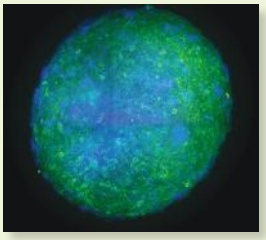
Visikol® Services

Advanced Drug Discovery

Our services include advanced imaging and image analysis techniques as well as cutting-edge 3D cell culture models and custom solutions

3D Cell Culture Assays

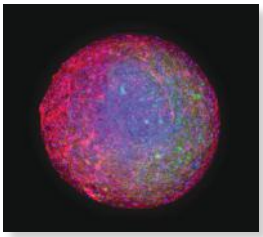
Simple to highly complex discovery assays



- Immune Cell Infiltration
- Antibody Penetration
- Phenotypic Screening
- Cytotoxicity
- Drug Induced Liver Injury
- Fibrosis, Cholestasis, NASH
- Cell Proliferation
- High Content Confocal Imaging

3D Cell Culture Models

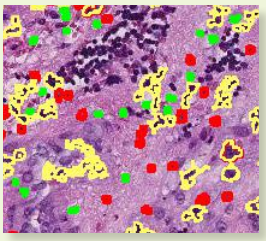
Improve translation between *in vitro* and *in vivo*



- HepG2 and HepaRG Spheroids
- HepaRG or Human Hepatocyte & Non-Parenchymal Co-cultures
- Custom PDX Model Development
- iPSC Derived
- Cell Lines
- Primary Cells
- Various Species

Digital Pathology

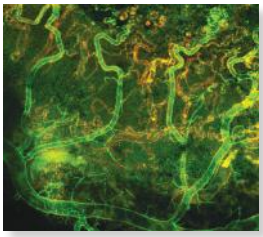
Quantitative analysis of tissue sections or other image data sets



- Machine Learning Analysis
- Slide Scanning
- Tumor Area Quantification
- Quantitative Scoring and Measurements of IHC Slides
- Phenotype Classification
- Custom Algorithm Development
- 21 CFR Part 11 Compliant Software

3D Tissue Imaging

Image your entire tissue instead of a slice

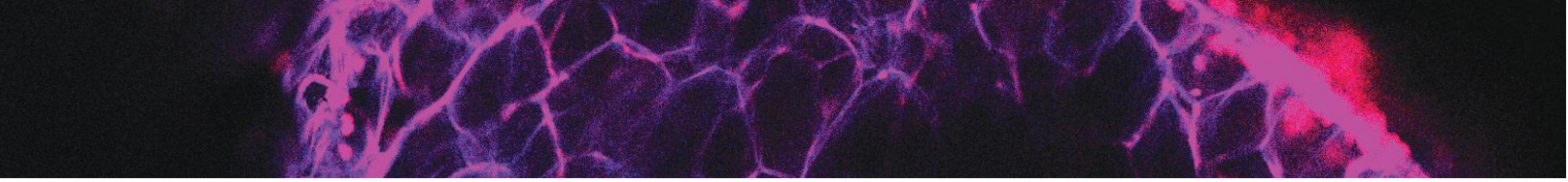


- Vasculature Mapping
- Target Identification
- Antibody Penetration
- Viral Infection
- Whole Brain Imaging
- Whole Mount Imaging
- Eyeball Whole/Flat Mount Imaging
- Neuron Counting and Classification

Custom Drug Discovery Projects

Imaging, analysis and 3D *in vitro* models

- OCT, OPT, MRI, CT, Ultrasound Imaging and Analysis
- *In vivo* Animal Projects
- Validation of Biological Target
- Bioprinting



3D Cell Culture Assays

Experts in Imaging and Image Analysis

The Visikol Difference

While there are many CROs offering 3D cell culture assay services, none offer the spectrum of imaging end-points that Visikol offers from simple plate reader-based luminescent ATP assays to high content confocal 3D analysis of cell subpopulations. These assays leverage our proprietary 3Screen™ image analysis software as well as the patented Visikol® HISTO-M™ tissue clearing reagent and several proprietary tissue processing techniques that facilitate characterization of every cell within a 3D cell culture model, as opposed to just a few outside layers.

