SYNVIVO

REALISTIC. DYNAMIC.

3D Tissue and Organ-on-Chip Models

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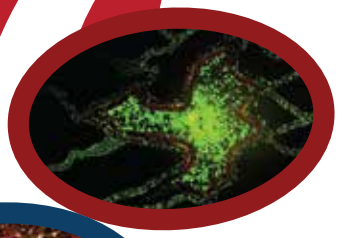
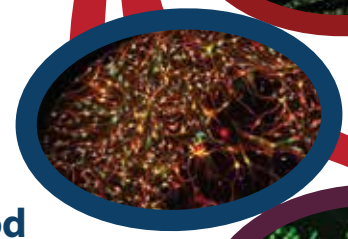
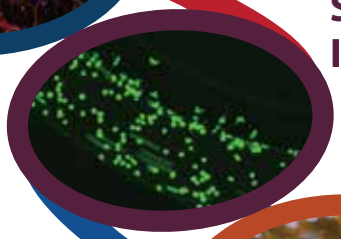


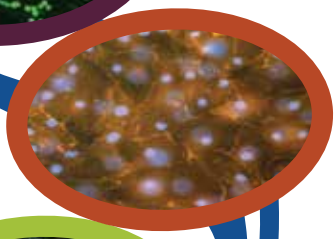
SynTumor Cancer Model



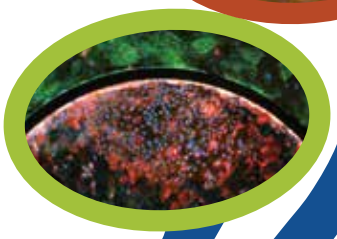
SynBBB Blood Brain Barrier Model



SynRAM Inflammation Model



SynALI Air-Liquid Interface Lung Model



SynTox Toxicology Model

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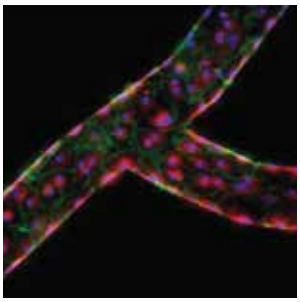
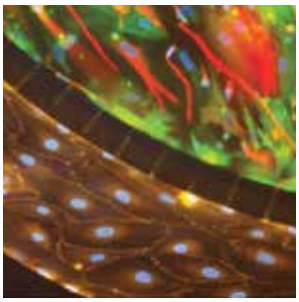
3D Tissue and Organ-on-Chip Models

SynVivo® is a cell-based microfluidic platform that provides a biologically realistic microenvironment for the analysis of cellular behavior, drug delivery and drug discovery. SynVivo 3D Tissue and organ-on chip models recreate complex in vivo microenvironments including scale, morphology, hemodynamics, and cellular interactions. Validated Models include SynBBB Blood Brain Barrier, SynTumor for Oncology applications, SynRAM for Inflammation, SynALI Air-Liquid Interface for Lung and SynTox for Toxicology applications.

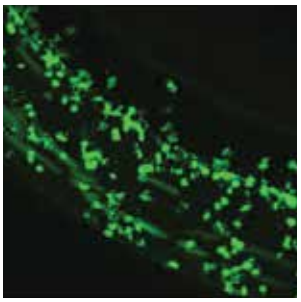
- **Side by side architecture**
  Develop complex co-culture morphology while maintaining real time visualization and quantitation.
- **In vivo like vascular morphology with fully formed lumen**
  Deliver drugs in biologically realistic conditions
- **Real time monitoring of cellular responses**
  Analyze Cell-Drug and Cell-Cell interactions in a controlled environment



