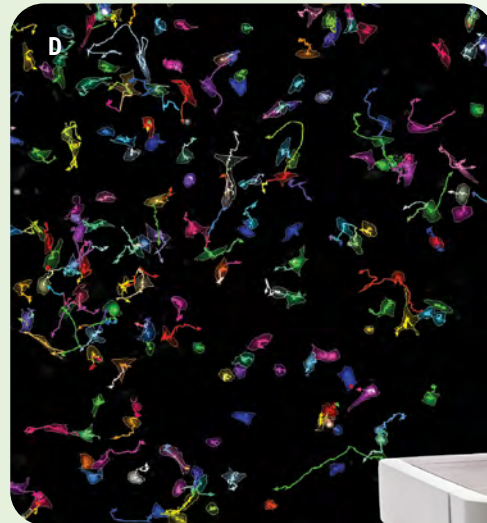
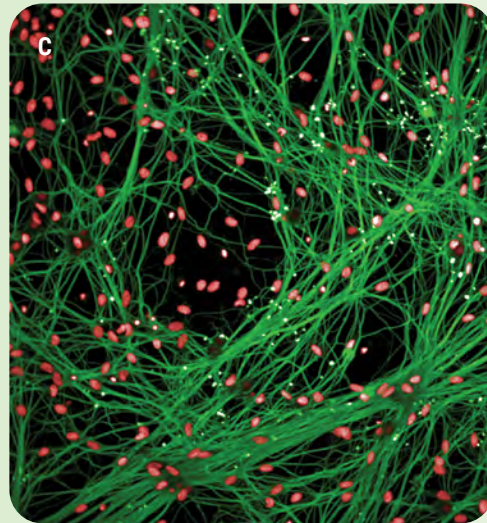
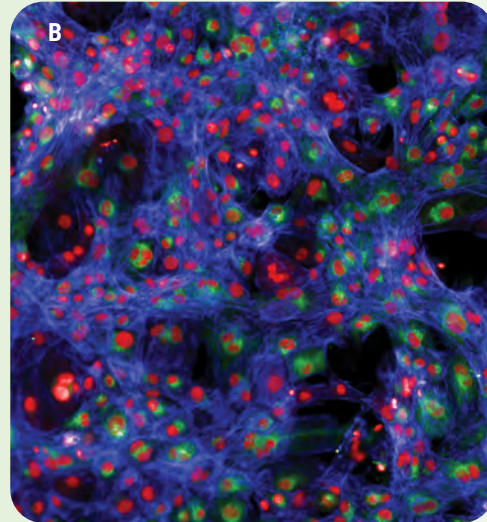
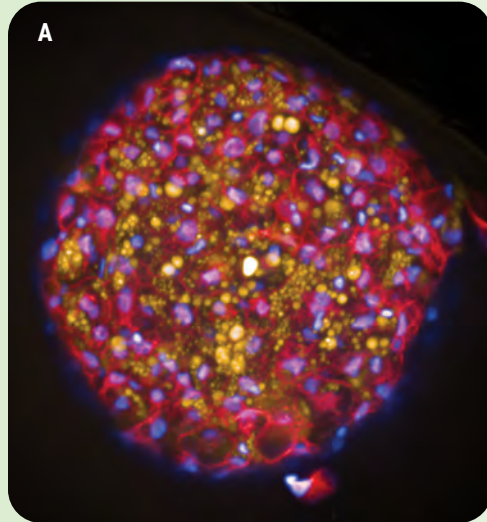




WHEN BIOLOGY IS COMPLEX
SIMPLIFY YOUR DISCOVERY



Operetta® CLS™ High-Content Analysis System



The System That Makes the Everyday Extraordinary

Today's drug discovery labs gain information and insights from a whole spectrum of assay types – fixed- and live-cell assays, 3D and complex cell models, cell painting, phenotypic fingerprinting, and protein-protein interaction assays, as well as everyday routine applications. So for these labs, flexibility is everything.

The **Operetta® CLS™ high-content analysis system** is built for flexibility, giving you the tools and technologies to glean more physiologically relevant information from the whole spectrum of assay types – quickly and simply, whether performed by novices or experts.

What's more, the Operetta CLS system is part of our comprehensive HCS workflow solution – everything from systems, reagents, and microplates to automation and informatics – all from one trusted source. Together with our **Harmony® high-content imaging and analysis software** – the easy-to-learn, easy-to-use software that empowers biologists to do their own analysis – you have everything you need to run your everyday (and complex) analyses.



A. HepG2 microtissue stained with Nile Red to study hepatosteatosis, 20x W objective. Cells provided by InSphero AG.

B. Human cardiomyocytes labeled with the hypertrophy marker proBNP/488, Rhodamine-Phalloidin, Hoechst and CellMaskBlue, 20x W objective. Cor.4U cardiomyocytes provided by Axiogenesis AG.

C. Embryonic rat dorsal root ganglion (DRG) neurons stained with Alexa Fluor® 488 anti-TUJ1 (axons) and DRAQ5 (DNA). Courtesy of Dr. York Rudhard, Evotec AG.

