SYNVIVO

REALISTIC. DYNAMIC.

Organ-on-Chip Models

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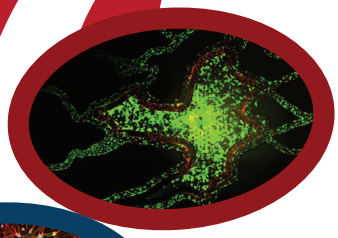
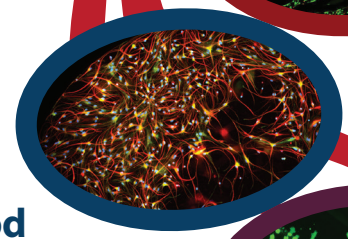
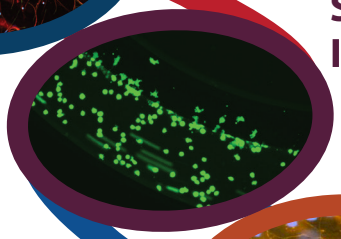


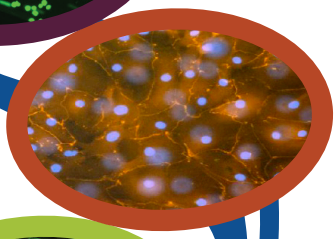
SynTumor Cancer Model



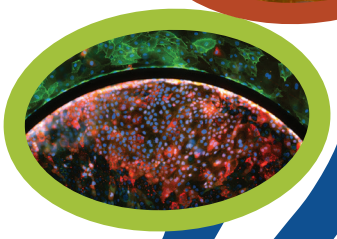
SynBBB Blood Brain Barrier Model



SynRAM Inflammation Model



SynALI Air-Liquid Interface Lung Model



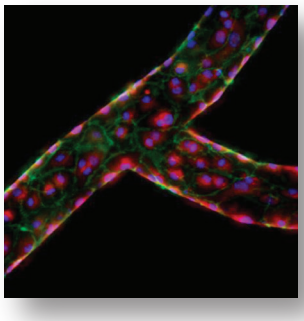
SynTox Toxicology Model

www.synvivobio.com

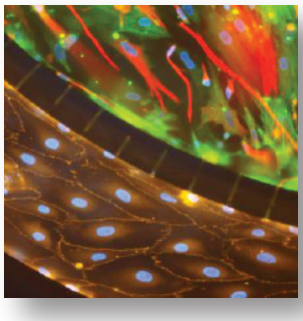
3D Tissue and Organ-on-Chip Models

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.

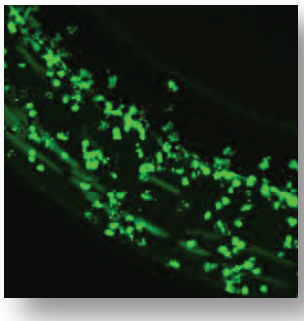
- **Side by side architecture**
  Develop complex co-culture morphology while maintaining real-time visualization and quantitation.
- ***In vivo* like vascular morphology with fully formed lumen**
  Deliver drugs in biologically realistic conditions
- **Real-time monitoring of cellular responses**
 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



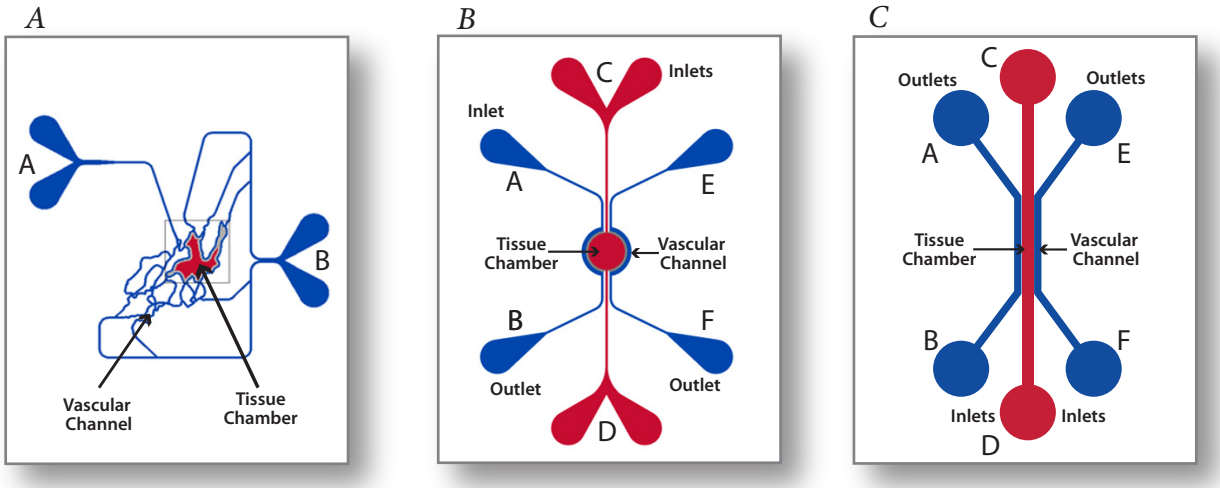
Confocal image of a fully formed vascular lumen



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



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



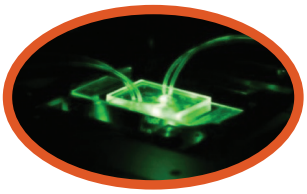
*SynVivo microfluidic chip designs are based on actual microvascular network images **(A)** or Idealized vascular networks **(B&C)** to support replication of the unique features of any tissue or organ in vitro.*

Perform biologically realistic assays

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

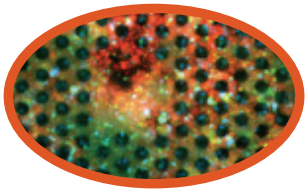
Products

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.

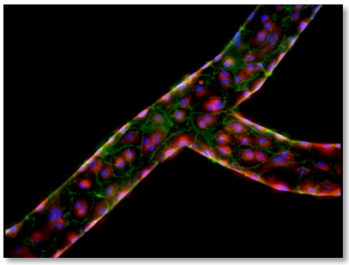
- Screening Services include Target Validation, Compound Screening, Biomarker Analysis, ADME/Tox and Mechanism of Action studies using our validated models.
- Assay Development services can be performed to develop and optimize new models, assay end-points or custom chip designs.
- Deliverables include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

