

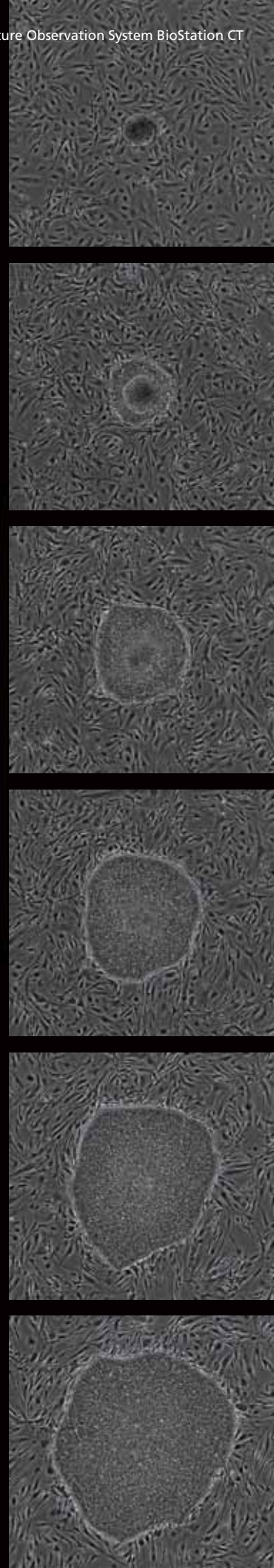
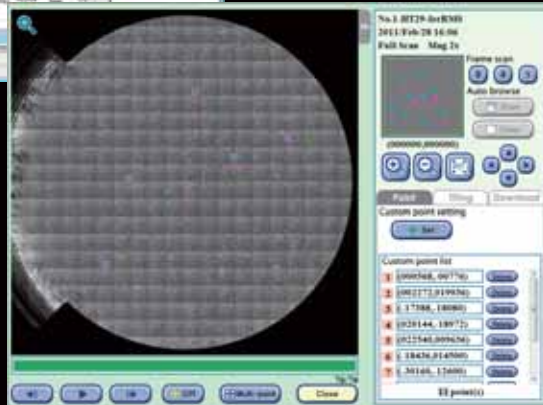
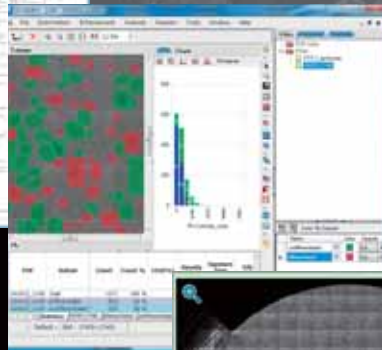
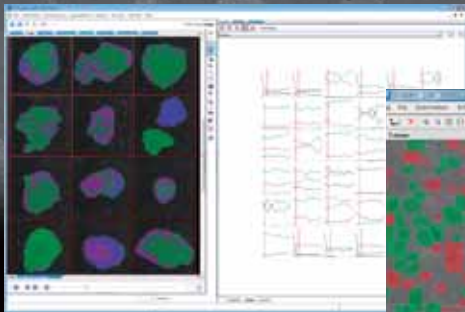


# Imaging Solutions for Stem Cell Research

Cell Culture Observation System

Cell Tracker

# BioStation CT



# Stem cell screening inside the incubator

With conventional cell monitoring procedures, a culture vessel has to be taken out of the incubator for microscope observation, where cells are subjected to stressful environmental changes and vibration. Researchers then have to spend additional time repositioning the vessel to find the same observation points. Nikon's BioStation CT eliminates these problems by providing a stable environment so that the cultures don't suffer while they are being imaged and allowing for a complete trace of the same live cells, including stem cells.