How We Work With Clients

We work with Clients in a number of ways; Clients can send us a library of compounds for execution of end-to-end 3D cell culture assays or Clients can send us a plate of fixed and labeled models for imaging and analysis. For Clients that wish to internalize assays, we also assist with protocol and/or software development and implementation.

We work very closely with Clients to design the best possible approach to conducting experimental procedures, image processing, and data analysis. We go the extra mile to make sure our customers are satisfied with the quality of our work.

Applications

Liver Toxicity & Pathology

Drug Induced Liver Injury

- Cholestatic
- Non-cholestatic
- Idiosynchratic (i.e. immune mediated)

NAFLD / NASH

- Steatosis
- Inflammation
- Fibrosis

Cancer Drug Screening

- Apoptosis
- Cell-cell Junctions
- Cell Proliferation
- Cell Viability
- Drug Efficacy

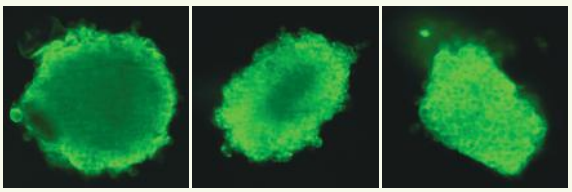
Other

- Antibody Penetration
- Angiogenesis
- Cell Migration / Extravasation
- Cell Viability / Cytotoxicity
- High Content Screening
- Hypoxia
- Mitochondrial Health + Toxicity
- ROS Generation
- Spatial Dose Response
- Immune Cell Invasion
- Phenotypic Screening
- Skin Anti-Aging Assay

Image-Based Assay Spotlight

Antibody Penetration

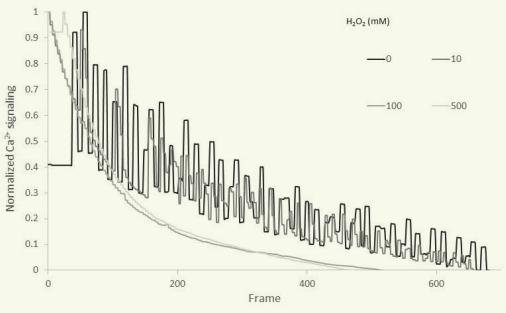
With the growth in development of biologics-based therapeutics, there has been a growing need to quantitatively assess antibody penetration into complex 3D tissues. Visikol's antibody penetration assay meets that need, with the ability to analyze penetration depth, width of penetration zone as well as target localization.



Functional Assay Spotlight

Cardiotoxicity

While quantification of viability and of certain biomarkers can provide some insight into drug dose-response or mechanism of cytotoxity, often times more functional measures provide additional understanding. For example, in our 3D cardiotoxicity assays, analysis of beating frequency and calcium flux can provide supplementary functional data.



3D Cell Culture Models
Application Specific Models

The Visikol Difference

At Visikol, we recognize that 3D cell culture models are not miniature organs in a dish and all of these models have their inherent advantages and disadvantages in regards to cost, throughput, complexity and *in vivo* relevancy. That is why we work closely with researchers to identify the model that is best for their specific research question while minimizing cost and increasing throughput. We are also committed to developing industry consensus around which models are best for specific applications and have recently launched our OpenLiver™ initiative to open source a suite of 3D cell culture liver models. Through this effort we are helping researchers determine the ideal model for their research question as well as how to reproducibly generate an appropriate model.

Shift Your Biology to 3D

We have an in house cell culturing facility and an expertise in transforming traditional 2D *in vitro* systems into 3D cell culture models. We have worked with many Clients on custom 3D cell culture model development from single cell type spheroids to complex iPSC-derived organoids.