Confocal image of a fully formed vascular lumen

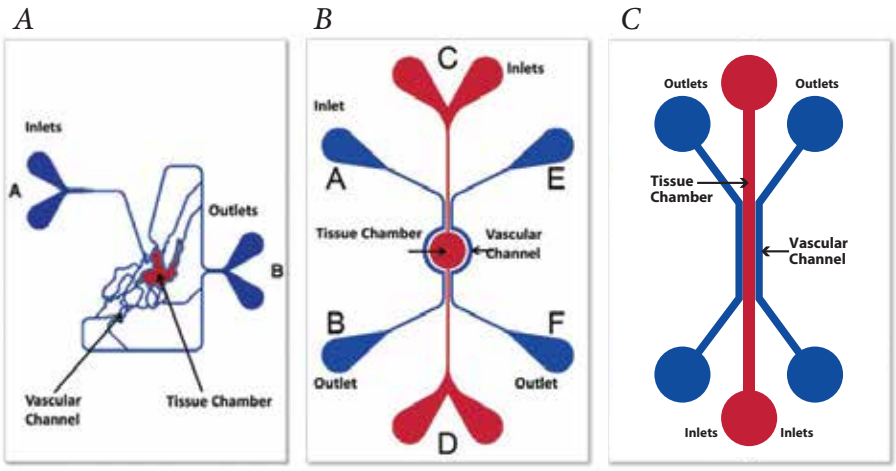


SynBBB Blood Brain Barrier model with endothelial cells, astrocytes and pericytes



Real time visualization of rolling, adhesion and migration of immune cells

SynVivo microfluidic chip designs are based on actual microvascular network images (A) or Idealized vascular networks (B&C) to support replication of the unique features of any tissue or organ in vitro.

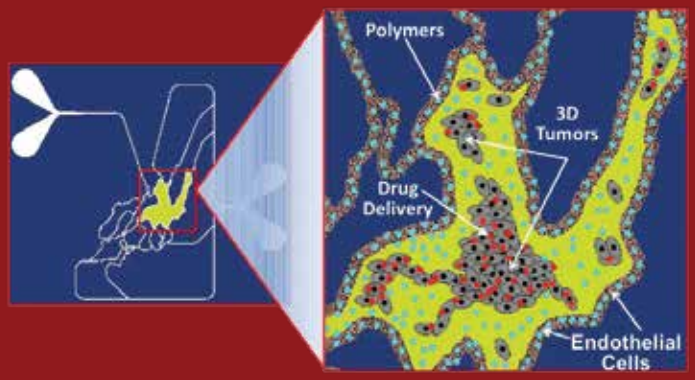


Perform biologically realistic assays

SynTumor 3D Cancer Model

The SynTumor™ 3D tissue model allows real-time visualization and quantitative assessment of cell-cell and cell-drug interactions in a physiologically realistic tumor microenvironment. The system enables analysis of circulation in the microvasculature, transport across the vessel walls, and drug delivery to tumors.

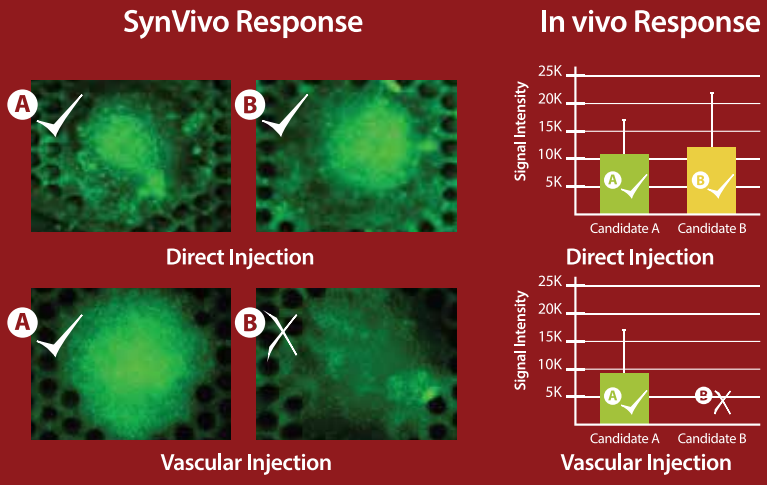
- Side by side architecture enables quantitative real-time visualization
- Physiological leaky vasculature with engineered porous structures
- Morphologically realistic in vivo based architecture
- Monitor interactions between tumor, stromal, vascular and immune cells



Starting with scans of vascular networks incorporated with interstitial and tissue/tumor spaces, the SynTumor model recreates an in vitro tumor microenvironment akin to a viable histological slice.

SynTumor Predicts in Vivo Drug Delivery Responses

A 3D cervical cancer model was developed using SynTumor to evaluate gene delivery efficiencies of nanopolymer formulations. GFP gene delivery using both direct and vascular injection routes were compared. In contrast to static well plate assays, he SynTumor model was successful in correctly predicting the in vivo responses of the nanopolymers. Both polymers "A" and "B" had uniform GFP transfection of the 3D tumors following direct injection similar to in vivo observations. However, following vascular injection only polymer "A" was able to diffuse across the endothelium and uniformly transfect the 3D tumor replicating the in vivo response.