## Advanced basic functions

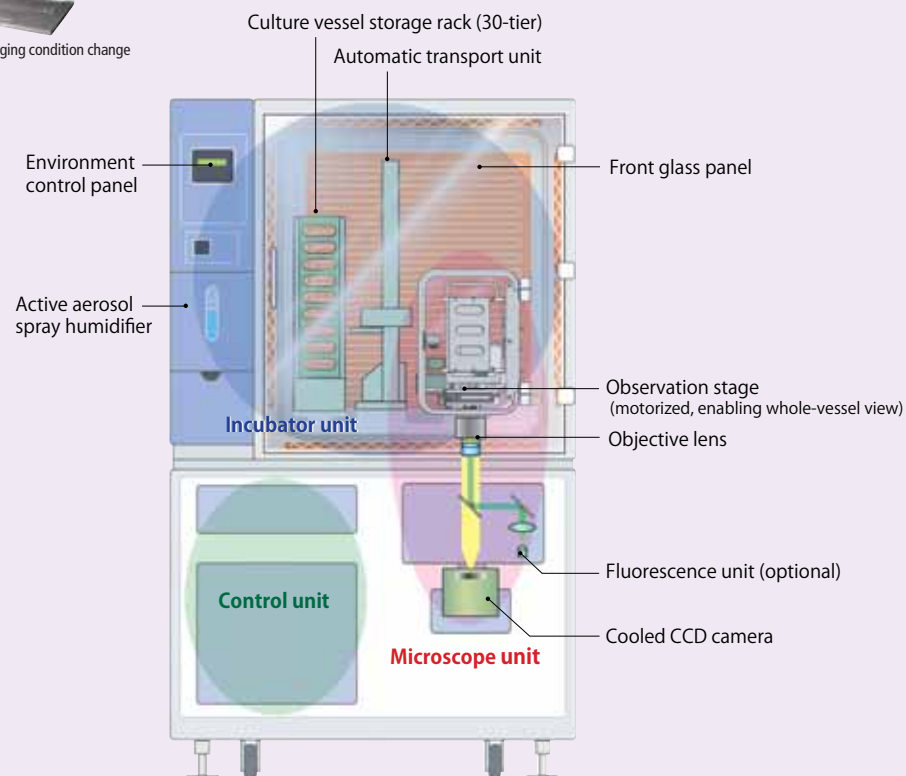
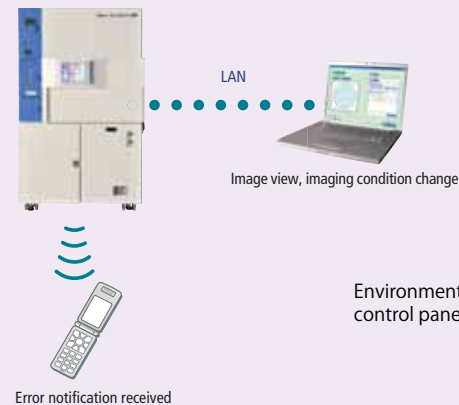
### Automatic image capture

The autofocus mechanism allows the capture of in-focus images. Z-stack imaging in phase contrast observation, multi-sample imaging and multi-point imaging are possible with multiple magnifications. User-configured imaging conditions that can be saved in BioStation CT support the repeatability of observations.



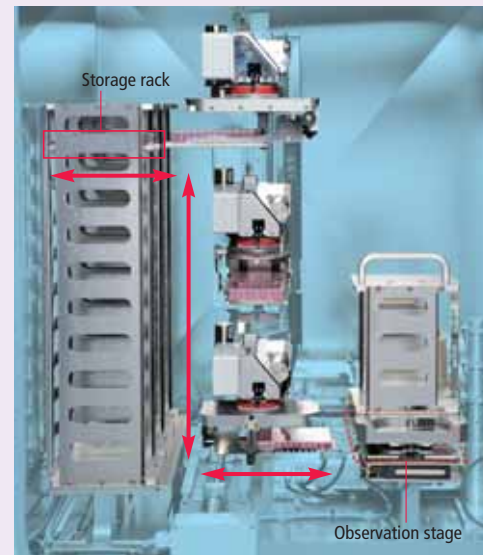
### Remote access

Configuring the imaging settings, scheduling a time-lapse experiment, and viewing the cell images are possible via a network. The captured data can be automatically downloaded to the user's local computer. This enables users to monitor the cell status away from the laboratory. When a culture environment (temperature, humidity, CO<sub>2</sub> concentration) control error occurs, BioStation CT can notify the users of the error by e-mails.



