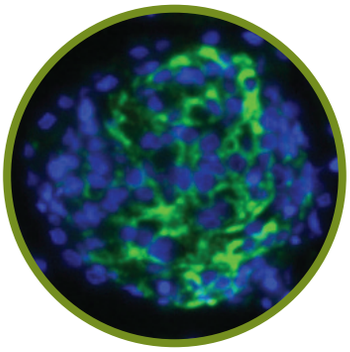
inSphero
Biomimetic Microtissue Technology



Immunofluorescence of Collagen type IV (green) and nuclei (blue) after TGF-β stimulation

3D InSight™ Human Liver Fibrosis Model

The InSphero 3D InSight™ Human Liver Fibrosis Model is a primary human liver microtissue for *in vitro* screening of anti-fibrotic drug efficacy, and for studying mechanisms of fibrosis induction *(Figure 1)*. The model includes the critical liver cells needed to recapitulate the fibrotic disease state upon induction, and serves as a powerful model for fibrosis drug discovery and development.

- **Rely on a physiologically relevant model** composed of primary human hepatocytes (PHHs), hepatic stellate cells (HSCs), Kupffer cells, and liver endothelial cells (LECs)
- **Expand your assay window** by leveraging a pre-qualified model that exhibits pro-fibrotic marker induction reflecting the *in vivo* disease state: ACTA2 (>5x) and COL1A1 (>3x)
- **Perform reproducible, throughput-compatible anti-fibrotic drug screening** using a standardized, assay-ready 96-well model system, amenable to a host of certified application endpoints

Certified Applications

Designed for assessment of:	Options:
Efficacy screening of anti-fibrotic drugs	● ● ●
Testing pro-fibrotic potential of drugs	● ●
Anti-fibrotic drug mechanism of action	● ●
Combined efficacy and toxicity testing of anti-fibrotic drugs	● ●
Mechanism of disease progression	● ●
Contribution of cell types to disease progression	● ●

● Microtissue ● Service ● Protocol

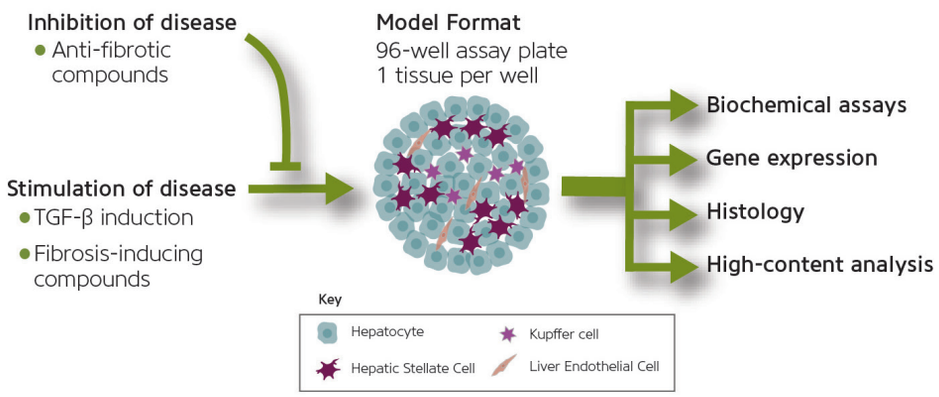


Figure 1: Disease Model Concept. *The 3D InSight™ Human Liver Fibrosis Model enables the study of liver fibrosis induction and inhibition of disease progression. The screening-compatible 3D microtissue format provides maximal endpoint compatibility.*

Liver Fibrosis Model Characterization Data

Induction of liver fibrosis requires the presence of HSCs, which are activated by pro-fibrotic stimuli, such as TGF-β. Kupffer cells (specialized macrophages located in the liver) and LECs influence liver fibrosis and are thus required for a physiologically, mechanistically relevant *in vitro* model system. The 3D InSight™ Human Liver Fibrosis model includes these relevant primary liver cell types, with robust induction of liver fibrosis biomarkers at the mRNA level observed upon TGF-β treatment (Figure 2). On histological examination, fibrotic biomarkers were also highly increased on the protein level (Figure 3). Concomitant treatment of TGF-β with an ALK5 inhibitor completely abolished progression of liver fibrosis (Figure 3), demonstrating suitability of the model system for testing pro- and anti-fibrotic compound efficacy.

