

HEPATOPAC Technology

Long-term, Stable *In Vitro* Hepatic Model

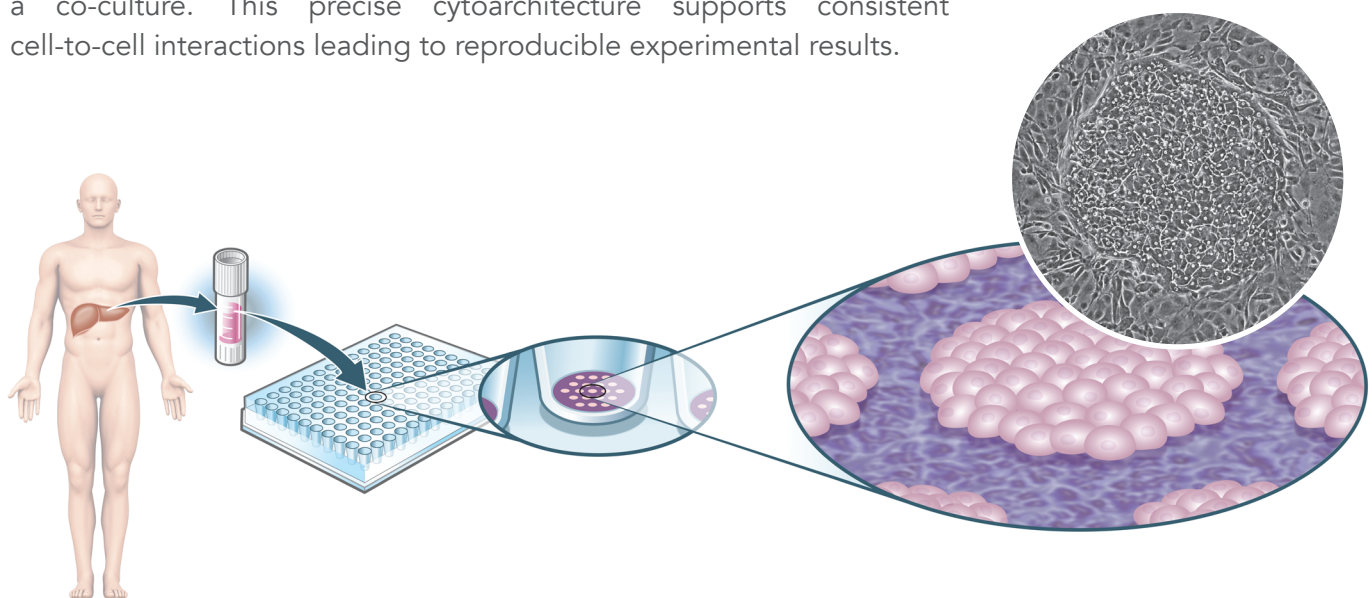
HEPATOPAC® Technology is used to create stable *in vitro* liver models that enable long-term hepatic metabolism and toxicity studies. HEPATOPAC cultures, formed using a proprietary patterning method, consist of hepatocyte “islands” surrounded with supportive stromal cells. This specialized architecture replicates the physiological microenvironment of the liver. Hepatocytes remain healthy and viable in the HEPATOPAC platform, and demonstrate physiologically-relevant transporter function and phase I and phase II metabolic activity for over four weeks.

HEPATOPAC models show better *in-vitro in-vivo* correlations (IVVC) than conventional hepatocyte models, especially for medium- and low-turnover compounds.

HEPATOPAC Architecture: Micropatterned Hepatocyte Co-cultures

HEPATOPAC cultures have a unique specialized architecture and an optimal ratio of hepatocyte islands to stromal cells. This gives the hepatocyte co-cultures greater longevity and stable metabolic activity compared with other *in vitro* models. The process to create a HEPATOPAC culture starts by selecting primary hepatocytes from a species of interest. The cells are then micropatterned on industry-standard plates creating the islands; stromal cells are added, forming a co-culture. This precise cytoarchitecture supports consistent cell-to-cell interactions leading to reproducible experimental results.

Micropatterned Hepatocyte Island
(10x magnification)



Research Applications for HEPATOPAC Technology

Metabolite Identification

The HEPATOPAC model has been demonstrated to identify phase I and phase II metabolites (including primary, secondary and tertiary metabolites) with greater accuracy than can be achieved with conventional models. Additionally, the HEPATOPAC model displays species-specific metabolism recapitulating *in vivo* metabolic profiles and enables adherence to the 2016 FDA Guidance for Industry, "Safety Testing of Drug Metabolites."

Metabolic Stability

Compared to other *in vitro* models, the HEPATOPAC model provides superior metabolic activity and IVIVC, especially for medium- and low-turnover compounds.

Toxicity Evaluation

The HEPATOPAC model is a robust methodology for assessing the toxic effects of drugs because it recapitulates key *in vivo* biochemical mechanisms and pathways. The long-term viability and extended functionality of the model enables repeat-dose experiments making it more predictive of clinical results, compared to conventional systems.

See How We Helped Others

Loratidine (LOR, Claritin) and its metabolite desloratidine (DL, Clarinex) are antihistamines approved in 1993 and 2001 respectively, to treat allergic rhinitis. The major human circulating and urinary metabolite of LOR, 3-OH-DL glucuronide, was not detected in microsomes, S9, or hepatocyte suspensions. Furthermore, this metabolite was not generated in appreciable amounts during preclinical safety studies in mice, rats, and monkeys, a concern during the FDA approval process. However, 3-OH-DL glucuronide was detected in human HEPATOPAC cultures. Study results were published in *Bioanalysis* in 2016¹. The success of the HEPATOPAC model in generating *in vivo* relevant metabolites can help minimize drug candidate failures and delays in bringing new drugs to patients.

1. Aratyn-Schaus Y, Ramanathan R *Bioanalysis*. 2016 Aug;8(16):1645-62. doi: 10.4155/bio-2016-0094. Epub 2016 Jul 27

HEPATOPAC Kits

HEPATOPAC technology is available in ready-to-use HEPATOPAC kits. Application-specific kits are available in a variety of sizes and formats including human, rat, monkey, dog, multi-species and multi-donor plates and systems are amenable to high-content imaging. Kits contain everything needed to perform an assay including:

- High throughput: 24-well or 96-well HEPATOPAC plates
- Maintenance and Application Medium components
- Maintenance and Quick Start Guides
- Application Protocols



How to order:

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