The Gulf Coast Consortia's High Throughput Research and Screening Center at the IBT

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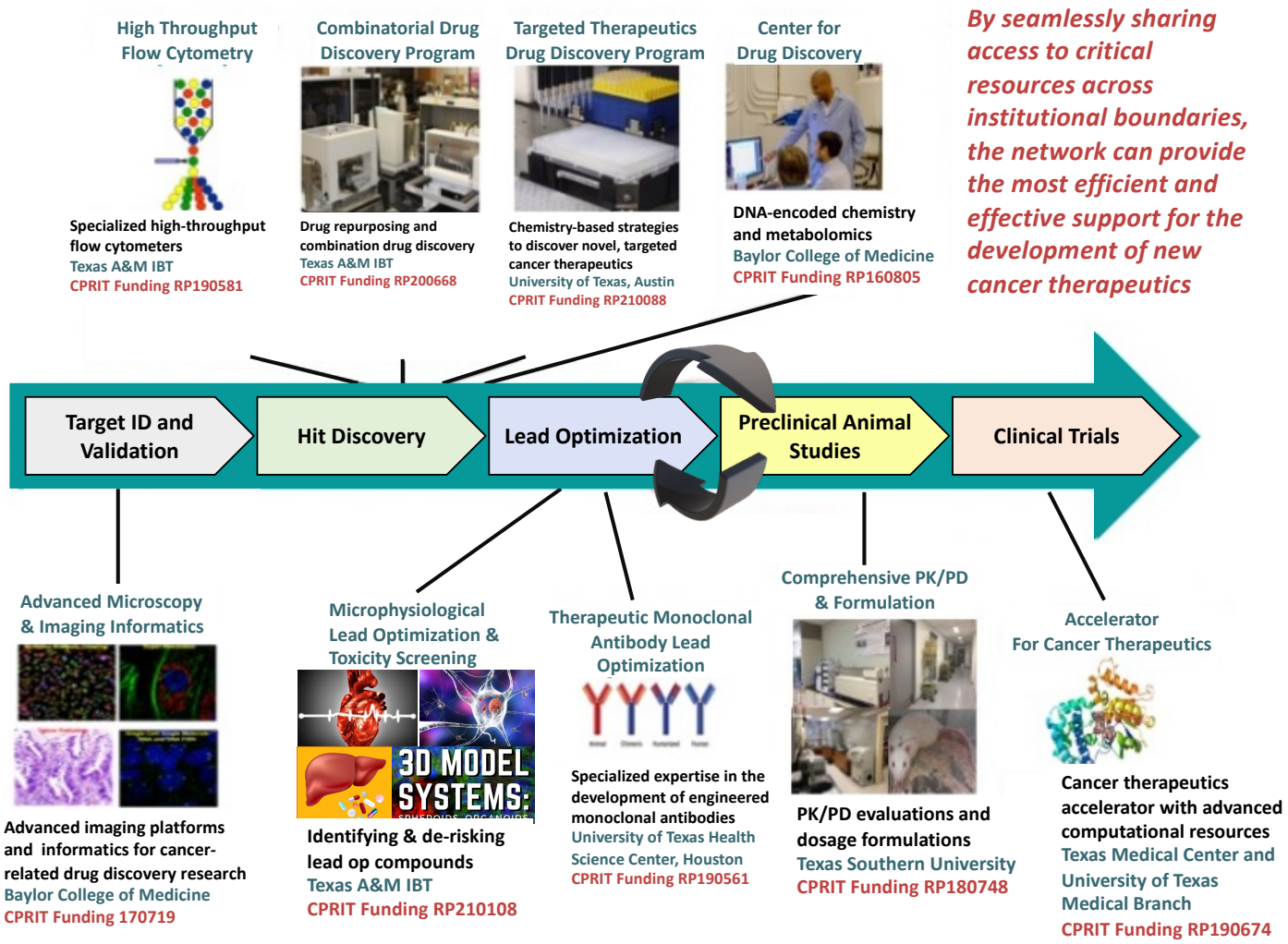
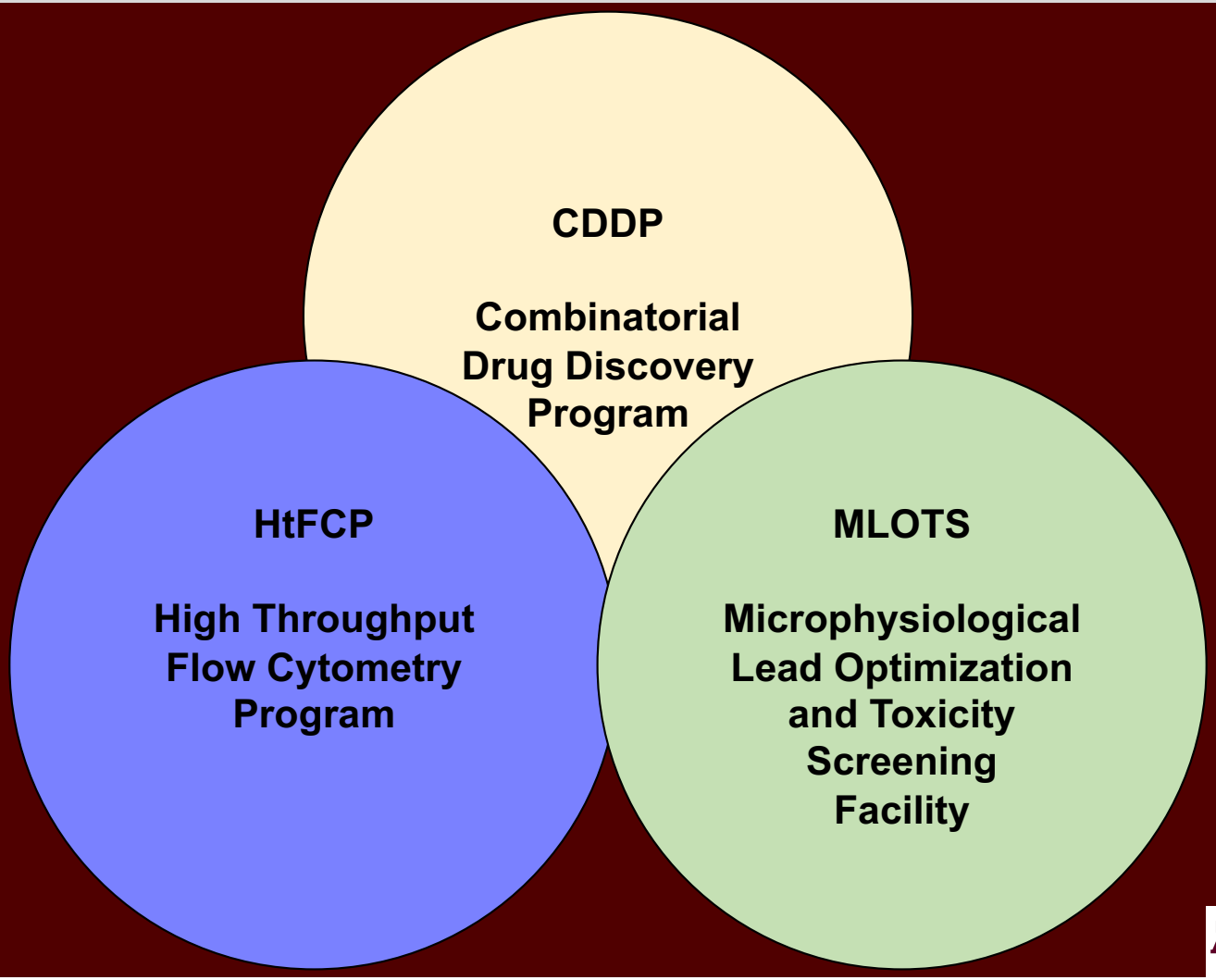
Scientific Director
cstephan@tamu.edu