Products and Services

- OpenLiver™ HepG2 Spheroid
- OpenLiver™ HepaRG™ Spheroid
- OpenLiver™ HepaRG™ NP 3D
- Primary Murine Cardiomyocyte 2D and 3D Cell Culture
- PDX 3D Cell Culture Models
- Custom Cell Line 3D Cell Culture Generation
- Custom Model Development
- Tissue Bioprinting

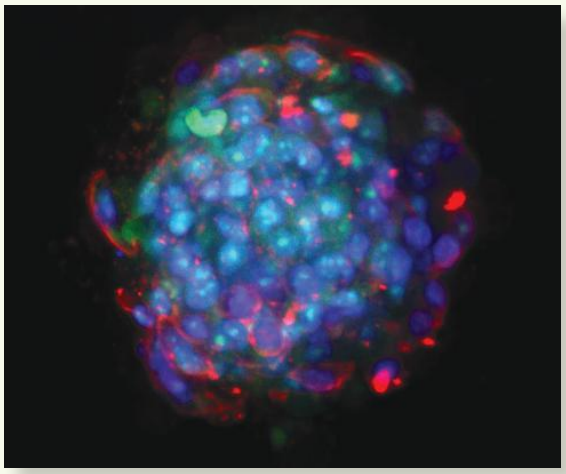
Commitment to Transparency

We strongly believe that our biology should not be proprietary and have thus open sourced all of our 3D cell culture models such that our results can be easily reproduced. Furthermore, our models can be internalized by our Clients if they so choose.

Model Spotlight

OpenLiver ™ HepaRG™ NP 3D

This pharma-validated 3D model was designed to be highly reproducible through the combination of HepaRG™ with non-parenchymal cells as well as affordable starting at $1,400 per 96 well plate (ask us about bulk pricing). We can use this model internally in a service project or ship it to you for use in your lab. We leverage our manufacturing facility in the US to quickly and effectively deliver to our customers.



Digital Pathology

Transforming Images Into Quantitative Insights

The Visikol Difference

The analysis of digitized histological slides has become commonplace in the study of biology, and many tools exist to facilitate quantitative measurement of tissue sections. However, we find that there is no one-size-fits-all solution and that researchers often need support in transforming their physical slides or digital files into reliable quantitative insights. Furthermore, most existing software tools are built for processing single slides, requiring manual, time-consuming technical work. Using our suite of proprietary 3Screen™ software, we execute on simple projects from quantifying tumor area or percent positive cells to building customized machine learning programs to identify novel biomarkers or building 21 CFR part 11 compliant software for use in a clinical setting. We specialize in large datasets, and can rapidly turn over huge image libraries. Our team is comprised of experts in image processing and computer science that look forward to partnering with you on your research efforts.

How We Work With Clients

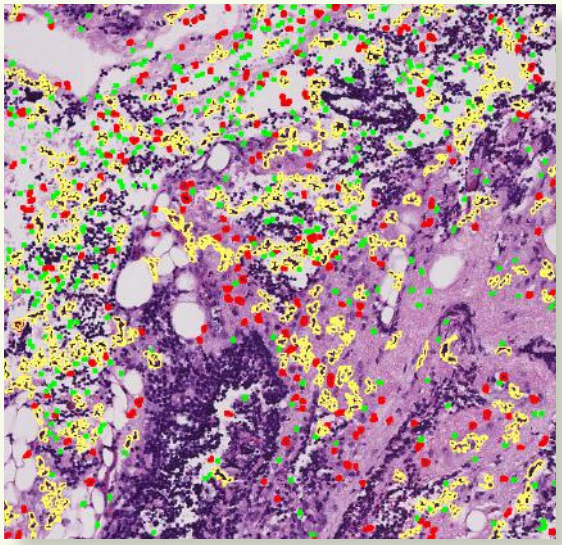
Typically, Clients send us either physical glass microscope slides for scanning and analysis or hard drives of scanned microscope slides. We also can conduct end-to-end tissue processing, sectioning, scanning and analysis if required as well.

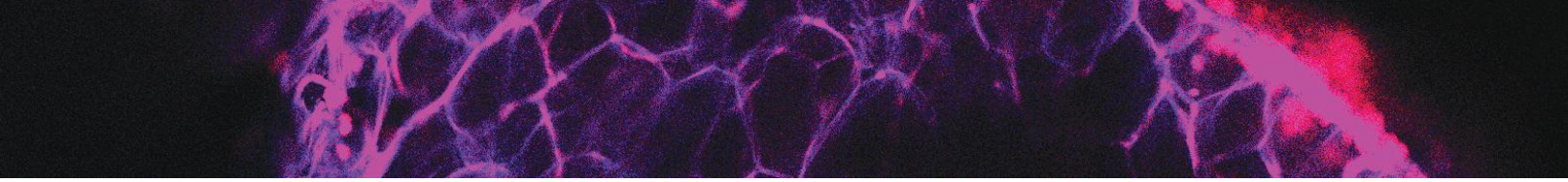
Services

- Slide Scanning
- Tumor Area Quantification
- Quantitative Expression Scoring
- Cell Counting
- Large Image Library Processing
- IHC Slide Quantification
- Nuclear Morphology Assessment
- Machine Learning Analysis
- Software Development and Implementation
- 21 CFR Part 11 Compliant Software Development and Validation
- Data Storage

