SYNVIVO

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BIO EXCELLENCE®

REALISTIC. DYNAMIC.

3-D TISSUE MODELS AND SERVICES

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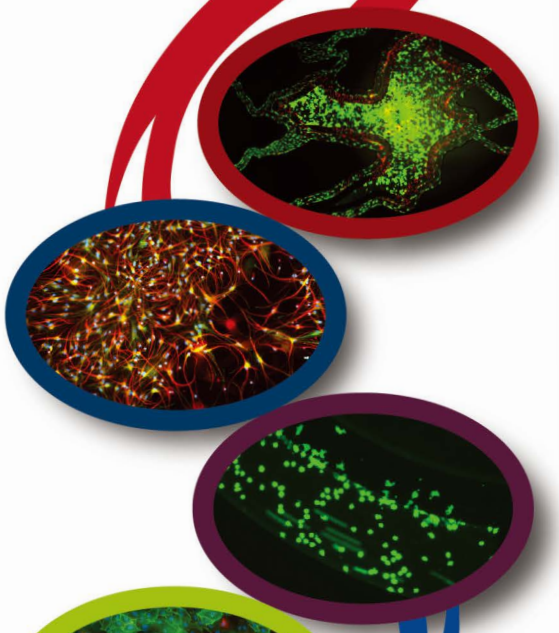

SynTumor 3D Cancer Model

Physiologically realistic 3D tumor microenvironment with real-time visualization of cellular responses

SynBBB 3D Blood Brain Barrier Model

The only in vitro 3D blood brain barrier model with real-time visualization of cellular and barrier functionality

SynRAM 3D Inflammation Model

Real-time visualization and quantitation of immune cell rolling, adhesion and migration in a single experiment

SynTox 3D Toxicology Model

Organ on a chip models for analysis of toxicity responses with real-time monitoring at specific cellular layers

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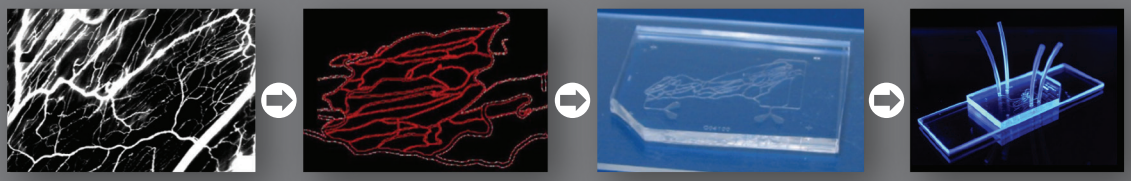
3D Tissue Models

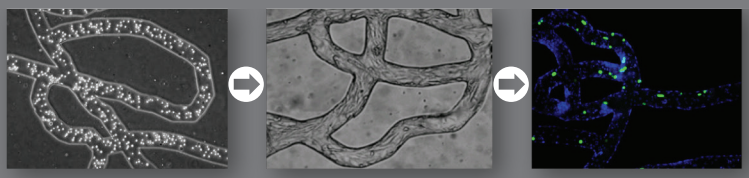
SynVivo® is a physiological, cell-based microfluidic platform that provides a morphologically and physiologically realistic microenvironment allowing real-time study of cellular behavior, drug delivery and drug discovery. SynVivo 3D tissue models recreate complex in vivo microenvironment including scale, morphology, hemodynamics, and cellular interactions with a side-by-side architecture enabling real-time visualization and analysis. The SynVivo 3D tissue models have been extensively validated for oncology, neuroscience, inflammation and toxicology applications. Available models include SynTumor (Cancer), SynBBB (blood brain barrier), SynRAM (Inflammation) and SynTox (Toxicology).