INSTITUTE OF BIOSCIENCES AND TECHNOLOGY
TEXAS A&M UNIVERSITY

GCC Consortium for Innovative Drug Discovery and Development (IDDD)



GCC Drug Discovery Cores at the Texas A&M IBT



INSTITUTE OF BIOSCIENCES AND TECHNOLOGY
TEXAS A&M HEALTH SCIENCE CENTER

GCC Drug Discovery Cores at the Texas A&M IBT

Automated liquid handling platforms + TC Incubators

- Plate washers

- Tecan Evo

Robotically integrated Detection systems

- ImageXpress Micro confocal & IN Cell 6000

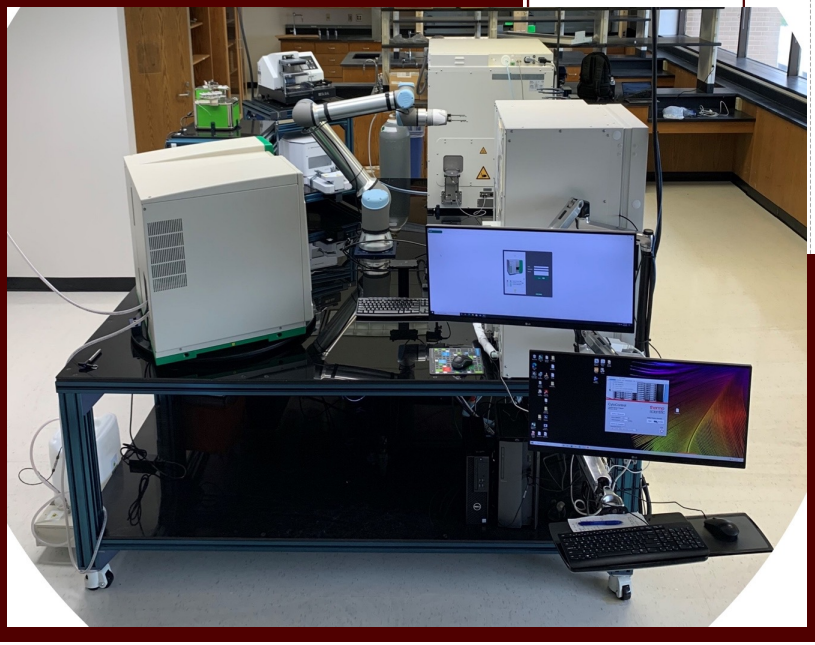
- MP-FLIM

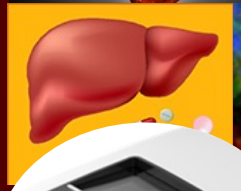
- ZE5 flow cytometer

- Neo Synergy2 & Tecan M1000 readers

Data & Image processing and secondary analysis

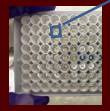
- Biovia Pipeline Pilot
- Deep Learning Studios
- Python
- Fiji/ImageJ

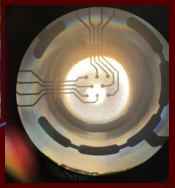




3D MODEL SYSTEMS:

PHEROIDS, ORGANOIDS.





GCC Drug Discovery Cores at the Texas A&M IBT

Each of the Cores is:

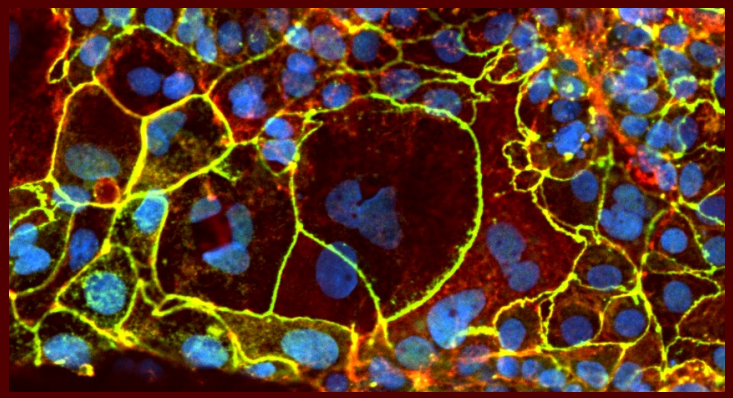
- A unique, highly productive multi-institutional screening resource
- Available to academic, private, and corporate investigators
- Easily accessible – Your neighbor in the Texas Medical Center located in the Texas A&M Institute of Biosciences and Technology
- Part of the GCC, the organization that lowers the barriers to collaboration for the member institutions

IBT Combinatorial Drug Discovery Program

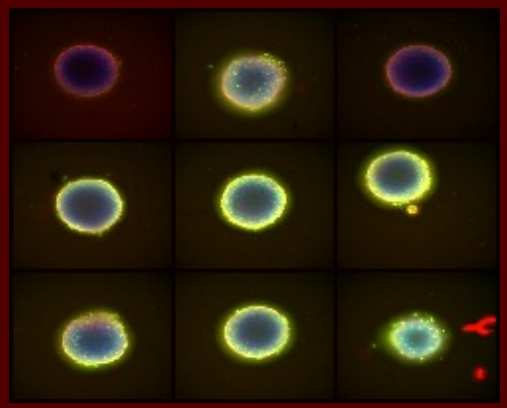
- **Assay development and pilot screens**
  - Bench to HTS
  - Grant support
- **Single agent screens**
  - Probe identification and Mechanism of action studies
  - Focused screens
- **Combinatorial screens – "Repurposing"**
  - Identifying therapeutic leads that can be rapidly advanced to preclinical and clinical evaluation
  - Multi-component drug combinations (cocktails)
  - Targeted agents overcoming resistance or lowering toxicity
- **Secondary analysis**
  - Pharmacogenomics/transcriptomics analysis
  - Biostatistics, conventional modeling, and deep learning

CDDP Target-Based & Phenotypic Drug Discovery Model Systems

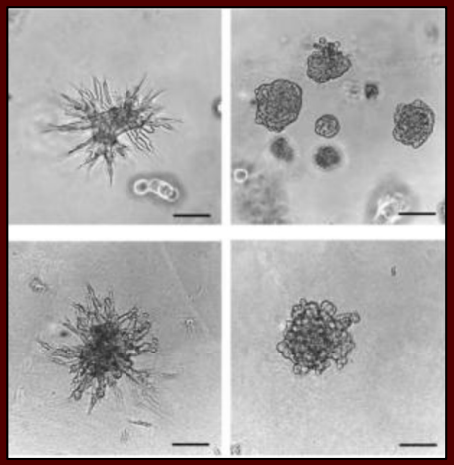
Proteins (enzymes)



