YOKOGAWA

Co-innovating tomorrow™

Confocal Quantitative Image Cytometer

Cell Voyager CQ1

Confocal Quantitative Image Cytometer

Bulletin 80J01A01-01E

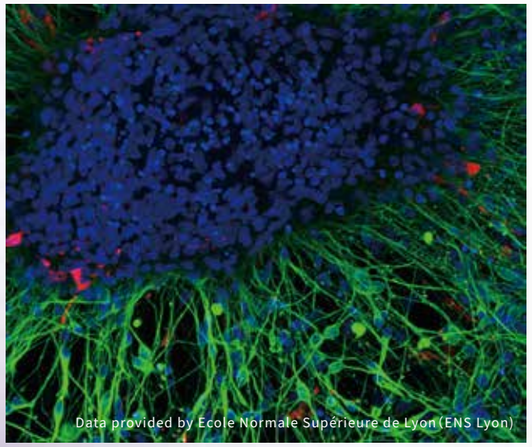
Summary

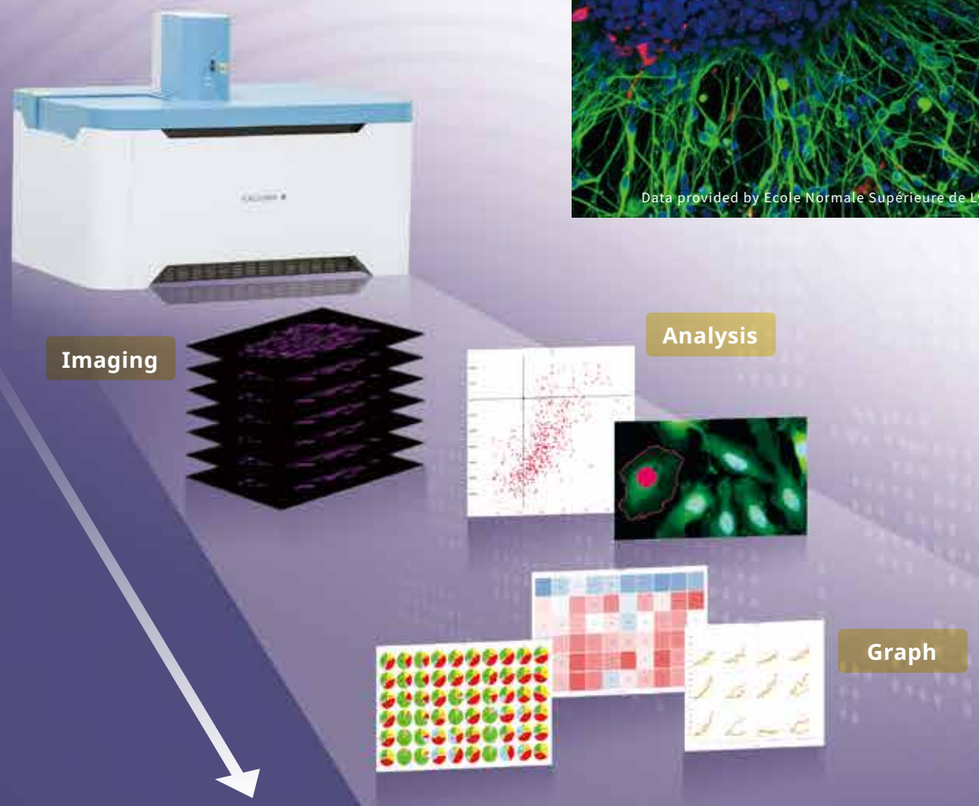
Confocal Quantitative Image Cytometer

Cell Voyager CQ1 offers a new approach to cell measurement

Confocal Quantitative Image Cytometer

Clear 3D images obtained from confocal microscopes have been enabling advancements in cell biology research for many years.
This imaging technology combined with population analysis now provides a significant advancement for cytometry.
The CQ1 enables clear 3D imaging, object recognition, and rapid quantification of live cells and cell clusters.
The data from the images help in the understanding, and enhance the reliability of data.
The CQ1's live cell chamber acts as a cellular incubator enabling is used to many times lapse imaging while the CQ1's unique imaging technology is gentle on the cells.
The Yokogawa CQ1 is an easy to use all-in-one confocal microscope for are asonable price.
The CQ1 comes with a number of configurable options andcan be integrated into a fully automated screening system.


Data provided by Ecole Normale Supérieure de Lyon (ENS Lyon)



Raise your high content analytics to the next level!

Enables measurement of spheroids, colonies and tissue sections.

- Possible to measure cells in culture dish without preprocessing such as cell peeling, unlike a flow cytometer
- Thanks to Yokogawa technology the confocal disk confocal, 3D images are acquired rapidly and gently
- Max.10 colors emission with 4 colors excitation and transmission illuminataion imaging
- Live cell chamber and time-lapse measurements
- Accurate feature extraction to facilitate sophisticated cell analysis
- Wide FOV and tiling function make easy to get imaging of large sample

Compact footprint, light weight bench-top system; no need for darkroom

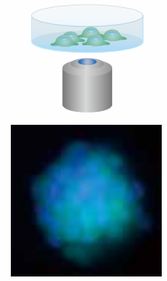
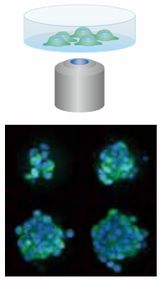
Offers the similar capabilities as flow cytometery

- Analyzed data displayed in real-time with image acquisition (On the fly analysis)
- Application protocols guided by templates
- Ability to trace back to the original image from a data point in a graph and to remeasure
- All-in-one system with easy operation

Open platform

- Output FCS/CSV/ICE data format readable by third-party data analysis software
- Connectable with external systems via plate handling robot
- A variety of cell culture and sample vessels are applicable

Contrast of measurement methods

Flow cytometer	Non-confocal imaging system	Confocal imaging system
•Cell peeling treatment is necessary. •Risk of damaging to cell		
		
Unable to re-measure nor confirm by image	Imaging is difficult sample is thick.	3D imaging of thick sample **In addition, CQ1 is high-throughput and gentle with cell.**

Example of setup

Multiple Functions Fully Integra ted in a Compact Box

Cell Voyager CQ1 — Confocal Quantitative Image Cytometer

Microscope Unit

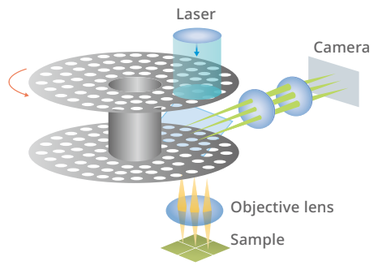
Maximal performance objective lens (super apochromat) and the widest field/ highest-resolution sCMOS camera achieve high-throughput measurements of submicron sample.

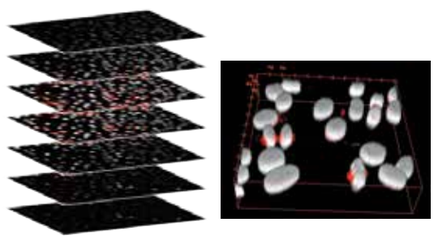
Emission Filter

Up to 10 Emission filters can be mounted. Measurement of multiple markers can be achieved in just one experiment.

Confocal Scanner Unit

Multi-beam scan by “Microlens enhanced dual Nipkow disk confocal” achieve high-throughput 2D/ 3D imaging with minimum damage to samples.