SynVivo and in vivo response show that both the nanopolymers labeled A and B transfect the core of the tumor with uniform GFP expression following direct injection. In contrast, vascular injection route in SynVivo shows uniform transfection of the tumors only for nanopolymer labeled A matching the results observed in vivo.

Monitor Phenotypic Behavior of Tumor Cells in Real-Time

The microenvironment of two different breast tumors were created using the SynTumor model to evaluate their metastatic potential over a four week period. The highly metastatic tumor cells intravasated the vascular channels and rapidly invaded the adjacent tissue chambers and highlighted spindle morphology, a classical sign of invasive tumor cells. In contrast, the non-metastatic tumor cells grew slowly in clusters indicative of a benign tumor.

A metastatic tumor (left image) rapidly spreads to adjacent chambers while a non-metastatic tumor does not. Inset shows stained images highlighting elongated protrusions for metastatic tumor in contrast to non-metastatic tumor. This model can be used to screen tumor cell populations for their metastatic potential.

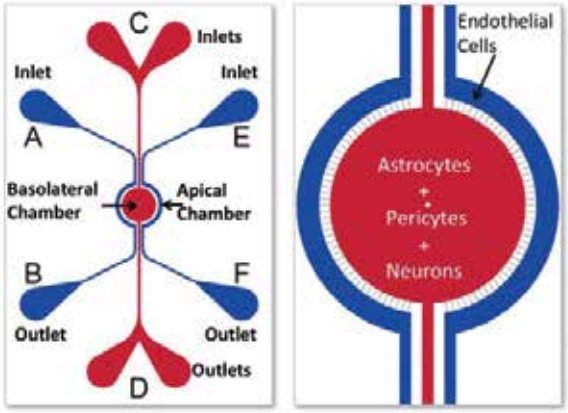
Recreate the tumor microenvironment

SynBBB 3D Blood Brain Barrier Model

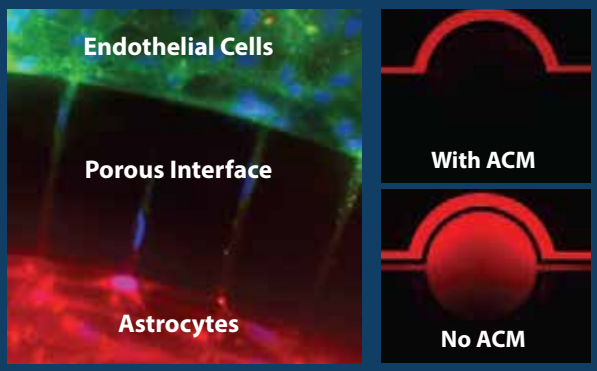
SynBBB™ recreates the in vivo brain microenvironment by replicating a histological slice of brain tissue cells in communication with endothelial cells across the blood brain barrier (BBB). Interactions between brain tissue cells and endothelial cells are readily visualized in the SynBBB model using biochemical or electrical analysis.

SynBBB is the only in vitro BBB model with:

- Accurate in vivo hemodynamic shear stress
- Real-time visualization of drug transport, cellular and barrier functionality
- Compatible with standard analytical instrumentation
- Robust and easy to use protocols

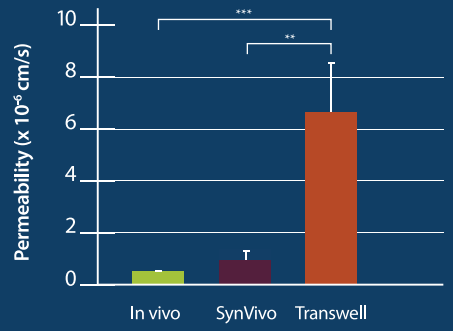


Schematic of the SynBBB Model. Apical chamber (outer channels) are for culture of vascular (endothelial cells) while basolateral chamber (central chamber) are for culture of brain tissue cells (astrocytes, pericytes, neurons). Porous architecture enables communication between the vascular and tissue cells.