More information at www.synvivobio.com

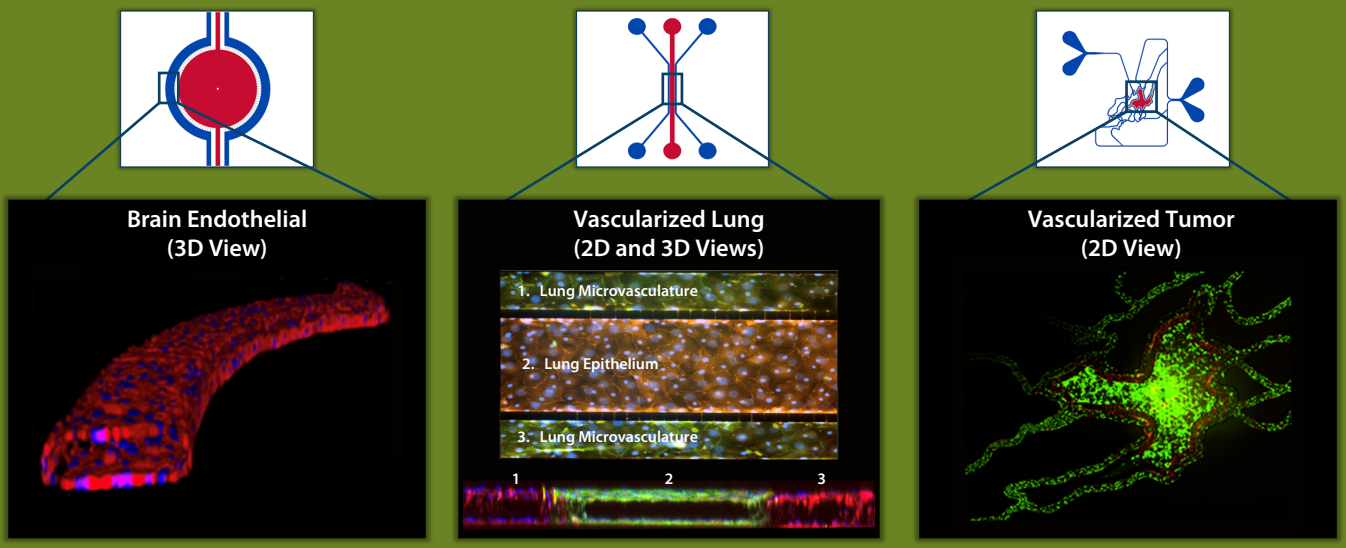
Contact us to discuss your research needs

Vasculature-on-Chip for Drug Efficacy and Safety Studies

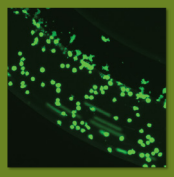
SynVivo's Vasculature-on-Chip models accelerates preclinical drug testing by testing compounds for safety and efficacy when administered under physiological flow conditions. Changes in barrier integrity and vascular injury across multiple organ types can be assessed using permeability, TEER, neutrophil adhesion and migration in response to drugs.

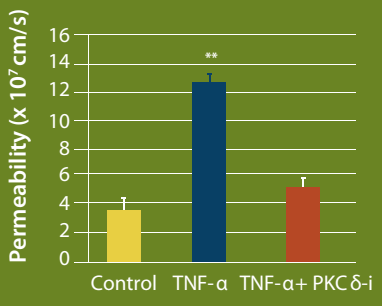


Examples of Vascularized Models on-Chip

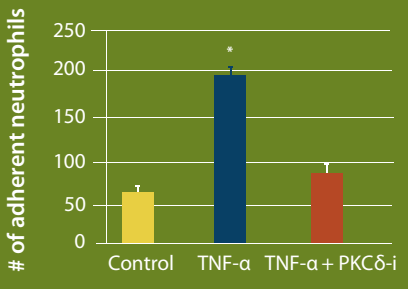


Screen anti-inflammatory therapeutics in organ-matched endothelial vessels

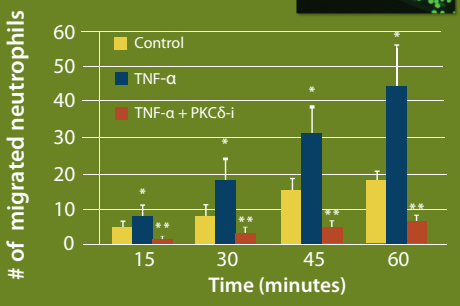




Permeability with fluorescent dextrans



Neutrophil Adhesion



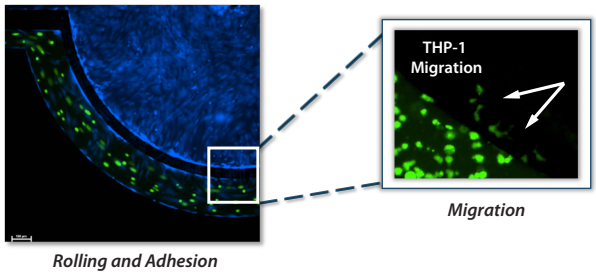
Neutrophil Migration

Endothelial cells treated with TNF-α display inflammation-induced vascular injury that can be assessed with permeability, TEER, neutrophil adhesion or migration readouts. Anti-inflammatory compound PKC- δ inhibitor was able to prevent TNF-α induced inflammation and vascular leakage.

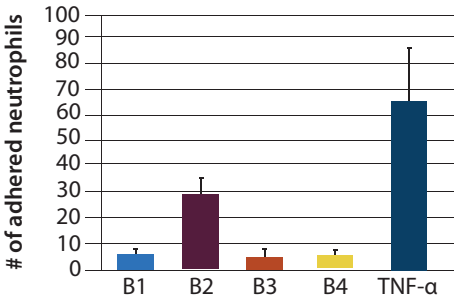
Discover the Future of Drug Testing with Human-Based In Vitro Vascularized Models

Uncover Drug induced vascular injury and inflammation. Assess changes in barrier integrity, monitor vascular injury, and explore the dynamic responses of multiple organ types.

Cardiac Co-culture Model

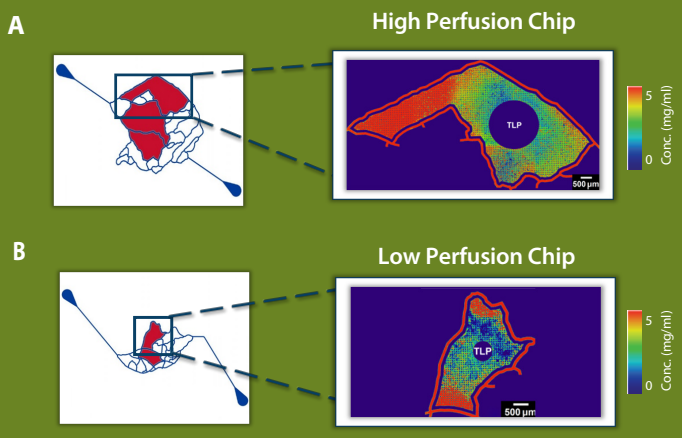


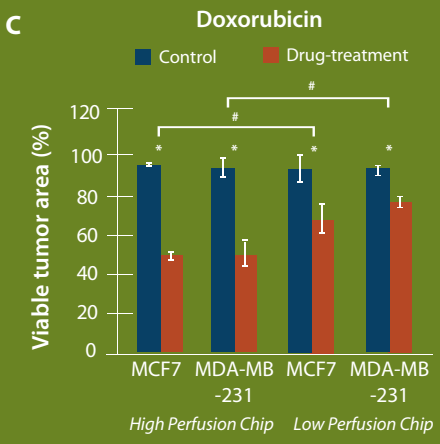
Co-culture of human aortic endothelial cells and cardiac smooth muscle cells treated with drug compounds and assessed for inflammation.



