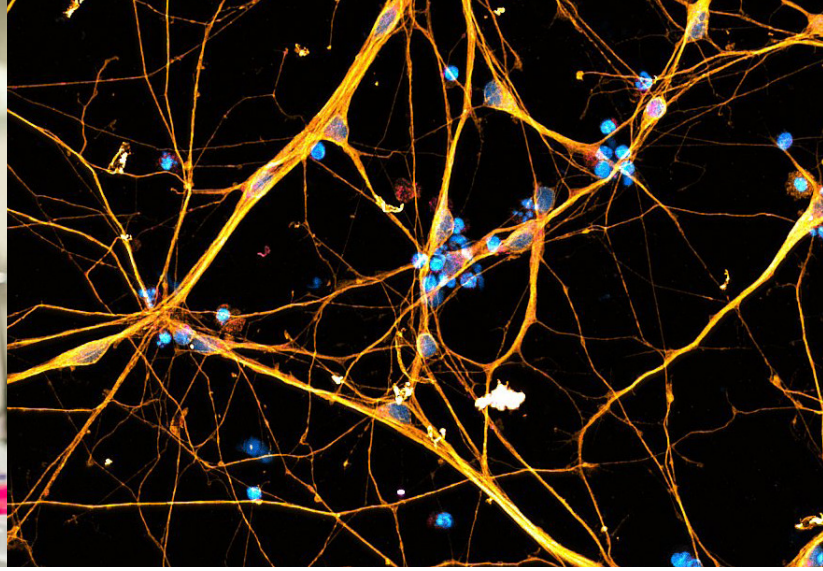

PHENOVISTA
YOUR COLLABORATIVE DISCOVERY PARTNER
www.phenovista.com



ABOUT US

We are a contract research organization (CRO) based in San Diego whose mission is to support our clients in the development of safer and more effective therapies. We believe that the use of more relevant in vitro disease models is critical towards this mission, but can be challenging to implement because of the difficulties in culturing and analyzing them.

Recognizing this challenge, PhenoVista was founded in 2014 by scientists from MIT and UCSD to offer their expertise in generating highly complex models as a service. Since then, we have grown to include expertise in high-content imaging and analysis (HCA) alongside our cell culture services because it is one of the few, but definitely most powerful, methods for analyzing these models while still intact, thus offering a more relevant readout for drug discovery.

Target Discovery › **Hit Generation** › **Lead Optimization** › **Early Pre-Clinical**

90% of the world's top-20 pharmaceutical companies work with us.

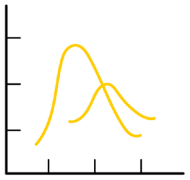
FUJIFILM Cellular Dynamics's preferred provider of cell-based assay services.

200+ companies throughout the US, UK, Europe, and Asia have worked with us over almost a decade.

Ranked #1 by Science Exchange for high-content assay services.

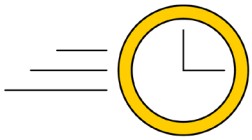
FOCUSED BEYOND THE IMAGE

We pride ourselves in tailoring our services to not only answer your biological questions, but also your overall business needs, through three core competencies: Developing assays that use the most relevant *in vitro* models, generating high-quality images, and using high-content analysis. We keep our focus narrow to deliver high-quality, reliable data to our customers.

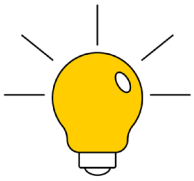


Partner with a talented, collaborative scientific team focused on delivering relevant data through quality control.

Get **deeper insights** and unique perspectives on disease by leveraging our expertise in high-content imaging.



Save time and resources with immediate access to established technologies and deep expertise vs. investing in building in-house capabilities.



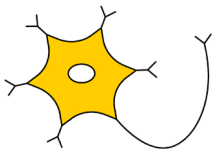
Enable more innovation by exploring risky projects with a team you can trust to generate high-quality, actionable data.

"PhenoVista provided high-quality cell analysis services for us quickly and cost-effectively. Our expectations were exceeded in terms of data quality and their collaborative, adaptable nature of engagement. I would heartily recommend working with PhenoVista."

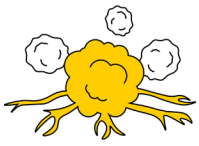
- Dr Robert S. Hillman, CEO CeleCor Therapeutics

THERAPEUTIC AREAS

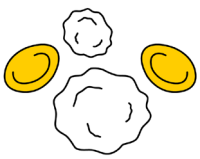
One of our core expertise is in assay design using cellular models that are highly relevant to the question at hand, ranging from 2D mono-cultures of immortalized cell lines to 3D tri-cultures of iPS-derived neurons in a microfluidic device.