Project Spotlight

We recently partnered with Enzyvant Therapeutics Inc to help them develop a machine learning based digital pathology software platform for the characterization of thymus tissue prior to transplantation for patients with Complete DiGeorge Syndrome. Like many of our projects, this project began as a research pilot project and transformed into a software development, validation and implementation project. We developed this software application as a validated 21 CFR part 11 complaint assay in accordance with the ICH analytical assay guidelines that is capable of determining if a tissue is of high enough quality to transplant. This is one of the first machine learning digital pathology algorithms to go in front of FDA for a BLA submission.





3D Tissue Imaging

Shift the Paradigm of Histology to 3D

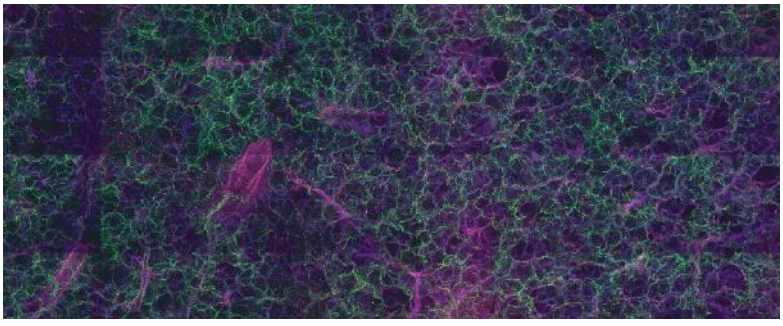
The Visikol Difference

Since the introduction of the microscope, researchers have characterized tissues using ultra-thin two-dimensional slices which can be limited in describing complex or heterogenous tissues. To address this problem, we have developed our patented Visikol® HISTO™ tissue clearing reagent which when paired with fluorescent labeling and confocal/light sheet microscopy allows for the complete 3D visualization of tissues.

Whole mount analysis of tissues provides many advantages over tissue sectioning. Firstly, far more of the tissue can be sampled and quantified, leading to more accurate results. Secondly, whole mount analysis greatly simplifies tissue prep, since we start with the intact organ, eliminating tedious sampling of regions of tissues and biases induced from improper sampling. Furthermore, many tissues and substructures are very delicate, causing their harvest to be difficult and time consuming. Thirdly, processing whole mount tissues allows for quantification of aspects of the tissue by region within the tissue, providing great insights about the effect of a particular drug or nature of a disease.

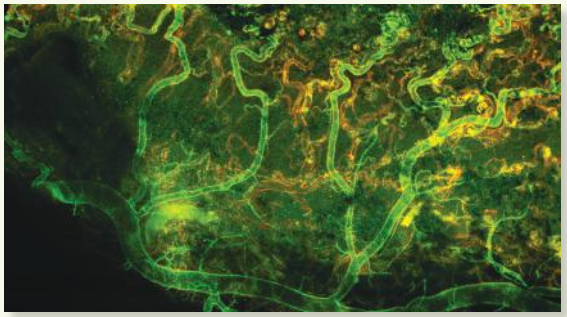
How We Work With Clients

We work closely with Clients to identify the exact needs for 3D tissue imaging projects. A detailed discussion of the requirements of a particular project is conducted, and our staff communicates closely with our Clients to ensure that our study plan, image processing, and data analysis meet all of the needs of our Clients. We will discuss end-point needs in depth with our Clients to be certain that we can provide the best possible insights while minimizing costs.



