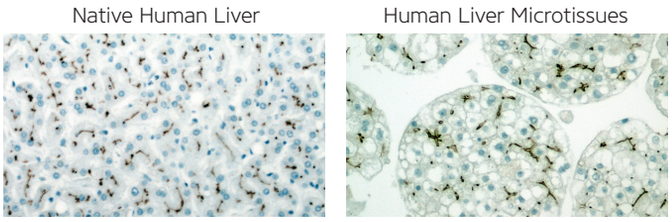
insphero
Biomimetic Microtissue Technology



An intact bile canaliculi network expressing bile salt export pump (BSEP) protein (brown) and hepatocyte nuclei (blue) in native human liver and in 3D InSight™ Human Liver Microtissues.

3D InSight™ Human Liver Microtissues

3D InSight™ Human Liver Microtissues are prequalified, long-lived liver models designed for drug safety and efficacy testing, and the study of healthy and diseased liver function. Composed of the primary human liver cells necessary for core liver functions, these microtissues are delivered assay-ready, in a lab-automation-friendly plate format ideal for screening.

- **Rely on physiologically relevant models** composed of primary human hepatocytes (PHHs), Kupffer cells (KCs), and liver endothelial cells (LECs). Monoculture models are also available.
- **Achieve 2X higher sensitivity for DILI prediction** over traditional 2D PHH due to active metabolism, intact hepatobiliary export, native-like mitochondrial function, immune competence, and possibility for long-term compound exposure
- **Increase confidence in decision making** with models that contain PHHs from 10 donors in a standardized format amenable to certified application endpoints.

Certified Applications

Designed and tested for:	Options:
DILI prediction screening	● ● ●
Mitochondrial toxicity testing	● ●
Inflammation-mediated toxicity testing	● ● ●
Cytochrome P450-mediated toxicity testing	● ●
Study of drug-Induced steatosis	● ●
Omics profiling	● ●

● Microtissue ● Service ● Protocol

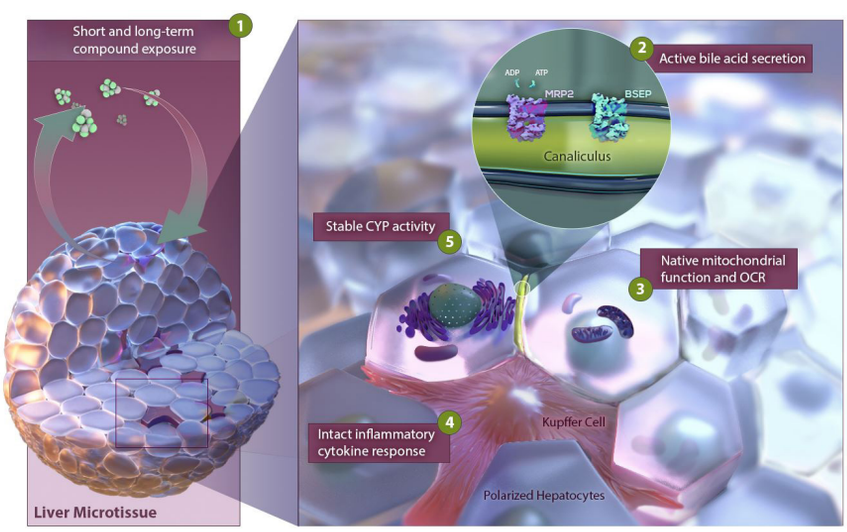


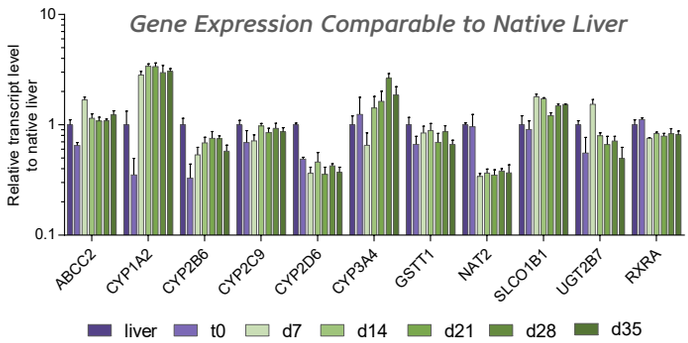
Figure 1: A physiologically relevant, functionally active human liver model. *3D InSight™ Human Liver Microtissues facilitate the study of liver function and response to 1 compound exposure by accurately recapitulating key liver functions typically compromised by disease or toxicity, including 2 bile acid secretion, 3 mitochondrial function and oxygen consumption rate (OCR), 4 inflammatory cytokine response, and 5 Cytochrome P450 activity.*