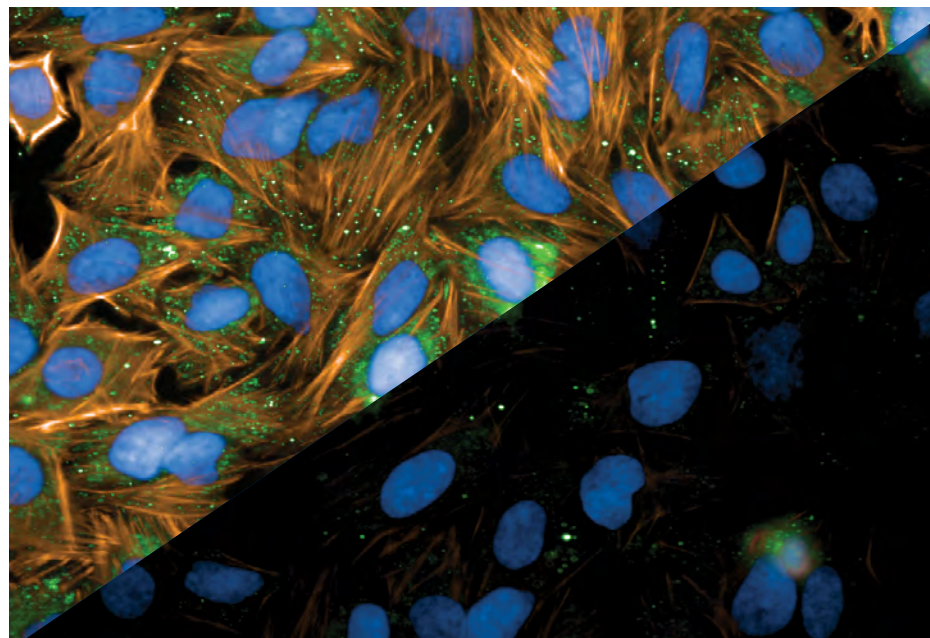
D. HeLa cells tracked using the digital phase contrast mode.

When Great Technologies Combine, the Results Are Illuminating

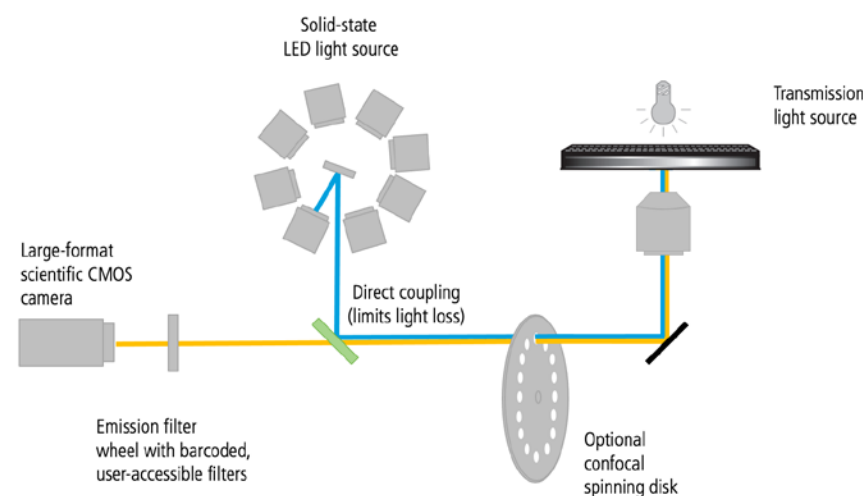
At the core of the Operetta CLS system is a light path that ensures highly efficient excitation of your samples and careful collection of emitted signals. Direct coupling of the excitation source into the optical path limits the light loss that's typical of light guides or fibers. The built-in 8x LEDs let you choose the optimal wavelength for excitation of your fluorophore and deliver the power directly to your cellular samples, while user-accessible emission filters let you further optimize detection.

With optional temperature and CO₂ control, you can run your live-cell assays knowing that the changes you're seeing are due to the biology, not the technology. Once your assay parameters are optimized, you know you can trust your results, time after time.

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Top corner: HeLa cells stained with Hoechst (DNA), Alexa Fluor™ 488 labeled anti-tubulin and TRITC-Phalloidin (actin) imaged with a high NA 40x water immersion objective (NA 1.1). Bottom corner: Same sample imaged with a 40x air objective NA 0.75 with the same exposure settings resulting in a dimmer image as the objective captures fewer photons.