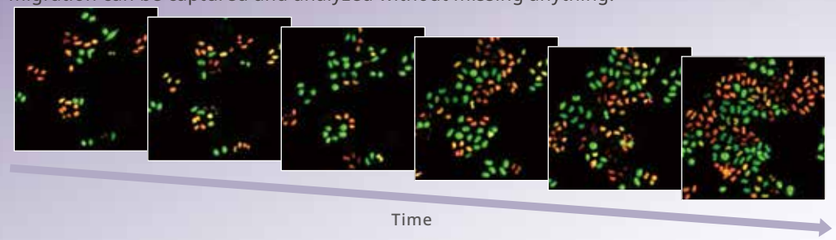




Example: Cellcycle measurement of cancer cells

Stage Incubator

The stage heater controls the temperature, humidity, and CO_2 / O_2 concentration of the sample environment to maintain the incubation environment and makes possible time-lapse imaging.
By using 3D time-lapse imaging, detailed reactions of intracellular organelles and dynamic movements such as cell migration can be captured and analyzed without missing anything.

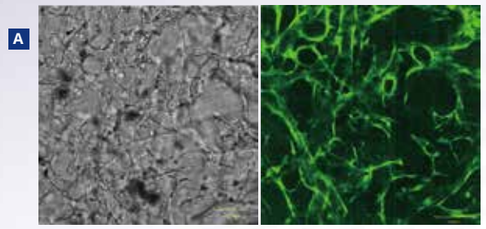


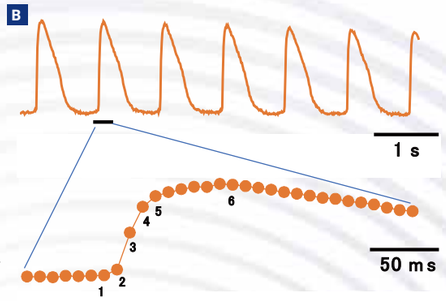
Stage Heater*1

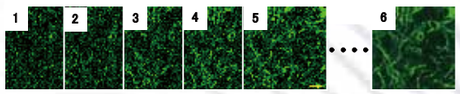
Fast Time Lapse Function

NEW!

Capable of capturing up to 100 images per second (100 fps).
It makes possible to capture high-speed phenomena that were previously difficult to capture.



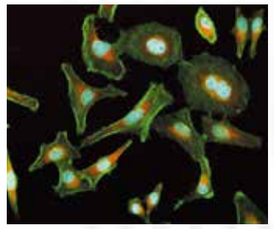


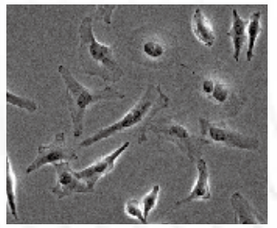


A: Gelatin fiber substrate for cell culture (Genocell® Plate for Myocardial Evaluation, Japan Wool Co. A: iPSC-derived cardiomyocytes in culture on a gelatin fiber substrate for cell culture (Genocell® Myocardial Evaluation Plate, Japan Wool Co.
Bright field image (left), stained with calcium-sensitive fluorescent dye (right).
B: Calcium signal waveform fluctuating periodically in response to myocardial pulsation (upper panel).
High-speed imaging at 100 frames per second allows the fast-rising portions of the waveform to be captured at a sufficient sampling frequency. High-speed imaging at 100 frames per second allows the fast-rising portions of the waveform to be captured at a sufficient sampling frequency.

Light Sources

Up to 4 laser sources for confocal imaging can be installed. Also, light source for phase contrast and bright field imaging is installed as a standard function, which is extremely useful when confirming sample shapes.





Sample vessels

Imaging with a variety of containers is possible.

Microplate

35 mm dish*1

60 mm dish*1

Slide glass*1

Cover glass chamber*1

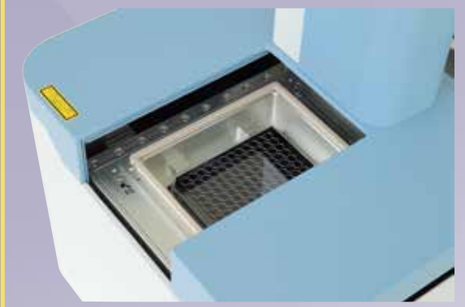
*1 Option

Set the protocol and One Click! -Easy & Universal Software-

Cell Voyager CQ1 Confocal Quantitative Image Cytometer

START!

Sample Loading



Step 1

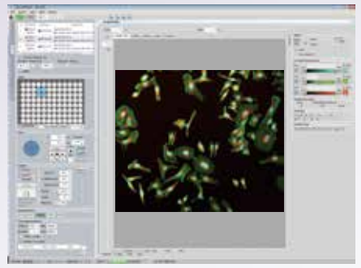
Acquisition Setting

Set wells, fields, focus, color, time-intevalof imaging.

Step 2

Acquiring

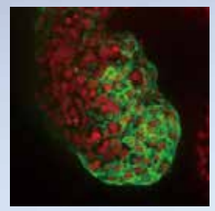
Images of samples are acquired full-automatically by set condition.



Acquiring

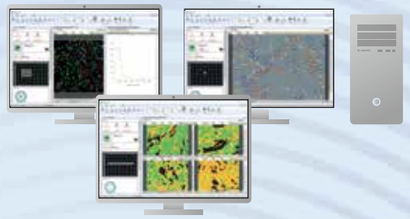
Image Data

Beautiful confocal images can be used foryour presentation, documentation and so on*1.
Also, images can be loaded to third party*2 analysis software.



Analysis Data

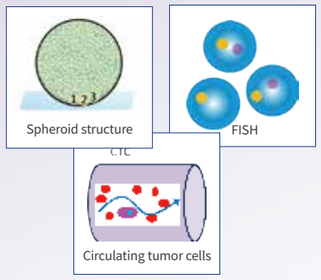
CellPathfinder allows for more advanced analysis



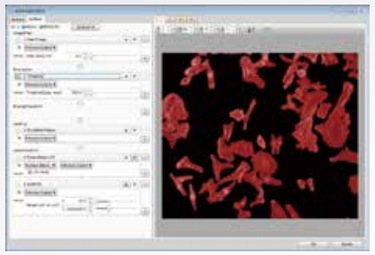
Step 3

Recognition, Analysis Setting

Set image recognition parameters and extract the structures to be recognized.



Various analysis template are prepared.
Complicated settings are not needed.



Also, detail recognition/ analysis condition can be set by customer.

1 Click!

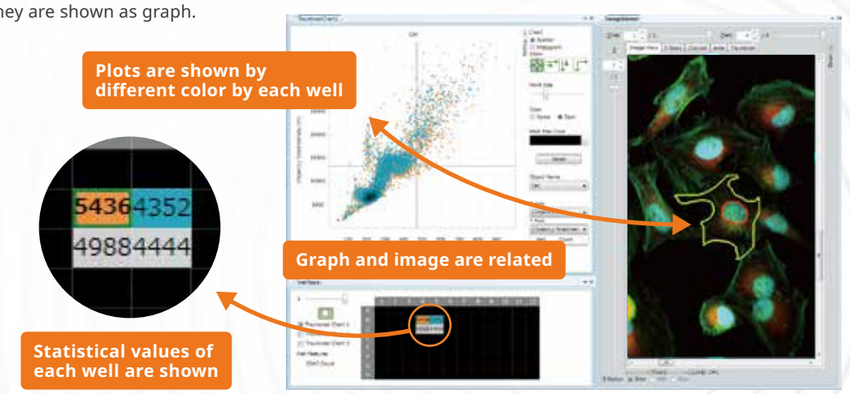
Automatic Measurement

Imaging and analysis, is performed by One Click.

