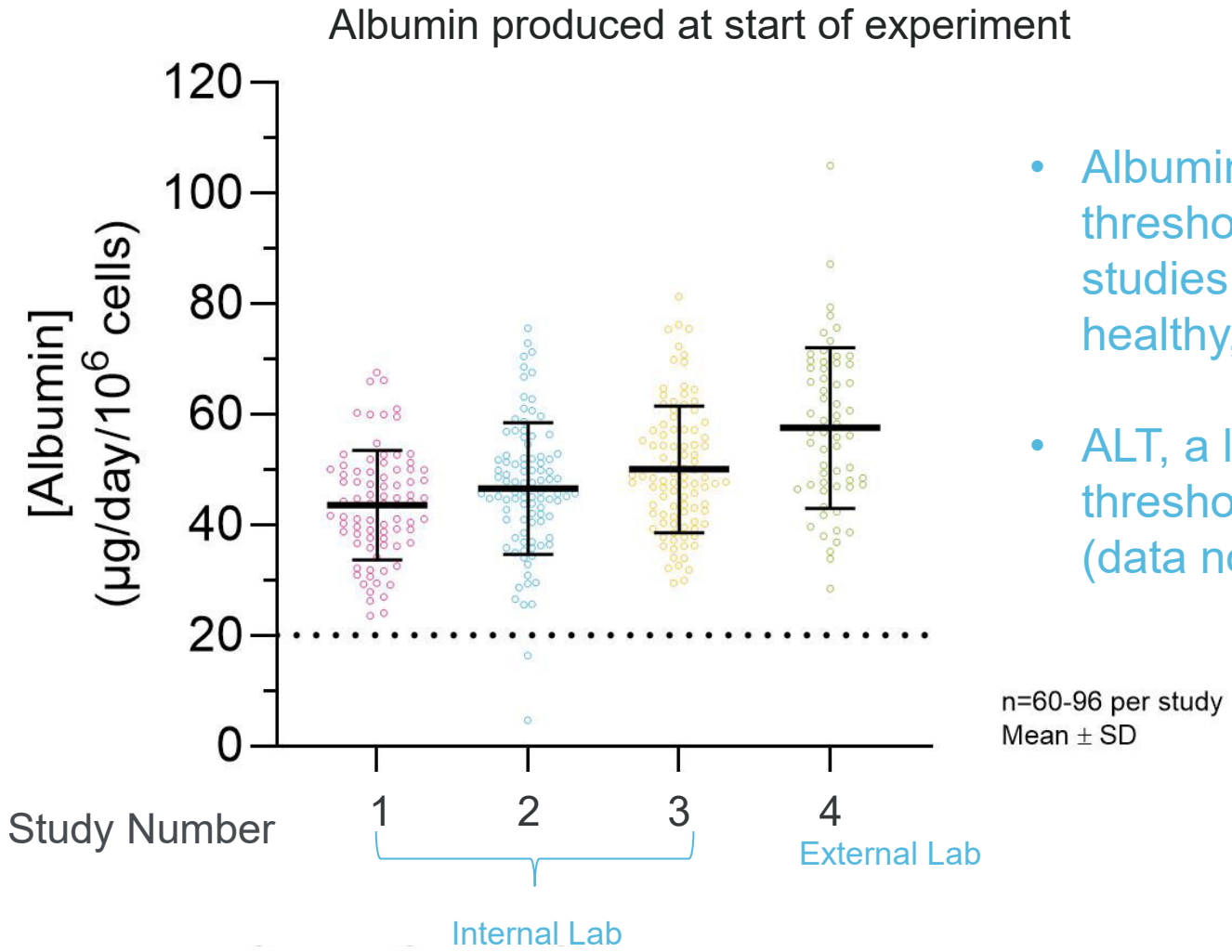
Microfluidic flow, a key component of the microphysiological microenvironment, has CV's of <5%

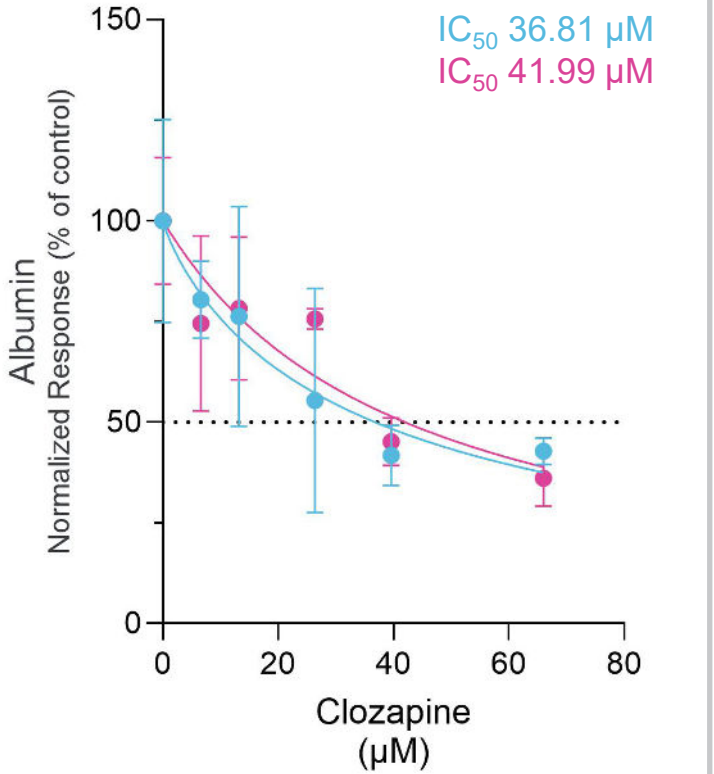
Reproducible Biological Performance Across Studies