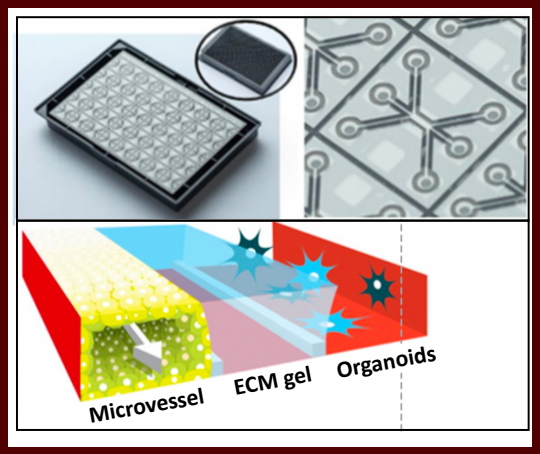
Cells



Spheroids



Organoids



Tissue Chips

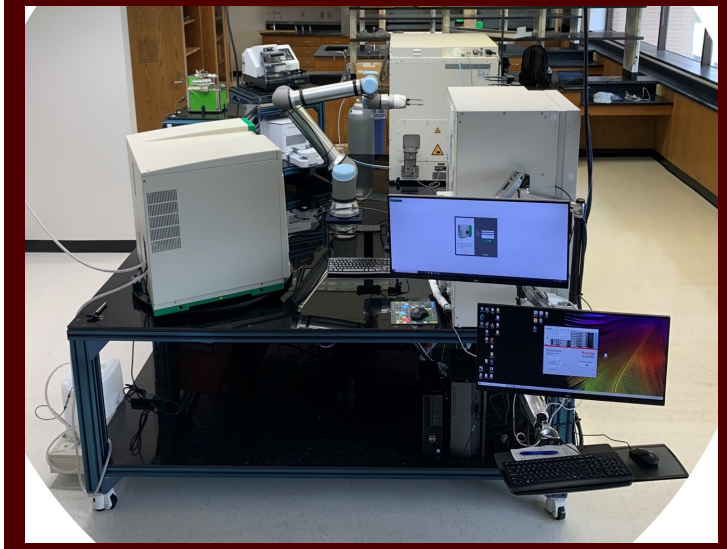
Simple model organisms

CDDP Drug and Compound Collections

Library Focus		Library Focus
Approved Drug Library		Stem cell Differentiation Compound Library
		Cell cycle related compound Library
Oxidation-Reduction Compound Library		Apoptosis Compound Library
Anti-Metabolism disease Compound Library		Autophagy Compound Library
Mitochondrial Targeting Compound Library		DNA Damage _ Repair Compound Library
Epigenetics Compound Library		Ion Channel Inhibitor Library
		Endocrinology-Hormones Library
PI3K-AKT-mTOR Compound Library		Neuronal Signaling Compound Library
MAPK Inhibitor Library		
Tyrosine kinase inhibitor library		JAK STAT Compound Library
		Wnt_Hedgehog_Notch Compound Library
Selleck Bioactives Collection		
		Fluorochemical Library
Prestwick/Microsource Collections		Natural Compound Library

CDDP maintains a collection of drugs and investigational agents approved for use in humans, bioactive compounds, natural products, and some small molecules. The Core maintains > 35,000 testable agents.

High Throughput Flow Cytometry Program - HtFCP



BioRad ZE5 cell analyzer

Services provided with automated HT flow cytometry for drug discovery:

- **Speed**: automated HT drug screening in hours vs days
- **Scalability**: can run large scale drug screens > 9,000 samples/day
- **Customized projects**:
  - Ability to multiplex endpoints
  - Detection of extracellular vesicles, exosomes, and nanoparticles (LOD 0.2µm)
  - Informatics analysis with machine learning and AI

Major equipment:

Bio-Rad ZE5 High Throughput Flow Cytometer

- 5 laser and 30 detectors
- Continuous 24hr sampling from tubes or multiwell plates

BD Biosciences FACSFusion Cell sorter

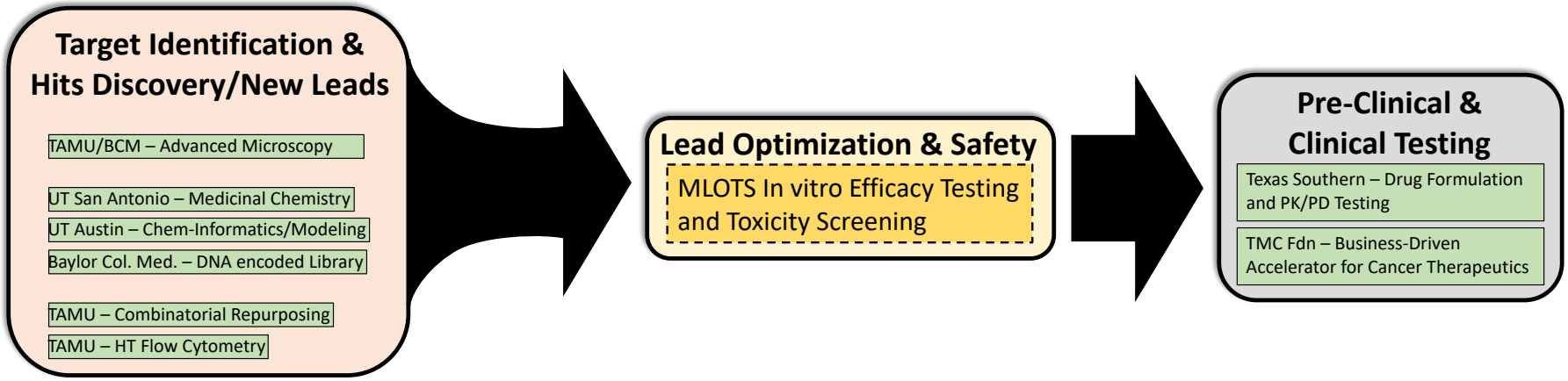
- 4 lasers (405 nm, 488 nm, 561 nm, and 640 nm) and 15 filters
- BSL2 level sorting of single cells into bulk tubes or 96 well plates

Cytek Aurora Spectral Flow Cytometer

- 3 lasers (488, 567, and 640 nm) and 32 fluorescent channels
- full imaging spectral flow cytometry

Microphysiological Lead Optimization & Toxicity Screening - MLOTS

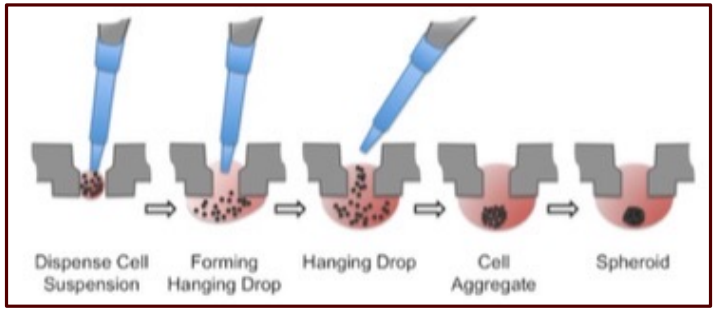
Drug Discovery and Development Pipeline

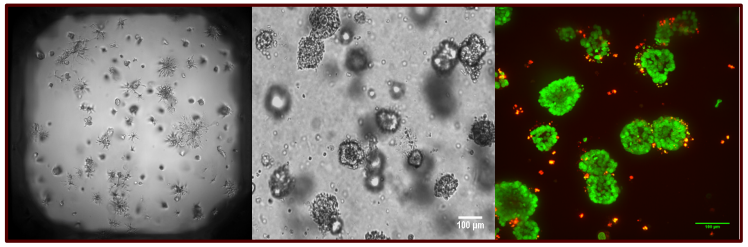


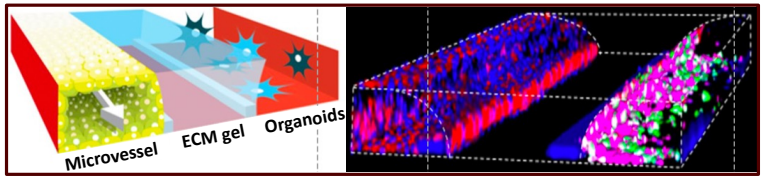
- Current CPRIT-Funded resources for drug discovery in the Texas Medical Center and the region.
- MLOTS fills a perceived void in the pipeline for efficacy testing in 3D and microfluidic models and early toxicity testing (CV, CNS, Liver)

Microphysiological Lead Optimization & Toxicity Screening - MLOTS

MLOTS - 3D Model Efficacy Testing for Lead Optimization







Cellular Spheroids

- Hanging drop
- Ultralow attachment
- n3D Magnetic beads

Cellular Organoids

- Cells cultured in ECM
- Stem cell focused

Microfluidic, Multicellular Models

- High throughput (96/64/48 well)
- Vascularized organoids

Microphysiological Lead Optimization & Toxicity Screening - MLOTS

MLOTS – Fail Early/Tox Identification Testing for Lead Optimization

Liver Toxicity Testing – Initial Model

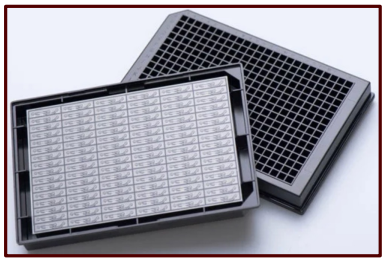
› Toxicology. 2021 Feb 28;450:152667. doi: 10.1016/j.tox.2020.152667. Epub 2021 Jan 6.