GOAL!

Image Analysis, Result Output

Attribute of extracted structures (size, intensity, location and so on) are quantified and they are shown as graph.

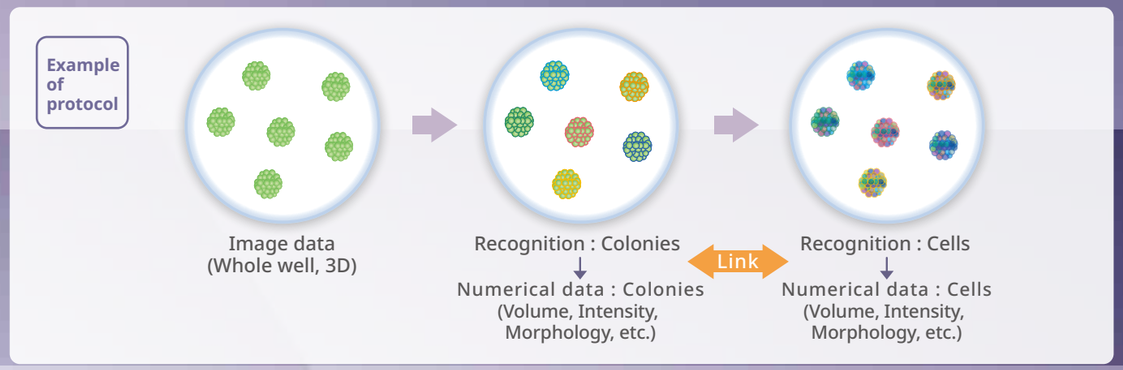


*1: Output by PNG, JPG or 8bit-TIFF format *2: Output by OME-TIFF format

Measurement example

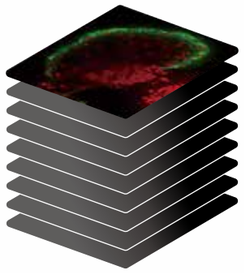
Let's start the easiest 3D Measurement!

The CQ1 is the easiest way 3D measurement system
Simple cell identification, colony counting,
and complex colony property analysis are available.
Of course you can do whole well imaging and analysis.

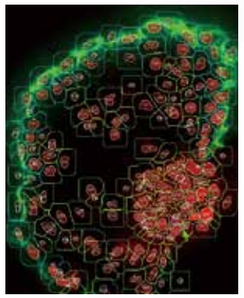


Quality control

High-speed · High resolution · 3D · Multi-color



Slice images

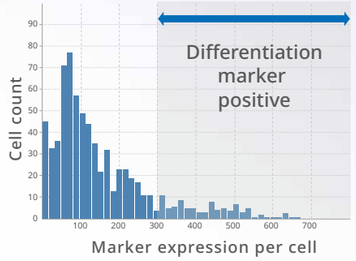


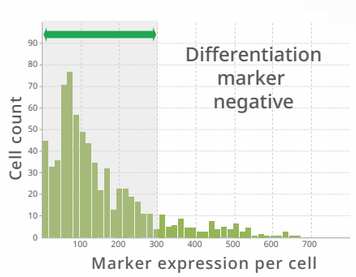
Cell recognition

Undifferentiated

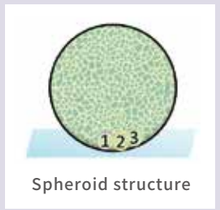
Partially differentiated

Partially differentiated





Aggregated cell images were taken in slices and presented as 3D.
Marker expression level as well as spatial information of individual cells were quantified via image analysis.



Spheroid structure

Template

■ Spheroid structure

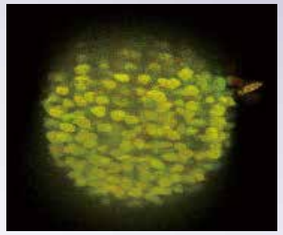
Cell-by-cell measurement of aggregated cells like spheroids.

■ Applications

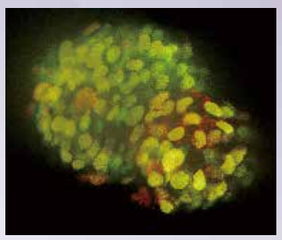
- Sheroids
- Differentiation

Quality control

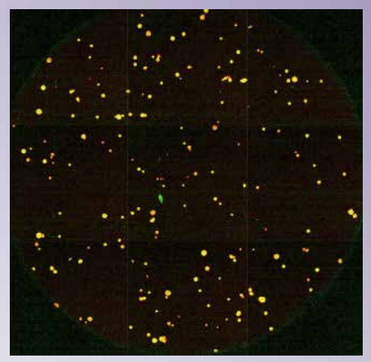
High-speed · High resolution · 3D · Multi-color



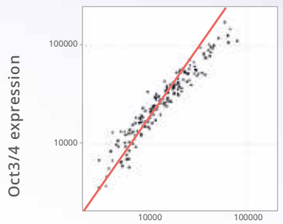
Uniform pluripotent state

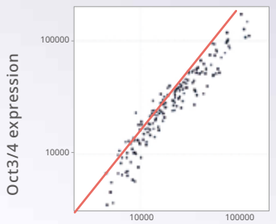


Non-uniform sphere



Whole well tile image





Sphere shape and pluripotencymarker expression level are suitable index for evaluation of quality of pluripotent state of human iPSC sphere.

Sphere shape and pluripotencymarker expression level are suitable index for evaluation of quality of pluripotent state of human iPSC sphere.

Data provided by ReproCell

Colony measurement.

Template

■ Colony measurement

Cell-by-cell measurement of aggregated cells like spheroids

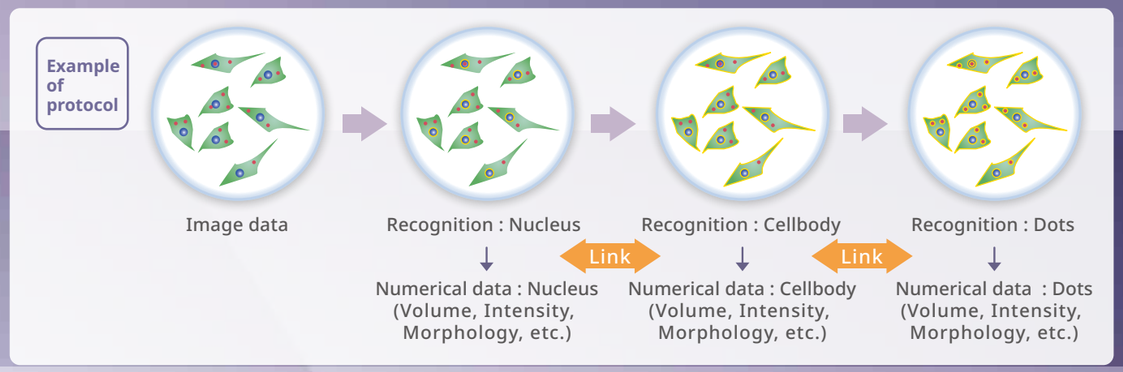
■ Applications

- Colony growth evaluation
- Differentiation

Measurement example

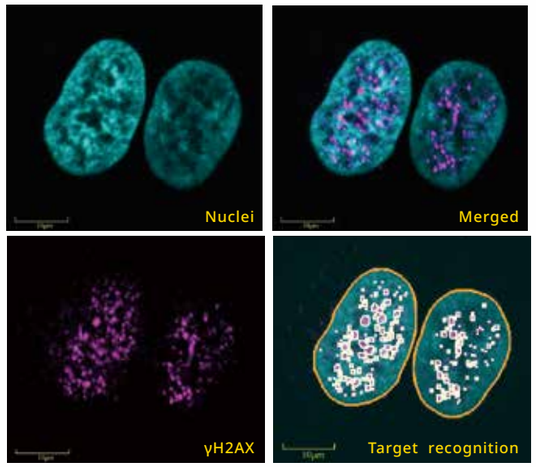
Want to go more deeper analysis!

