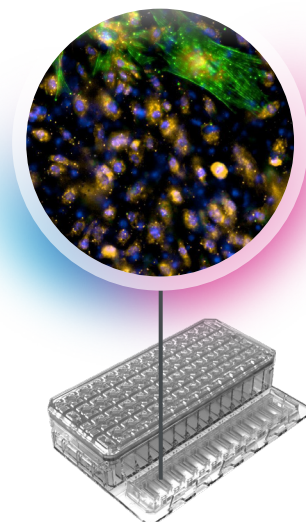


Liver-Chip Array Quad-Culture BioKit

A scalable model for human-relevant assessment of drug toxicology, efficacy, and ADME profiles.



Overview

The Liver-Chip Array BioKit brings Emulate's established human Liver-Chip model to the higher-throughput Chip-Array™ format for use with the AVA Emulation System™. The model combines four primary human hepatic cell types within the dynamic, two-channel microenvironment of the Chip-Array Organ-Chip consumable, enabling researchers to recreate key aspects of human liver physiology at a greater experimental scale. Together, the Liver-Chip Array BioKit and AVA Emulation System provide a standardized, scalable platform for human-relevant assessment of drug toxicology, efficacy, and ADME profiles.

Model Configuration

The Liver-Chip Array model is a quad-culture configuration incorporating primary human hepatocytes, liver sinusoidal endothelial cells (LSECs), stellate cells, and Kupffer cells within the Chip-Array Organ-Chip consumable (**Figure 1**). Each Chip-Array contains 12 independent Organ-Chip Emulations in an automation-compatible SBS plate format. Used with the AVA Emulation System, the Liver-Chip Array BioKit enables studies of up to 96 independent Liver-Chip Emulations per run with integrated microfluidic perfusion, incubation, and imaging functions. Constructed from low-absorption rigid thermoplastics, Chip-Array also improves recovery of compounds prone to absorption in PDMS-based devices.

1. Top Channel
2. Extracellular Matrix
3. Hepatocytes
4. Porous Membrane
5. Stellate Cells
6. Kupffer Cells
7. Liver Sinusoidal Endothelial Cells
8. Bottom Channel

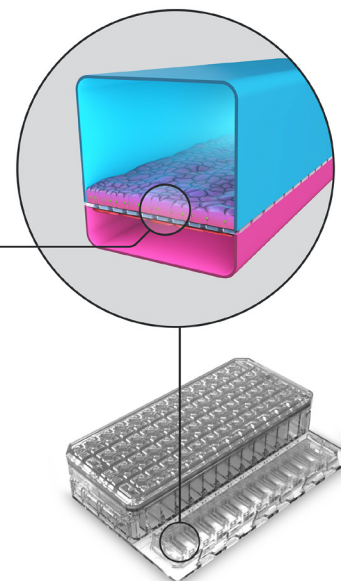
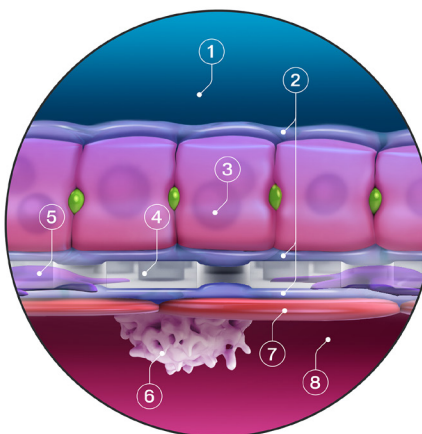


Figure 1: Liver-Chip Array Cross Section.

Model Characterization

The multicellular configuration of Liver-Chip Array supports complex cell-cell interactions that contribute to hepatic physiology and drug response. Continuous perfusion exposes cells to physiologically relevant shear stress while supporting the maintenance of hepatic morphology and function over the experimental window. Liver-Chip Array displays morphological and functional characteristics of mature hepatic tissue for up to twelve days in culture, with a window of up to seven days for drug exposure and assessment of cellular response.

- **Human-based model:** Avoids translational issues caused by species differences.
- **Multicellular complexity:** Incorporates four hepatic cell types to capture complex cell-cell interactions.
- **Scalable, reproducible performance:** Maintains consistent albumin secretion across multiple Chip-Arrays, with low variability between Chip-Arrays and all Emulations exceeding the healthy secretion threshold. (**Figure 2**).