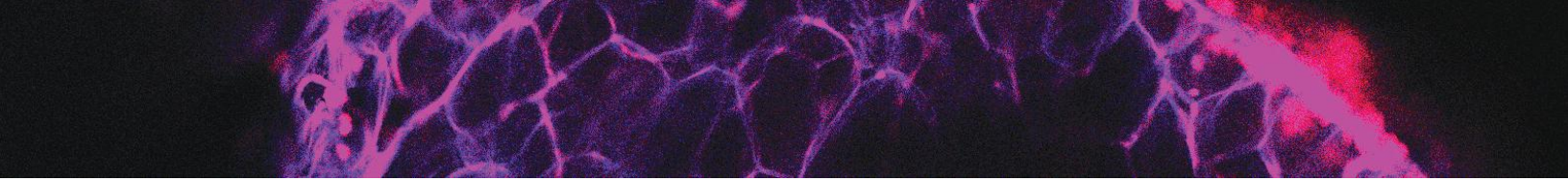
Our Approach

Many researchers have struggled to adopt 3D tissue imaging and analysis techniques due to their complexity. At Visikol, we have developed a suite of optimized tissue clearing and labeling protocols for various tissues and pair this expertise with a strong focus on imaging and image analysis. We partner with our customers to understand the minimum requirements for their research question such that we can minimize project costs while increasing throughput and sample size.



Project Spotlight

3D tissue imaging allows for complex features and heterogeneously expressed biomarkers to be characterized in their entirety. This is incredibly useful for complex features such as neurons and vasculature which are challenging to depict with conventional histology. An example of this work is the imaging of retina vasculature to quantify how various compound treatments effect several conditions which alter retina vasculature phenotype. Through combining 3D tissue imaging with 3D tissue analysis, we can quantify complex 3D features such as branching, tuberosity, volume, branch points and redundancy.



Custom Drug Discovery Projects
Images to Insights

The Visikol Difference

While we have a suite of standard assays and services that we offer to our Clients, a large portion of the work we do is bespoke projects for Clients or customizations of our existing services. We pride ourselves on our ability to partner with Clients to come up with customized solutions to help them address their research questions.

How We Approach Custom Projects

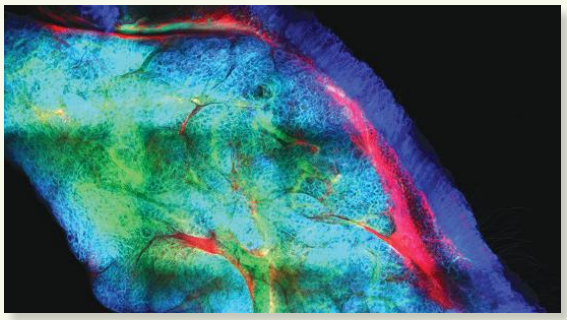
We have access to the most cutting-edge biology, imaging tools and image analysis solutions in the drug discovery space. We partner with Clients to intimately understand their research question and then begin each project by defining a possible solution to addressing this problem. We actively work with our Clients to minimize cost and increase throughput as well as to define the specific endpoints for the project. The goal of all of our projects is to distill down a large set of data to an actionable report that can be used to make a more informed decision during the drug discovery process. We typically stage our custom projects with several stage gates and begin with a small pilot study before moving into the majority of the project.

Example Projects

- Machine learning software development for custom tissue classification
- Development of thymus organoid model
- Assessment of bioprinting for the recapitulation of tumor microenvironment
- Mapping and quantifying blood vessel regression in retina
- Tau protein burden in whole mouse brains
- Tracking Zika spread from mother to infant via breast milk
- Echocardiogram image analysis
- Development of X-ray CT software for skeletal evaluation

When to Partner with Visikol

As a company, our core expertise is in imaging, image analysis and advanced *in vitro* biology. We find that we provide the most value to our Clients when a project requires one of these domain experiences. However, our expertise spans many types of imaging modalities from X-ray CT to confocal microscopy, many different tissue types from animal studies to organoids and many disease applications from cancer to toxicology. We are agnostic to the type of project we are working on with our Clients and our team is continually excited by the diversity and complexity of the projects we work on.



How to Get Started

All of our projects begin with a conversation to discuss the specific aims of a project and the desired deliverables. Our aim is always to transform tissues or images into quantitative insights. To work with us, Clients send antibodies/compounds for end-to-end testing, image data sets on a hard-drive, physical glass slides for scanning or whole tissues for a wide range of different types of processing.