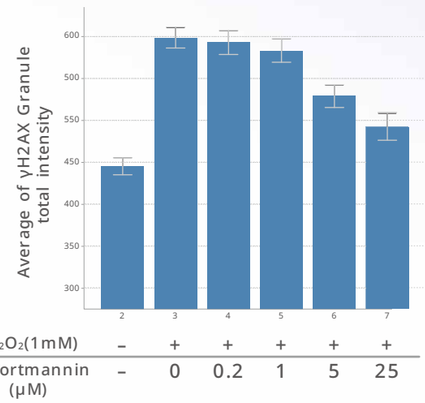
High quality confocal images from the CQ1 can be used for more detailed image analysis.
Morphology change, particle analysis and other
High Content Analysis that require high resolution images.
Of course the CQ1 can work like simple Confocal Microscopy to
geta nalyzed data and images.



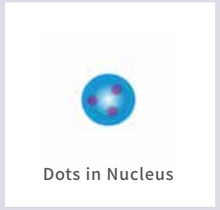
Analysis: gamma-H2AX focus formation

Quantitative | High resolution





The phosphorylation of histone H2AX Ser139 (gamma-H2AX) is one of the significant events upon the breakage of double strand DNA. Quantitative measurement of gamma-H2AX focus formation can be easily performed by using the high-speed confocal image acquisition in combination with the Granule Analysis Template.


Dots in Nucleus

Template

Dots in Nucleus

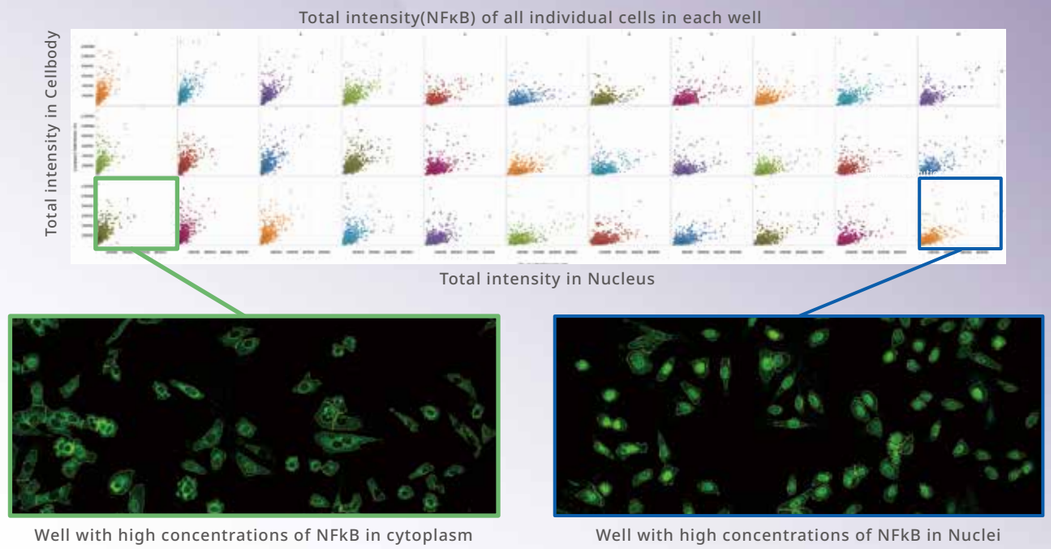
Measurements of dots in cytoplasm and nuclei
Precise separation of individual dots by the confocal unit

Applications

- FISH
- GPCR

Nuclear translocation

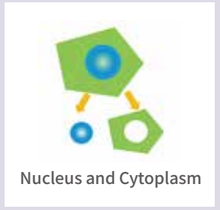
Quantitative | High resolution



Well with high concentrations of NFkB in cytoplasm

Well with high concentrations of NFkB in Nuclei

NFκB is one of the famous transcription factor of DNA. NFκB plays a key role in regulating the immune response and inflammation and is attracting attention as a tumor therapy and anti-inflammatory drug target. NFκB is located in the cytoplasm with IκB which is inhibitory protein. Once the signaling pathway has been activated by the cytokine stimulation via cell membrane receptor, dissociate IκB from NFκB and activate NFκB. Then NFκB translocate into the nucleus to bind specific sequence of DNA, which induce inflammation. Nucleus and intracellular NFκB level indicates protein level between cytoplasm and nucleus.


Nucleus and Cytoplasm

Template

Nucleus and Cytoplasm

Measurements of nuclei and cytoplasm
Precise separation of localization by the confocal unit

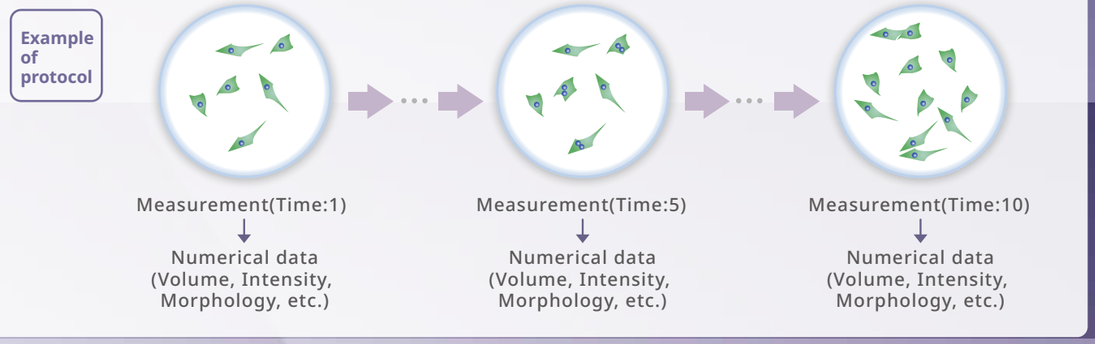
Applications

- Nuclear translocation
- Membrane translocation

Measurement example

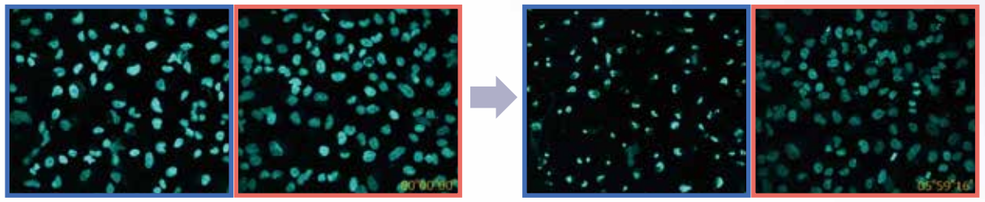
Try time lapse imaging!