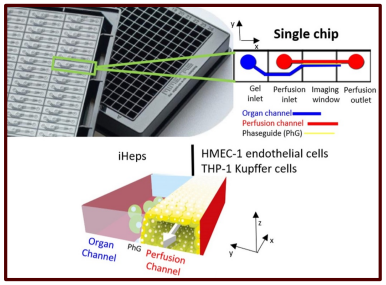
A 3D microfluidic liver model for high throughput compound toxicity screening in the OrganoPlate®

Kristin M Bircsak [1], Richard DeBiasio [2], Mark Miedel [2], Alaa Alsebahi [3], Ryan Reddinger [3], Anthony Saleh [3], Tongying Shun [2], Lawrence A Vernetti [2], Albert Gough [4]

Affiliations + expand

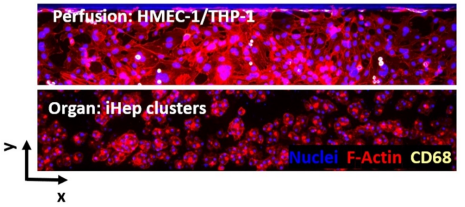
PMID: 33359578 DOI: 10.1016/j.tox.2020.152667



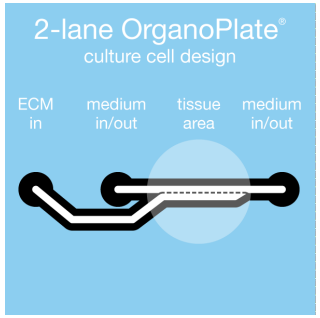


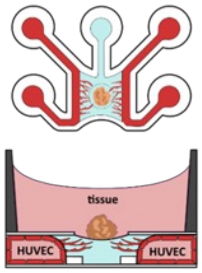
Multi-well plate format
96 ‘Chips’/plate

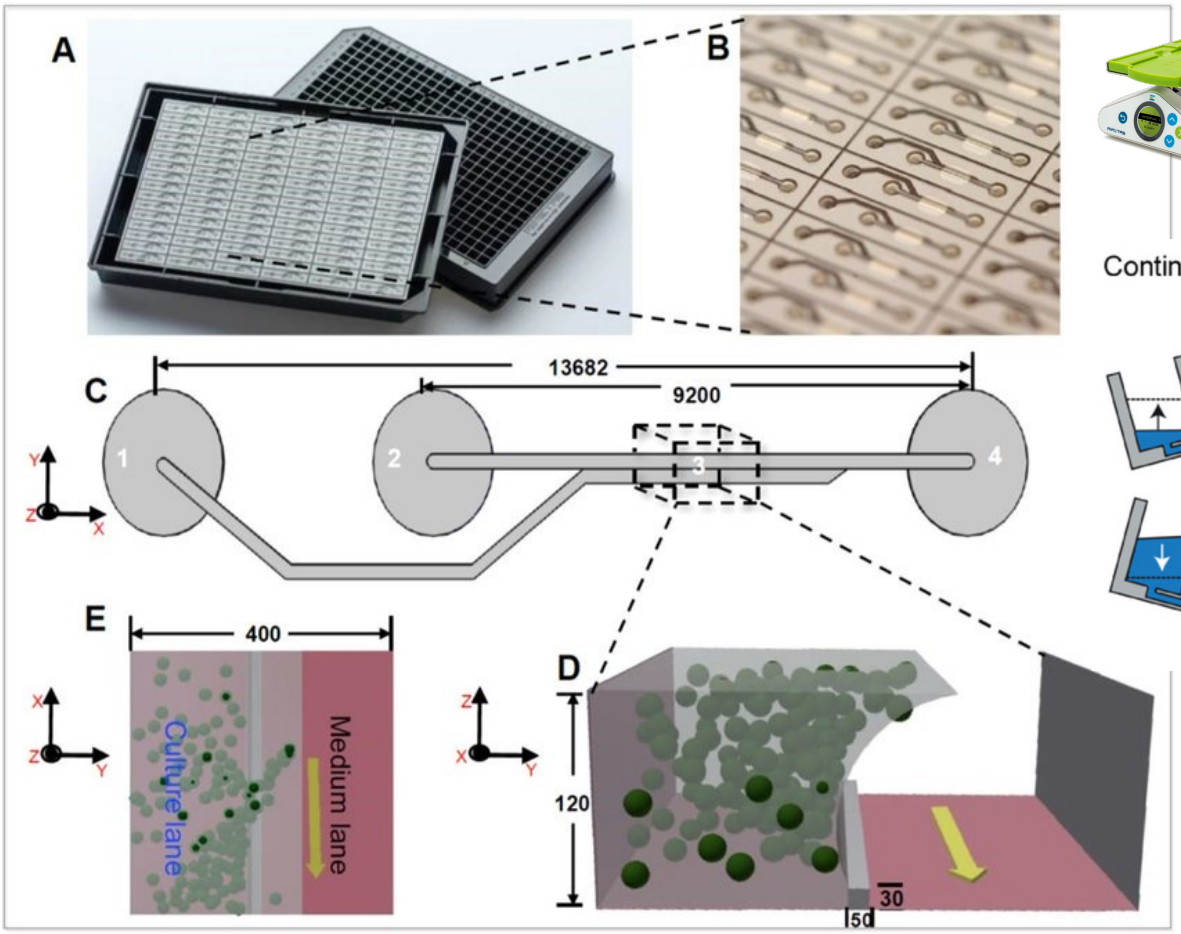
Multi-cellular
Vascular channel
with perfusion