Immune cell adhesion levels on aortic endothelial cells following TNF-α or drug treatment

Assess drug delivery and efficacy in tumors with varying vascular geometries





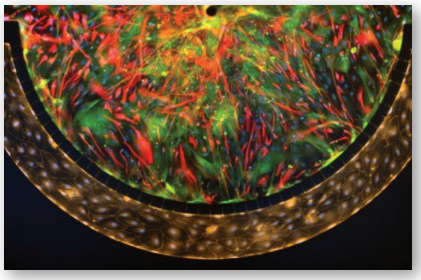
*High Perfusion **(A)** and Low Perfusion **(B)** vascular profiles show differences in tumor cell killing **(C)** with Doxorubicin.*

Vasculature-on-Chip models are available in monoculture with primary endothelial cells or co-culture with tissue/stromal cells

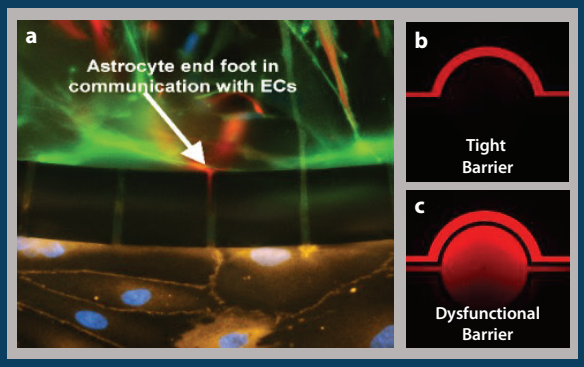
Find our publication list at: www.synvivobio.com/publications

SynBBB Blood Brain Barrier Model

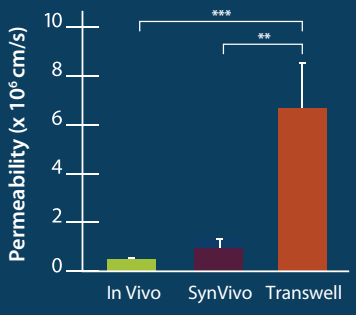
SynBBB Blood Brain Barrier (BBB) on-Chip recreates an *in vivo* like BBB with brain endothelial cells, astrocytes and pericytes with physiological flow to model blood flow and shear stress. SynBBB can be used to detect permeability of compounds from small molecules to biologics. Measure antibody or viral transport across the BBB using receptor mediated transcytosis assays. Measure drug or inflammation induced BBB injury and test drugs that repair a leaky BBB. Model neuroinflammation and test for anti-inflammatory therapeutics.



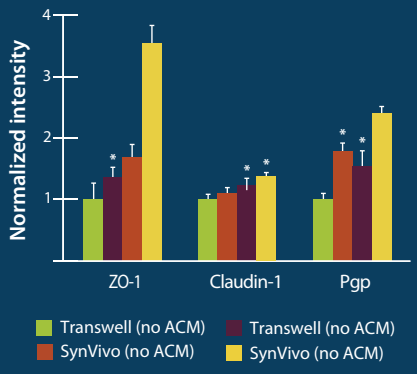
CONTACT US FOR CONTRACT RESEARCH SERVICES USING SynBBB-on-Chip



(a) Human primary cell tri-culture BBB model showing astrocyte end foot in communication with endothelial cells. (b,c) Real-time visualization of small molecule permeation

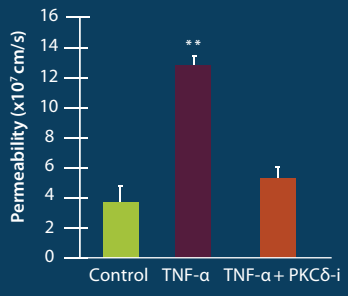


Small molecule permeation data validating the SynBBB model against in vivo and transwell permeability



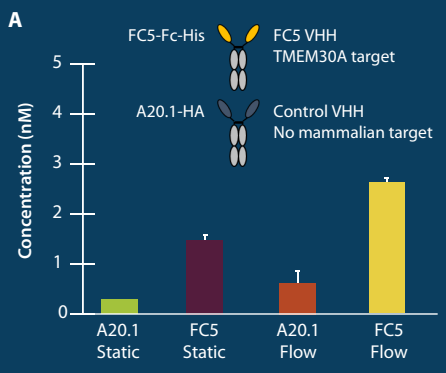
Flow increases the expression of tight junction proteins and transporters when compared to static assays

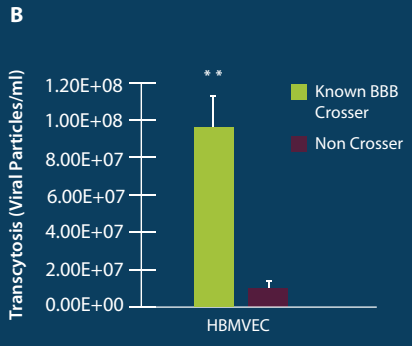
Modeling Neuroinflammation



Permeability assay in human brain endothelial cells inflamed with TNF-α vs control. PKC-δ inhibitor prevents TNF-α induced vascular leakage.

Modeling Antibody and Viral Transcytosis



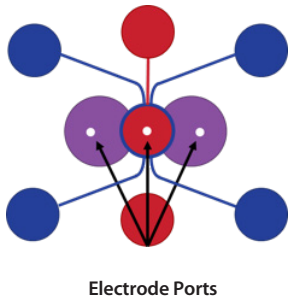


(A) Antibody transcytosis across the SynBBB model. Known crosser FC5-Fc-His vs non-crosser A20.1 tested under static and flow based dosing conditions. (B) AAV Viral Transcytosis with a known crosser vs non crosser in the human SynBBB model.

Recreate Normal and Dysfunctional Blood Brain Barrier Models

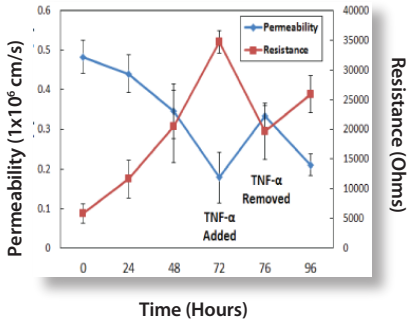
SynBBB TEER Chips Allow Measurement of Resistance on Chip

A



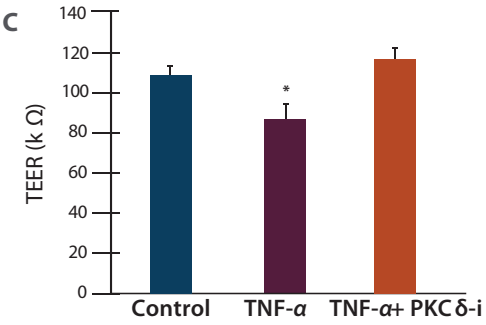
(A) Cartoon showing TEER enabled SynBBB chip

B



(B) SynBBB TEER chip can be used to measure barrier integrity after treatment with inflammatory cytokines over time.