Simple, Low Cost Fabrication



Tissue Image | Digitized Network | Microfabricated Chip | SynAssay Platform

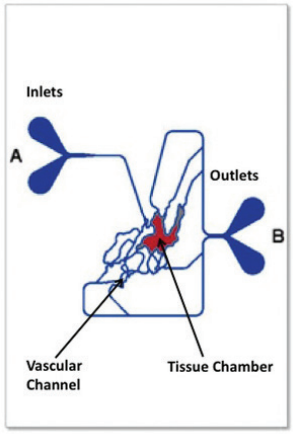
Simple, Robust Protocols

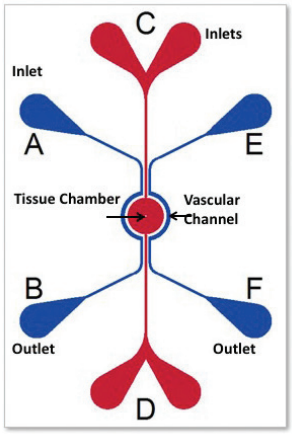


Cell Seeding (-5 min) | Cell Culture (12-48 hrs) | Experiment (hours-weeks)

SynVivo microfluidic chip designs are based on actual microvascular network images or an idealized vascular network to support in vivo replication of physiological, morphological and cellular makeup for cell-cell and cell-drug interaction assays.

Realistic Microvascular Networks: Replicate in vivo physiological, morphological and cellular makeup for cell-cell and cell-drug interaction across the vascular-tissue interface.





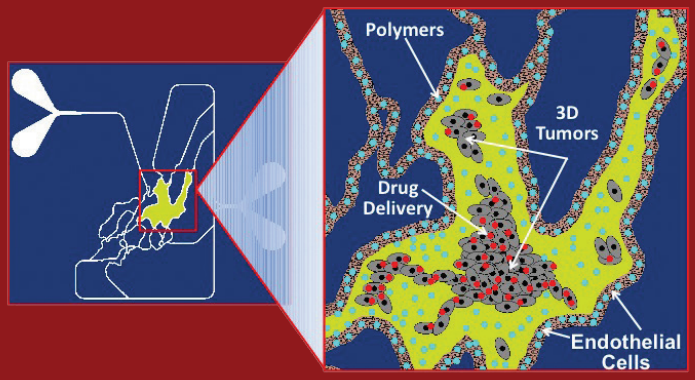
Idealized Microvascular Network: Replicate in vivo fluidic and cellular makeup for cell-cell and cell-drug interaction across the vascular-tissue interface.

Perform morphologically and physiologically 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.

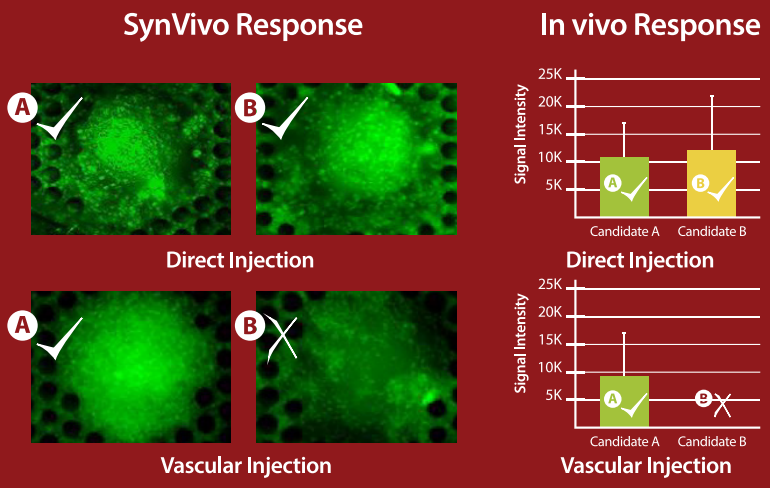
- Side by side architecture enables quantitative real-time visualization
- Physiological leaky vasculature with engineered porous structures
- Morphologically realistic in vivo based architecture
- Monitor interactions between tumor, stromal, vascular and immune cells