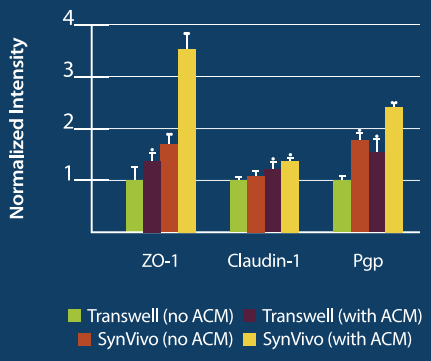


LEFT: *Co-Culture of endothelial cells (stained with CD31) and astrocytes (stained with GFAP) in the SynBBB model highlighting communication across the porous interface.*

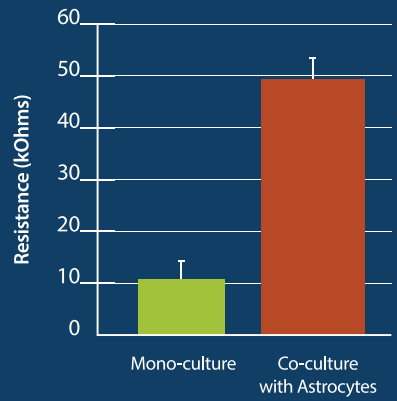
RIGHT: *Real-time visualization of fluorescently labeled small molecule permeation across the BBB. Flow and Astrocyte Conditioned Media (ACM) synergistically control tight junction formation.*



Small molecule permeation data validating the SynBBB model against in vivo. SynBBB model prediction matched very well with in vivo measurements.



Western blot analysis demonstrating strong up regulation of tight junction and transporter molecules in SynBBB model.



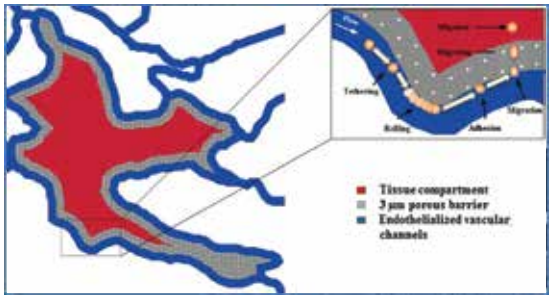
Electrical resistance based analysis of tight junction formation.

Recreate normal and dysfunctional blood brain barrier models

SynRAM 3D Inflammation Model

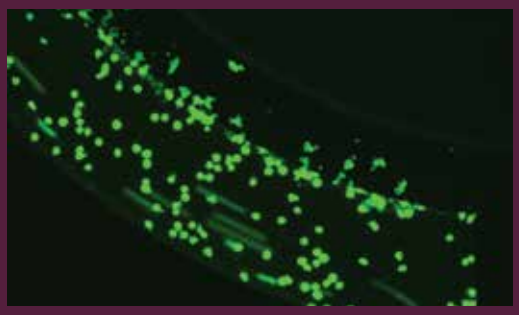
SynRAM™ allows the study of the entire inflammation pathway in a realistic and dynamic environment. By a histological slice of co-cultured tissue and/or tumor cells with a lumen of endothelial cells, SynRAM delivers a physiologically realistic model and enables real-time tracking of rolling, adhesion and migration processes. SynRAM has been successfully validated against in vivo studies showing excellent correlation with rolling velocities, adhesion patterns and migratory processes.

- Physiological flow within a microvascular environment
- In vivo like vascular morphology with fully formed lumen
- Co-culture capability for cell-cell interactions
- Quantitative real-time rolling, adhesion, and migration data from a single experiment

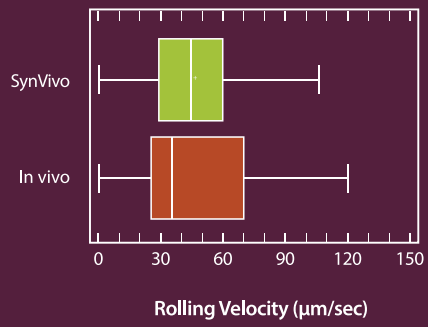


SynRAM enables real-time assessment of cellular interactions comprising of rolling, adhesion and migration through multiple cellular layers in a single experiment with close correlation to in vivo results.