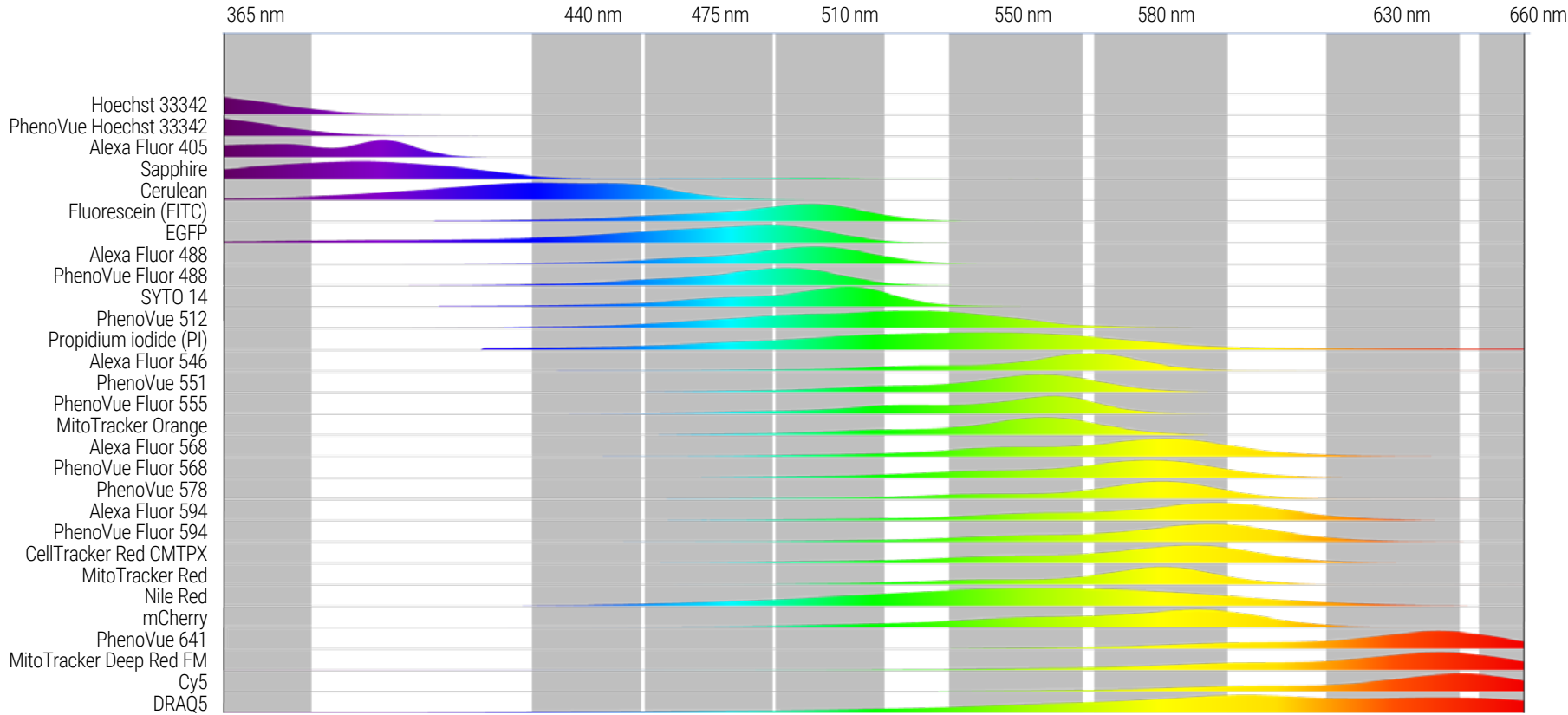


More Light on the Subject

Proprietary automated water-immersion objectives with very high numerical aperture deliver and capture more photons and provide a higher resolution in XYZ than conventional objectives – in fact, they capture up to four times more light than high numerical aperture air objectives can. You can benefit in two ways: delicate live-cell samples can be excited with less light to protect them from photodamage or you can significantly increase the throughput of applications such as 3D stack acquisition.

The Perfect Way to Image

The Operetta CLS system’s proven spinning disk technology minimizes photobleaching and phototoxicity and provides several advantages over conventional confocal microscopy techniques: since multiple points are collected simultaneously rather than by scanning a single point at a time, the imaging process is much faster and gentler, enabling efficient background rejection, live-cell experiments, and 3D imaging. What’s more, the large-format sCMOS camera delivers low noise, wide dynamic range, and high resolution – perfect for sensitive and quantitative measurements at short exposure times.



Up to eight LEDs excite a wide range of fluorophores, from UV to NIR, including DNA stains, live-cell stains, fluorescent proteins, and typical covalent labels. Some popular dyes are shown here.

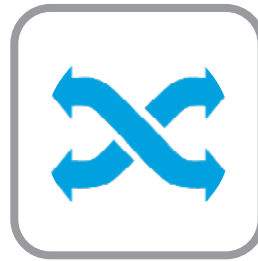
A Configuration for Every Need

Whatever your application, there's an Operetta CLS system to fit your requirements – and it's modular, so it can change with your research demands.



Operetta CLS Quattro

With four LEDs and widefield fluorescence, the basic configuration is ideal for common applications that need sensitivity and resolution, with the capacity to grow if the need arises.



Operetta CLS FLEX

With eight LEDs and confocal and widefield fluorescence, this configuration offers flexibility in excitation and imaging modes for many challenging applications – and it can be upgraded to even higher performance.



Operetta CLS LIVE

With all the features of the FLEX configuration, plus gas and temperature control and water-immersion objectives, this system is ideal for gentle yet highly sensitive live-cell imaging.