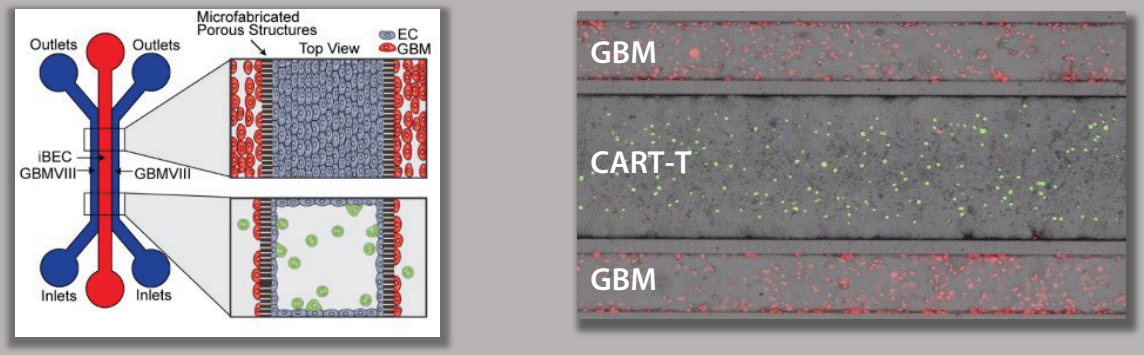
C



(C) Changes in barrier integrity measured using TEER after TNF-α, or TNF-α plus PKC-δ inhibitor compared to control.

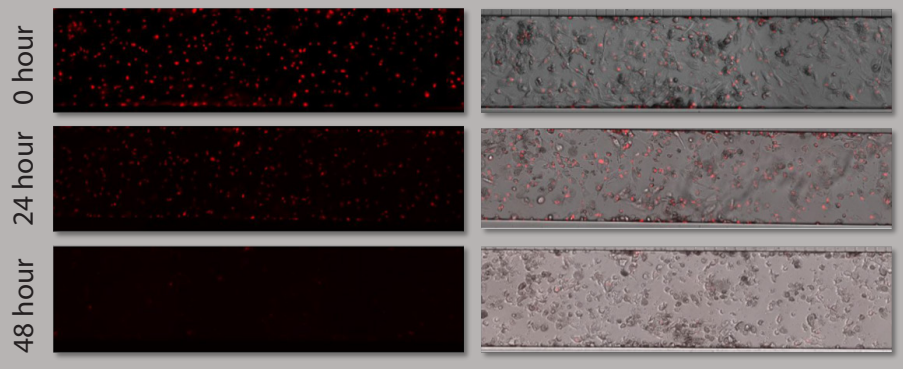
SynBBB Blood-Brain Tumor Barrier Model

A



(A) Extravasation of CAR-Ts targeting U87MG human Glioblastoma (GMB) cells.

B



(B) GBM Cytotoxicity after CAR-T extravasation

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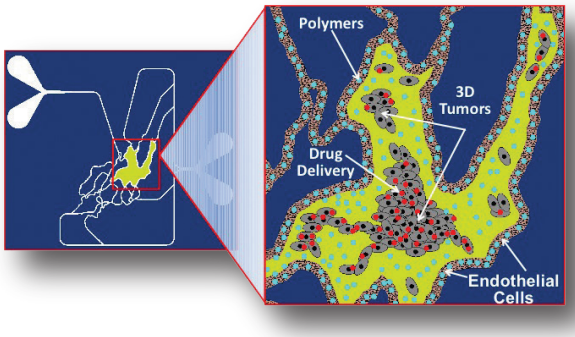
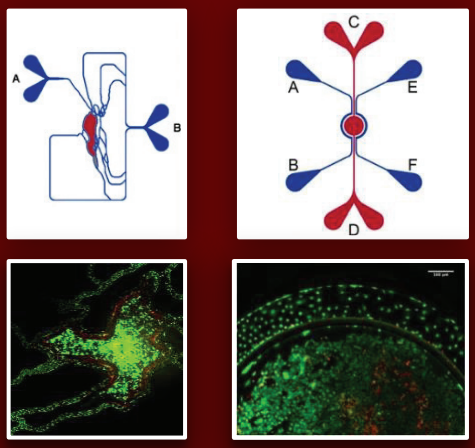
SynTumor Vascularized Cancer Models

SynTumor vascularized Tumor-on-Chip models allow real-time visualization and quantitative assessment of cell-cell and cell-drug interactions in a physiologically realistic tumor microenvironment. The tumor models enable analysis of circulation in the microvasculature, transport across the vessel walls, and drug delivery to tumors.

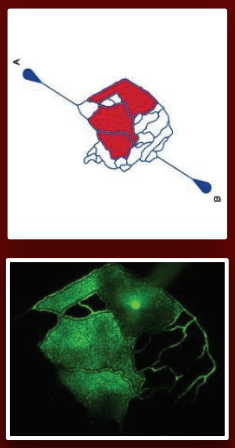


- Morphologically realistic *in vivo* based architecture
- Engineered porous structures recreate fluid-filled interstitial spaces
- Side-by-side architecture enables quantitative real-time visualization
- Recreates a viable histological slice by incorporating geometries of actual microvascular networks with interstitial spaces and tissues/tumors
- Monitor interactions between tumor, stromal, vascular and immune cells

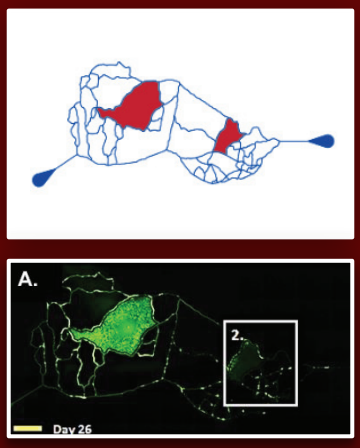
Microvascular or Idealized Network Co-culture Chips



Multi-Chambered Chips High or Low Perfusion



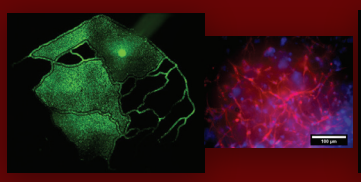
Tandem Design with Separate Vascular Network Beds



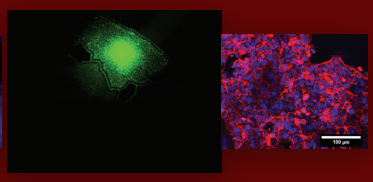
Multiple device architectures are available including the idealized IMN2 (radial or linear) devices, or microvascular (SMN2) network chip configurations in single or multi-chamber formats. Chips can be selected to accommodate 2D (IMN2, SMN2 chips) or 3D (IMN3, SMN3 chips) tumor cultures.