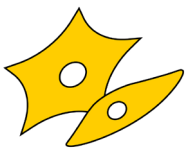
CNS



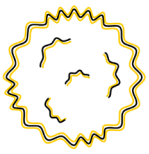
Oncology/ Immuno-Oncology



Immunology & Inflammation



Fibrosis



Rare Diseases

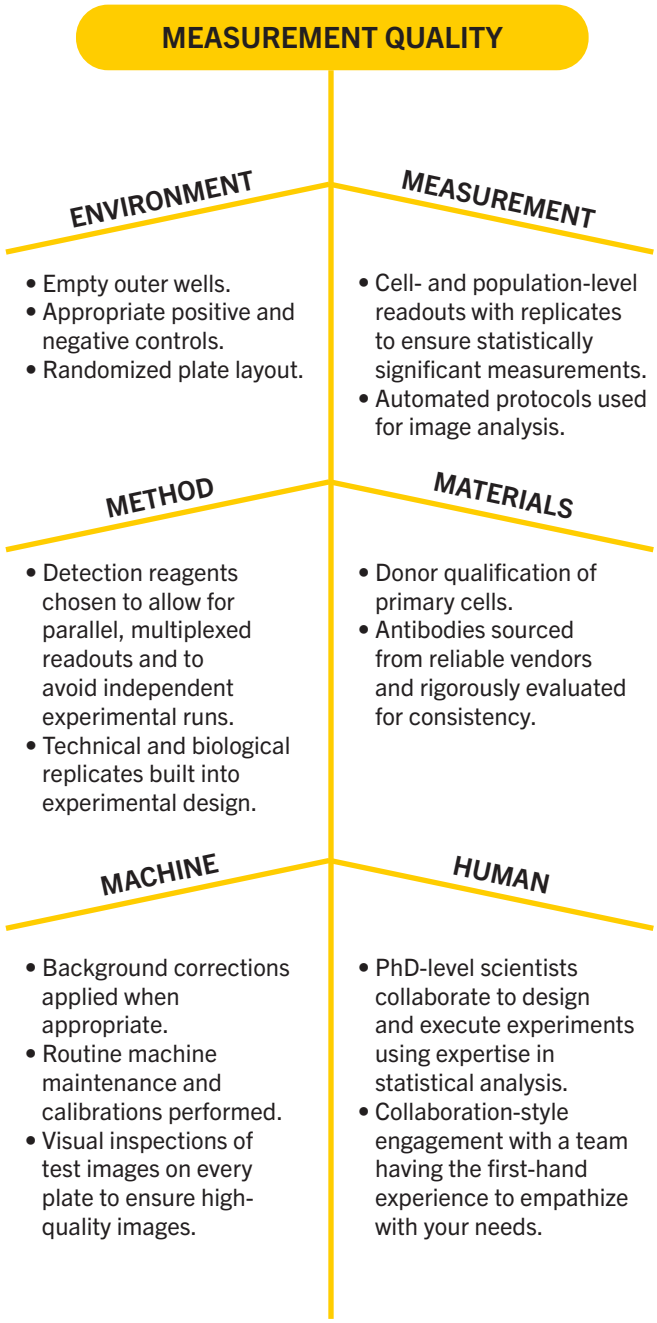
..and more!

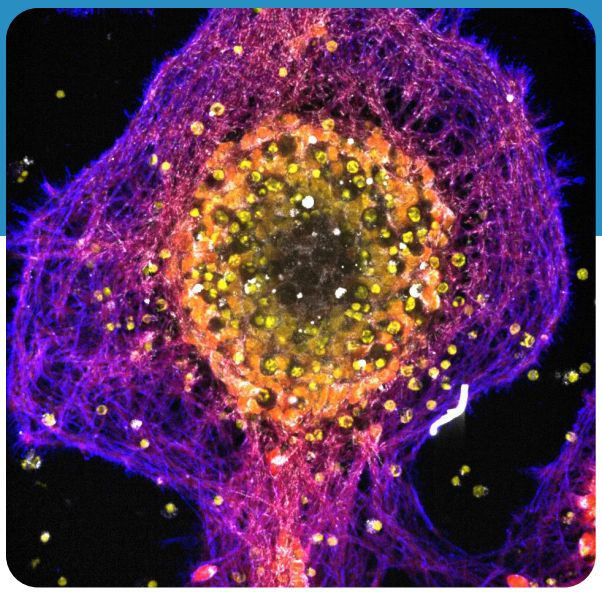
QUALITY IS ONE OF OUR CORE VALUES

The field of cell biology finds its origins in microscopy, which was used to first describe a cell in the 1600's. Since then, the immeasurable impact of microscopy on cell biology has been undeniable. With the recent, significant advancements in technological and data-storage capabilities, the nature of microscopy as purely qualitative, observational technique has shifted to a highly quantitative approach that can be used to not only see, but also measure biological phenomena. The quality of quantitative cell measurements, like any other measurement, depends upon the quality of the measurement process.