### Automatic vessel transportation

BioStation CT incorporates a transport unit that provides stable vessel transportation within the heated and humidified incubation area. The high-precision motorized stage in the observation unit allows for automated imaging of the entire area of a well in all culturing formats.

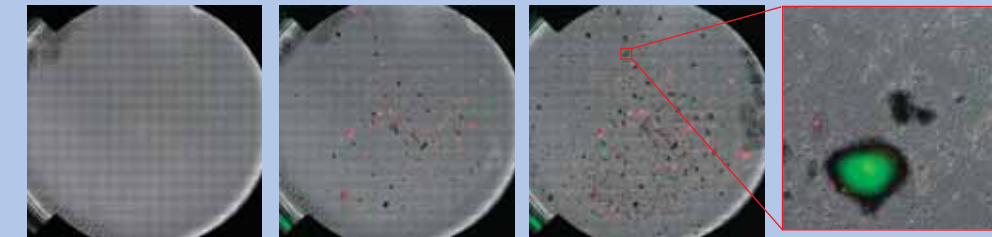


The transport unit carefully conveys the vessels from the storage rack to the observation stage in accordance with configured schedules.

## Various functions

### Full-well scan imaging and highly magnified image stitching NEW

High-resolution full-well scans are reconstructed by stitching captured adjacent images. This enables clear detection of an iPSC colony, which is difficult to detect because of its low induction efficiency, no matter where it forms in the vessel. The specified position of the vessel can be highly magnified with high resolution. BioStation CT also offers cell registration to allow for repeated visits to the same location. These time-lapse sequences can be created even when a vessel is removed from the BioStation CT for medium exchange.



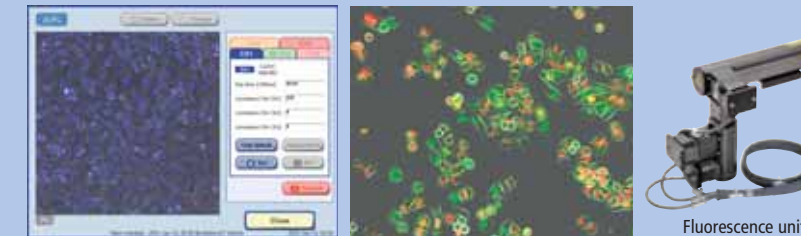
Day 5 of culture      Day 13 of culture      Day 18 of culture

### Mouse iPSC cells reprogramming

GFP: Nanog-GFP  
DsRed: retrovirally transduced  
Vessel: 100 mm culture dish  
Magnification: 2x  
Culture period: 3 weeks  
Imaging interval: 4 hours  
Courtesy of Dr. Hidemasa Kato, Saitama Medical University

### Fluorescence observation (optional)

Long-life and low-cost LED illuminator is employed as a light source. Up to five fluorescence filter cubes can be mounted. Up to three channels can be used with simultaneous multi-channel acquisition. The expression of fluorescence proteins such as CFP, YFP, Kusabira Orange, DsRed, Texas Red and Cy5 can be observed effectively in fluorescence observation.