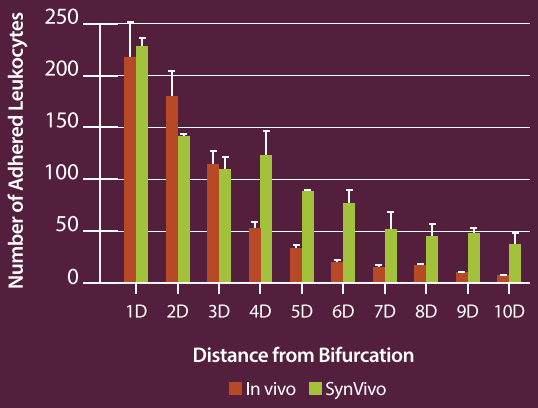
The SynRAM model reproduces inflammation responses observed in vivo



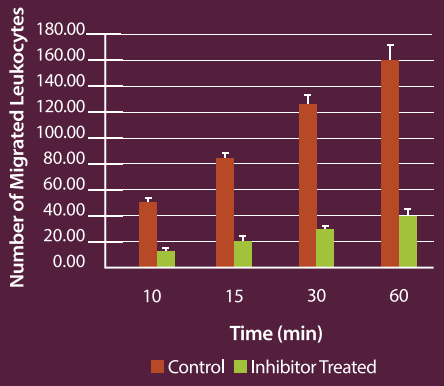
Real-time visualization of leukocyte rolling, adhesion and migration across an inflamed endothelium in the SynRAM 3D model.



Leukocyte rolling velocities are similar to those observed in vivo.



Leukocyte adhesion pattern in SynRAM model matches leukocyte adhesion in vivo.



Screening of inhibitors in SynRAM model. In the presence of inhibitor, migration drops significantly (by more than 75%) compared to control conditions.

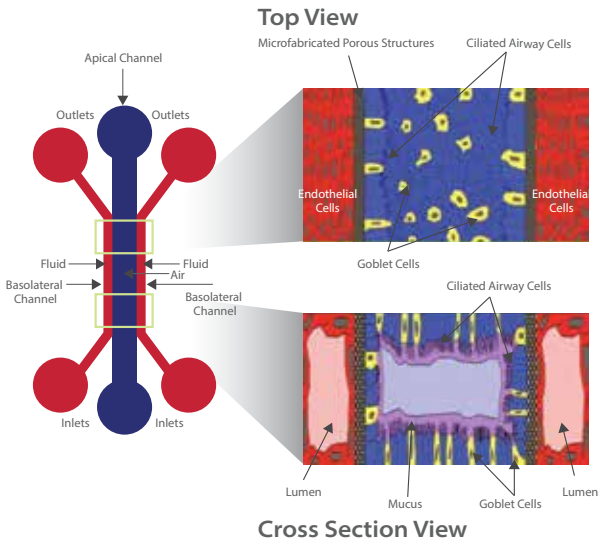
Simultaneously visualize rolling, adhesion and migration in a single experiment

SynALI: Air-Liquid Interface Based Lung Model

SynVivo has developed a novel Air Liquid Interface (ALI) model mimicking the lung architecture. The microfluidic device is functionalized with epithelial cells surrounded by vasculature comprised of endothelial cells. This structure maintains an Air Liquid Interface (ALI) across the airway cells, allowing theformation of airways tubules that transport mucus and are maintained by the surrounding endothelium. Cell morphology, airway structure, cell-cell interactions and functions of the airway (e.g. mucus transport, ciliary beating, therapeutic induced improvement) can be visualized and quantified in real-time on both diseased and treated conditions.

Unique features include:

- Morphologically realistic airway structure and environment
- Air Liquid Interface (ALI) across the epithelium and endothelium
- in vivo hemodynamic shear stress
- Real-time visualization of cellular and barrier functionality
- Mucus, ciliary beating, immune cell interactions and therapeutic screening



Schematic of the device used to develop the air-liquid interface across the cells. The air (or epithelial) channel is separated from two fluid (basolateral) channels by a micro-fabricated porous structure. Right panel shows the orientation of cells when seen from top and cross-section views