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

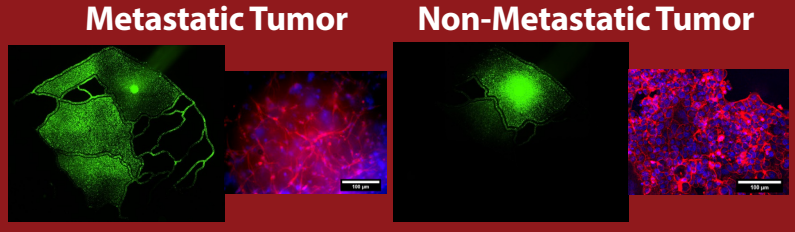
A 3D cervical cancer model was developed using SynTumor to evaluate gene delivery efficiencies of nanopolymers being evaluated for use in a clinical trial. GFP gene delivery using both direct and vascular injection routes were compared. In contrast to static well plate assays, the SynTumor model was 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.

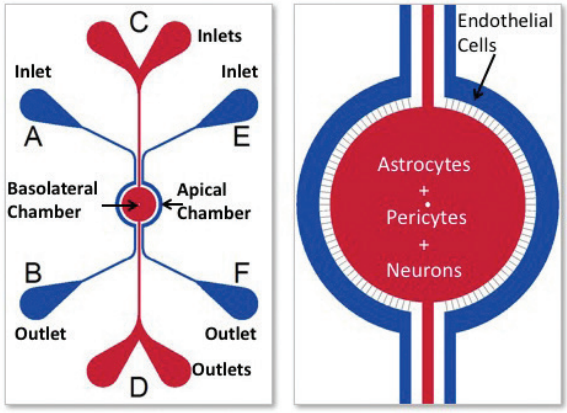
Recreate the tumor microenvironment

SynBBB 3D Blood Brain Barrier Model

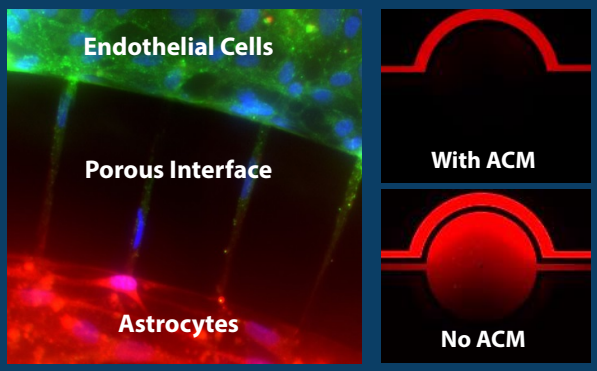
SynBBB™ recreates the in vivo brain microenvironment by replicating a histological slice of brain tissue cells in communication with endothelial cells across the blood brain barrier (BBB). Interactions between brain tissue cells and endothelial cells are readily visualized in the SynBBB model using biochemical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

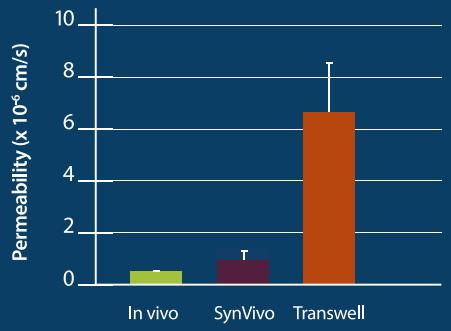


Schematic of the SynBBB Model. Apical chamber (outer channels) are for culture of vascular (endothelial cells) while basolateral chamber (central chamber) are for culture of brain tissue cells (astrocytes, pericytes, neurons). Porous architecture enables communication between the vascular and tissue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

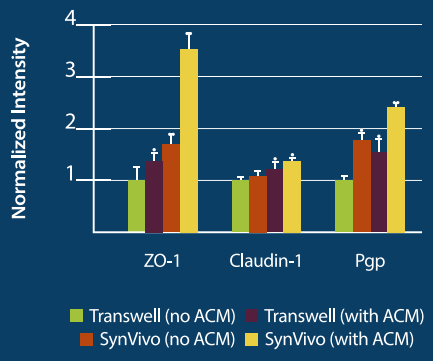


LEFT: *Co-Culture of endothelial cells (stained with CD31) and astrocytes (stained with GFAP) in the SynBBB model highlighting communication across the porous interface.*