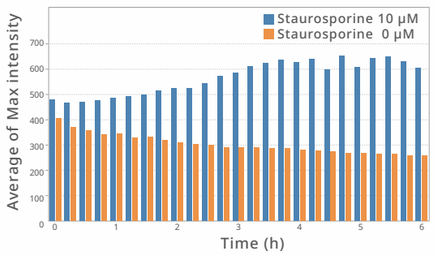
Keep cells happier in incubator to see how they react on live.
The CQ1 is installed with Yokogawa's proprietary technology CSU,
which is very gentle to cell-friendly, low photobleaching and low phototoxicity.
Long-term time lapse are possible while minimizing the effects of multiple measurements.

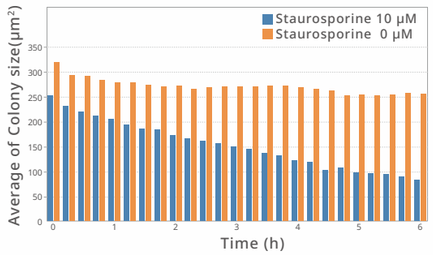


Time lapse analysis: Apoptosis

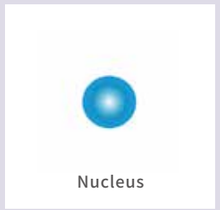
Time-lapse Quantitative







Spread HeLa cells to 96well microplate with 10,000 cells/well.
Stain with Hoechst 33342 (1 µg/ml, 30 min, 37 °C) and treat with Staurosporine (0 - 10µM) and capture image every 15 min. Recognize DNA fragmentation area of nuclei at Staurosporine 10 µM treatment.



Template

Nucleus

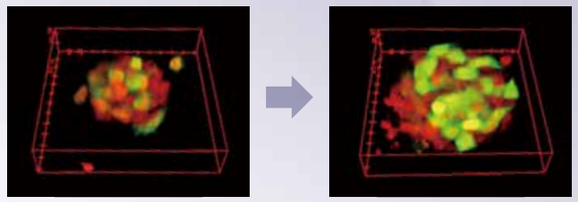
Measurements of Volume, Intensity and Morphology

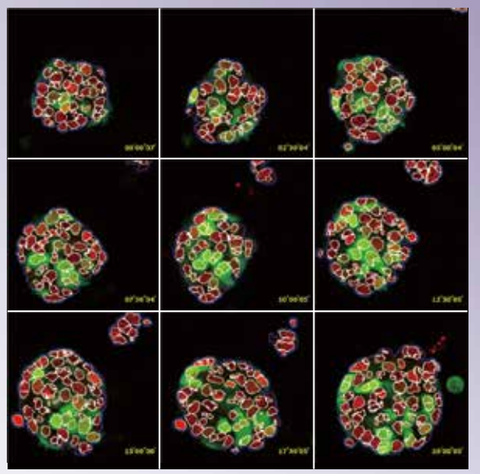
Applications

- Cellcycle
- Apoptosis

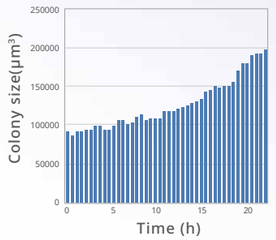
Time lapse analysis: ESC colony

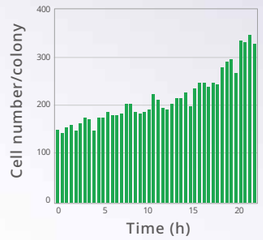
Time-lapse Quantitative 3D Multi-color





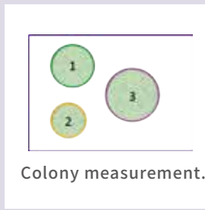
3D imageing(Z=11)
Cells were cultured in CellASIC®(Merck Millipore)





Time lapse analysis of colony size and individual cells allow to monitor colony formation state. CQ1's image can perform image acquisition with low photo-toxicity.

Data provided by Kyoji Horie,ph.D, Physiology II, Nara Medical University



Colony measurement.

Template

Colony measurement

Time course measurement allows to monitor cell colony growth

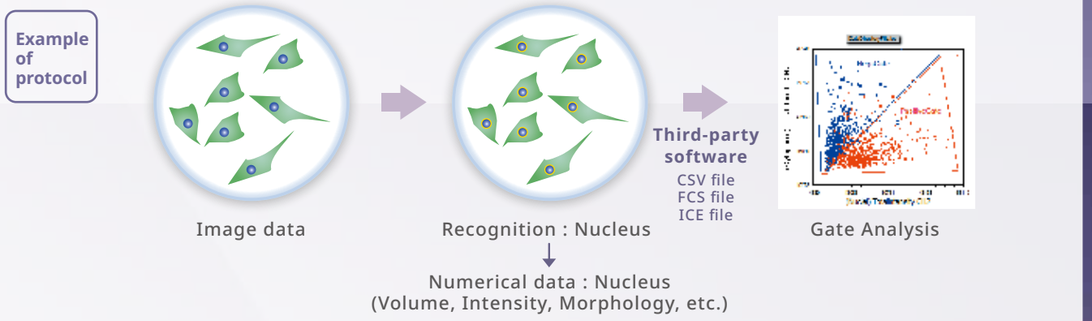
Applications

- Cell colony growth
- Differentiation

Measurement example

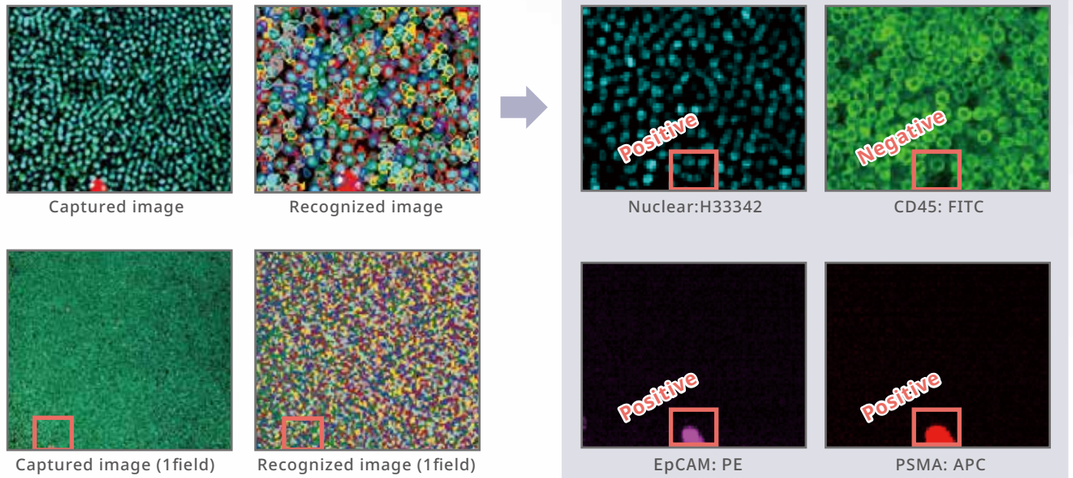
Want to try the measurement again...

Cells can be imaged at culture plate, no need to prepare single-cell suspension, and you can use same sample to different measurement.
Image and analysis data are associated together and its help to pick up tiny difference.