The PhenoVista team is comprised of scientists and engineers with advanced degrees across the life sciences, statistics, and related fields with extensive experience in the process of quantitating cell images (see diagram on right for a select few of the quality procedures we implement). This diversity in background uniquely positions us to integrate a quality control perspective into designing relevant in vitro assays to meet your research needs.

These capabilities are the foundation of PhenoVista. By working with us, you will obtain high-quality data afforded by state-of-the-art imaging instrumentation and advanced, in-house informatics to propel your research forward.





OVERVIEW OF OUR SERVICES

Using the workflow outlined below, we can assist you with early, feasibility studies, assay development, or full screening campaigns. Our collaborative style of engagement offers great flexibility in our service offerings, which include Custom Assays, Ready-2-Go, Cell Painting, and Imaging & Analysis.

Consultation & Scope > Assay Design > Assay Prep > Image Cells > Analyze > Report

CUSTOM ASSAYS

- Tailor your assay to better answer your questions.
- Answer more specific, complex biological questions with more detailed data.

READY-2-GO

- Defined, fixed offerings across a range of disease and therapeutic areas.
- Faster turnaround.
- More cost effective.

CELL PAINTING

- Compare your compounds' effects against those of reference compounds.
- Broadly assess your test articles before implementing more targeted, sophisticated assays.

IMAGING & ANALYSIS

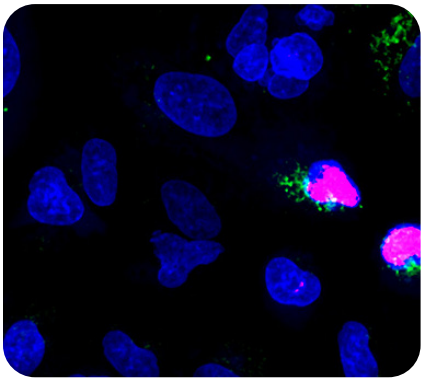
- You send us plates with cells that have been fixed & stained, and we'll send you data.

	CUSTOM*	READY-2-GO*	CELL PAINTING BASE OFFERING*	IMAGING & ANALYSIS*
Cell Model	Your choice	Select from available options	A549 cells	Client provided
Fluorescent Dyes & Stains	Your choice	Pre-determined	Pre-determined (see page 11)	Client provided
Timepoint(s)	Your choice	Pre-determined	Pre-determined	Client provided
Compounds	Your choice	Your choice	Your choice	Client provided
Workflow Stages Included	All	All	All	Consultation & scope, Image, Analyze, and Report

*Some technical limitations apply

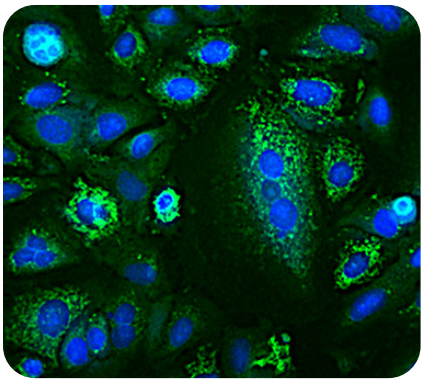
READY-2-GO ASSAY SERVICES

Our team has extensive experience developing and executing custom assay services for clients whose highly complex assays require outside-the-box approaches to deliver impactful results. Building upon that foundational experience, our Ready-2-Go (R2G) assay services robustly and efficiently address general, biological questions. For the complete list of R2G services, visit https://phenovista.com/r2g-assay-services



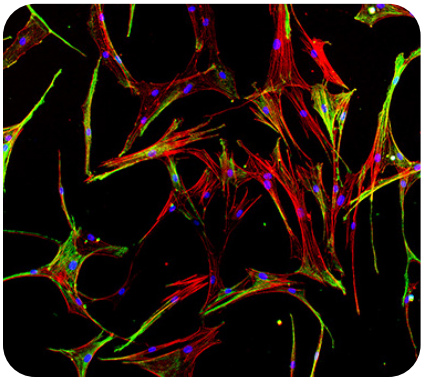
CELL HEALTH

Assessments of cell health are typically limited to classification of cells as “live or dead”, but cell health is more nuanced than this bimodal categorization. Our R2G Cell Health Assay Service takes a multiplexed approach to measure proliferation, apoptosis, and viability.