### Storage rack drawer (optional) NEW

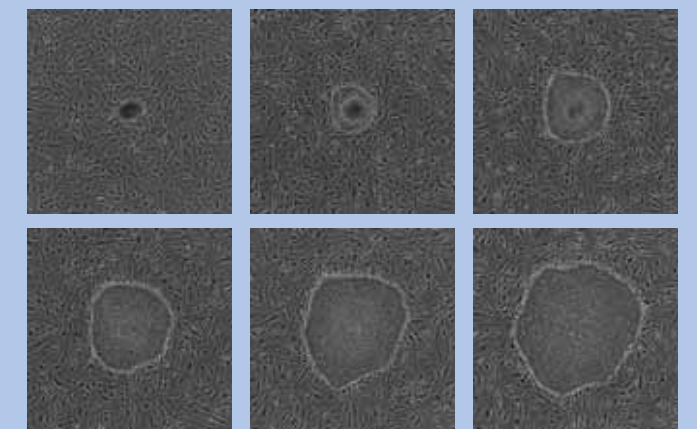
The sliding storage rack enables the installation of multiple vessels at one time.

### Reduced phototoxicity

The excitation period is shortened by synchronizing the camera exposure with the excitation illuminator. This prevents photobleaching of the specimen and minimizes the phototoxic damage on the cells.

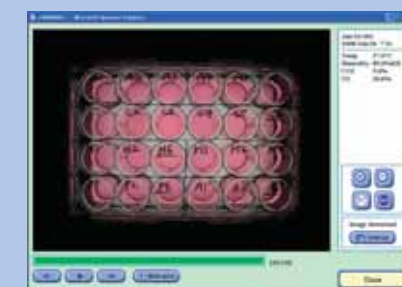
### Micro observation

Phase contrast and fluorescence images can be captured with the high-sensitivity cooled CCD camera. These images can be magnified in 2x, 4x, 10x, 20x and 40x. Up to 40 phase contrast images can be captured along the Z axis with the Z-stack function.



### Macro observation

Brightfield image of the whole vessel provides users outside the BioStation CT with information such as handwritten information on the vessel, medium color and whether mold is growing or not. In addition, alkaline phosphatase stained cell counting is available as an option.





# Stable culture environment maintenance



## Precise temperature control

The inside temperature is directly controlled by panel heaters embedded in the incubator's six sides. This allows highly precise temperature maintenance.

## Humidity control with air-flow type active aerosol spray humidifier

Distilled water is automatically sprayed inside the incubator to keep the optimum humidity. Water can be supplied to the tank without opening the incubator door. This air-flow type humidifier reduces contamination risks compared to the water bath type.



## Hypoxic culture capability

Hypoxic culture observation is possible with the optional oxygen regulator and nitrogen generator.



## Environment data recording

The culture environment is constantly monitored and recorded. The environment data can be accessed at anytime.



CO<sub>2</sub> incubator environmental graph screen

## Smooth vessel transportation

The waver of liquid surface during the transportation is less than 2 mm. The drift and stress of cells are reduced.



## Reduced contamination risk

The incubator interior can be sterilized using hydrogen peroxide gas. (This is optional, and a 200 V power source is necessary.)

# Compatible with various culture vessels



96-well plate  
Up to 30 plates stored in a storage rack  
Up to 25 observation points in a well



48-well plate  
Up to 30 plates stored in a storage rack  
Up to 25 observation points in a well



24-well plate  
Up to 30 plates stored in a storage rack  
Up to 25 observation points in a well



12-well plate  
Up to 30 plates stored in a storage rack  
Up to 25 observation points in a well



6-well plate  
Up to 30 plates stored in a storage rack  
Up to 25 observation points in a well



4-well plate  
Up to 30 plates stored in a storage rack  
Up to 25 observation points in a well



100 mm culture dish  
Up to 30 dishes stored in a storage rack  
Up to 25 observation points in a dish



60 mm culture dish  
Up to 60 dishes stored in a storage rack  
Up to 25 observation points in a dish



35 mm culture dish  
Up to 150 dishes stored in a storage rack  
Up to 25 observation points in a dish



75 cm<sup>2</sup> culture flask  
Up to 30 flasks stored in a storage rack  
Up to 25 observation points in a flask