CTC (Circulating tumor cells)

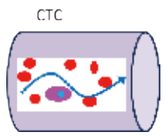
High-speed Quantitative Multi-color



Totall cells (count)	113443
CTCs (count)	2 (0.001%)

Example of CTC quantitate (spiking experiment). CTC : CD45 is only Negative.
Data provided by Yusuke Tomita, Min-Jung Lee, Jane B Trepel , Developmental Therapeutics Branch, National Cancer Institute, National Institutes of Health, , Bethesda, MD 20892 USA

CTCs are tumor cells which circulate in peripheral blood. Developed tumors metastasize through the bloodstream and lymph fluid. Therefore, tumor cells exist in the bloodstream when metastasis occurs. The detection of CTCs makes it possible to diagnose recurrence and metastasis at an early tumor stage. CTCs' numbers are very small as only less than 100 CTCs are contained in more than 1x106 of blood cells in 10 ml of cancer patient's blood. Therefore it is difficult to detect CTCs with a flow cytometer because they detect CTCs as noise. However, it is very easy to detect rare CTCs with an Image cytometer.



Circulating tumor cells

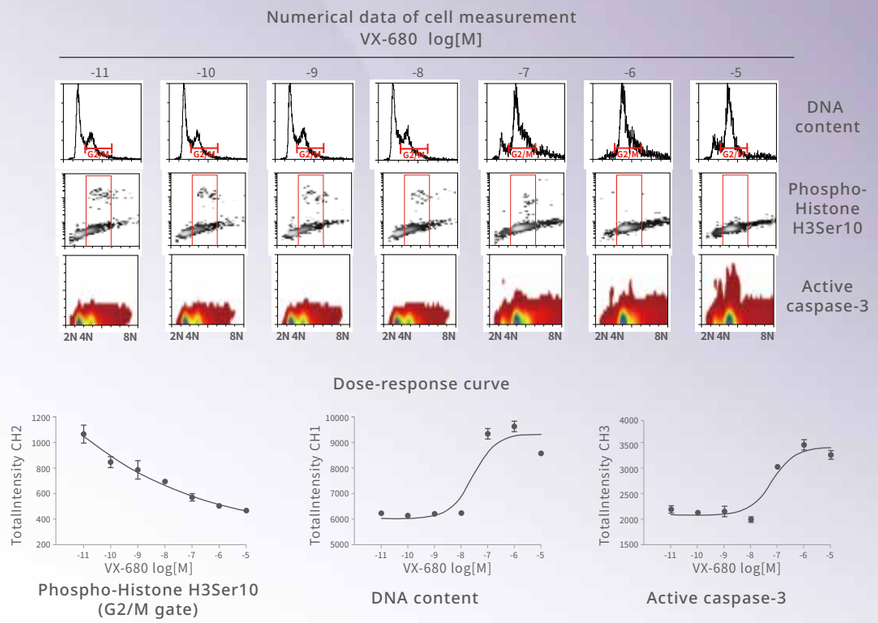
Template

CTC

You can detect multiple marker expression of the cell. Not only for circulating tumor cells, but also for the other specific marker can be detected.

Cell cycle analysis: M-phase inhibitor

High-speed Quantitative



Cell cycle analysis in relation to H3Ser10P immunofluorescence by utilizing the CQ1's multi-color channel capabilities. Histone molecules are phosphorylated during cell cycle progression with phosphorylation of the 10th serine of histone H3 being one of the well characterized events of late-G2 to M progression.

CellCycle

Template

CellCycle

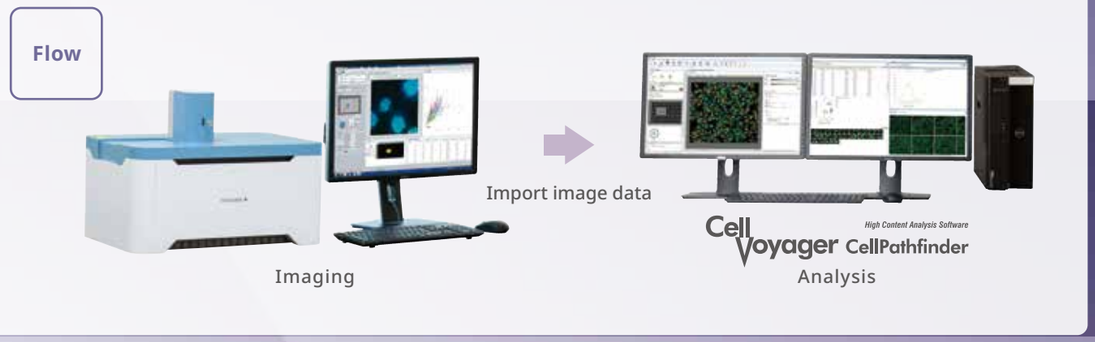
You can detect cell cycle to verify drug treatment efficiency. This is available by the flow cytometer, but CQ1 can analyze more items which typical at the image cytometer.

Analysis example

Make analysis easier!

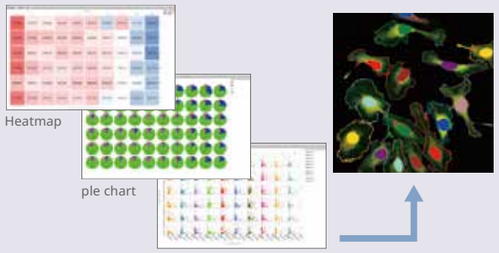
NEW!

The dedicated analysis software "CellPathfinder" can analyze a large amount of image data from multiple angles and easily lead to a graphical display.
In addition to the machine learning function,
the new Deep Learning option dramatically improves the recognition of analysis targets, making it powerful not only for bright field image analysis,
but also for difficult analysis such as 3D culture systems and live cell imaging.



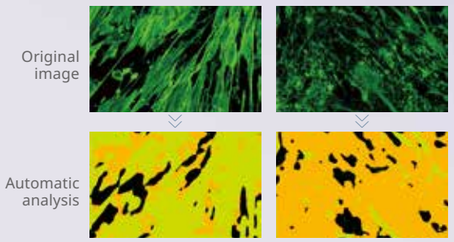
Fast results for immediate verification and study

Computed numeric data can be displayed in a variety of ways.
Graph plots and cell images are linked,
making for easy result verification and inquiry



Unbiased phenotype evaluation via AI

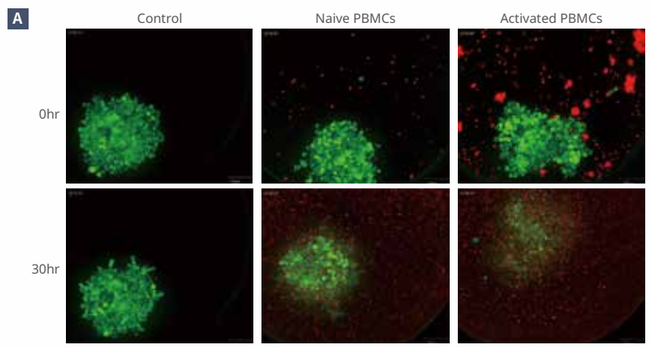
machine-learning also provides bias-free digitization of visually-evaluated experiments.
Automatic recognition is made possible simply by clicking the shape you want the software to learn.