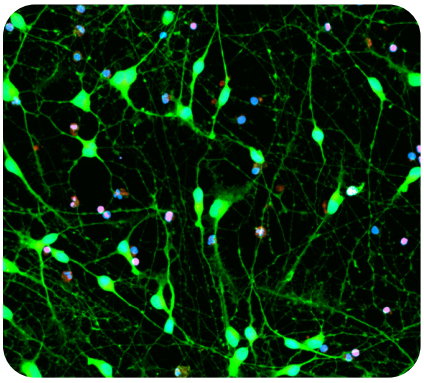
MITOCHONDRIAL HEALTH

Mitochondrial health can be an early indicator of toxicity, but typically requires single-cell resolution to get meaningful data, which many assays do not provide. Our Mitochondrial Health Assay Services measures changes in mitochondrial membrane potential at the single-cell and population level, enabling us to assess the effects of drug candidates as a continuum of cell health.



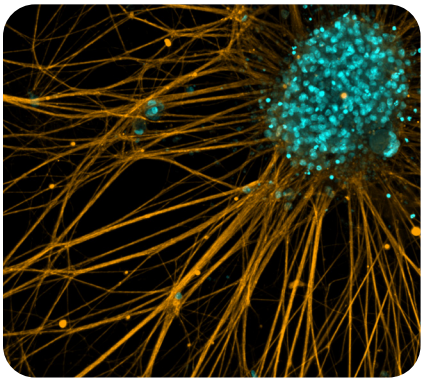
LUNG FIBROSIS

Our Lung Fibrosis Assay Services uses primary, normal human lung fibroblasts (NHLF) cultured using an optimized protocol that limits basal induction of fibrosis. This affords enhanced control of fibrotic induction in a format amenable to higher-throughput therapeutic profiling than other commonly used fibrosis assays.



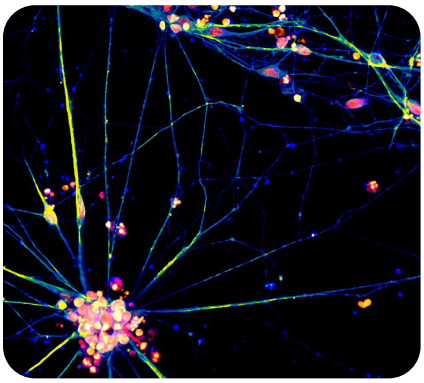
NEURONAL APOPTOSIS & VIABILITY

Evaluating and identifying potential neurotoxic effects of therapeutics is essential to any drug-discovery/development campaign. Our R2G Neuronal Cell Health Assay Service uses iPSC-derived neuronal cells to provide you with a robust, accurate quantification of your test articles' impact on neuronal apoptosis and viability.



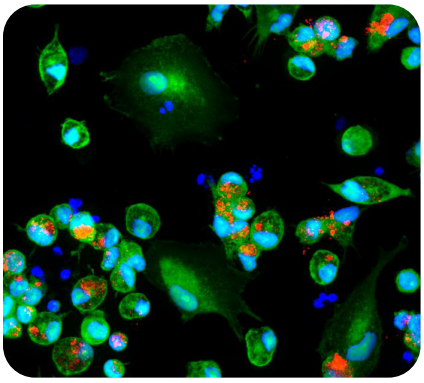
NEURITE OUTGROWTH & NETWORK DYNAMICS

Neurodegenerative diseases are often associated with altered connections in neural networks. Typical assays measuring these dynamics use immortalized neuronal cell lines, which may not be physiologically relevant, or use costly and highly variable primary neurons. Our R2G Neurite Outgrowth and Neurite Network Dynamics assays use iPSC-derived neurons with culture conditions optimized to provide accurate initial neurite outgrowth measurements with the flexibility to assess changes in steady-state neurite network formation.



NEURONAL MITOCHONDRIAL HEALTH

Neurons are uniquely sensitive to disruption of mitochondrial activities due to their specialized functions that require high amounts of energy. These mitochondrial perturbations are thought to play a major role in many neurodegenerative diseases. Our R2G Neuronal Mitochondrial Health Assay Service measures changes in mitochondrial function in iPSC-derived neurons to help you assess your test articles' impacts on this biological process.