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Your Instrument, Your Choices

High-Efficiency Solid-State Excitation Source

Choice of up to eight excitation lines built into your system

Environmentally Controlled Sample Chamber

Compatible with robotic automation

User-Accessible Emission Filters

Your choice from more than 10 different filters

Water Immersion Objectives

Built-In supply and waste bottles

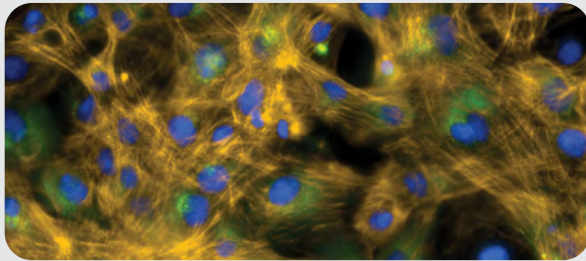
Widefield and Confocal Imaging Modes

Switchable imaging mode depending on your needs



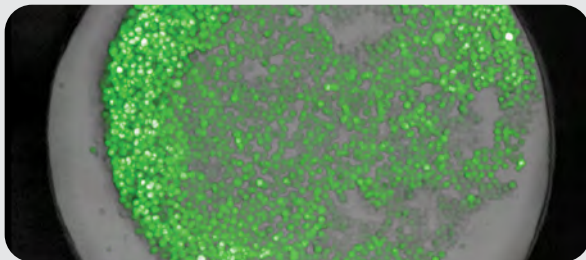
Your Science in Every Cell

From everyday assays to more demanding applications, the Operetta CLS high-content analysis system delivers just the right combination of flexible excitation, sensitive optics, and advanced software features to enable you to gain deeper biological insight from all your critical applications.



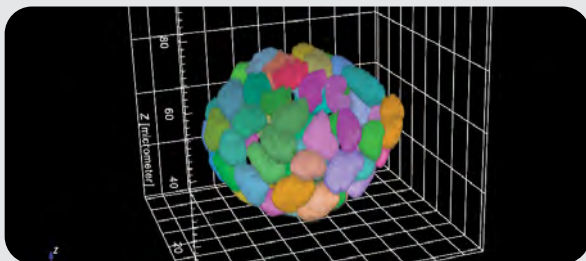
Fixed-Cell Assays

You can choose from fluorescent widefield and confocal spinning-disk imaging with up to eight high-power excitation sources and user-accessible emission filters for maximum flexibility – so you can optimize your assays quickly.



Live-Cell Assays

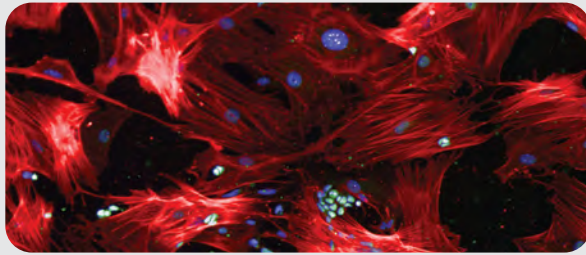
Meaningful live-cell assays depend on stable excitation and minimal photodamage, spinning disk confocal optics, and synchronized LED illumination. For live-cell analysis without fluorescent labels, you can also choose brightfield or digital-phase contrast imaging modes.



3D Cell Models

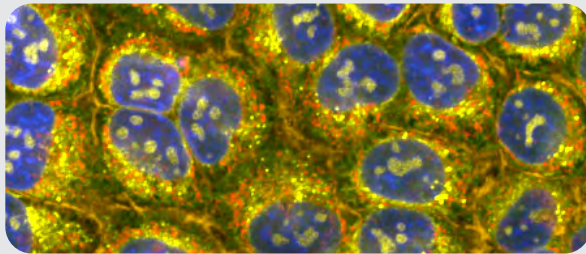
Spinning disk confocality and water-immersion objectives combine to collect up to four times more light from samples and increase X, Y, and Z resolutions, for high-quality images from 3D samples. And Harmony software lets you acquire, visualize, and analyze 3D samples on one platform, for more physiologically relevant results.

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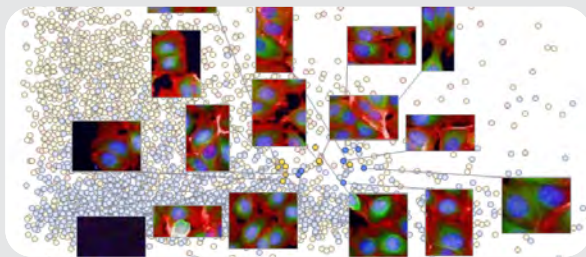
Complex Cell Models

The Operetta CLS combines a large-format sCMOS camera with water-immersion objectives for sensitivity and high resolution, while machine-learning-based PhenoLOGIC™ software helps you distinguish and characterize cell types based on morphology, fluorescence intensity/distribution, texture, and more.



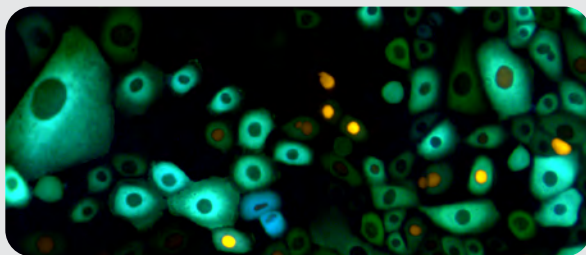
Cell Painting

Cell painting is a powerful application of high-content screening technology. In cell painting, specific cellular compartments are stained with six different fluorescent bioprobes simultaneously, followed by imaging and analysis to phenotypically profile the cells and elucidate their behavior.