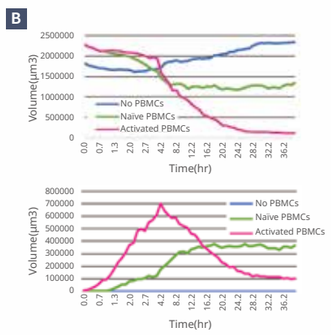


Immuno Oncology

– Immune-cell infiltration into Tumor Microtissue –

Time lapse | Quantitative | Multi-color





A. Merged images of 488 nm and 640 nm of each condition after 0 and 30 hrs.
A 3D tumor microtissue treated with the activated PBMCs was destructed 30hrs later.
B. Top: The volume of 3D tumor microtissue.
Bottom: The total volume of immune cells touching to the 3D tumor microtissue.

Objective lens: 20x / Ex: 488 nm (A549-GFP), 640 nm (CellMask™)
Time lapse: 39 hrs at 10 min interval (timepoint 1-20) and 60 min interval (timepoint 20-56)
Wardwell-Swanson, J., Suzuki, M., et al., A Framework for Optimizing High Content Imaging of 3D Models for Drug Discovery. SL AS Discovery. 2020, Aug;25(7): 709-722

inSphero Biomimetic Microtissue Technology

3D tumor microtissues comprised of A549-GFP (human lung cancer) cells were exposed to either naïve or CD3/CD28-activated
immune cells labeled with CellMask™ Deep Red. Time-lapse imaging was performed for 39 hours.

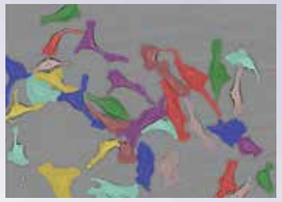
Deep Learning

Deep Learning

No expertise in image analysis required. Save time for creating analysis protocols

Cell Recognition : Deep Area Finder

You can recognize targeted objects, such as cells and intracellular organelles,by painting them using not only fluorescence images but also bright field images. This function is useful when the analysis accuracy with conventional analysis methods are not enough.

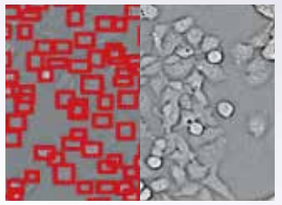


Cell Classification : Deep Image Gate

You can classify phenotypes that are difficult to quantify but appear to be "something different". Simple operation of selecting the cell groups to be classified. No need to select effective features or set thresholds.

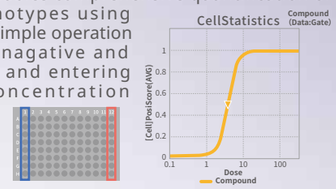
Cell Counts : Deep Detection

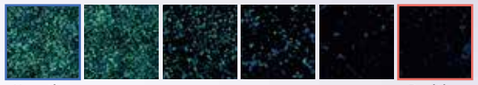
This function detects cells with with simple operation of enclosing cells. No experties are required. It is possible to count cells in high-density on bright field images as well as fluorescence images.



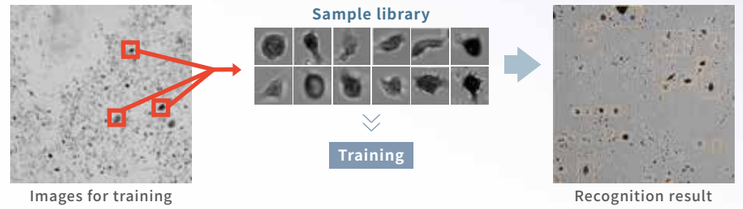
EC50/IC50 Calculation : Deep Image Response

This function enables comprehensive quantification of cpmplex phenotypes using whole images. Simple operation of selectiong nagative and positive wells and entering compound concentration information. Any protocol to segment cells is not necessary.





Application:Measurement of inhibition of osteoclast differentiation



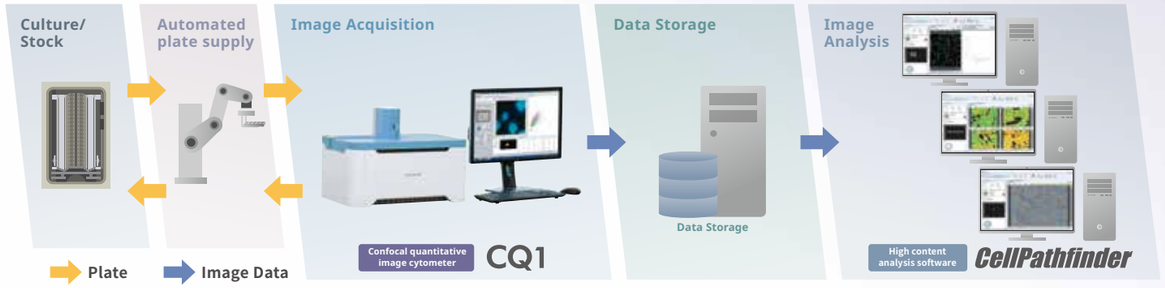
RANKL was added t o RAW 264.7 cells to promote their differentiation int o osteoclasts, and differentiated cells were detected by TRAP staining. Using CellVoyager (CQ1, CV 8000), we acquired the stained cells, and after learning the osteoclast images differentiated by the deep learning function, we analyzed them quantit atively. We can search for foods, cosmetics, medicines, etc.

System integration

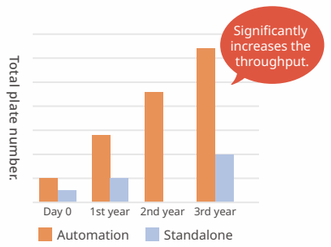
CQ1 in Integrated Automation

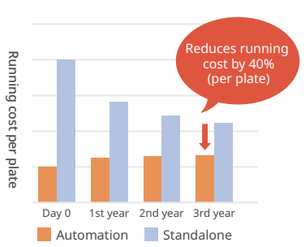
There are many advantages to automating CQ1 as a system.
Not only does it increase throughput, but it also reduces human error by reducing human intervention, and maintains the experimental environment even in live screening where results tend to be unstable.

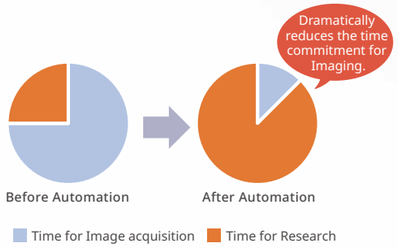
System Integration



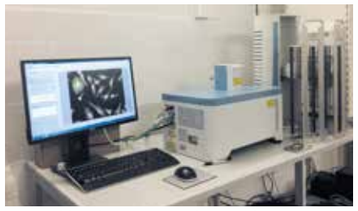
Benefits of Robotic automation



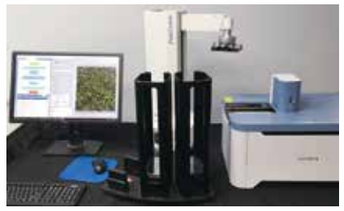




Robot automation not only reduces the running cost, it also saves time and significantly reduces the time required to complete a project. This not only shortens the imaging and screening cycle, but also allows researchers to focus on their own research.