MICROGLIA PHAGOCYTOSIS

To date, most assays developed for microglial research are conducted using immortalized and murine cell lines that do not adequately mirror human biology. Our R2G Microglia Phagocytosis Assay Service overcomes this issue by using iPSC-derived human microglia. Choose from wild-type and TREM2-mutant cells to measure your test articles' effects on phagocytosis in a fluorescent, kinetic assay.

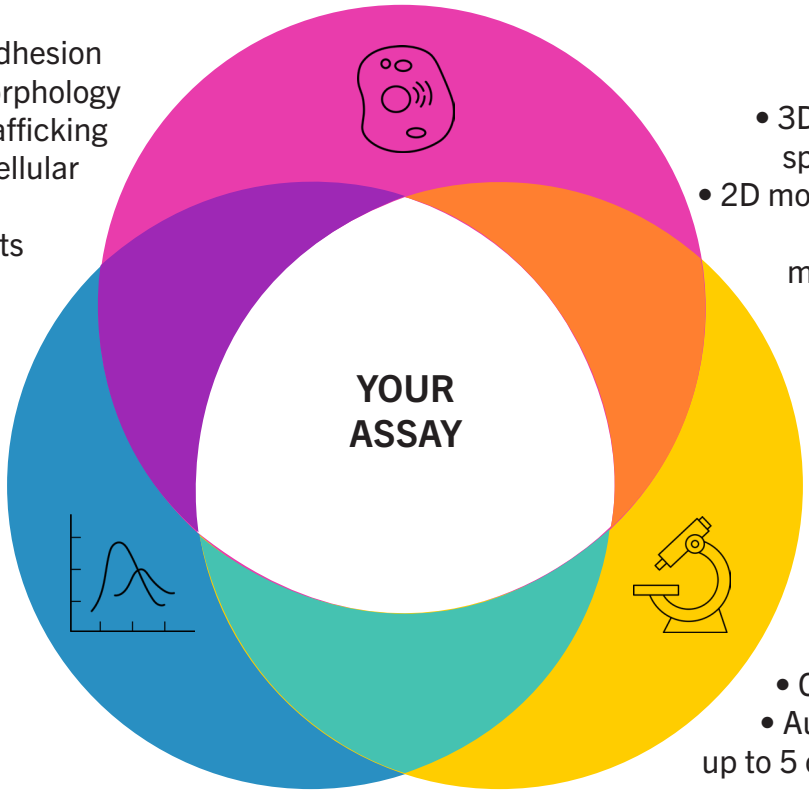
CUSTOM ASSAY SERVICES

We work with you to design and tailor experiments to help get answers to your most difficult and complex biological questions.

Cell Models
- iPSC-derived cells
- Patient-derived cells
- Immortalized cell lines
- Ex vivo tumor fragments

Assay Types
- Cell/mitochondrial health and proliferation
- Cell migration & adhesion
- Cell painting & morphology
- Cell signaling & trafficking
- Protein and sub-cellular localization
- Functional readouts

...and more!



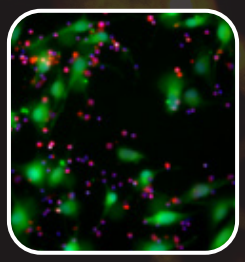
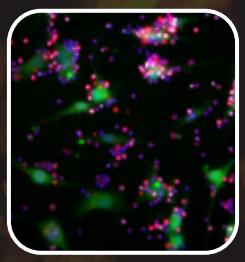
Assay Formats
- 3D cultures - including spheroids & organoids
- 2D mono- and co-cultures,
- Bioprinting and microfluidics platform

Imaging
- Live or fixed
- Confocal or widefield
- Automated imaging of up to 5 channels in 2D & 3D

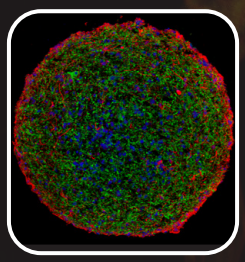
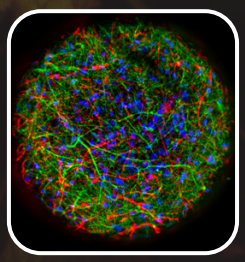
Data Analysis
- Proprietary data and statistical tools for downstream analysis and data visualization
- Professionally-managed IT environment with encryption, data backup, and disaster recovery
- Representative images provided with data report

Image Analysis
- Commercial image analysis software for 2D and 3D images – HCS Studio, CellPathfinder, Imaris, Huygens etc.

