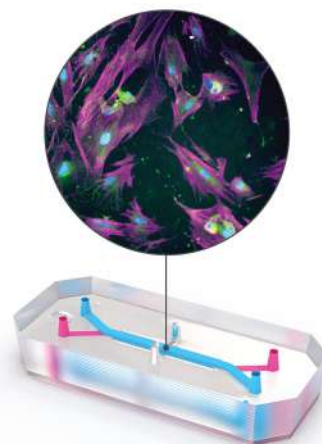


Emulate Human Liver Bio-Kit

Confidently predict drug safety and evaluate AAV gene delivery of preclinical candidates.



Overview

Drug-induced liver injury (DILI), despite being a primary concern during pharmaceutical development, remains poorly understood due to the limited predictivity of models typically used to analyze it. Animal models, for example, suffer from species differences in drug toxicity, while conventional 2D cell-based systems lack the cellular complexity to predict the diverse mechanisms of drug toxicity in humans. To avoid these pitfalls, the Emulate Liver-Chip combines up to four human cell types in a dynamic microenvironment for human-relevant functionality and response to drug candidates, overcoming the limitations of conventional preclinical models. It can be used in drug discovery and development, including general, predictive, and mechanistic assessments of candidate drug toxicity.

Model Configuration

The Liver-Chip is available in co- or quad-culture configurations, depending on study requirements. The co-culture configuration includes primary human hepatocytes and liver sinusoidal endothelial cells, while the quad-culture configuration includes these cell types as well as stellate and Kupffer cells. Both model configurations enable researchers to recreate complex cell-cell interactions that are crucial for modeling hepatic physiology and drug response. Unlike static hepatocyte sandwich monocultures, albumin and urea secretion are comparable to *in vivo* ranges and sustained over time, indicating enhanced functionality.

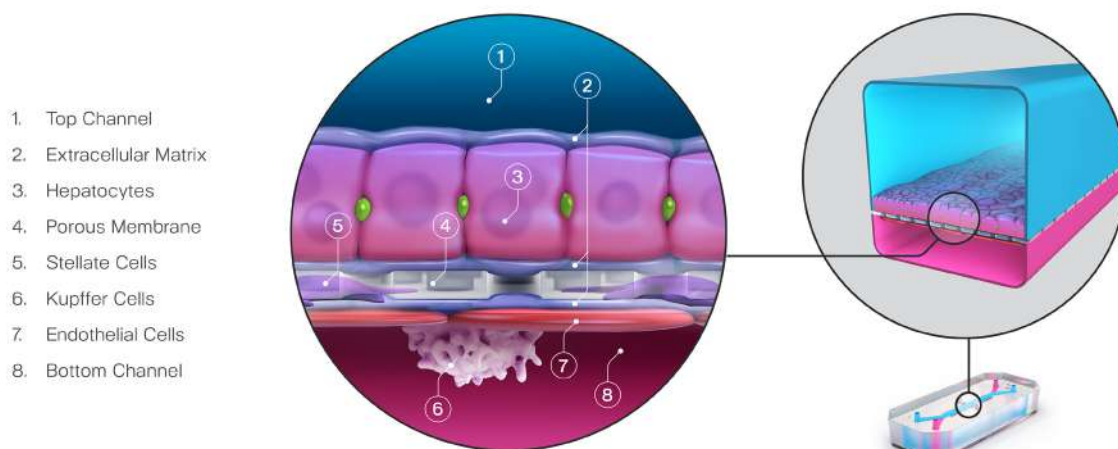


Figure 1: Liver-Chip Cross Section.

Model Characterization

The Liver-Chip provides the specific 3D multicellular architecture, physiological functions, and mechanical forces—such as shear stress—necessary to recapitulate the relevant aspects of the liver. This chip demonstrates morphological and functional characteristics of mature hepatic tissue for up to fourteen days in culture. Hepatocytes exhibit physiological cobblestone morphology and form branched bile canicular networks lined by functional MRP2 efflux transporters.