Phenotypic Fingerprinting

At the core of successful phenotypic assays is the ability to create robust fingerprints of subtle differences. The Operetta CLS system combines high-resolution imaging with advanced software tools such as STAR morphology and machine learning for true multiparametric hit selection.



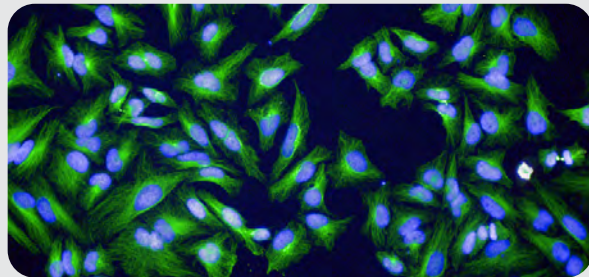
Protein-Protein Interaction Assays

FRET is a powerful tool for investigating conformational changes and protein-protein interactions. With a good FRET sensor, it's possible to track activity of kinases such as ERK in live cells and much more. And with imaging and dedicated analysis tools for ratiometric imaging, robust results are easy to obtain.

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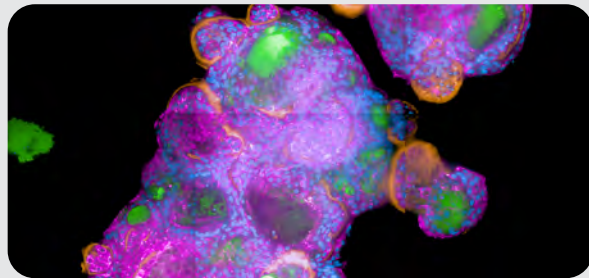
Exceptional Imaging and Analysis for Your Disease Models

Our high-content screening workflow provides disease researchers the tools that enable insights and interactions between cell types and organ systems that lead to breakthroughs in prevention, early detection, and treatment of diseases.



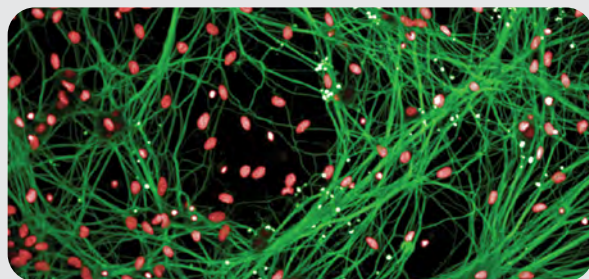
Cancer Research

Cellular imaging is a proven, powerful tool for improving understanding of cancer biology, allowing you to visualize tumor cell mobility, invasion, metastasis, angiogenesis, and more. Whether you're exploring complex biological pathways or investigating how drugs affect those processes, we have cellular imaging tools to advance your research and discovery.



Infectious Diseases

Fully automated imaging and unbiased quantitative image analysis take advantage of the full potential of microscopy, allowing the characterization of pathogens and host-cell phenotypes. Infection rates can be determined with high sensitivity, since individual infected cells can be identified. Infection can be described with up to hundreds of readouts per cell, allowing the linkage of infection rates to other readouts, such as host-cell morphology or signaling.



Neuroscience

High-content analysis provides rich data for neuroscience research, including assays that can quantify various aspects of dendritic trees, protein aggregation, transcription factor translocation, neurotransmitter receptor internalization, neuron and synapse number, cell migration, proliferation, and apoptosis.

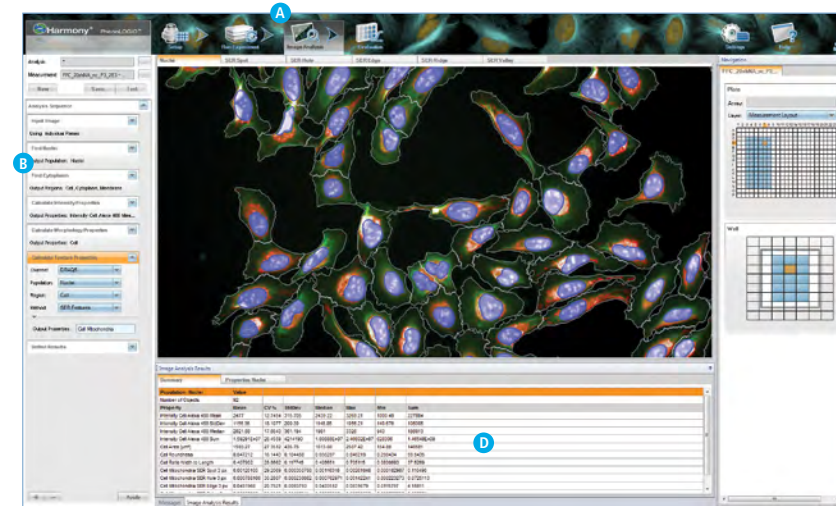
Everything Comes Together in Harmony

Simple, powerful **Harmony high-content imaging and analysis software** provides a complete solution, enabling you to set up assays and automate high-content imaging experiments, acquire images and analyze data, and store, retrieve, and present those results in meaningful ways. Its workflow-based interface makes the whole process simple and straightforward, even for new users with little microscopy or programming knowledge.