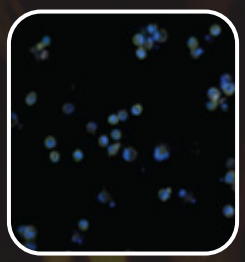
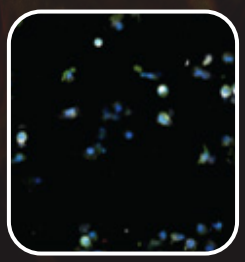
DIVERSE PORTFOLIO OF CUSTOM CAPABILITIES

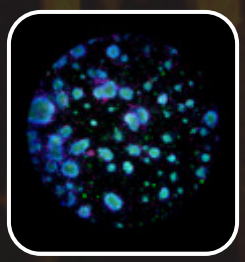
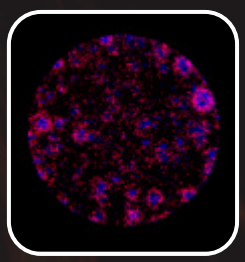
ONCOLOGY & IMMUNO-ONCOLOGY
- 2D co-culture
- Primary immune cells
- Unique analysis: Cluster index
- 4-color assay, widefield imaging

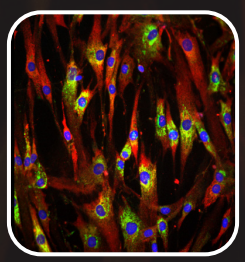
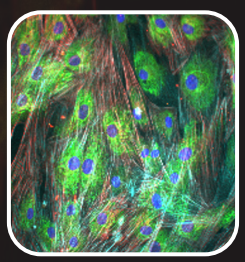
NEUROBIOLOGY
- 3D co-culture, organoid
- iPSC-derived neurons & glia
- Unique analysis: Neurite area
- 3-color assay, confocal imaging

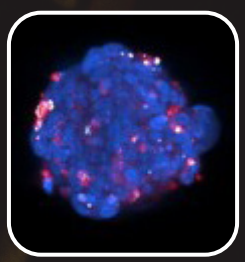
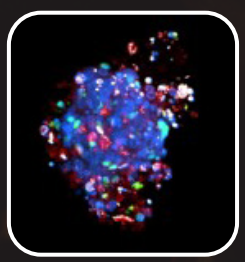
IMMUNOLOGY & INFLAMMATION
- 2D monoculture
- iPSC-derived human microglia
- Unique analysis: Puncta per cell
- 3-color assay, widefield imaging

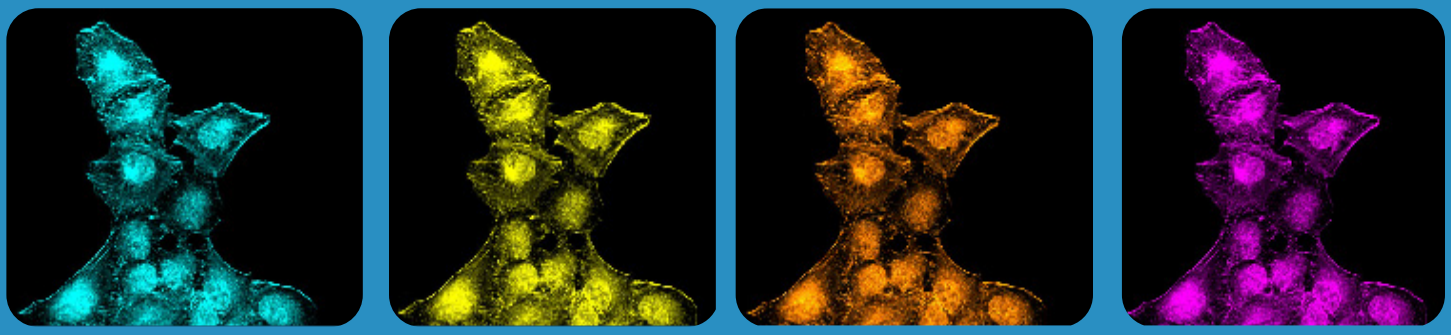
ONCOLOGY & IMMUNO-ONCOLOGY
- 3D culture
- *Ex vivo* patient-derived tumors
- Unique analysis: Metabolic activity
- 3-color assay, widefield imaging

FIBROSIS
- 2D mono-culture
- Primary, human stellate cells
- Unique analysis: Fiber alignment
- 3-color assay, widefield imaging

CELL & GENE THERAPY
- 3D co-culture
- Tumor spheroid
- Unique analysis: Tumor penetration
- 4-color assay, confocal imaging



CELL PAINTING SERVICES

Cell Painting is an unbiased, image-based profiling method that is revolutionizing the drug-discovery process in the biotech and pharmaceutical industries. However, this method is inaccessible to smaller or more academic laboratories because it:

- Requires high-content imaging.
- Requires the generation of large datasets, enabled through high-throughput automation.
- Requires a combination of expertise in cell biology, microscopy, automation, and data science.