25 cm<sup>2</sup> culture flask  
Up to 30 flasks stored in a storage rack  
Up to 25 observation points in a flask

## Tray holders for various culture vessel types



For well plate



For nunc 4-well plate



For 100 mm culture dish



For 60 mm culture dishes



For nunc 60 mm culture dishes



For 35 mm culture dishes



For Falcon 35 mm culture dishes



For 75 cm<sup>2</sup> culture flask



For 25 cm<sup>2</sup> culture flask

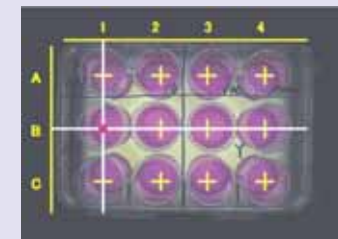
## Different GUI for each vessel type



Vessel type icons



GUI for 12-well plate



Wells to be observed can be chosen on the touchscreen.

# Easy operations

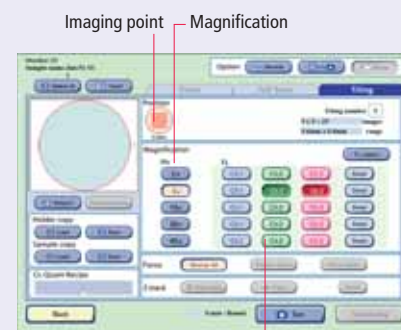
## Vessel installation



### Culture vessel installation into the storage rack

Efficient installation with the optional sliding storage rack that enables multiple vessels to be installed at one time

## Imaging parameter setting



Fluorescence channel

### Easy touchscreen operation

Time-lapse imaging configurations such as magnification, imaging point, fluorescence channel and stage motion speed can be set.

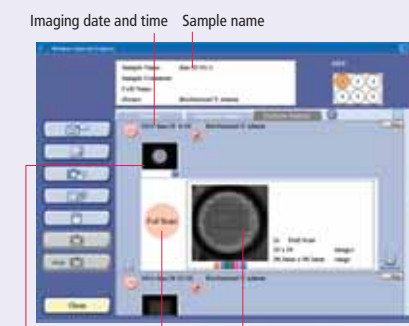
## Scheduling



### Time-lapse imaging schedule

The imaging interval and total period can be set. The shortest time-lapse imaging interval is one minute.

## Captured image view

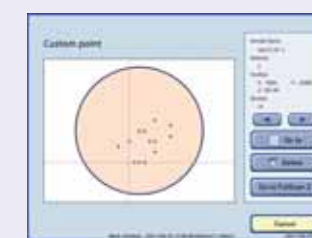


Macro image thumbnail  
Imaging point within the vessel  
Micro image thumbnail

### Culture history data management

The time-course change of a specimen can be observed easily in sequentially displayed captured images.

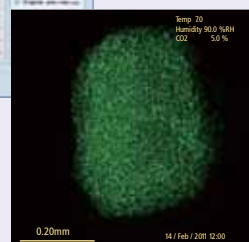
## Medium exchange



### High-precision repeatability

Accurate tracing of same cells, even after medium exchange, is possible using a dedicated tray holder, as BioStation CT records culture history, such as medium exchange and subculture, as well as X-Y positions for each vessel.