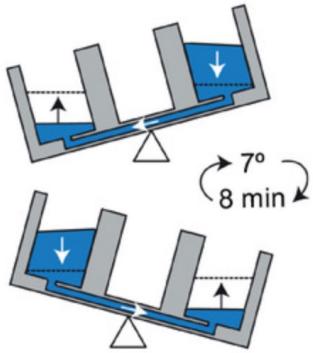
Mimetas Technology Platform



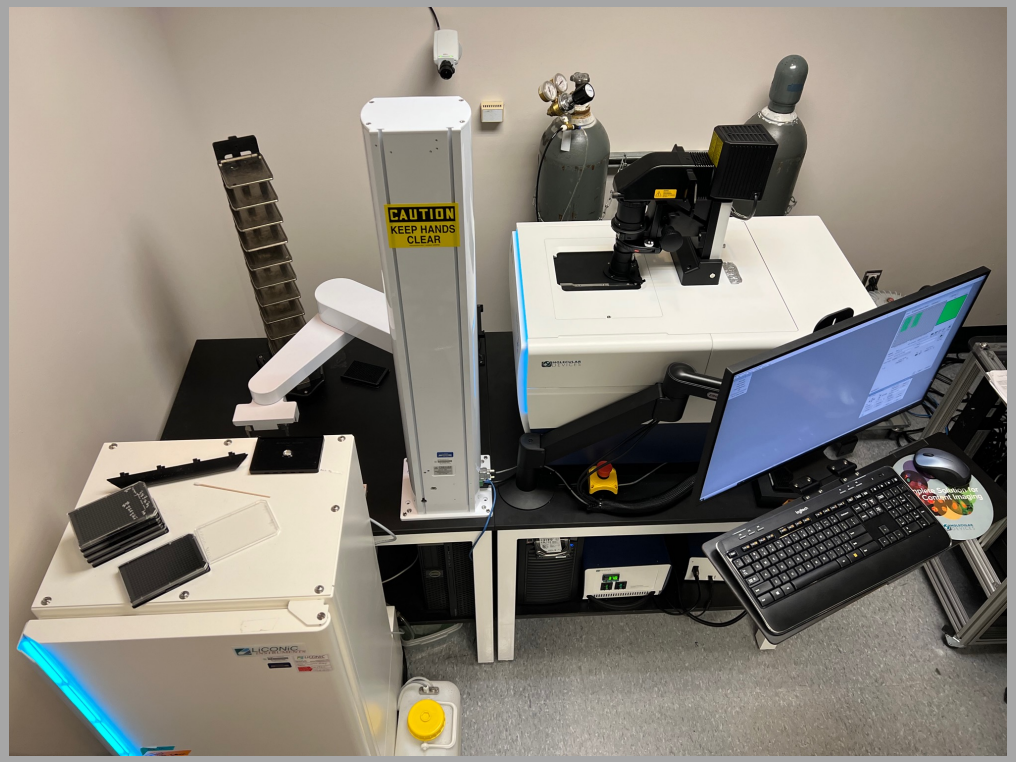




Continuous bi-directional flow



IBT Mimetas Imaging Automation Platform



The Mimetas Microfluidic Platform – Neural Applications

Open Access | Published: 09 December 2016

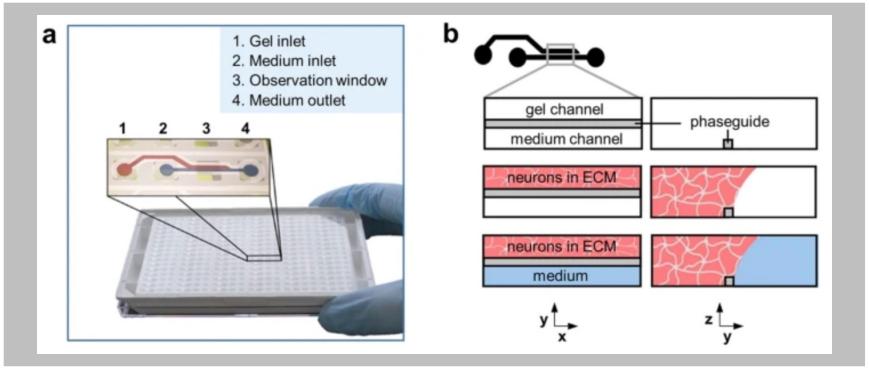
High-throughput compound evaluation on 3D networks of neurons and glia in a microfluidic platform

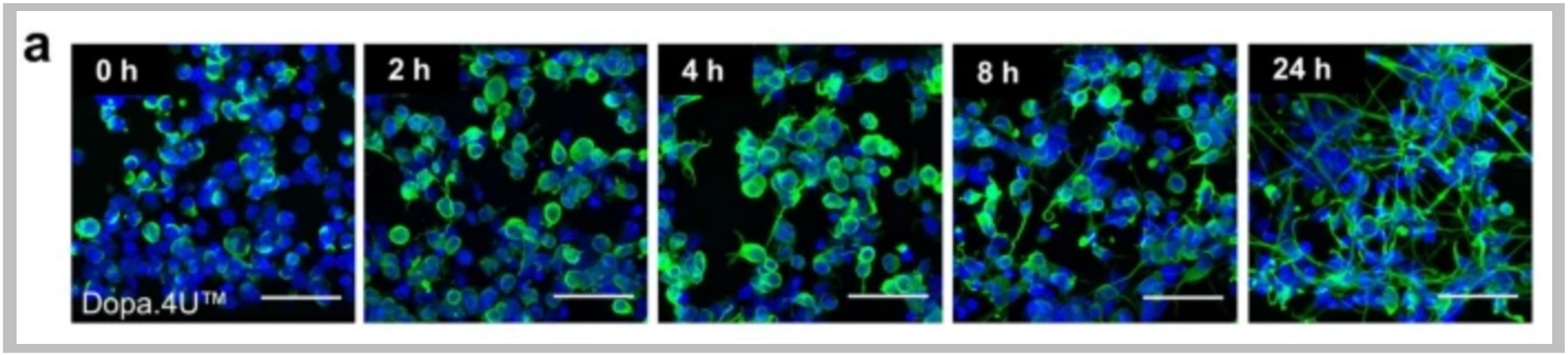
Nienke R. Wevers, Remko van Vught, Karlijn J. Wilschut, Arnaud Nicolas, Chiwan Chiang, Henriette L. Lanz, Sebastiaan J. Trietsch, Jos Joore & Paul Vulto

Scientific Reports **6**, Article number: 38856 (2016) | Cite this article

11k Accesses | **85** Citations | **15** Altmetric | Metrics

PMID: 27934939





The Mimetas Microfluidic Platform – Neural Applications

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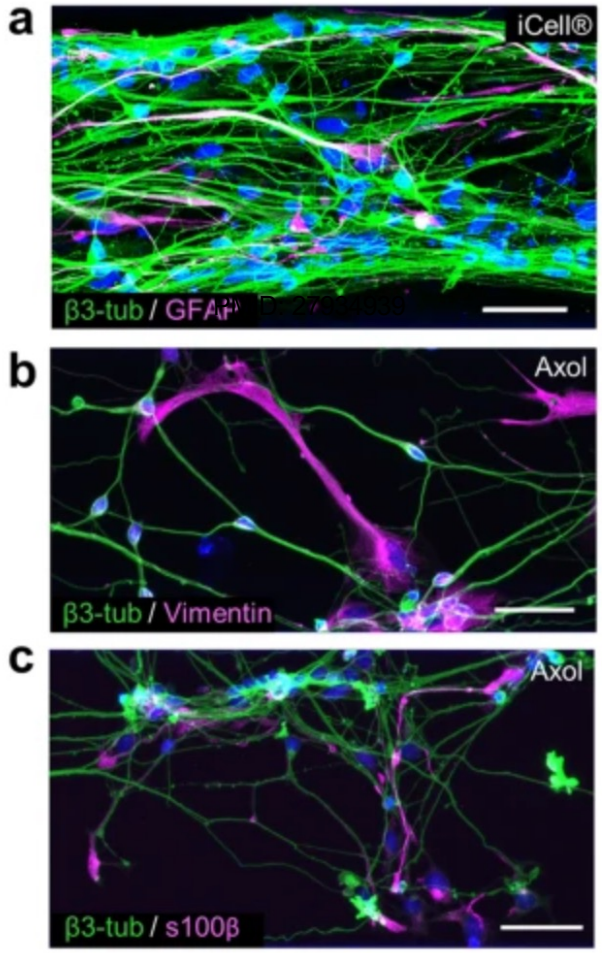
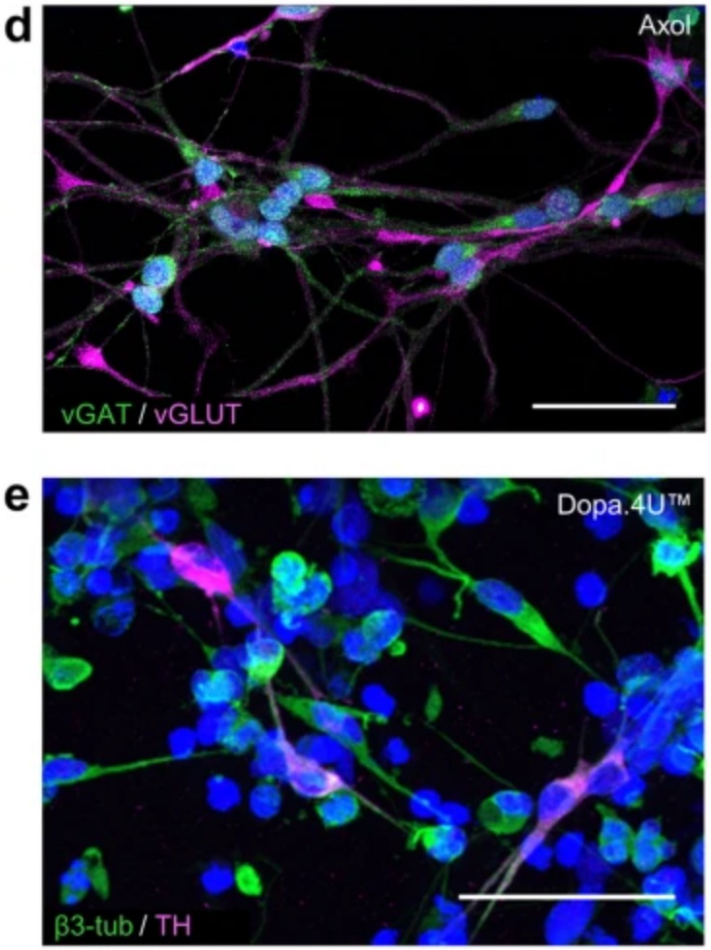




The OrganoPlate® supports growth and differentiation of various cerebral cell types.