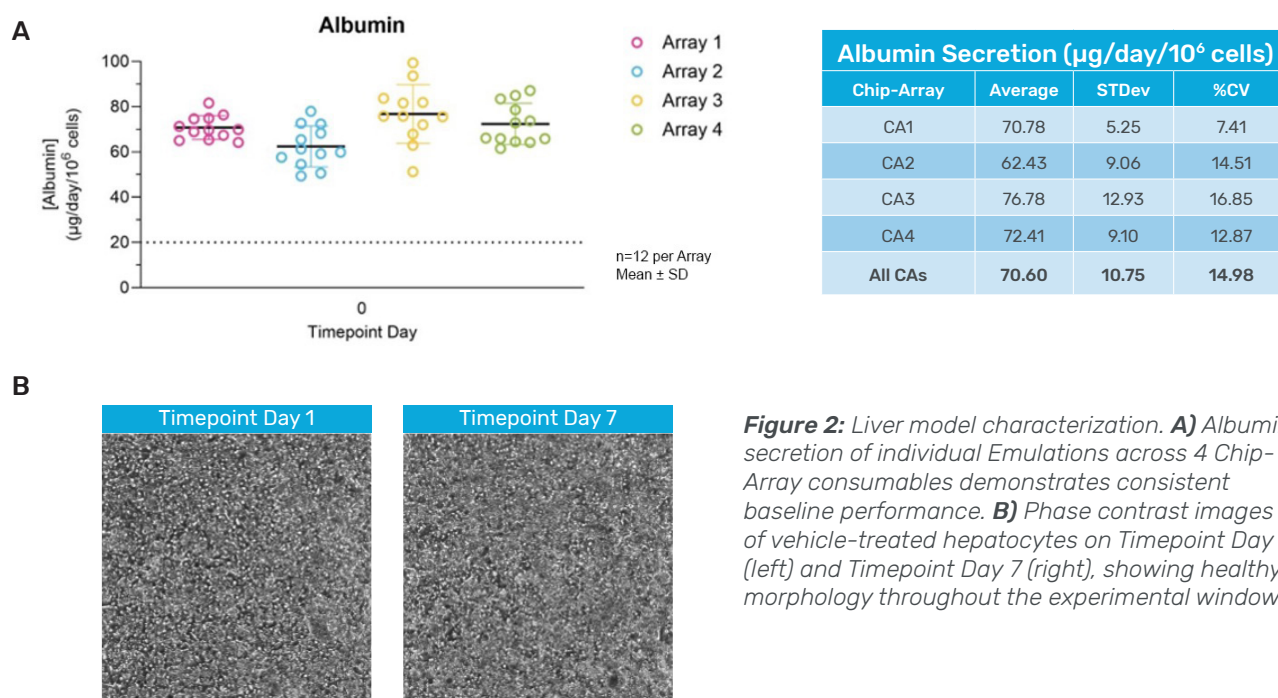


Figure 2: Liver model characterization. **A)** Albumin secretion of individual Emulations across 4 Chip-Array consumables demonstrates consistent baseline performance. **B)** Phase contrast images of vehicle-treated hepatocytes on Timepoint Day 1 (left) and Timepoint Day 7 (right), showing healthy morphology throughout the experimental window.

SUPPORTED APPLICATION

Toxicology

A clinically useful liver toxicology model must be capable of distinguishing between compounds with similar chemical structures but different hepatotoxic potential. To demonstrate this capability, Liver-Chip Arrays were treated with increasing concentrations of two structurally related drugs with different clinical hepatotoxicity profiles: clozapine, which is associated with severe hepatotoxicity, and olanzapine, which has a lower hepatotoxic risk. (Figure 3).

Clozapine produced a clear time- and concentration-dependent reduction in albumin production accompanied by increased ALT protein release. In contrast, olanzapine produced a substantially different response across the same concentration range, enabling the Liver-Chip Array to discriminate between the hepatotoxic profiles of these structurally related compounds.

Toxicology (cont.)

These results demonstrate the sensitivity of the Liver-Chip Array to compound-specific hepatic responses and support its application to higher-throughput comparative toxicology and compound prioritization studies.