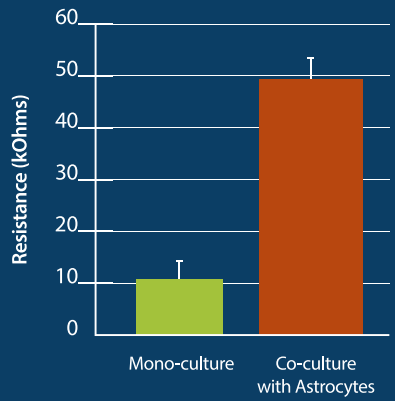
RIGHT: *Real-time visualization of fluorescently labeled small molecule permeation across the BBB. Flow and Astrocyte Conditioned Media (ACM) synergistically control tight junction formation.*



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.



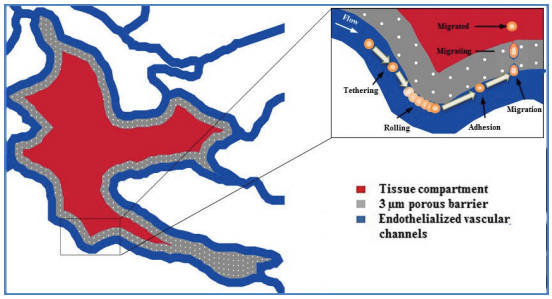
Electrical resistance based analysis of tight junction formation.

Recreate normal and dysfunctional blood brain barrier models

SynRAM 3D Inflammation Model

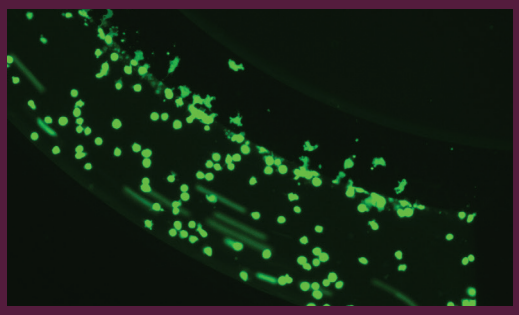
SynRAM™ allows the study of the entire inflammation pathway in a realistic and dynamic environment. By a histological slice of co-cultured tissue and/or tumor cells with a lumen of endothelial cells, SynRAM delivers a physiologically realistic model and enables real-time tracking of rolling, adhesion 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

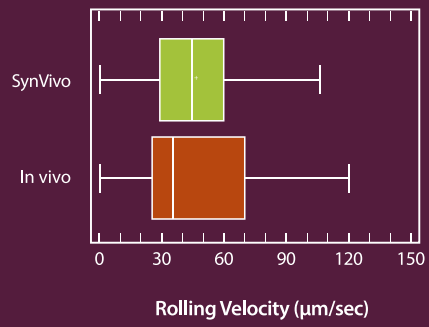


SynRAM enables real-time assessment of cellular interactions comprising of rolling, adhesion and migration through multiple cellular layers in a single experiment with close correlation to in vivo results.

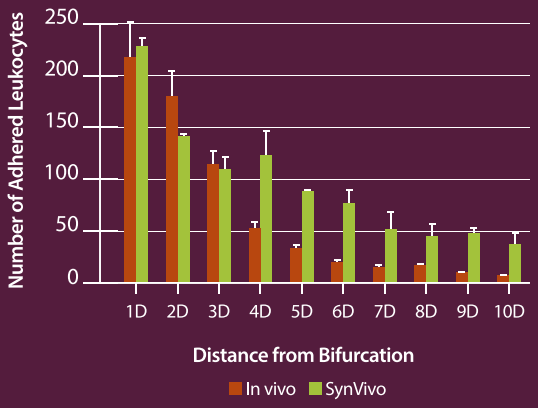
The SynRAM model reproduces inflammation responses observed in vivo



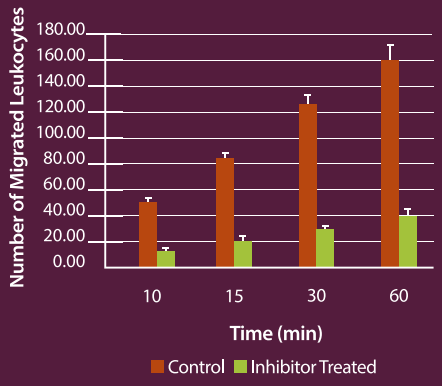
Real-time visualization of leukocyte rolling, adhesion and migration across an inflamed endothelium in the SynRAM 3D model.