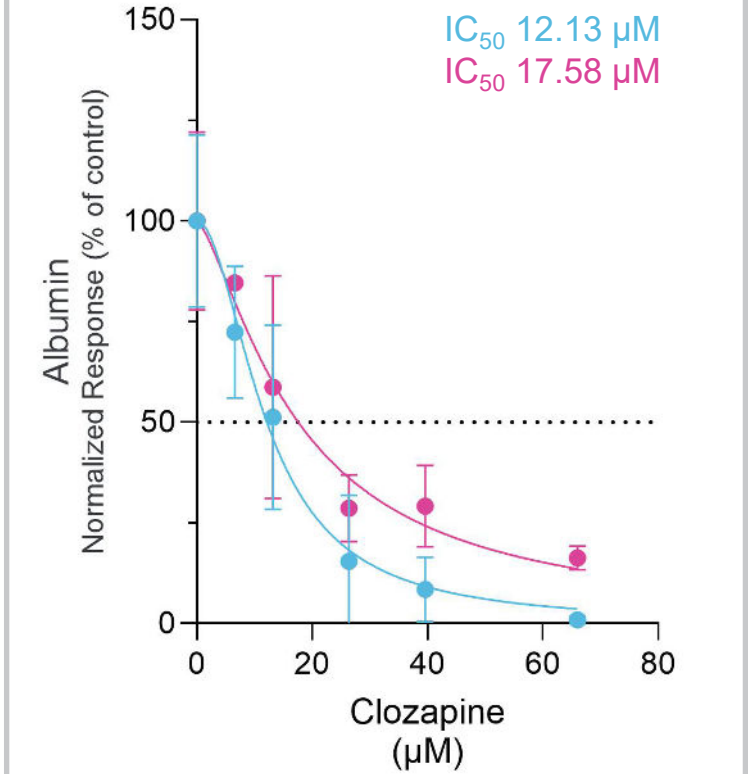
- Albumin secretion is above minimum threshold across three separate internal studies and one external study indicating healthy, functional hepatocytes
- ALT, a liver injury marker, is below the threshold again indicating healthy cells (data not shown)

Reproducibility of Clozapine Hepatotoxicity Across Labs

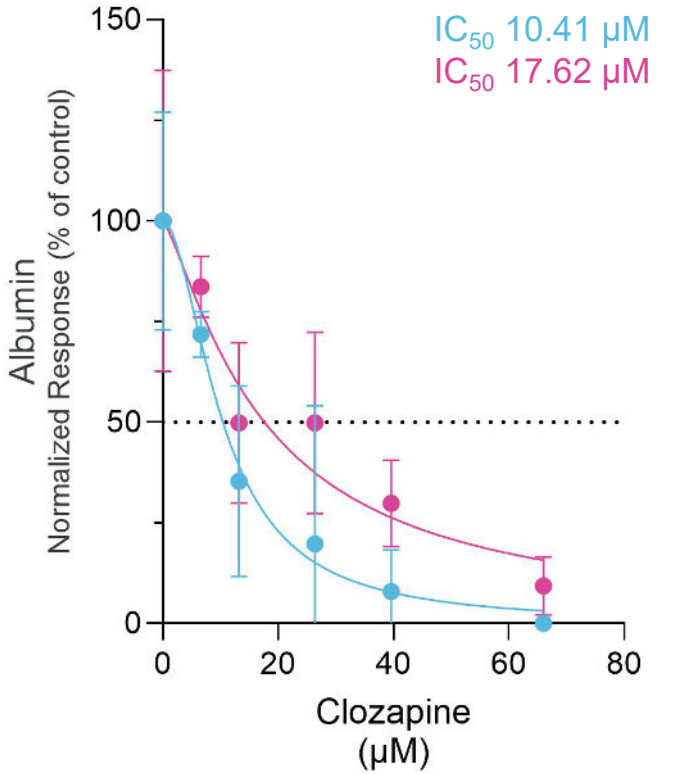
Day One Post-Treatment



Day Three Post-Treatment



Day Seven Post-Treatment



For 50% albumin reduction with 80% confidence at a 0.05 significance level requires 3.45, 4.6, and 2.60 Emulations on Day 1, 3 and 7 respectively

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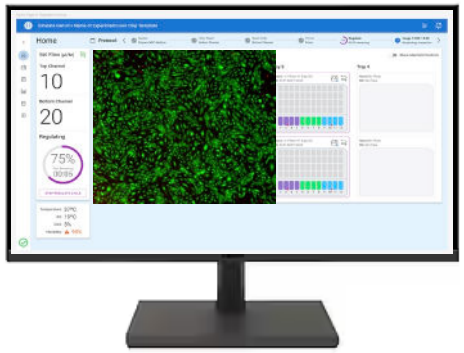
Internal laboratory data; External laboratory data

Streamlined Workflows Reduce FTE Requirements

60% reduction in hands-on, in-lab time for 96-Chip experiments*

Experiment Timeline By Day

	Model Preparation Phase Seeding, connection, and flow stabilization	Experimentation Phase Drug Treatment, QC, Media Exchange	Analysis Phase Imaging, Drug Response
In Lab Work	41 hours → **22 hours**	25 hours → **17 hours**	27 hours
Out of Lab Work			**15 hours** Review imaging/ biology anywhere, any time



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*Compared to equivalent experiments on Zoë Culture Module

Summary

- Human Organ-Chips generate translational data for drug discovery workflows
- Pharma recognize biological value but want reproducibility, throughput and application to decision making for routine adoption
- AVA aims to support routine adoption and reproduces performance of the Liver-Chip in predicting drug induced liver injury as well as distinguishing hepatotoxicity of structural analogs
- Platform robustness and biological reproducibility demonstrated by successful technology transfer