Maximum projections of immunofluorescent images:

(a) A co-culture of mature iCell® neurons (β3-tubulin) and astrocytes (GFAP) at day 14.

(b,c) Axol Huntington neural stem cells have differentiated into neurons and astrocytes @ 6wks

(d) Axol neural stem cells show both glutamatergic (vGLUT) and GABAergic (vGAT) neurons @ 6 wks

(e) Dopa.4U™ neurons at day 5

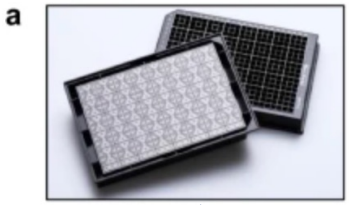
The Mimetas Microfluidic Platform – Neural Applications

Modeling ischemic stroke in a triculture neurovascular unit on-a-chip

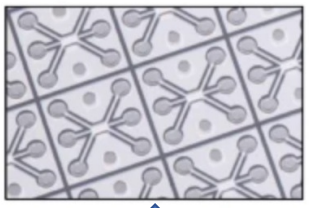
Nienke R. Wevers, Arya Lekshmi Nair, Tania M. Fowke, Maria Pontier, Dhanesh G. Kasi, Xandor M. Spijkers, Charlie Hallard, Gwenaëlle Rabussier, Remko van Vught, Paul Vulto, Helga E. de Vries & Henriëtte L. Lanz

Fluids and Barriers of the CNS **18**, Article number: 59 (2021) | Cite this article

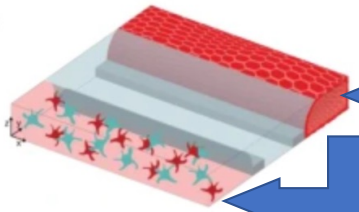
3339 Accesses | **1** Citations | **7** Altmetric | Metrics PMID: 34906183



3-Lane Plate

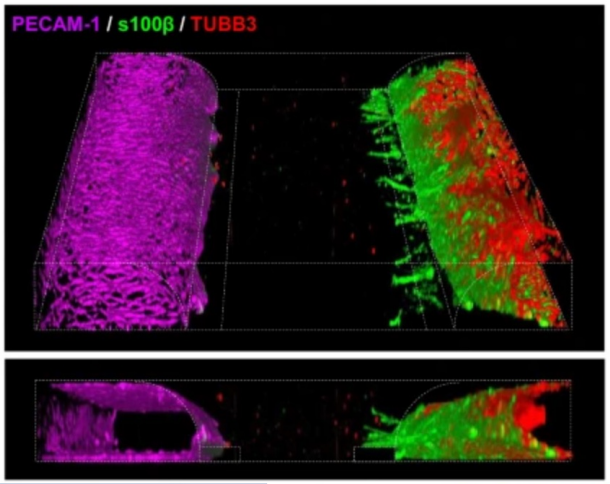


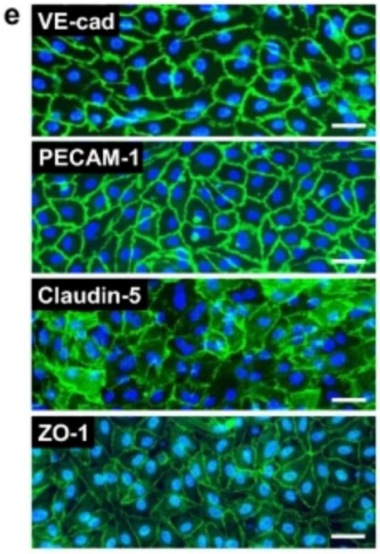
40 Chips/Plate

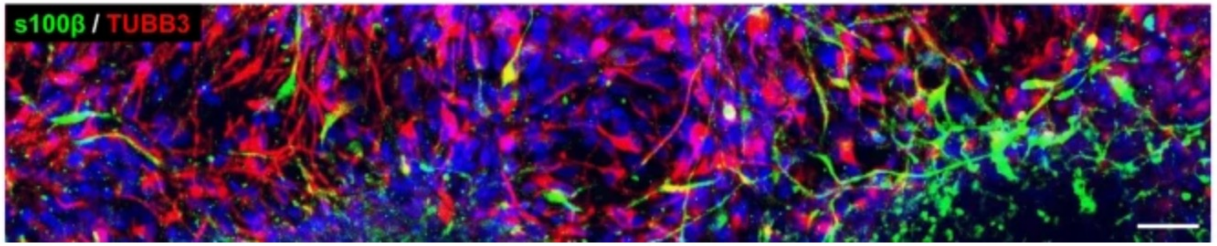


1º Brain endos

iPSC-derived neurons and astrocytes







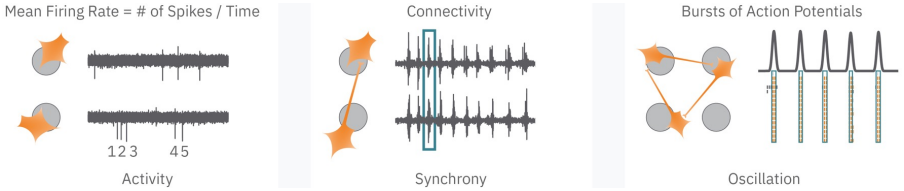
Microphysiological Lead Optimization & Toxicity Screening - MLOTS

MLOTS – Fail Early/Tox Identification Testing for Lead Optimization

Cardiovascular and CNS

action potential morphology & characterization

cardiac field potential



iPSC cardiovascular and neuronal cells

Neural – Measure the key parameters of neural network function, including activity (functional), synchrony (synapses), and oscillation (networks).

Cardiac – Record the four key measures of functional cardiac performance, label free and in real time in multiwell plates: action potential (LEAP assay); field potential; propagation; and contractility.

MEA Viability – orthogonal measure

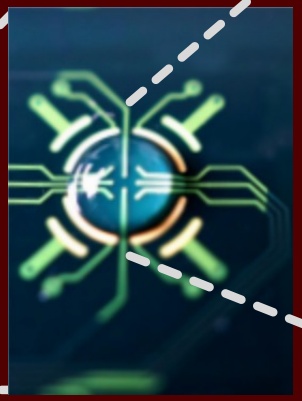
Impedance to track cell growth and morphology in real-time

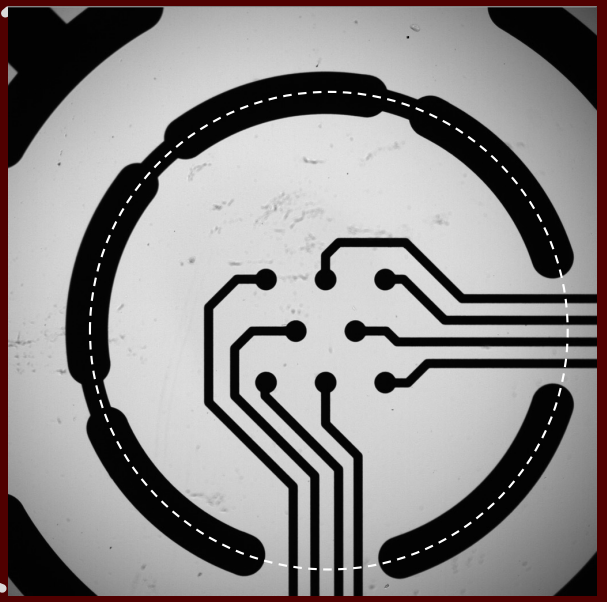
Microelectrode Array (MEA) Technology Platform