Monitor Phenotypic Behavior of Tumor Cells in Real-Time

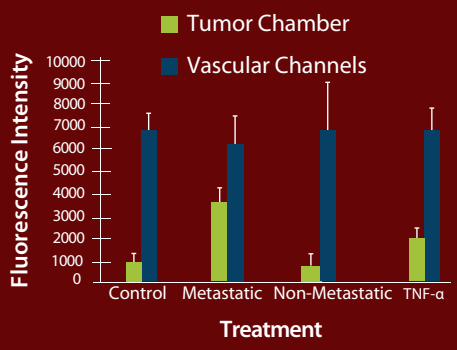
Metastatic Tumor



Non-Metastatic Tumor



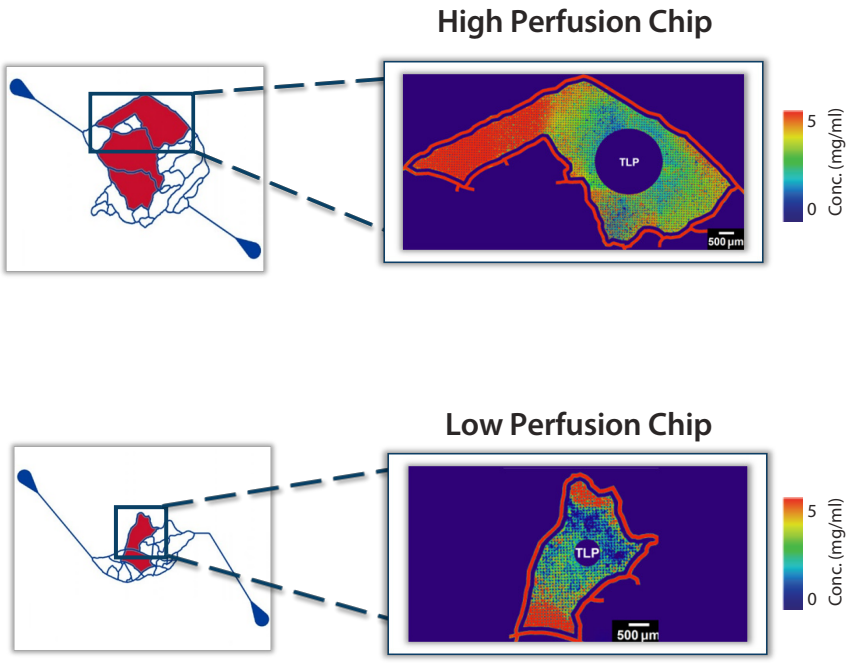
A metastatic tumor (left) rapidly spreads to adjacent chambers, while a non-metastatic tumor does not (right). Insert shows immunocytochemistry-stained images highlighting spindle cell morphology for metastatic tumor cells in contrast to non-metastatic tumor clusters.

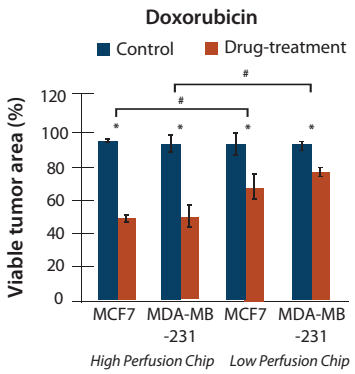


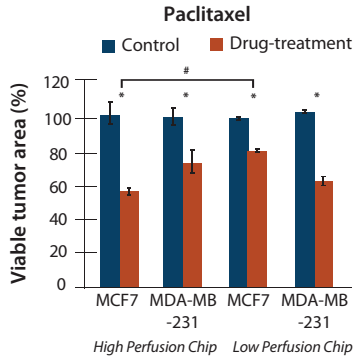
Macromolecular tracers such as fluorescently labeled dextran can be used to measure the permeability of the tumor-endothelial co-cultures. Secretion of proteases by metastatic tumors increases tissue permeability and increases the accumulation of the tracer in the tumor channel similar to the vascular channel. In a non-metastatic tumor, there is very little accumulation of the tracer in the tumor chamber.

Impact of metastatic vs. non-metastatic cells on vasodilation can be evaluated.

Modeling Unique Microenvironments







SynTumor models can investigate factors influencing drug delivery and efficacy including various flow effects in areas of high and low perfusion.

Assay Development and Screening Services using SynTumor

Real-time Monitoring of Cancer, Stromal, Immune, and Vascular Cell Interactions

SynTumor Models Available	• Monoculture using tumor cell lines • Co-Culture with endothelial cells • Tri-Culture with stromal and endothelial cells • Tri-Culture with stromal, endothelial and immune cells
Assays available:	• Efficacy and toxicity screening • Cell proliferation, morphology, viability • Tumor-induced vascular leakage • Tumor Intravasation and extravasation • Tumor Immune Cell interactions • Drug delivery, uptake, and efficacy • Biomarker analysis • On-chip or off-chip analysis

Selected Publications using the SynTumor Models

(1) **Rapid Assessment of Nanoparticle Extravasation in a Microfluidic Tumor Model**
Mai N. Vu et al (2019). *ACS Applied Nano Materials* 2 (4), 1844-1856.

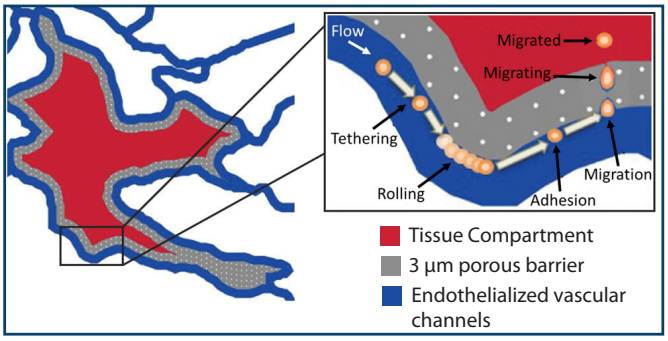
(2) **A Microvascularized Tumor-mimetic Platform for Assessing Anti-cancer Drug Efficacy**
Pradhan, S. et al (2018) *Scientific Reports* Volume 8, Article number: 3171.

(3) **A Biomimetic Microfluidic Tumor Microenvironment Platform Mimicking the EPR Effect for Rapid Screening of Drug Delivery Systems**
Tang Y et al (2017). *Scientific Reports* 7, Article number: 9359.

(4) **Microfluidic Co-Culture Devices To Assess Penetration Of Nanoparticles Into Cancer Cell Mass**
Jarvis, M et al (2017). *Bioeng Transl Med.* Sep 26;2(3):268-277.

SynRAM 3D Inflammation Model

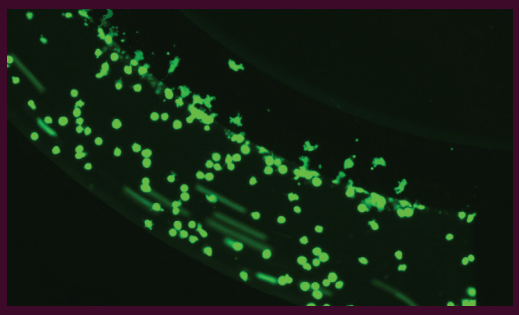
SynRAM™ allows the study of the entire inflammation pathway in a realistic and dynamic environment. By a histological slice of co-cultured tissue and/or tumor cells with a lumen of endothelial cells, SynRAM delivers a physiologically realistic model and enables real-time tracking of rolling, adhesion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



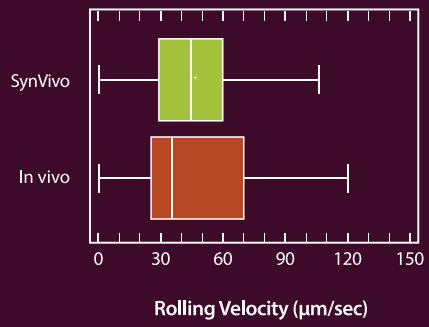
SynRAM enables real-time assessment of cellular interactions compromising of rolling, adhesion and migration through multiple cellular layers in a single experiment with close correlation to in vivo results.