Cell Painting requires a significant financial investment to support the equipment and personnel with the expertise to carry out the assays. PhenoVista's Cell Painting Assay Service makes this method accessible to scientists who are interested exploring this powerful methodology but do not have the resources to invest in its in-house development. Our service also provides scientists who already have Cell Painting capabilities to contract out their work to meet quickly approaching deadlines.

KEY BENEFITS

- **Short turnaround time because Cell Painting requires little assay optimization steps.**
- **The use of a palette of dyes, as opposed to anti bodies, affords less variability in data.**
- **High sensitivity of the assay detects nuanced differences in cell phenotypes while still capturing whole-cell information.**

KEY CHALLENGES

- **Due to its high sensitivity, technical artifacts and additional noise are often and unknowingly detected as the disease profile, leading to many issues downstream.**
- **The amount of data or 'curse of dimensionality' can be difficult to overcome.**
- **Can be difficult to interpret results, particularly if deep learning methods are employed.**

CELL PAINTING CAN BE USED ACROSS DRUG DISCOVERY

QUALITY CONTROL
The technique is highly sensitive to changes in phenotypes that may be useful for detecting assay instability.

MECHANISM OF ACTION
Mechanism of Action (MOA) Identification: Image profiles generated by Cell Painting are clustered by similarities in the phenotypic readouts. The close clustering of a novel compound with unknown MOA to that with compounds that have a known MOA suggests that they share a common or similar MOA.

ASSAY DEVELOPMENT FOR PHENOTYPIC SCREENING
Cell Painting can be used to discover phenotypic differences between a disease model and a healthy cell model. If differences are found, then it can potentially be used as the readout of a screening campaign.

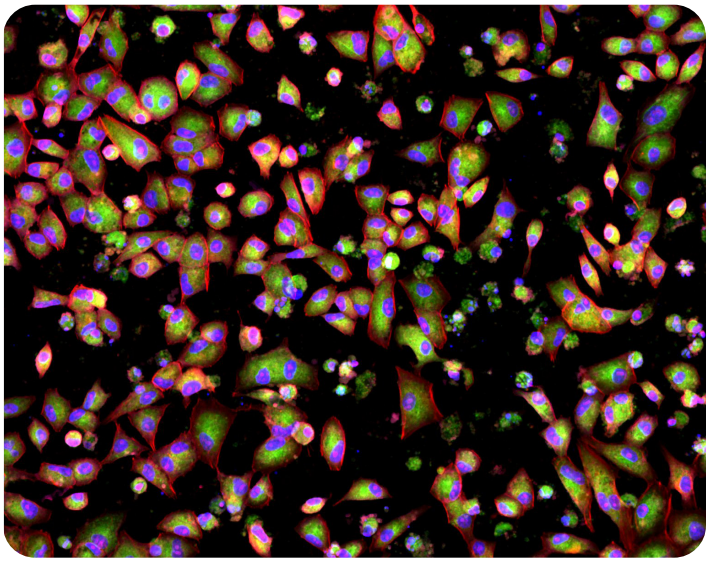
HOW IT WORKS

Cell Painting is an image-based, phenotypic profiling method that uses morphological features extracted from images of cells stained with a set of fluorescent dyes that label a generic set of cell organelles and components (see table). Unlike screening, there is not a pre-defined phenotype being identified in Cell Painting; rather, it is an unbiased approach that aims to cluster similar phenotypic profiles together to attribute phenotypic fingerprints to specific conditions.