- Easily set up acquisition channels and parameters
- Utilize more than 30 ready-made solutions for common assays
- Use image analysis building blocks to create, configure, and customize your own protocols
- Get detailed cellular phenotype descriptions for more robust, reproducible classification with advanced analysis features
- Automatically store metadata such as assay layout, instrument settings, analysis results, and user-defined keywords and annotations
- Visualize and analyze your samples in 3D for more physiologically relevant information and insights

Harmony software also powers the Opera Phenix™ Plus high-content screening system so you can transfer your Operetta CLS assays to higher throughput with ease. And with regular updates, it's a flexible solution for gathering unbiased data from your cell samples, keeping you ahead of your growing research needs.

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- A. Workflow-based interface with easy-to-read icons
- B. Analysis building blocks for easy protocol design
- C. Clear plate navigation and wizard for easy setup of new plate types
- D. Results summary with immediate numerical output for faster insights

Easily Quantify Cellular Phenotypes in Complex 3D Models

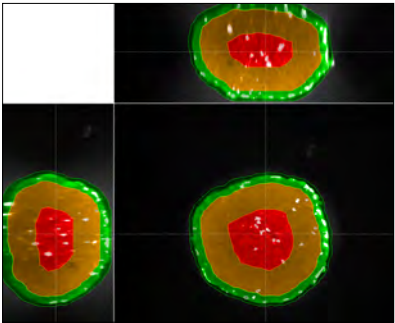
With **Harmony** software, you can speed up 3D image acquisition through targeted imaging independent of culture method, such as plates or hydrogels, and better understand your cell models by exploring them in 3D and XYZ viewers. You can measure morphology, volume, and texture in 3D; count nuclei within spheroids; and calculate XYZ positional properties. And you can quickly analyze your z-stack as maximum intensity projection, with 3D information preserved, using PlaneMap technology.

Accurately Target Objects of Interest for Greater Efficiency

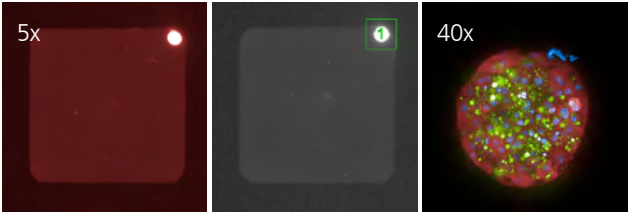
High-content screening can capture fine subcellular detail with very high resolution images, but this can slow down acquisition times and create large amounts of data. The **PreciScan** plug-in enables intelligent image acquisition to let you accurately target your objects of interest in X, Y, and Z dimensions, such as spheroids, stem cell colonies, or rare cell phenotypes. The software delivers a fully automated, integrated workflow of low-magnification prescans, image analysis, and higher magnification rescans to reduce acquisition times and data volume and speed up analysis significantly.

Become an Image Analysis Expert with Machine Learning

With the **PhenoLOGIC™** plug-in, you can recognize different cell populations and regions by example, making it easy to create optimized algorithms. Just click on a few cells of each type to show the software what you're looking for. PhenoLOGIC software then selects the most meaningful combination of parameters to robustly discriminate phenotypes or segment images based on texture features.



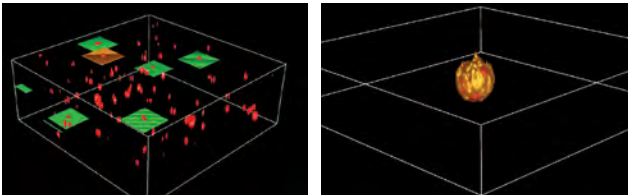
XYZ view showing positional analysis of dead cells using ring regions.
Green: Outer region
Orange: Inner Region
Red: Core Region



Step 1. Pre-scan at low magnification

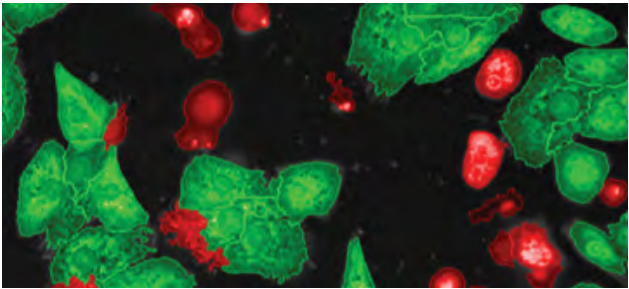
Step 2. Identify object of interest

Step 3. Re-scan at high magnification



10x pre-scan in x, y, and z dimensions.

63x magnification re-scan.



PhenoLOGIC classification of primary hepatocytes (green = healthy, red = dying).

Solutions to Optimize Your Workflow

Phenomenal Fluorescence

Our **PhenoVue™ cellular imaging reagents** complement our proven high-content screening instruments, image analysis software, microplates, and automation, providing an integrated solution across the entire cellular imaging workflow.

Building on our extensive expertise in imaging instrumentation, fluorescent dye chemistry, and assay development, our optimized and validated PhenoVue platform includes bright-organelle and cell-compartment stains, fluorescent-labeled secondary antibodies, and cell painting kits comprising six fluorescent probes and an optimized protocol to streamline your workflow.



The Perfect Plate for the Work You Do

For best results, choose the microplates designed specifically for high-end imaging systems. We've developed and validated a range of microplates for HCS applications, including **PhenoPlate™** (formerly CellCarrier™ Ultra) microplates with a unique patented design for high-content imaging readers.