- 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

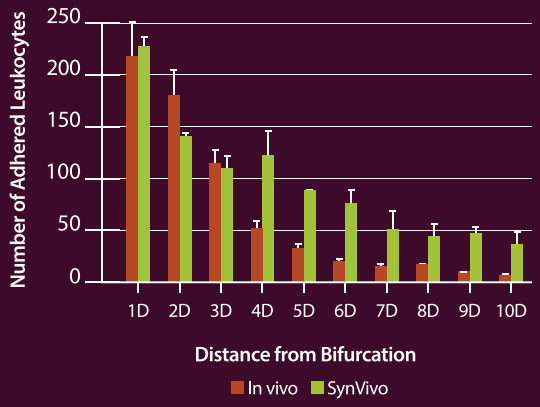
The SynRAM model reproduces inflammation responses observed *in vivo*



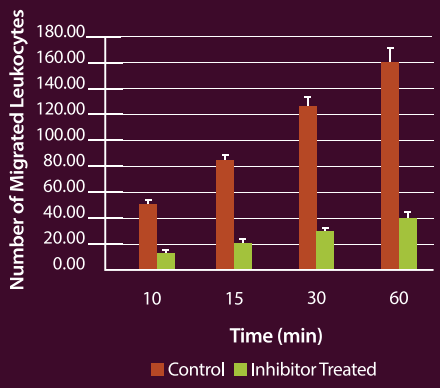
Real-time visualization of leukocyte rolling, adhesion, and migration across an inflammed endothelium in SynRAM 3D model.



Leukocyte rolling, velocities are similar to those observed in vivo



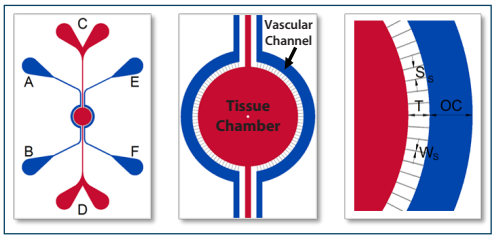
Leukocyte adhesion pattern in SynRAM matches leukocyte adhesion in vivo



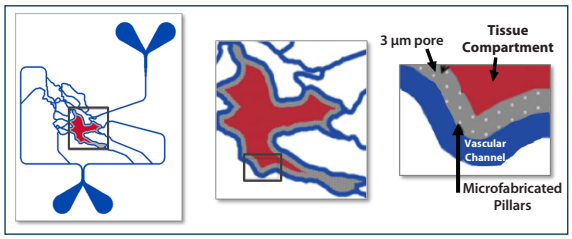
Screening of inhibitors in SynRAM model. In the presence of inhibitor, migration drops significantly (by more than 75%) compared to control conditions

Simultaneously visualize rolling, adhesion and migration in a single experiment

IMN2 Idealized network co-culture Chips



SMN2 microvascular network Co-Culture Chips



Chip Schematics - Depending on your specific research applications you can select from basic IMN2 or SMN2 microvascular co-culture chip configurations.

Assay Development and Screening using SynRAM

SynRAM Models Available	• Monoculture using primary endothelial cells/cell line • Co-Culture with stromal/tissue cells
Types of Service Projects	• Immune cells (primary, cell lines) rolling, adhesion and migration across the endothelium • Inflammation-induced vascular permeability • Drug-induced vascular injury • Inflammation-induced biomarker analysis • Therapeutic screening • Screening for cell surface biomarkers • Target Identification • Screening for activators/inhibitors of inflammation

Don't see your model or assay of interest?
Contact our expert scientific team to discuss your needs

Selected Publications using the SynRAM Model

(1) **The Role of Tyrosine Phosphorylation of Protein Kinase C Delta in Infection and Inflammation.**
Yang Q et al (2019). *Int J Mol Sci*. 2019 Mar 26; 20 (6)

(2) **PKCδ Inhibition as a Novel Medical Countermeasure for Radiation-Induced Vascular Damage.**
Soroush F et al (2018). *The FASEB Journal*. Vol. 32, No. 12.

(3) **A Novel Microfluidid Assay Reveals a Key Role for Protein Kinase C δ in regulating human Neutro-Phil-Endothelium Interaction.**
Soroush F et al (2016). *J Leukoc Biol*. 100:1027-1035.

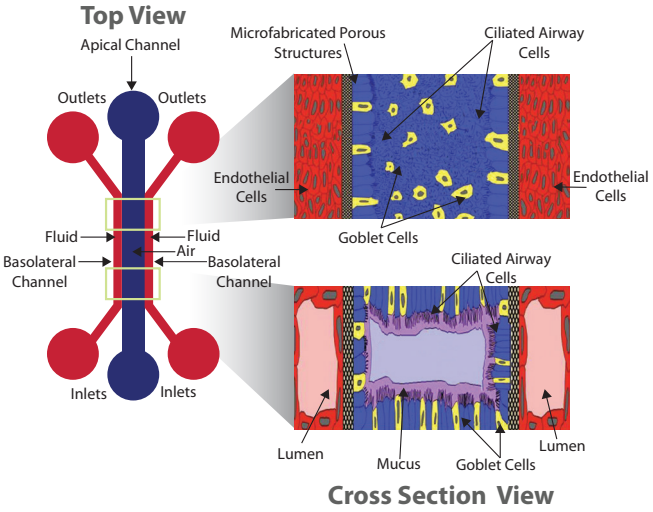
(4) **Bioinspired Microfluidic Assay for In Vitro Modeling of Leukocyte-Endothelium Interactions.**
Lamberti, G et al (2014). *Anal. Chem.* 2014, 86 (16), 8344-8351

SynALI: Lung Air-Liquid Interface-on-Chip Model

SynALI Lung model is functionalized with epithelial cells surrounded by vasculature comprised of lung microvascular endothelial cells. The functionalized model maintains an Air Liquid Interface (ALI) across the airway cells, allowing the formation of airway 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 in normal and diseased conditions.