Leukocyte rolling velocities are similar to those observed in vivo.



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



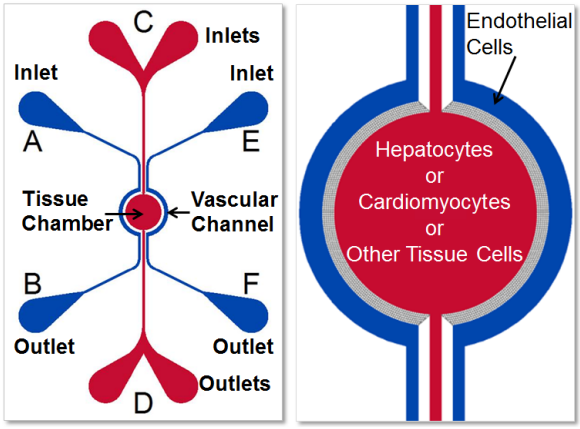
Screening of inhibitors in SynRAM model. In the presence of inhibitor, migration drops significantly (by more than 75%) compared to control conditions.

Simultaneously visualize rolling, adhesion and migration in a single experiment

SynTox 3D Toxicology Model

SynTox™ is the only commercially available 3D tissue model replicating a histological slice of a tissue with in vivo like multicellular architecture.

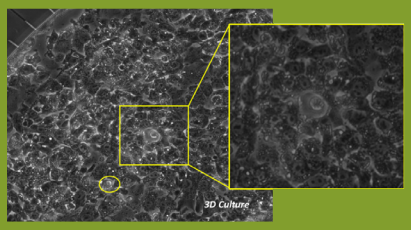
- Physiologically realistic vascular and tissue cell interactions
- Universal platform to model architecture specific to desired organs
- Real time monitoring of cellular responses
- Compatible with standard analytical instruments for both on chip and off chip assays including omic methodologies



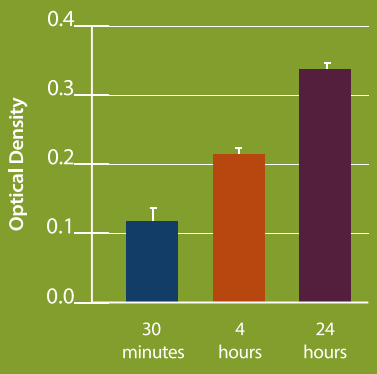
SynTox 3D Toxicology Model recreates the in vivo microenvironment by recreating a histological slice operating in an in vitro format.

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

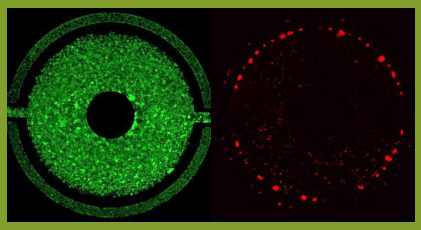
Liver and heart cells were co-cultured with their respective endothelial cells and analyzed for toxicity after treatment with various drugs.



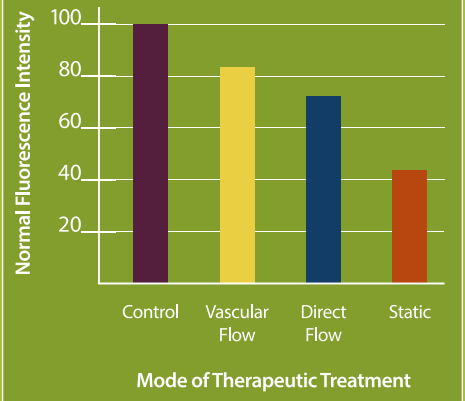
Hepatocytes form bile-canaliculi in SynTox model.