Electrode/ well	Electrode layout*
64 PEDOT CytoView MEA 6	
16 PEDOT CytoView MEA 24	
16 PEDOT CytoView MEA 48	
8 PEDOT CytoView MEA 96	

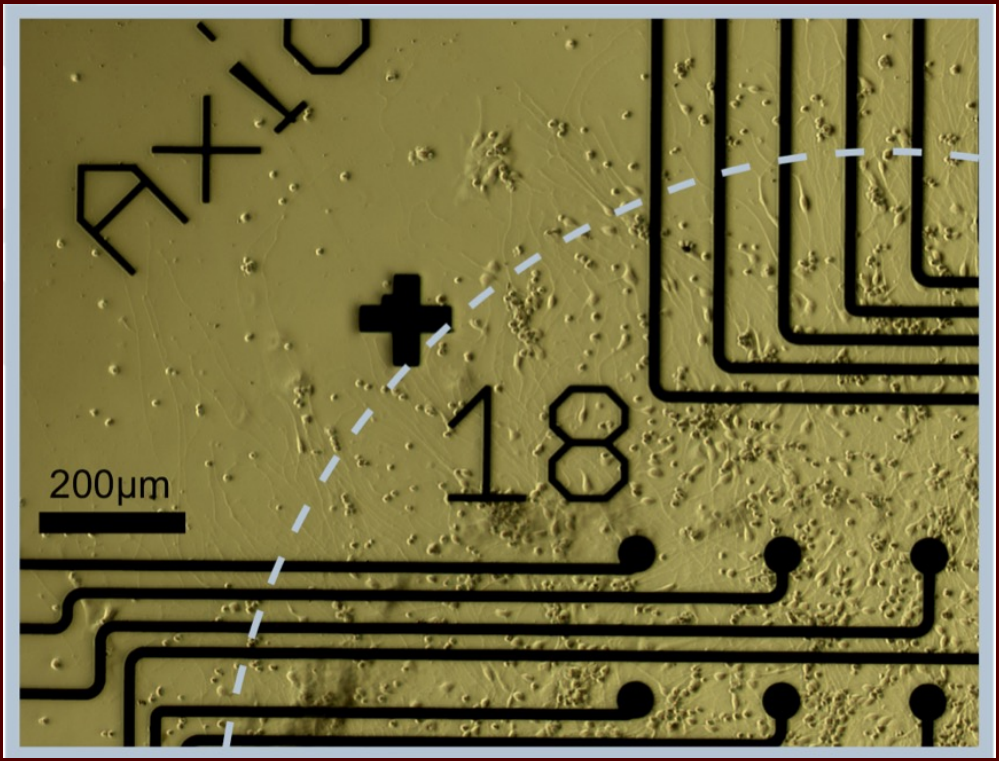
Axion MEA plate features allow real-time, label-free, and noninvasive electrophysiological assays:

- Up to 768 low-noise electrodes per plate
- Recording or stimulation capability for each electrode
- Integrated, independent ground electrodes
- Conical shaped wells, optical plate bottoms
- CO_2 + Evaporation-reducing lids with humidity chambers