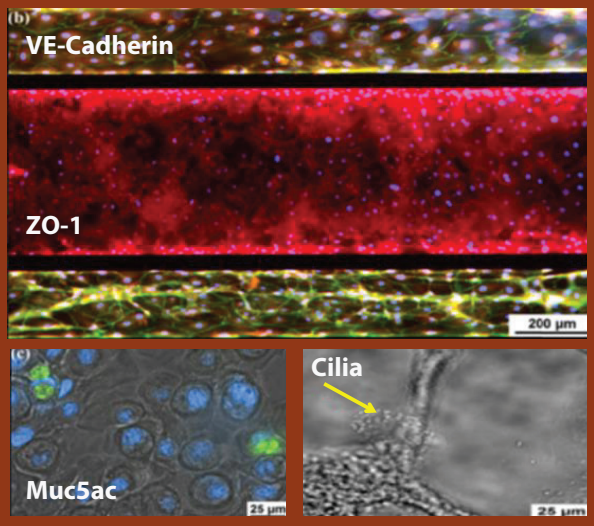
Unique features include:

- 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



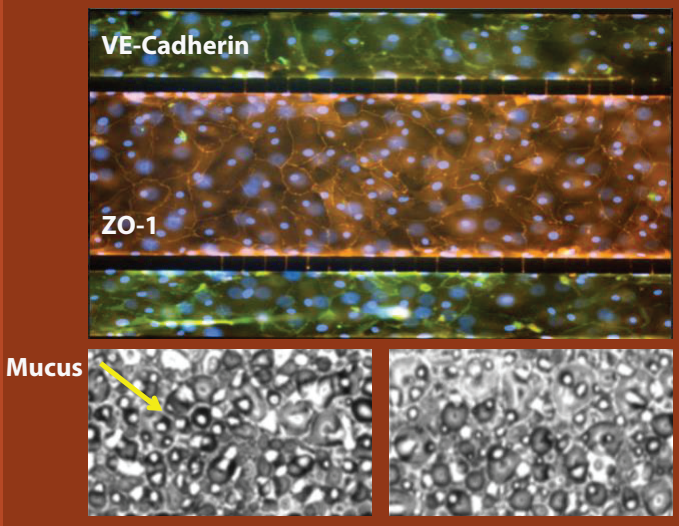
Schematic of the device used to develop the air-liquid-interface across the cells. The air (or epithelial) channel is separated from two fluid (basolateral) channels by a micro-fabricated porous structure. Right panel shows the orientation of cells when seen from top and cross-section views.

Small Airway Lung Model



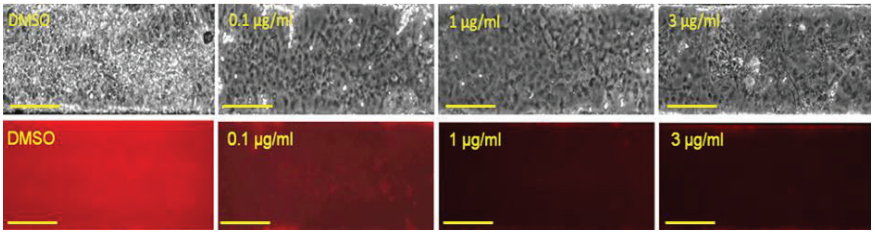
Co-culture human bronchial epithelial cells and human lung microvascular cells.

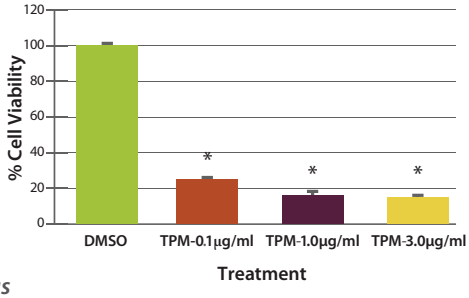
Alveolar Lung Model



Co-culture human microvascular lung endothelial cells, human alveolar epithelial cells type I and II.

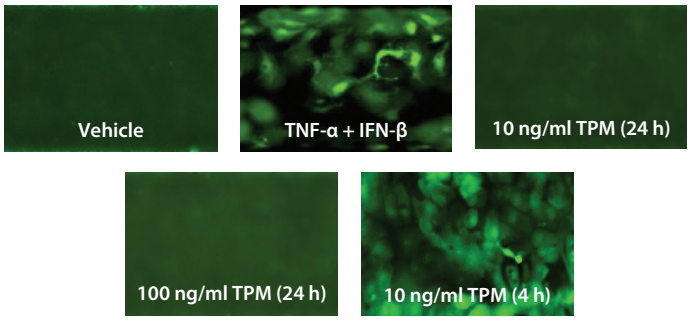
SynALI Lung-on-Chip model can quantitate lung epithelial viability after compound exposure

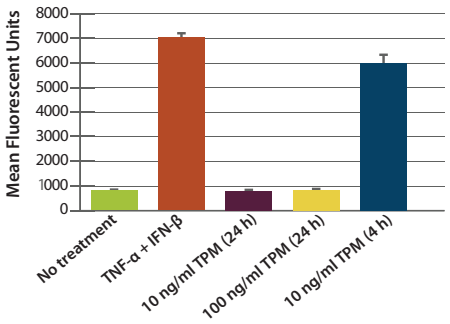




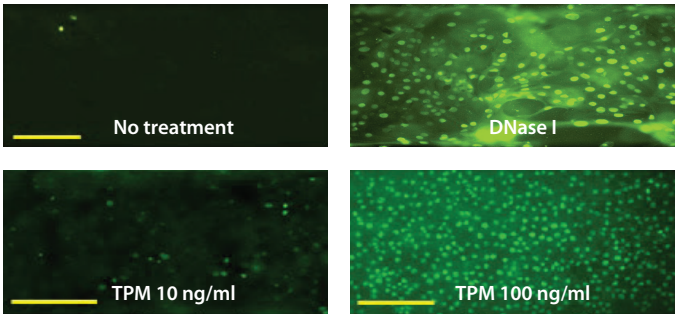
Viability of lung epithelium treated with equi-nicotine units of TPM was significantly lower than the DMSO-treated control

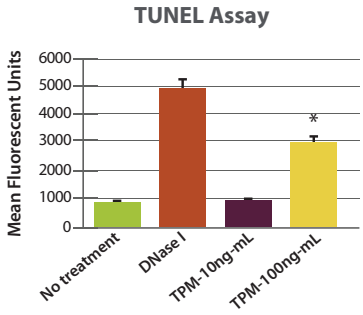
Lung epithelial oxidative stress and apoptosis visualized and quantified in SynALI





Cigarette total particulate matter increases oxidative stress measured at 4 hours and 24 hours post dosing.





Cells treated with10 ng/ml equi-nicotine units of TPM induced a moderate cell death; whereas, 100ng/ml equi-nicotine units of TPM enhanced apoptotic cell death.

Contract Research Services using the SynALI Model

Air Liquid Interface Models available:	• Monoculture using primary epithelial cells • Co-Culture with endothelial cells • Tri-Culture with fibroblasts
Assays available:	• Toxicity assays • Biomarker analysis • Therapeutic screening
Sample Endpoints:	Vascular Permeability, TEER resistance measurements, Viability, ROS, Real-time imaging of cellular changes, Biomarker analysis, Quantitation of immune cell interactions with the endothelium, Biomarker screening using immunoassays. Collect cells or effluents for down-stream genomic, proteomic or metabolomic analysis.