SynALI small airway model exhibits mucus formation and biomarker staining

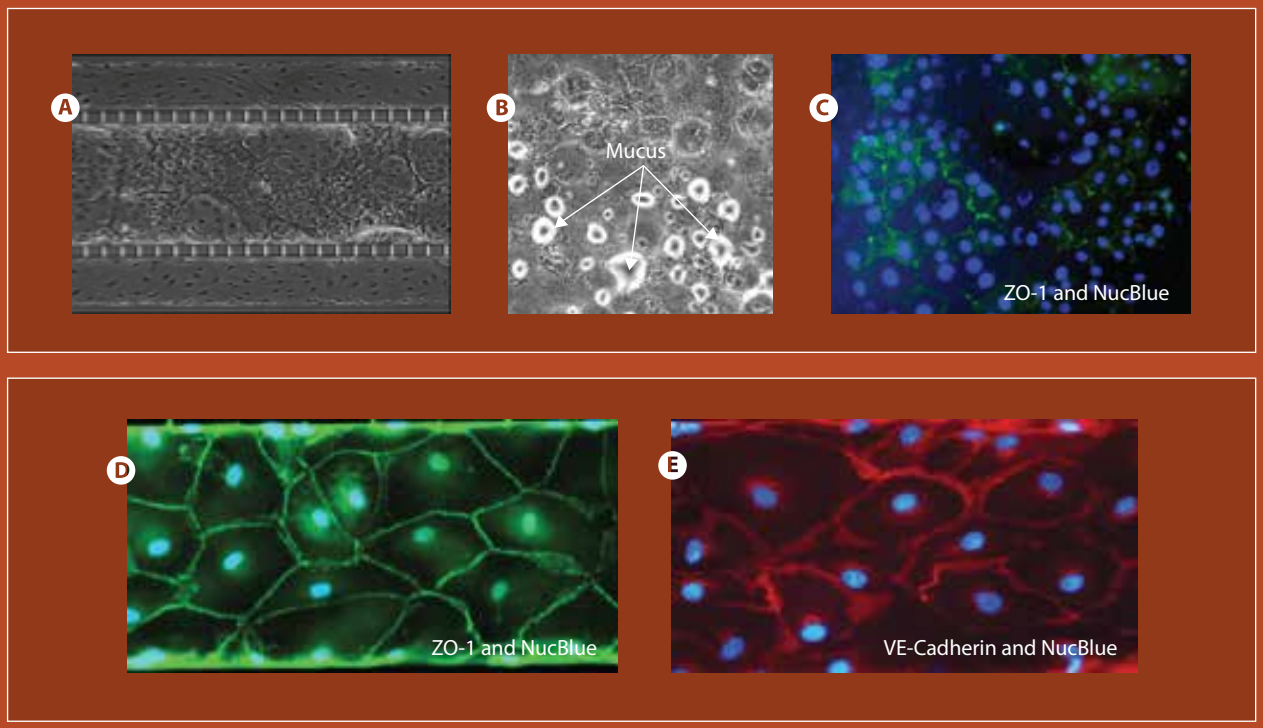


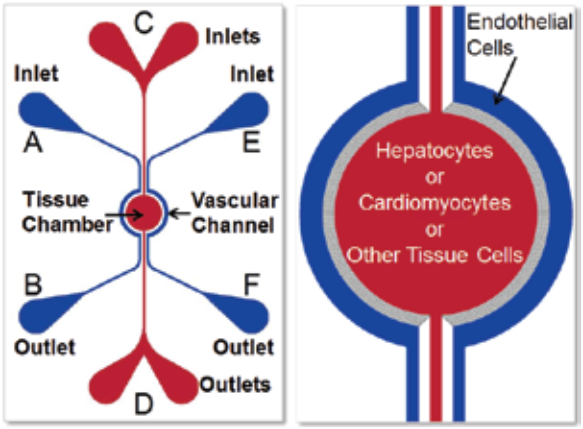
Figure 2: Top Panel. **A-C** *Confluent co-culture of endothelial and epithelial cells following ALI development highlighting mucus formation and staining of biomarkers in epithelial cells.* Bottom Panel. **D-E** *Biomarker staining for tight junction markers (VE-Cadherin and ZO-1) in endothelial cells.*

Small Airway and Alveolar Lung Models

SynTox 3D Toxicology Model

SynTox™ 3D toxicology model replicates a histological slice of a tissue with in vivo likemulticellular architecture.

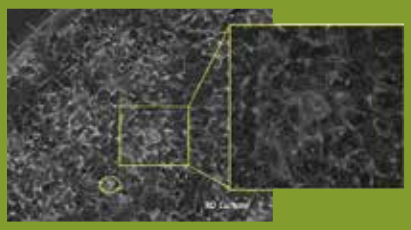
- Physiologically realistic vascular and tissue cell interactions
- Universal platform to model architecture specific to desired organs
- Real time monitoring of cellular responses
- Compatible with standard analytical instruments for both on chip and off chip assays including omic methodologies



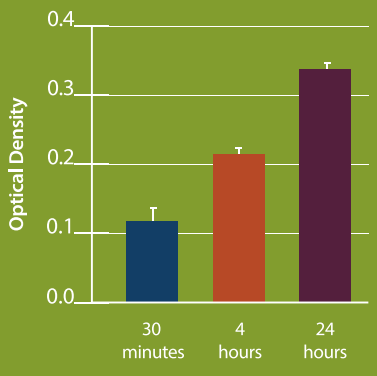
SynTox 3D Toxicology Model recreates the in vivo microenvironment by recreating a histological slice operating in an in vitro format.