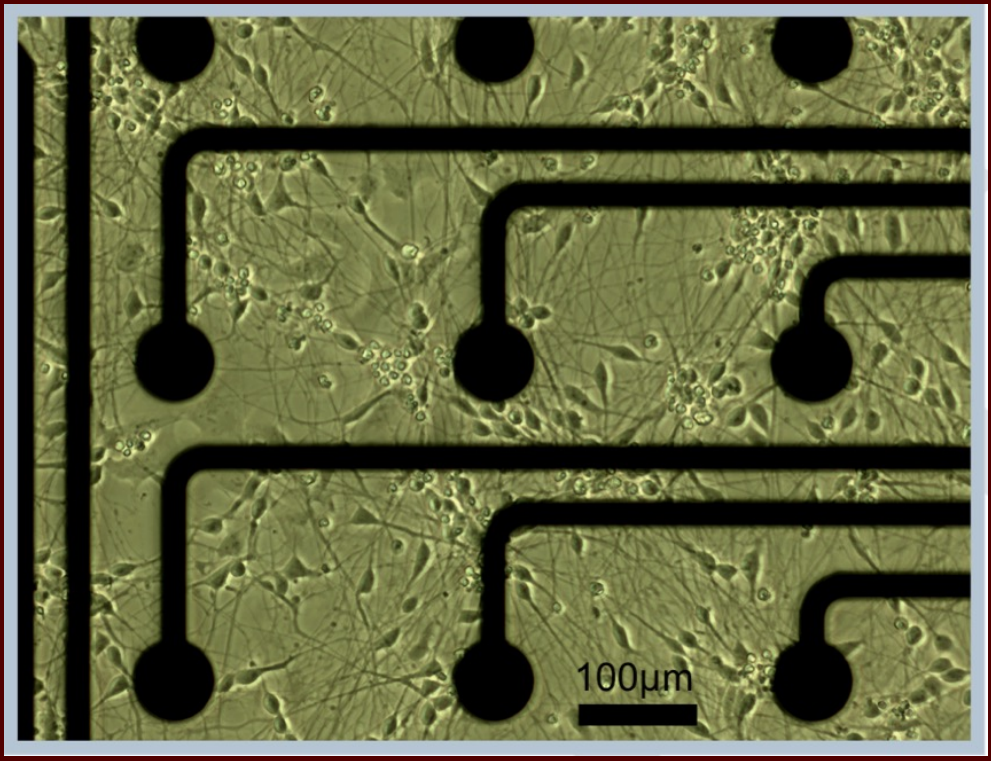




Human Cortical Neuron Morphology Cultured on CytoView MEA Plates

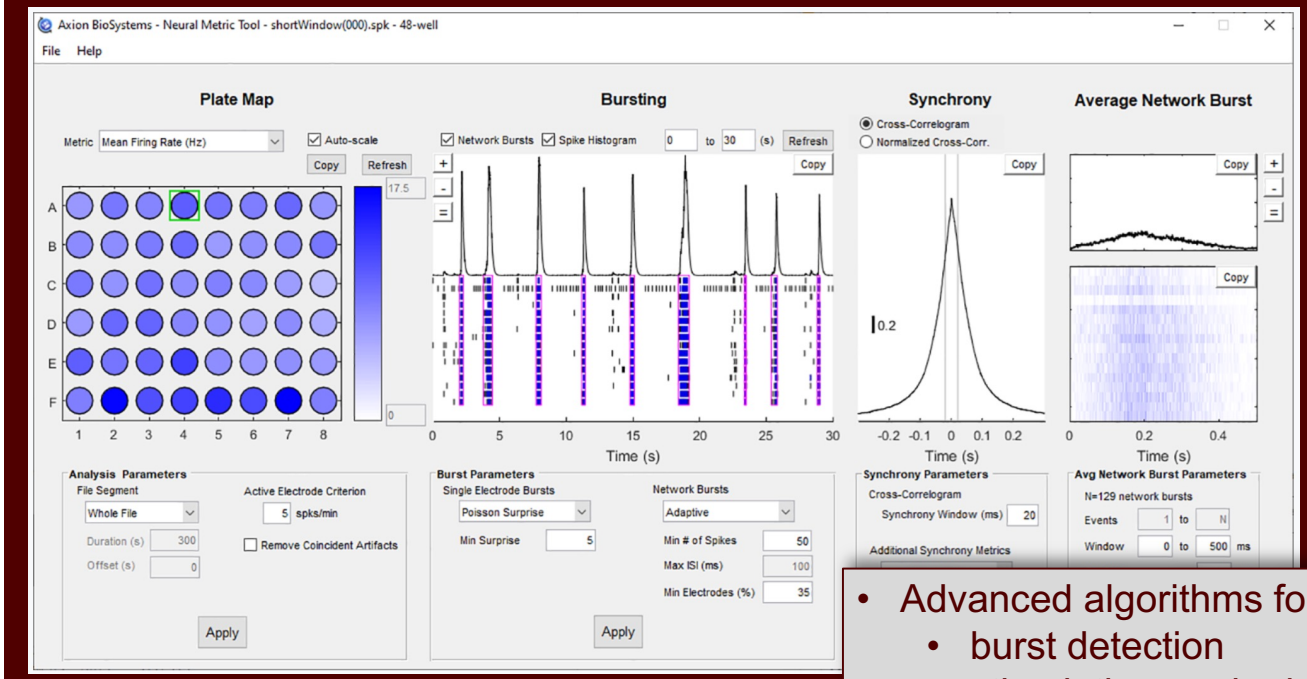


- Day 4 in culture
- 4X magnification
- Cells confined to the area indicated by the dotted line surrounding the grid of circular electrodes.



- Day 4 in culture
- 10X magnification
- Branching and neurite outgrowth is visible
- Optical bottoms allow for continuous cell monitoring

Record and Analyze Activity Using the Axion Neural Module Software



- Advanced algorithms for:
  - burst detection
  - stimulation-evoked activity analysis
- Generates plate map visualizations, raster plots, and synchrony cross-correlograms.
- Analyze/visualize single unit activity from sorted spikes.
- Explore high resolution rasters, analyze single unit participation in network events
- Characterize the response of single units to chemical, electrical, or optical stimulation.

Published Neuronal Applications from Axion Biosystems Internet Site

Development of a human derived induced pluripotent stem cell neuronal assay for early *in vitro* detection of seizure liability

K L Rockley[1]; R A Roberts[1]; M J Morton[1]
[1]ApconiX, Alderley Park, Alderley Edge, Cheshire, UK

APCONIX
a better decision

Identifying Seizures with MEA:
Complementary Human and Rat Neuronal Models Enhance Predictivity

You Feng, Jenifer Bradley, Sergiy Viatchenko-Karpinski, and Christopher Strock
Cyprotex US, LLC., an Evotec Company, Watertown, MA.

https://www.cyprotex.com/toxicology/neurotoxicity/eciphrneuro/

Derivation of peripheral nociceptive, mechanoreceptive, and proprioceptive sensory neurons from the same culture of human pluripotent stem cells

Saito-Diaz K, Street JR, et al. Stem Cell Reports. (2021) PMID: 33545066

Multi-electrode array of sensory neurons as an *in vitro* platform to identify the nociceptive response to pharmaceutical buffer systems of injectable biologics

Eaton M, Que Z, et al. Pharmaceutical Research. (2021) PMID: 34244893

Inhibition of sodium conductance by cannabigerol contributes to a reduction of dorsal root ganglion neuron excitability

Ghovanloo M-R, Estacion M, et al. British Journal of Pharmacology. (2022) PMID: 35297036

Publication Topics of Applications from Axion Biosystems

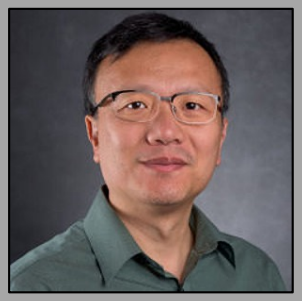
- Neural characterization and development
- Neural circuit and innervation
- Neural co-culture and glial interaction
- Neural optical and electrical stimulation
- Neural organoids
- Neurological diseases
- Neuromuscular junction
- Neurotoxicity and safety
- Pain
- Retina

IBT High Throughput Research and Screening Center

"Our Team"





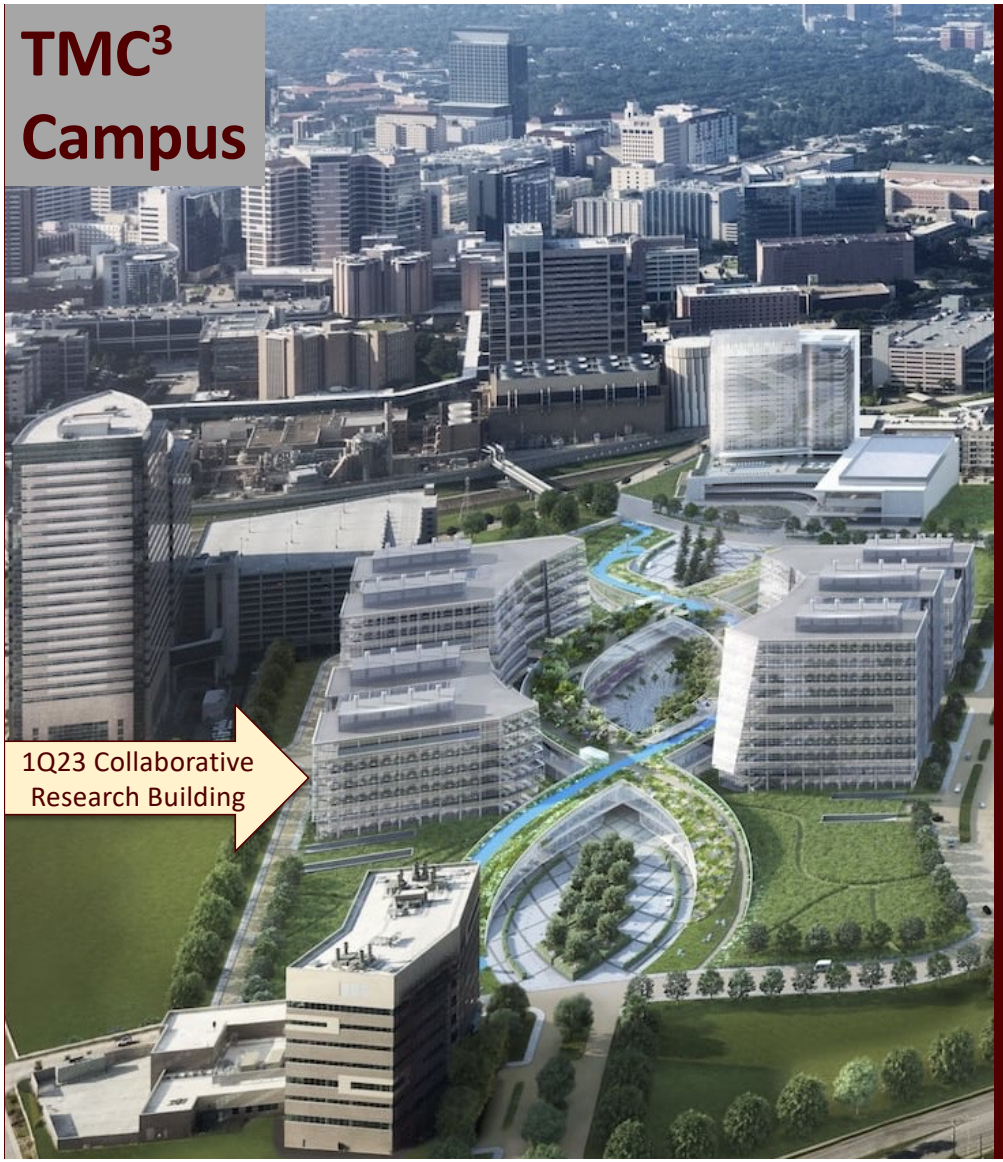



Specialized Expertise – "*The Heart of the Core*"

Scientific and Technical Staff:
Industry level HTS, Imaging and Data Analysis, Informatics, Robotics, Automation, Tissue culture





The Combinatorial Drug Discovery Core

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https://ibt.tamu.edu/cores/high-throughput

Main

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