- **Human-based model:** Avoids translational issues caused by species differences.
- **Multicellular complexity:** Contains four hepatic cell types for improved cell-cell interactions.
- **Enhanced hepatic functionality:** Produces albumin secretion (see **Figure 2**), urea secretion (see **Figure 2**), and cytochrome P450 activity that is significantly higher than in conventional static sandwich monoculture.

Learn more in the Liver-Chip [Characterization Note](#).

SUPPORTED APPLICATION

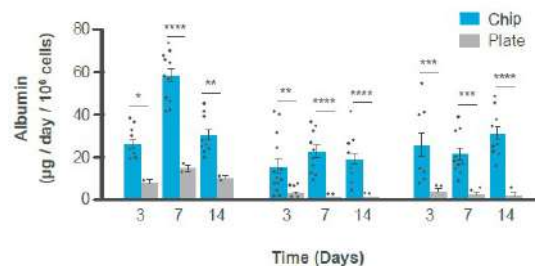
Toxicology

The Liver-Chip has been characterized as a model to [evaluate the hepatotoxicity](#) of preclinical drug candidates, a leading factor in clinical drug attrition, enabling researchers to improve the safety profile of drug candidates before they enter clinical trials. It has also been validated against [IQ MPS reference compounds*](#) in a large-scale, 870-chip study published in [Communications Medicine](#), exhibiting 87% sensitivity and 100% specificity against a set of 27 known hepatotoxic and non-toxic compounds. Key mechanisms of toxicity can be evaluated on-chip, including:

- **Hepatocellular injury:** Decrease in albumin secretion and elevated alanine aminotransferase (ALT), aspartate transaminase (AST) (See **Figure 3**), and glutamate dehydrogenase (GLDH)
- **Steatosis:** Lipid accumulation
- **Cholestasis:** BSEP/MRP2 inhibition as well as altered bile acid handling
- **Kupffer cell depletion:** Decrease in CD68-positive cells as well as in interleukin-6 (IL-6) and monocyte chemoattractant protein-1 (MCP-1)

*Validated against 18 of 20 IQ MPS reference compounds based on mechanism of toxicity

Albumin Secretion Comparison



Urea Secretion Comparison

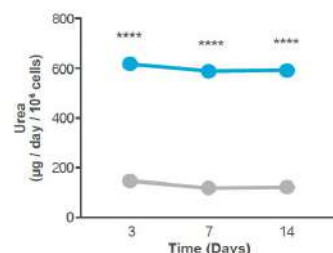
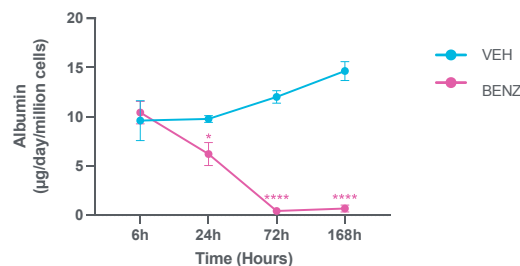


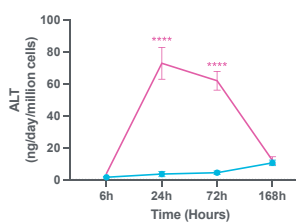
Figure 2: Albumin and urea secretion in the Liver-Chip compared to conventional static hepatocyte sandwich culture. Sidak's multiple comparisons test ($n=3-14$ independent chips, $n=3-9$ independent wells in plate). * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$. Error bars = mean \pm SEM.

Albumin Secretion



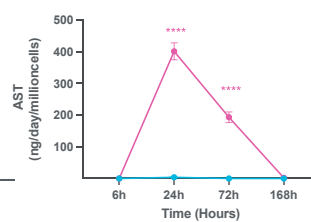
2-way ANOVA, Uncorrected Fisher's LSD Test
* $p < 0.05$; **** $p < 0.0001$
In comparison to the vehicle control at that timepoint

ALT Release



2-way ANOVA, Uncorrected Fisher's LSD Test
**** $p < 0.0001$
In comparison to the vehicle control at that timepoint

AST Release



2-way ANOVA, Uncorrected Fisher's LSD Test
**** $p < 0.0001$
In comparison to the vehicle control at that timepoint

Figure 3: Albumin secretion, ALT release, and AST release after Benzbromarone treatment at 100 μM in both top and bottom channels.