Discover the power of physiologically relevant 3D Liver Microtissues **www.insphero.com**

Native-like gene expression pattern preserved over weeks

Prevalidated and standardized, 3D InSight™ Human Liver Microtissues have been thoroughly characterized on a functional, transcriptomic, and proteomic level (Figure 2). The results demonstrate that this model represents a functional and physiologically relevant *in vitro* liver model that maintains stable function for more than 5 weeks in culture and is therefore well suited for a broad range of liver research applications, such as DILI prediction.
Reference: Messner *et al.* (2017) *Applied In Vitro Toxicology,* doi: 10.1089/aivt.2017.0022.

Figure 2: Relative transcriptional level of native liver in comparison to 3D InSight™ Human Liver Microtissues over 5 weeks in culture. Relevant transporters and Phase I/II/III metabolic enzymes are depicted. Stable gene expression is observed for most enzymes. (Data excerpt from Messner *et al.* (2017) *AIVT.)*



Highly suitable for DILI prediction and mechanistic assays

In a recent study, AstraZeneca and Genentech performed a systematic validation of 3D Human Liver Microtissues for their predictive value in discriminating between known hepatotoxicants and clinically safe drugs (Figure 3). The study tested 110 clinically known drugs on 2D PHH and 3D Human Liver Microtissues utilizing the same hepatocyte lot, compound concentrations and ATP-endpoint. *Reference:* Proctor *et al.* (2017) *Arch Toxicol,* doi 10.1007/s00204-017-2002-1.

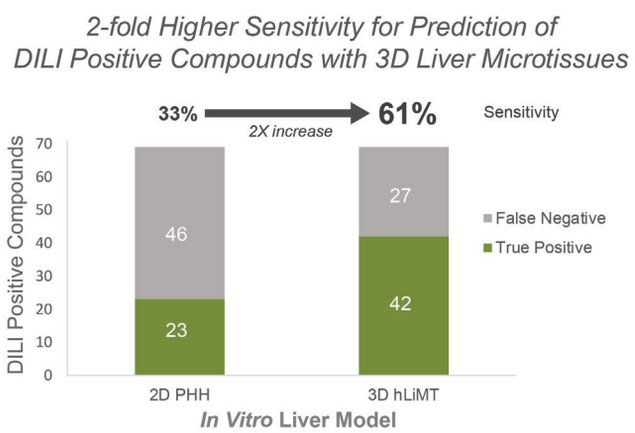
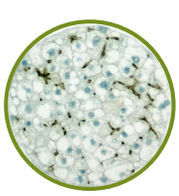


Figure 3: Study results confirm 3D Liver Microtissues outperform 2D PHH in culture for DILI prediction.

Key Findings

- Two-fold more sensitive in identifying known hepatotoxicants in comparison to 2D PHH (e.g., sensitivity 60.9% vs. 33.3%)
- Specificity for prediction of non-DILI drugs remained very high (90%), even after 14 days of compound exposure
- Enabled assessment of novel hepatic injury biomarkers, such as miRNA122, HMGB1 and α-GST

3D InSight™ Human Liver Microtissues



Liver model with PHHs, KCs, and LECs.

Available Assay-ready Models

- **Multi-donor PHH**
  Monoculture (MT-02-301-01)
  Co-culture with KCs and LECs (MT-02-302-04)
- **Single-donor PHH**
  Monoculture (MT-02-002-01)
  Co-culture with KCs and LECs (MT-02-002-04)

Format

- 96 microtissues, 1/well in Akura™ 96 plate

Related Products and Services

- 3D InSight™ Human Liver Fibrosis Model
- 3D InSight™ FFA-BSA Kit for induction of Steatosis in Human Liver Microtissues
- 3D InSight™ Toxicology Services

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