## Data report



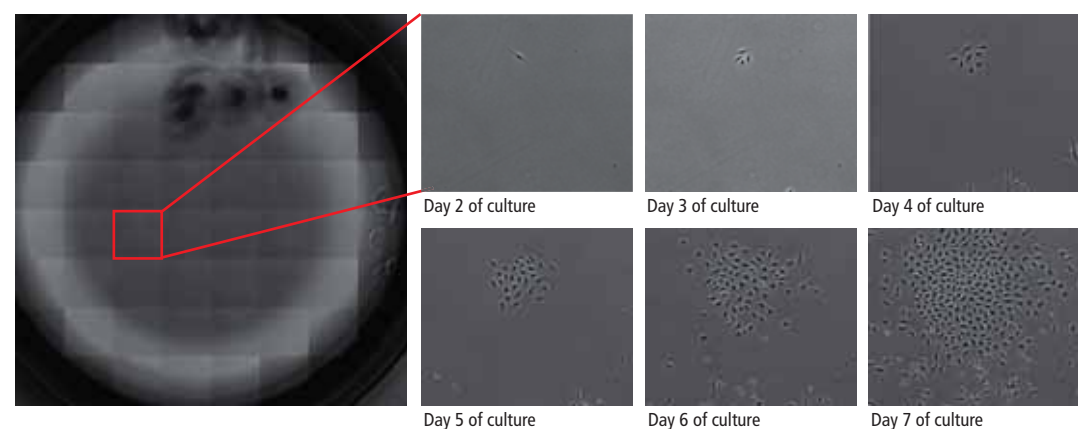
### Reliable data management and documentation support

Obtained data is duplicated and protected using uninterruptible power supply. Observation information such as temperature, humidity and imaging date can be written and displayed on the captured image to simplify presentation document preparation.



### High-resolution imaging

It is possible to track the clonal colony derived from a single cell by magnifying a desired area of the high-resolution whole-vessel image.

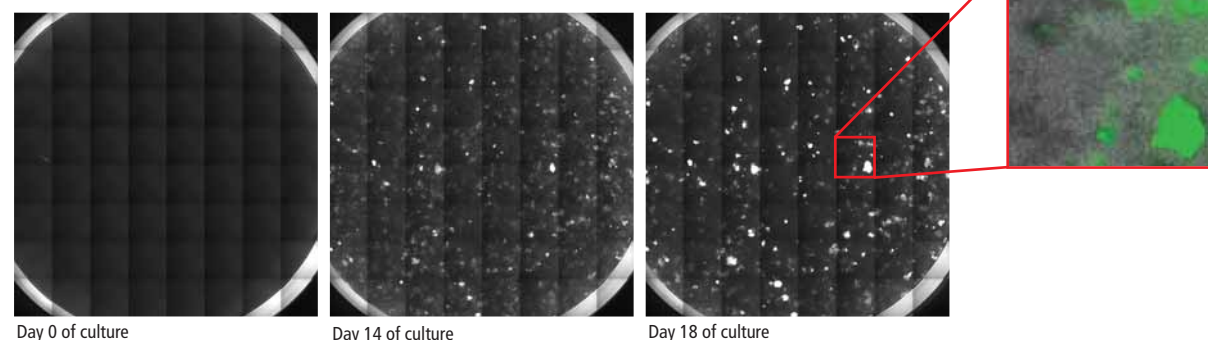


**Division process of human hepatic stem cells**  
 Vessel: 6-well plate  
 Magnification: 2x  
 Culture period: 1 week  
 Courtesy of Dr. Yun-Wen Zheng, Yokohama City University