SynTox used to model toxicity in liver, vascular and cardiac tissues

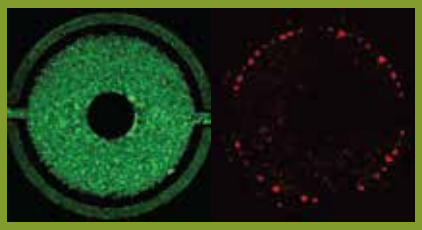
Liver and heart cells were co-cultured with their respective endothelial cells and analyzed for toxicity after treatment with various drugs.



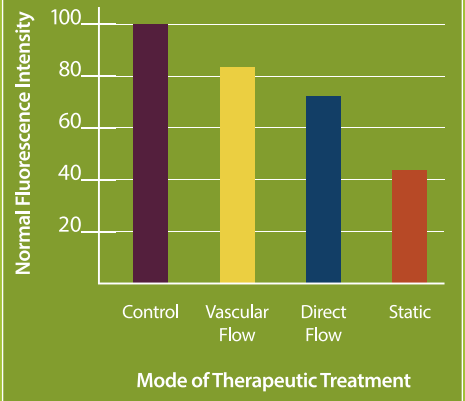
Hepatocytes form bile-canaliculi in SynTox model.



Hepatocytes secrete urea with increasing concentration in a time-dependent manner.

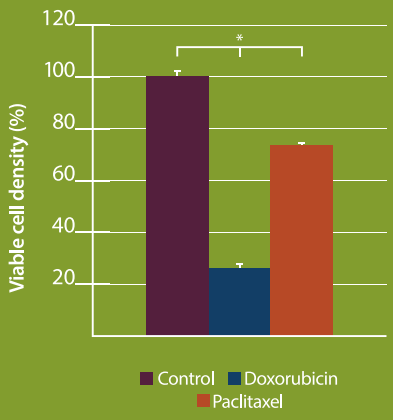


Acetaminophen toxicity on hepatocytes following bolus injection. Peripheral hepatocytes show severe toxicity.



Hepatocytes toxicity following different modes of treatment.

Drug toxicity on cardiac cells. Left panel indicates viable cells while right panel indicates mixture of live and dead cells following drug treatment.



Plot of vascular (endothelial) cell toxicity following treatment with chemotherapeutic. Endothelial cells are highly susceptible to the drugs.

Evaluate candidate drugs for organ specific toxicity responses

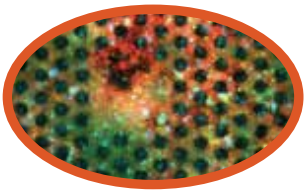
3D Tissue and Organ-on-Chip Models - Products, Training and Services

Products

Our exciting models – SynTumor for Oncology, SynBBB for Blood Brain Barrier, SynRAM for Inflammation, SynALI Air-Liquid Interface for Lung and SynTox for Toxicology applications can be purchased as kits or microfluidic chips to be functionalized with your choice of cells. Accessories and Instrumentation needed to run assays are also available. Detailed protocols and technical support are provided.

Training Workshops to Get You Started

SynVivo provides robust protocols and technical support along with all products. We also organize 2 and 4-day training workshops at our laboratory facilities in Huntsville, AL. You will work side by side with our expert scientists and receive hands on training specific to your application and interest. You will receive detailed protocols and an assay kit of your choice to take home with you.



Screening and Assay Development Services

SynVivo assays provide the realism of an in vivo microenvironment in vitro for modeling drug delivery, drug discovery and ADME/Toxicity.

- Screening Services include **Target Validation, Compound Screening, Biomarker Analysis, ADME/Tox and Mechanism of Action** studies using our validated models.
- Assay Development services can be performed to develop and optimize new models, assay end-points or custom chip designs.
- Deliverables include data or the validated model with relevant products, training and support for use in your research facility

More information at www.synvivobio.com

Contact us to discuss your research needs

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