CQ1 and incubator system integration
Components:incubator,plate stacker, barcode reader, plate handler robot
Data provided by :Dr. Manuel Kaulich, University Hospital Frankfurt, Goethe University



CQ1 and stacker system integration
Components:plate stacker, plate handler robot

Automation companies which have installed CQ1

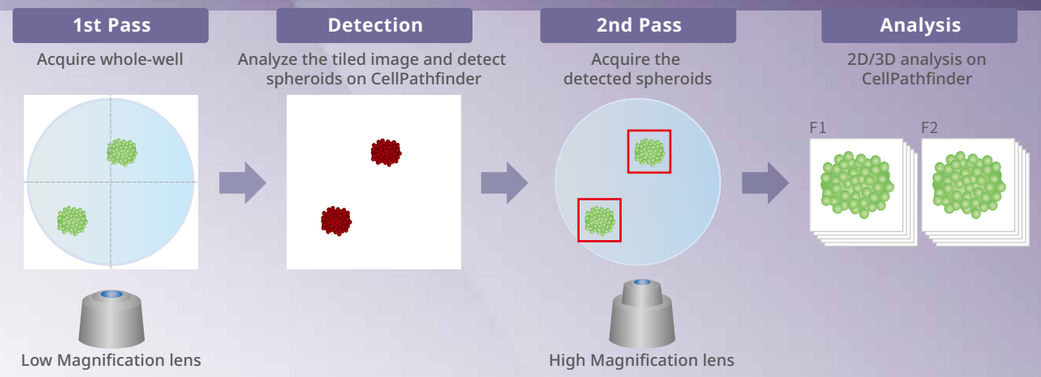
Advanced Solutions
Beckman Coulter Life Sciences
Hudson Robotics
PAA A Directech Company — At the heart of laboratory automation
WAYPOINT

We can also support manufacturers not on the list. Please feel free to contact us.

CellVoyager ACE Software for CellVoyager CQ1*1*2

It can can scan the entire well at low magnification, detect the position of the object based on the analysis results, and acquire images at high magnification. This makes it possible to image samples where it is not possible to know where the object is located in the well, or to image and analyze only the cells that match the conditions from among a large number of cells.

Targeted Imaging Overview

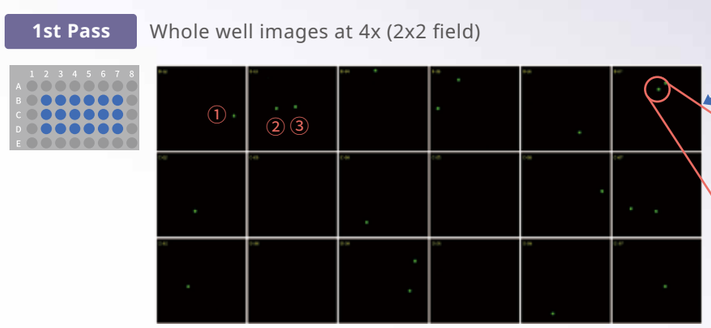


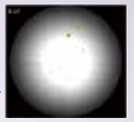
Advantage

- High magnification imaging only in the field where the target is detected, greatly reducing the amount of data and throughput.
- Reduce unnecessary images and tiling by imaging at the center of the target.
- Automation of the two imaging processes reduces human intervention time and human error.

Example: Detect Spheroids of GFP-expressing Hela

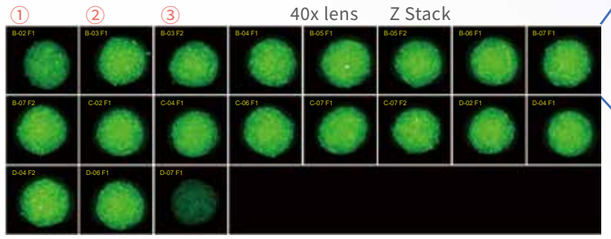
1st Pass Whole well images at 4x (2x2 field)

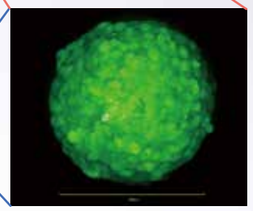




Merged image of GFP and bright field

2nd Pass Detected spheroid images at 40x (1 field, MIP)





MIP(1 field)

*1 This software is provided as free of charge only for our customers. We cannot guarantee performance of operations, in case of unexpected circumstances.
*2 To be able to use this software, the corresponding analysis software CellPathfinder is necessary.

Cell Voyager CQ1

Confocal Quantitative Image Cytometer

Optics	Microlens enhanced dual wide Nipkow disk confocal
Fluorescence	Laser : Choose Max.4 lasers from 405 / 488 / 561 / 640 nm EM Filter : Max. 10 filters (Included 1 filter for transmitted illumination)
Transmitted illumination	Phase contrast*1, Bright field Light source : LED
Camera	Number of effective pixels：sCMOS 2000 × 2000pixels、FOV：13.0 × 13.0mm
Objective lens	Max.6 lenses Dry : 2x, 4x, 10x, 20x, 40x Long working distance : 20x, 40x For thick bottom vessel : 20x Phase contrast*1 : 10x, 20x
Attachment	All wells imaging type, Chambered type*2
Sample vessel	Microplate (6, 12, 24, 48*3, 96*3, 384*3, 1536*3 well), Slideglass*4*5, Cover glass chamber*4, Dish*4 (35, 60 mm)
XY stage	High-precision XY stage, designated resolution: 0.1 µm
Stage heater (Option)	Stage heater with chamber Controllable temperature range : Room temperature +5 – +17°C, Max.40°C Settable temperature resolution: 0.1°C Humidity holding*6
Z focus	Electric Z motor, designated resolution: 0.1 µm
Autofocus	Laser autofocus, Software autofocus
Feature data	Number of cells / cellular granules, Intensity, Volume, Surface area, Area, Perimeter, Diameter, Sphericity, Circularity, Length, etc.
Data format	Captured image : 16 bit TIFF (OME-TIFF) Output image format : TIFF (16 bit, 8 bit) , PNG, JPEG Output movie format : WMV, MP4 Output numerical data format : FCS, CSV, ICE
Fast time lapse (Option)	Selectable from Max.100fps or Max.20fps
Workstation	Measurement and analysis workstation
Gas Mixer (Option)	CO_2 concentration : Atmospheric concentration – 7 % O_2 concentration : 3 % – Atmospheric concentration
Size / Weight	Main unit : 600 × 400 × 437 mm, 44 kg Utility box : 275 × 432 × 298 mm, 18 kg Gas Mixer (Option) : 170 × 260 × 280 mm, 5.2 kg
Environment	Main unit and Utility box : 15 – 35 °C, 20 – 70 % RH No condensation Gas Mixer (Option) : 20 – 30 °C, 10 – 85 % RH No condensation
Power consumption	Main unit and Utility box : 100-240 VAC, 800 VAmax Workstation : 100-240 VAC, 950 VAmax Gas Mixer (Option) : 100-240 VAC, 50 VAmax

*1 Phase contrast option is required
*2 Stage heater option is required to use environment keeping function
*3 Phase contrast observation is unavailable
*4 Option
*5 Environment keeping function is unavailable
*6 Humidity holding time is changed by condition

Safety Precautions

* Read the user's manual carefully in order to use the instrument correctly and safely.
* This product falls under the category of class 1 laser products.

Reliable after-service / Powerful technical support

We offer the best after-service program to meet your requirement and budget.
Our HCA experts will support you to obtain the best results easily.

CQ1 is sold under license from ThermoFisher Scientific patent portfolio related to High Content Screening and Analysis.

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https://www.yokogawa.com/solutions/products-platforms/life-science/

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