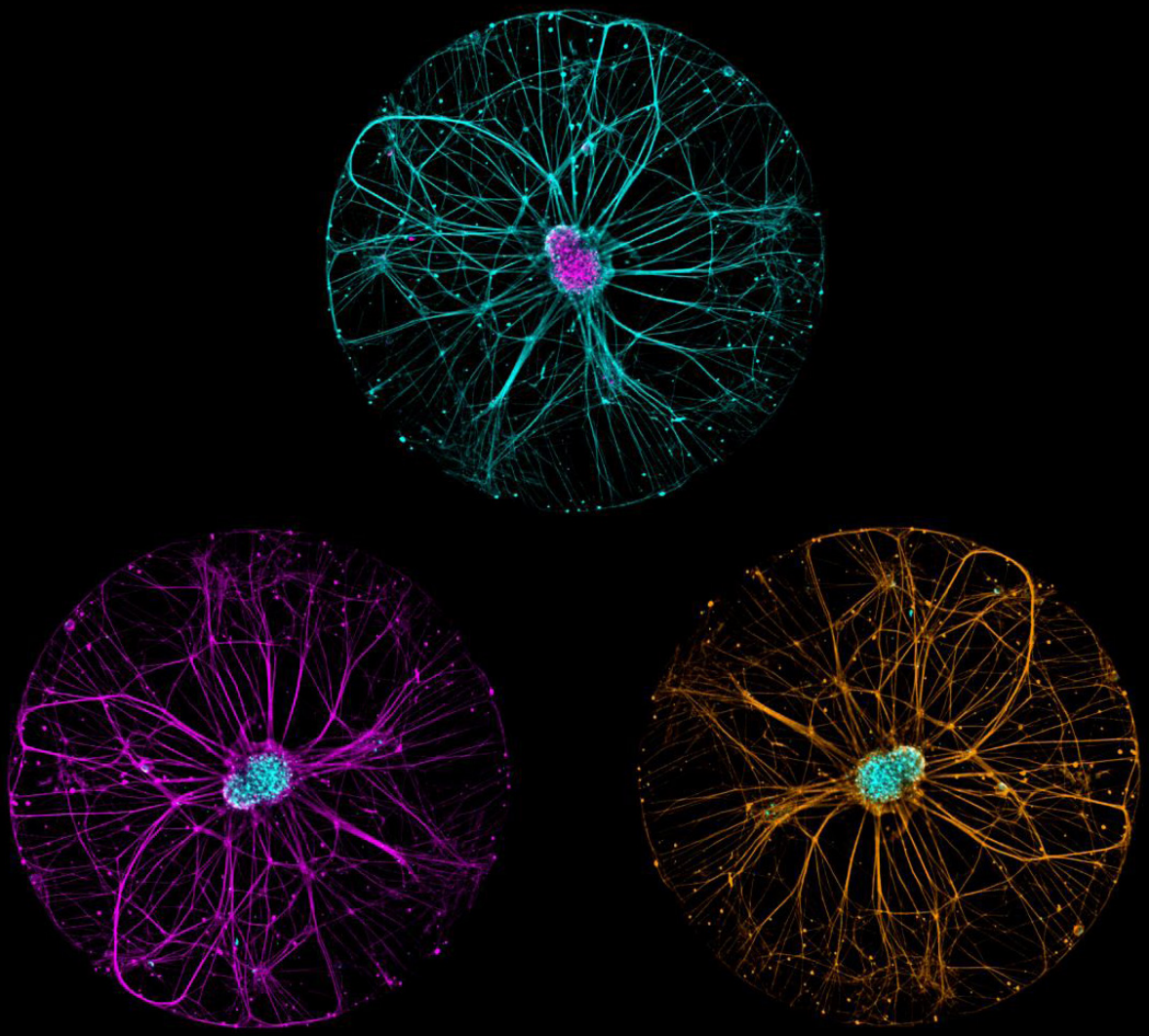
OUR CELL PAINTING SERVICE OFFERING

A549 cells are seeded into 384-well microplates and allowed to grow for one day. On day 1, 2% serum is added and treatement applied for 48 hours. On day 3, cells are fixed and stained using the dyes in the table below. Microplates are then imaged at 9 fields per well with a 20X objective on the Yokogawa CQ1.

Organelle or Structure	Dyes
Nucleus	Hoechst
Endoplasmic Reticulum	Concanavalin A (Alexa Fluor 488)
Nucleoli & Cytoplasmic RNA	SYTO 14
Golgi & Plasma Membrane	Wheat germ agglutinin
F-actin	Phalloidin (Alexa Fluor 568)
Mitochondria	MitoTracker Deep Red FM



	Cell Painting Base Offer	Custom
Cell Model	A549 cells	Your choice
Fluorescent Dyes & Stains	See table	Your choice
Timepoint(s)	48 hours	Your choice
Compounds	Minimum of 5	Minimum of 5



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