SUPPORTED APPLICATION

Adeno-associated Virus (AAV) Transduction

The Liver-Chip can be applied to test the [delivery efficiency and safety of AAV vectors](#) for human-relevant results in weeks—not months, like with animal models. This enables researchers to rapidly iterate AAV design in a human-relevant model of the liver sinusoid to accelerate vector optimization ahead of clinical trials. By administering a test vector in the epithelial channel, researchers can:

- Assess time- and concentration-dependent AAV transduction efficiency (see **Figure 4**)
- Evaluate the toxicity of AAV-based gene therapy
- Discriminate between the transduction efficiency of different AAVs

Part of the Human Emulation System®

The Liver-Chip is designed to be cultured using the Human Emulation System, a complete Organ-on-a-Chip platform that includes instruments, consumables, and software, providing the dynamic conditions needed to culture up to 12 Organ-Chips.

AAV Transduction

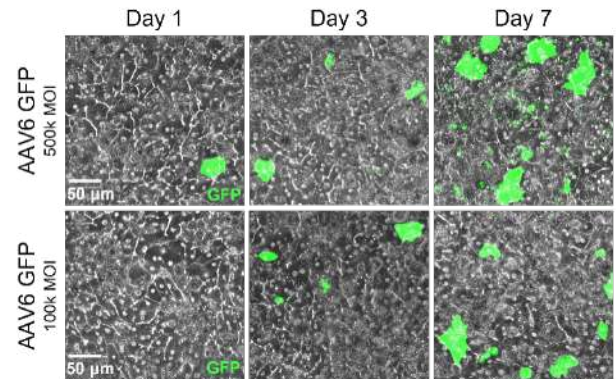


Figure 4: Brightfield imaging of the Liver-Chip epithelial channel after 24-hour administration of AAV6 vectors encoding green fluorescent protein.



Liver-Chip Specifications:

Specification

Validated applications

Storage conditions

Shelf life

Cell types

Characterization endpoints

Details

General toxicology and mechanistic toxicology

- Cells: Store in liquid nitrogen
- ER-1® Reagent: -20°C
- ER-2® Reagent: 2–8°C
- Other kit components: Ambient temperature (15–25°C)

1 year from date of manufacture

Available in two configurations, both using primary human cells:

- Co-Culture: Hepatocytes + liver sinusoidal endothelial cells (LSECs)
- Quad-Culture: Co-culture + Kupffer cells + stellate cells

- Immunofluorescent staining of MRP2 transporter, bile canicular networks, and stablin-1
- Albumin and urea secretion
- Cytochrome P450 enzyme activity

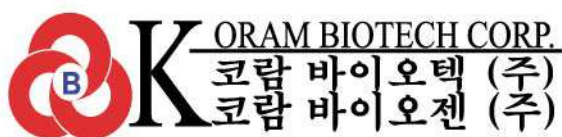
Ordering Information

Every Liver Bio-Kit includes the essential components needed to create the Liver-Chip—including Emulate-qualified cells—and is available in multiple configurations and kit sizes to meet various study needs. Each product is shipped with:

- Chip-S1® Stretchable Chips
- Pod® Portable Modules
- ER-1® / ER-2® Chip Activation Reagents
- Steriflip® Filter
- 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 Bio-Kit Co-Culture	Hepatocytes and LSECs	12	BIO-LH-C012
		24	BIO-LH-C024
Liver Bio-Kit Quad-Culture	Hepatocytes, LSECs, Kupffer cells, and stellate cells	12	BIO-LH-QUAD12
		24	BIO-LH-QUAD24



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