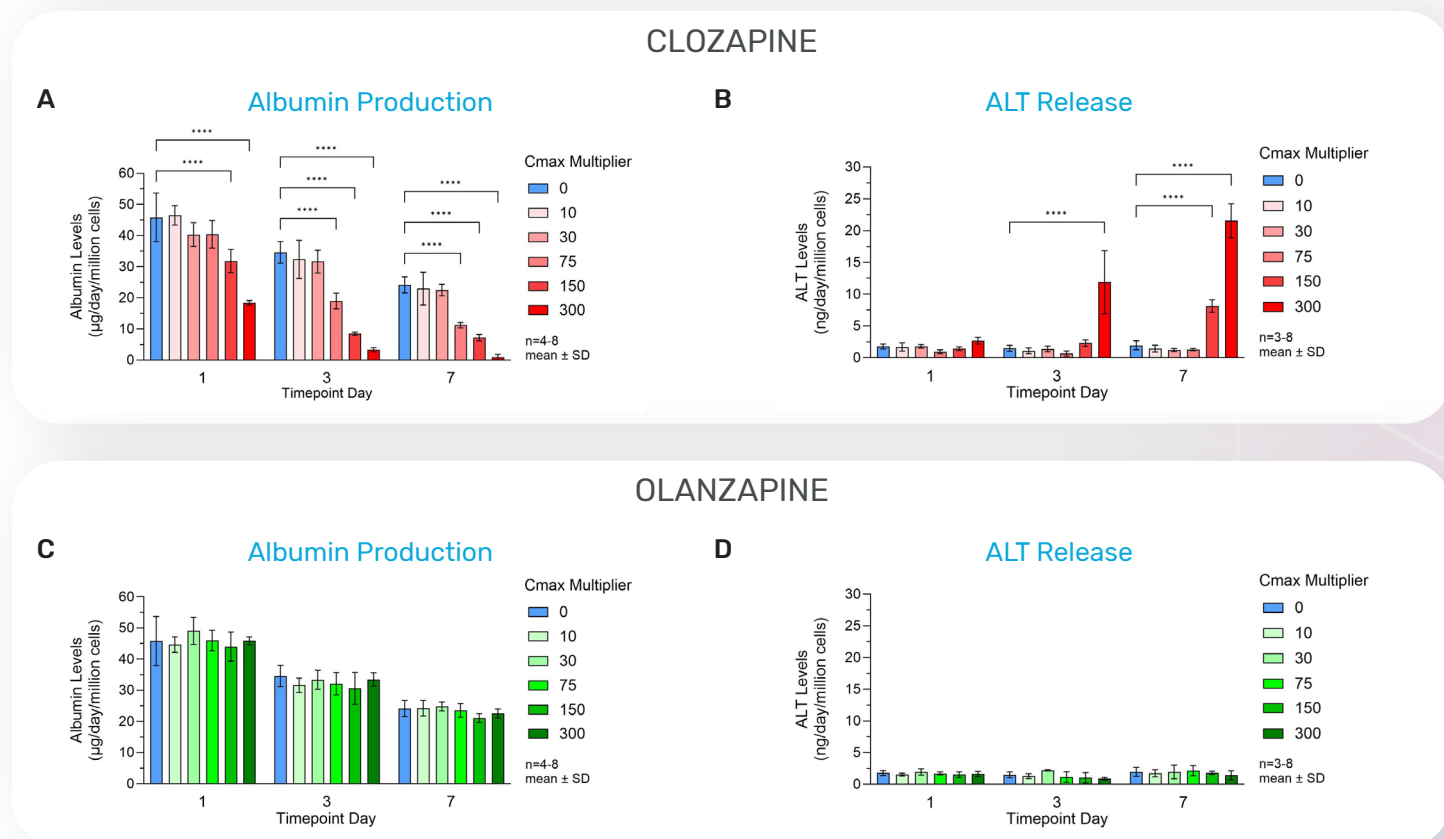
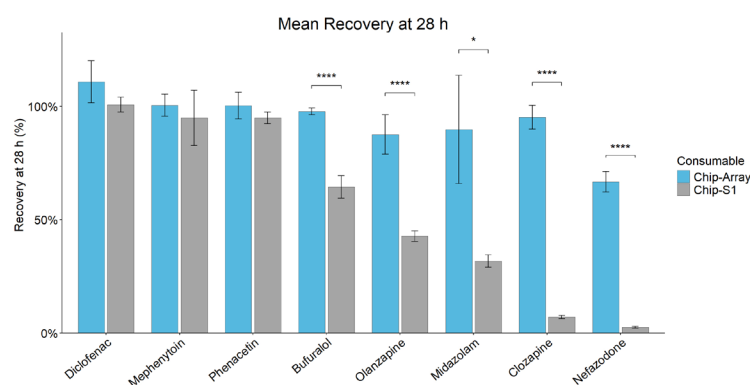