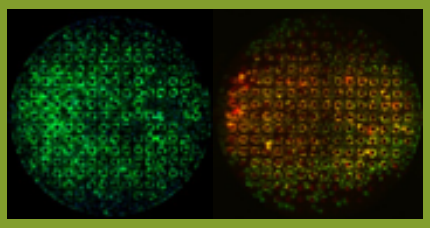
Hepatocytes secrete urea with increasing concentration in a time-dependent manner.



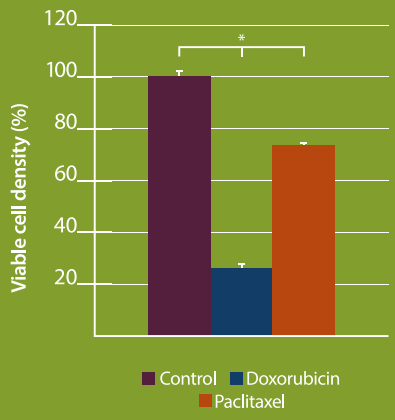
Acetaminophen toxicity on hepatocytes following bolus injection. Peripheral hepatocytes show severe toxicity.



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.

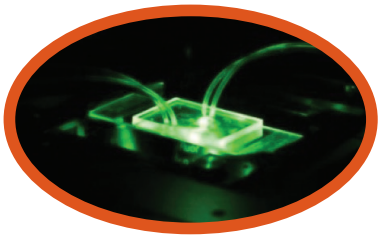


Plot of vascular (endothelial) cell toxicity following treatment with chemotherapeutic. Endothelial cells are highly susceptible to the drugs.

Evaluate candidate drugs for organ specific toxicity responses

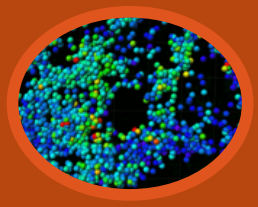
3D Tissue Models - Assay Kits and Chips

Our most popular 3D tissue models – SynTumor for oncology, SynBBB for blood brain barrier, SynRAM for inflammation, and SynTox for toxicology models can be purchased as starter kits, assay kits or the microfluidic chips alone. Kits include all the basic components required to create 3D tissue models to run assays in your specific application. Accessories including tubing, clamps, needles and syringes are included. Starter kits include the pneumatic priming device (required for running co-culture assays).



SynAssay Development and Screening Services

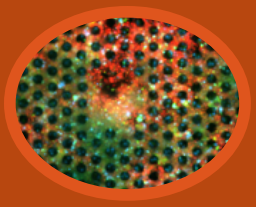
SynAssay provides the realism of an in vivo microenvironment in an in vitro platform for modeling drug delivery, drug discovery and ADME/Toxicity. We provide custom assay development and services specifically tailored to meet your goals. Our team of engineers and scientists will work closely with you to develop the right solution for your application.



Drug Delivery

Validated Data. Get Reliable Prediction!

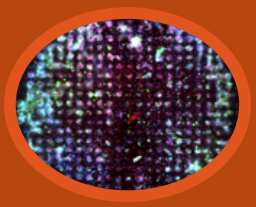
The SynAssay platform has been successfully validated for accurate prediction of in vivo responses. Use this unique platform for realistic assessment of drug delivery in vivo.



Drug Discovery

Understand Mechanism. Develop Better Drugs!

Use the SynAssay platform for real-time visualization and analysis of cell-cell, cell-drug and their underlying mechanisms. Use with confidence to innovate and accelerate your drug discovery pipeline.



ADME/Tox

Safety Concerns. Overcome Early Failures!

Recreate cellular and tissue architecture in an organ-on-a-chip format compatible with standard analytical equipment. The SynAssay platform reduces expensive and time-consuming preclinical or clinical trials.

Contact us to discuss your research needs