Cell Counting to Increase Accuracy and Accelerate Assay Prep

Counting cells is an essential step in determining cell concentration prior to cell passage and seeding. Automated cell counting reduces variations due to human error and improves robustness of HCS assays.

Nexcelom Cellometer® and **Cellaca™ automated cell counters** from PerkinElmer are designed to simplify the cell counting process, combining the basic principles of a hemocytometer with modern technologies like fluorescent microscopy, image cytometry, and automation to avoid the pitfalls of manual cell counting.

Cellometer Image Cytometers

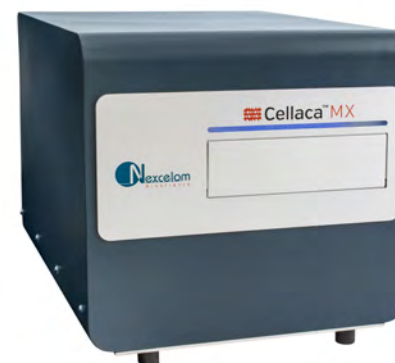
Automatically obtain cell images, counts, measurements, and viability calculations in less than 30 seconds per sample – and with disposable counting chambers, there are no time-consuming wash steps.



Cellaca MX High-Throughput Automated Cell Counter

Run 24 samples in less than three minutes with no reloading individual slides or waiting for small-batch counters to finish.

- Small sample volume – only 25 µl of sample required
- Cell viability with trypan blue or fluorescence
- Robotic integration with optional API
- 21 CFR Part 11 ready – optional add-on for audit trail, user access control, and digital signature



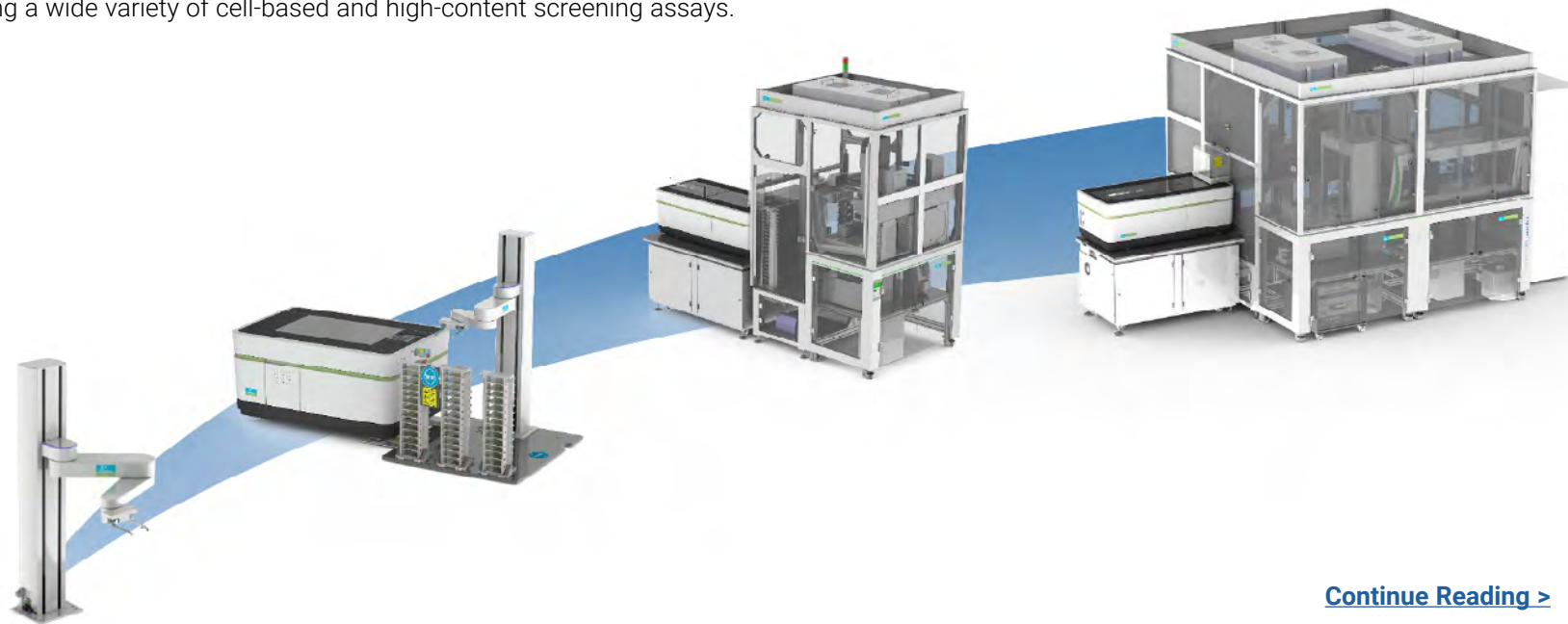
Speed Discovery by Integrating HCS Workflows

Higher throughput, improved efficiency, and greater productivity: these are the benefits of integrating your HCS workflows with automation and advanced data analysis capabilities. Whatever your screening needs, we have a solution that's right for your lab.