Figure 3: Liver-Chip Array distinguishes the hepatotoxicity of structural analogues. Albumin production and ALT protein release on days 1, 3, and 7 following treatment with clozapine (A, B) or olanzapine (C, D) at concentrations ranging from 0 to 300x free Cmax. Clozapine produced time- and concentration-dependent evidence of hepatotoxicity that was distinguishable from the response to olanzapine.

Minimal Drug Absorption

The rigid plastic design of the Chip-Array consumable significantly reduces drug absorption compared to the Chip-S1 Stretchable Chip. In a panel study with eight drugs of varying physicochemical properties, the acellular Chip-Array demonstrated markedly improved compound recovery for 5 of the 8 drugs, with no significant absorption observed for the remaining three drugs in either chip. This supports the utility of the Chip-Array consumable for ADME and toxicology applications, including drugs prone to PDMS absorption.



Bars show mean + SD; * adjusted $p < 0.05$, ** < 0.01 , *** < 0.001 , **** < 0.0001 . One-way ANOVA with Tukey's HSD for Diclofenac, S-Mephenytoin, Phenacetin, Bufuralol, and Olanzapine. Welch one-way ANOVA with Games-Howell for Midazolam, Clozapine, and Nefazodone.

Figure 4: Average compound recovery between 24–28 hours of flow.

Compatible with the AVA Emulation System™

The Liver-Chip Array is compatible with the [AVA Emulation System](#), a high-throughput Organ-Chip platform that supports up to 96 individual Organ-Chip “Emulations” per experiment.



Liver-Chip Array Specifications:

Specification	Details
Validated application	Toxicology
Storage conditions	- Cells: Store in liquid nitrogen - Other kit components: Ambient temperature (15–25°C)
Shelf life	- Cells: 6 months from date of shipment - Organ-Chip consumables: 1 year from manufacture
Cell types	Primary human cells: hepatocytes, LSECs, Kupffer cells, and stellate cells
Compatible assays	Live Imaging (via AVA Emulation System) - Phase-contrast microscopy for longitudinal assessment of cell morphology and tissue integrity - Fluorescence microscopy for longitudinal visualization of relevant cellular biomarkers and responses Endpoint Imaging (via third-party microscope) - Quantitative immunofluorescence microscopy for assessment of cell phenotype, tissue organization, and hepatic markers Effluent-Based Assays - Albumin secretion as a measure of hepatocyte function - ALT release as a marker of hepatocellular injury - Measurement of secreted biomarkers, cytokines, or other soluble analytes - CYP activity and metabolite formation, where applicable, to assess hepatic metabolic function Post-Experiment Off-Chip Analyses - Transcriptomic analysis of gene-expression changes - Proteomic analysis of cellular and secreted proteins - Metabolomic analysis of metabolic pathways and compound response

Ordering Information

Each Liver-Chip Array Quad-Culture BioKit includes the essential components needed to create the Liver-Chip Array—including Emulate-qualified cells—and is available in multiple sizes. Each kit contains:

- Chip-Array™ Organ-Chip consumables
- Steriflip® Filters
- Corresponding set of Emulate-qualified primary human cells, shown in the table below

To learn more, visit emulatebio.com/liver-chip

Product Name	Primary Human Cells	Chips per Kit	Catalog Number
Liver-Chip Array BioKit Quad-Culture	Hepatocytes, LSECs, Kupffer cells, and stellate cells	48	BIO-LH-QUAD48CA
		96	BIO-LH-QUAD96CA