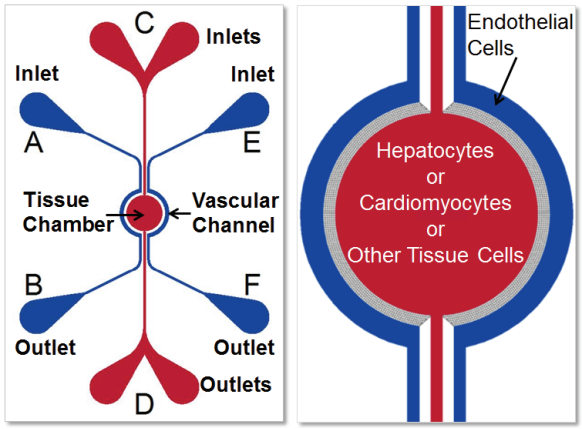
Publications using SynALI Lung Model

Co-Cultured Microfluidic Model of The Airway Optimized for Microscopy and Micro-Optical Coherence Tomography Imaging
Liu, Z. et al (2019). *Biomedical Optics Express* Vol. 10, Issue 10, pp. 5414-5430

SynTox 3D Toxicology Model

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

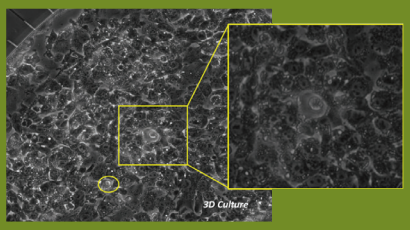
- Physiologically realistic vascular and tissue cell interactions
- Universal platform to model architecture specific to desired organs
- Real-time monitoring of cellular responses
- Compatible with standard analytical instruments for both on chip and off chip assays including omic methodologies



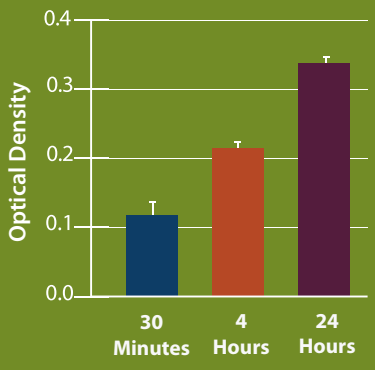
SynTOX 3D Toxicology Model recreates the in vivo microenvironment by recreating a histological slice operating in an in vitro format.

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

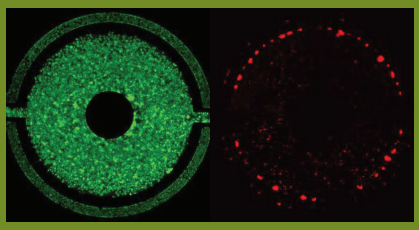
Liver and heart cells were co-cultured with their respective endothelial cells and analyzed for toxicity after treatment with various drugs.



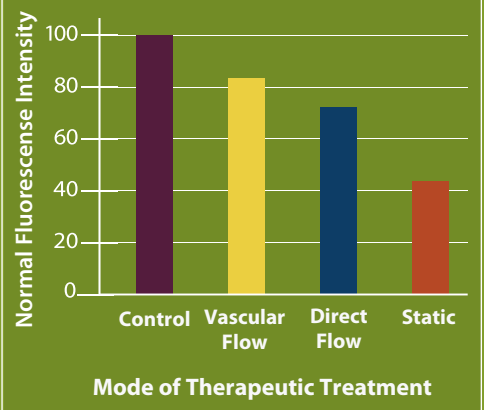
Hepatocytes form bile-canaliculi in SynTox model.



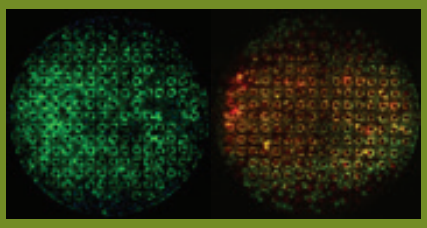
Hepatocytes secrete urea with increasing concentration in a time-dependent manner.



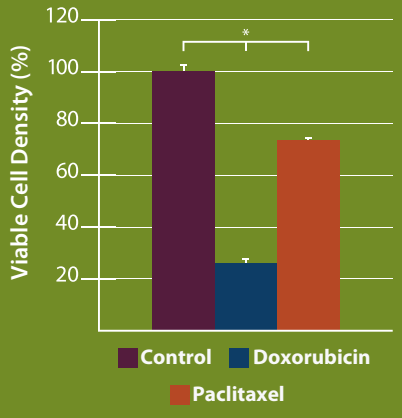
Acetaminophen toxicity on hepatocytes following bolus injection. Peripheral hepatocytes show severe toxicity.



Hepatocytes toxicity following different modes of treatment.



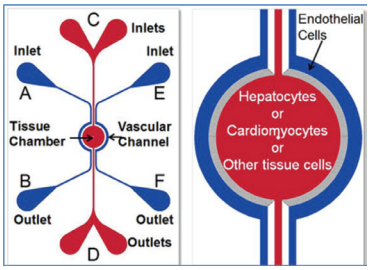
Drug toxicity on cardiac cells. Left panel indicates viable cells while right panel indicates mixture of live and dead cells following drug treatment.



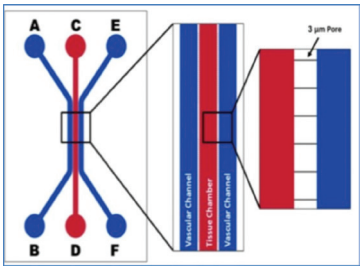
Plot of vascular (endothelial) cell toxicity following treatment with chemotherapeutic. Endothelial cells are highly susceptible to the drugs.

Evaluate candidate drugs for organ specific toxicity responses

Idealized network co-culture Chip (IMN2-Radial)



Idealized network co-culture Chip (IMN2-Linear)



Chip Schematics - Depending on your specific research applications you can select from basic IMN2 Radial or Linear chip configurations.

Contract Research Services using the SynTox Model

Real-time Monitoring of Organ and Species-Specific Drug Toxicity

SynTox Models Available	• Monoculture using endothelial cells • Co-Culture with stromal/tissue cells
Assays available:	• Drug-induced vascular leakage • Vascular inflammation • Biomarker analysis • Efficacy and toxicity screening • Dose-response • Cell viability • Mechanism of action studies
Sample Endpoints:	Sample Endpoints: Vascular Permeability measurements using fluorescent-tagged molecule. If untagged use mass spectrometry or other readouts from collected effluents, TEER resistance measurements, Viability, ROS, Real-time imaging of cellular changes, Biomarker analysis, Quantitation of immune cell interactions with the endothelium, Biomarker screening using immunoassays. Collect cells or effluents for downstream genomic, proteomic or metabolomic analysis. Contact us to discuss your specific project needs.

Publication using SynTOX Model

A 3-Dimensional Microfluidic Platform for Modeling Human Extravillous Trophoblast Invasion and Toxicological Screening

Yong Pu et al (2019). *Lab Chip*, 2021, 21, 546-557

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