It Pays to Automate

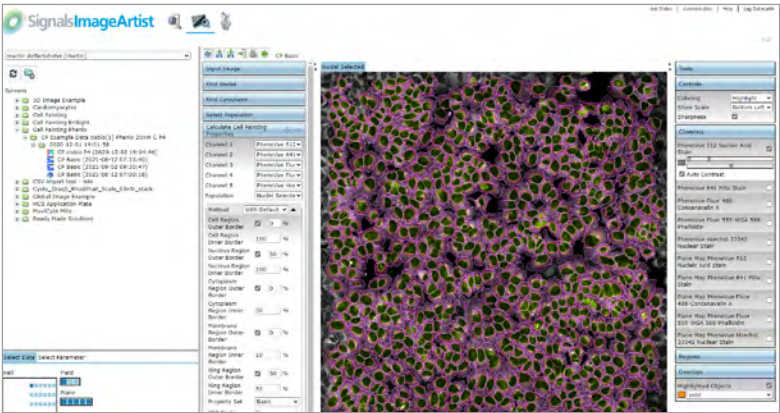
Whether you're integrating your Operetta CLS system with our **plate::handler™ FLEX system** for automated plate loading or integrating your entire HCS workflow with our **explorer™ G3 automated workstations**, you'll see increased productivity, less risk of human error, safer working conditions, and the ability to maximize your data for better results.

What's more, our experts have extensive experience developing integrated workstations for automating a wide variety of cell-based and high-content screening assays.



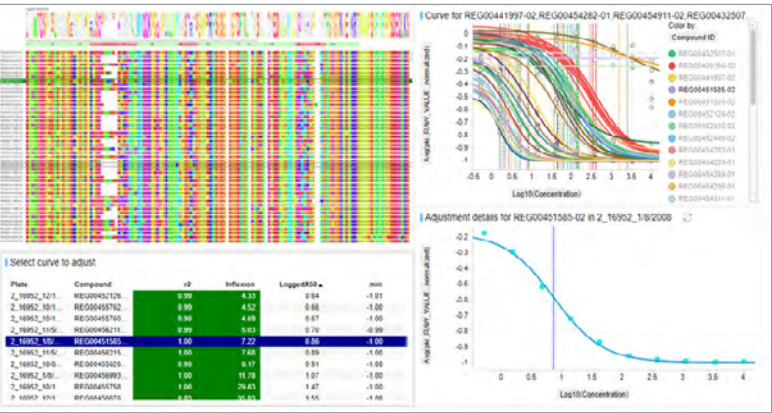
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Access and Analyze All Your HCS Data in One Place

For universal high-volume image data storage and analysis, **Signals Image Artist™ software** provides a central location to quickly process, analyze, share, and store the vast volumes of data generated by high-content screening and cellular imaging, including 3D imaging, phenotypic screening, and cell painting. Compatible with all major high-content screening and cell imaging systems, Signals Image Artist is a multiuser platform that can support your entire lab and is scalable to expand with your lab's data storage needs over time. It integrates seamlessly with the Operetta CLS and Opera Phenix Plus high-content screening systems, as well as the Signals VitroVivo™ software platform.



Analysis of All Your Assay and Screening Data

With **Signals VitroVivo™ software platform**, you can perform screening data analysis and validation, QC analyses, calculate reliable normalization, multivariate hit stratification, dose response curves, drug response profiling, and more. It unites assay development, low-throughput to ultrahigh-throughput production assays, high-content screening, and *in vivo* studies so users can explore all assay and screening data in a single platform.

Complete Services for Increased Productivity and Efficiency

Today's lab leaders are facing several challenges, from tighter deadlines to increased budget scrutiny to teams with various degrees of comfort with lab equipment. Time that could be spent getting ahead is spent on noncore activities.

To help you overcome barriers to success, OneSource® Laboratory Services has built a team of trained scientists and engineers who bring their real-life knowledge to you, helping increase your productivity with recommendations on how to best utilize your assets. With this knowledge, you can get back to your core mission.

We service our instruments, as well as equipment from other manufacturers – from contracts and performance maintenance to full-lab asset management delivered globally, we can help you make the most of your important lab assets. And for labs looking to introduce new equipment and techniques, we offer training at our facilities and yours.

Instrument Support Services

Maintaining labs is never easy, especially when an instrument is down. We know you're responsible for the performance of your laboratory, and we make sure nothing holds you back. Our field service engineers, manufacturing site technical services, and research and development teams are here at your disposal to ensure maximum uptime.

You need your instruments to be reliable and running with minimal downtime, and you want flexible service agreements that are easy to comprehend. We understand, and we're here to help.

Education Services

Whether you are looking for a basic instrument refresher course, simple troubleshooting techniques, general application support, or method optimization, our field application scientists or service engineers will come directly to your lab. Through education, you will gain knowledge and insights into the latest techniques, not only increasing your confidence, but also unlocking the full potential of your instrument.



OneSource Services

- Asset optimization
- Lab environment and instrument monitoring
- Asset location
- Education and training
- Technology and descriptive analysis
- IoT/Lab of the future
- Remote support
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- Compliance
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- IT solutions
- Instrument qualifications

[For more information visit www.perkinelmer.com/OperettaCLS](http://www.perkinelmer.com/OperettaCLS)

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