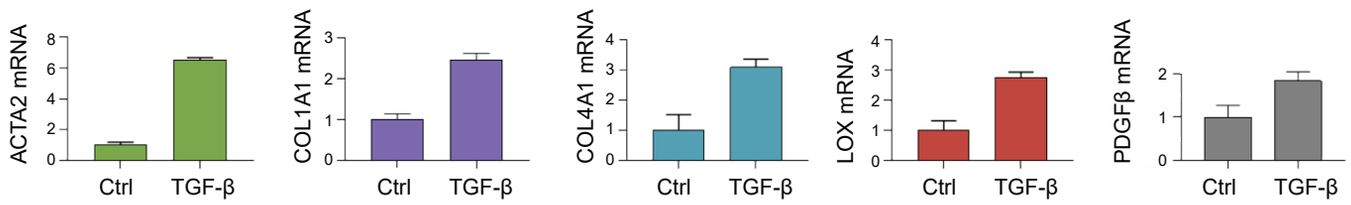


Figure 2: Robust induction of pro-fibrotic marker gene expression upon TGF-β stimulation. *After TGF-β treatment, a 5-fold induction of ACTA2 (α-SMA, stellate-cell activation marker), 4-fold induction of COL1A1 and COL4A1 (ECM markers), 3-fold induction of LOX (early fibrosis marker), and 2-fold induction of PDGFβ (stellate-cell activation marker) is observed.*

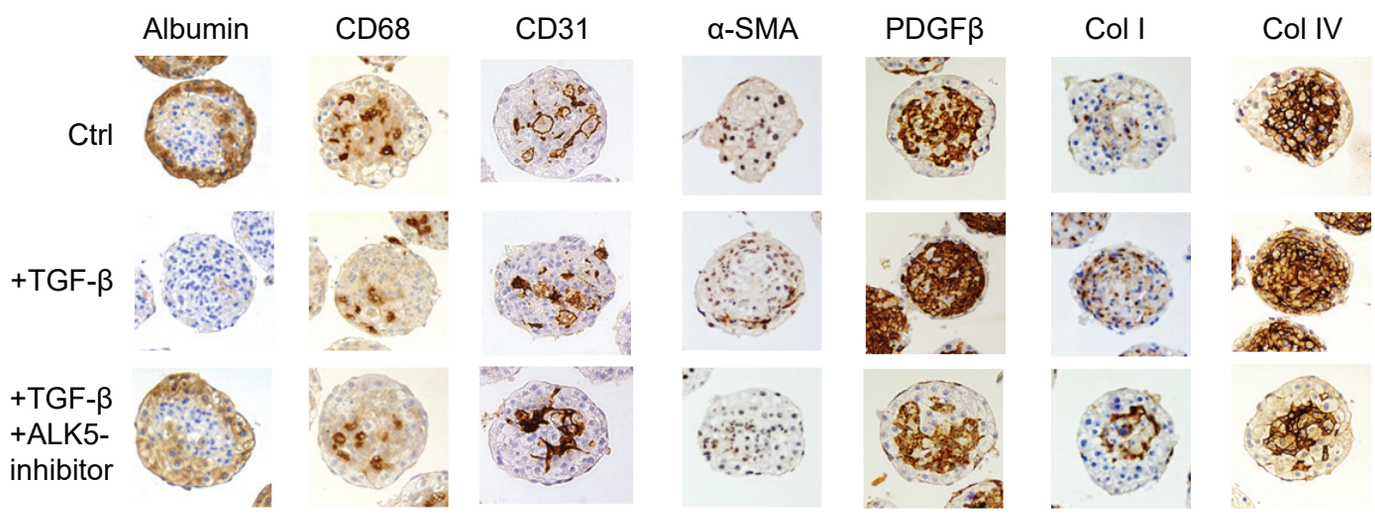
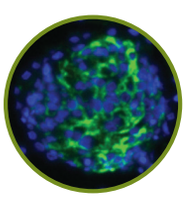


Figure 3: Histological characterization after TGF-β and disease inhibition. *Control tissues exhibit presence of hepatocytes (albumin), Kupffer cells (CD68), LECs (CD31), and stellate cells (PDGFβ). TGF-β treatment induces elevated expression of α-SMA, PDGFβ, Col I, Col IV, accompanied by decreased hepatocyte function as detected by decreased albumin expression. Simultaneous treatment of TGF-β and ALK5 inhibitor halts the induction of fibrosis biomarkers and rescues hepatocyte function.*

3D InSight™ Human Liver Fibrosis Model



Liver Fibrosis
Disease model

Model Specifications

- **Microtissue**
  3D InSight™ Human Liver Co-culture (PHHs, Kupffer cells, HSCs, and LECs)
- **Media**
  InSight™ Human Liver Maintenance Medium
- **Format**
  Akura™ 96 plate
  96 microtissues, 1 tissue/plate

Related Models and Platforms

3D InSight™ Liver Disease Discovery Platform

- 3D InSight™ Human Liver NASH Model
- 3D InSight™ Human Liver Steatosis Model

3D InSight™ Diabetes Discovery Platform

- 3D InSight™ Diabetes Type II Model
- 3D InSight™ Diabetes Type I Model

3D InSight™ Liver Toxicology Platform

IS-500-0029-01-Ad

InSphero AG
Schlieren, Switzerland
✆ +41 44 515 04 90

InSphero Inc.
Brunswick, ME, USA
✆ +1 800-779-7558

Email and Website
info@insphero.com
www.insphero.com

InSphero is ISO 9001:2015 certified