### Directed reprogramming

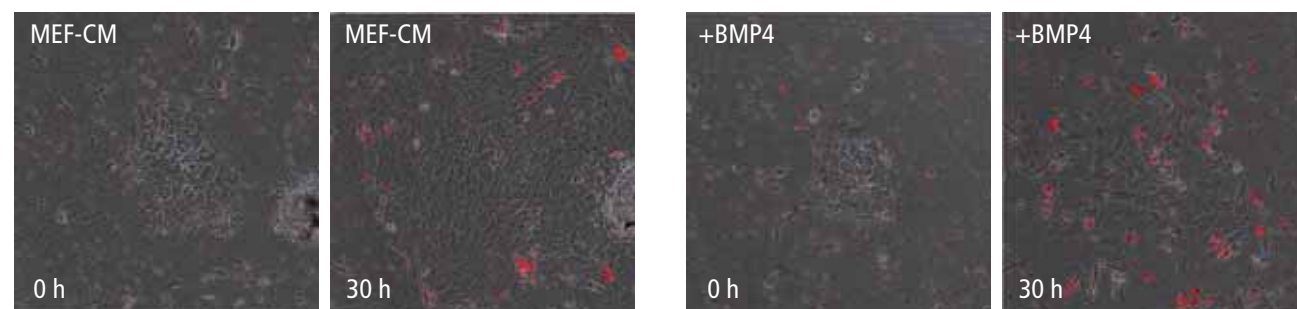
Mouse skin fibroblasts inserted with two reprogramming factors (c-Myc, Klf4) and a chondrogenic transcription factor (Sox9) by gene transfer were observed over time. Generation of chondrocyte-like cells directly from skin cells was successfully observed with the expression of a chondrocyte-specific marker, type XI collagen. This research was published in *the Journal of Clinical Investigation, 2011;121(2):640-657*.

- The whole area of the 6-well plate was observed at 2x magnification every second day.
  - Image of GFP, reporter of type XI collagen gene, merged with a phase contrast image (right)
  - Whole-well fluorescence images of the 6-well plate (below)
- Courtesy of Associated Professor Noriyuki Tsumaki, Department of Bone and Cartilage Biology, Osaka University Graduate School of Medicine



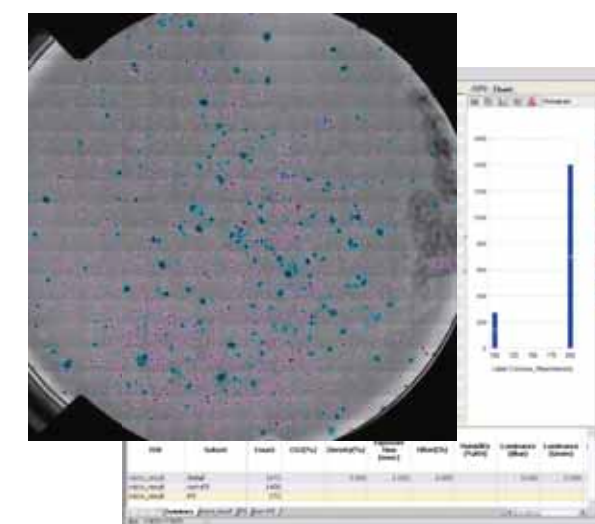
### Apoptosis

The apoptosis process of human ES cell line H9 cultured in the presence of MEF-CM on Matrigel® was observed. Annexin V (red fluorescence) was used as a detection probe for the cell membrane change that was caused by added BMP4.  
 Courtesy of Mr. Jamie McNicol, McMaster University



### iPS/non-iPS cell colony auto identification and colony counting Image analysis software CL-Quant (optional)

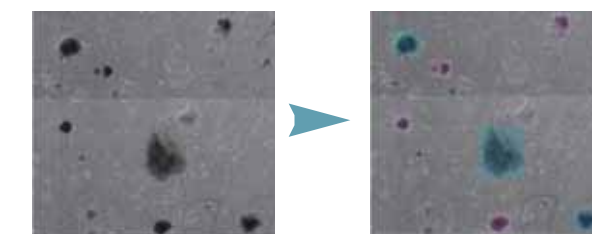
CL-Quant automatically detects cell colonies in a phase contrast image, and automatically distinguish iPS cell colonies from cell colonies with insufficient reprogramming. iPS and non-iPS cell colony area measurement and iPS cell colony counting are also possible.



#### Reprogramming process of mouse iPS cells

iPS cell colonies (blue) and non-iPS cell colonies (pink) are automatically distinguished based on expression/non-expression of Nanog-GFP, a marker for undifferentiated cells, and the colony information from a phase contrast image.

GFP: Nanog-GFP  
 DsRed: retrovirally transduced  
 Vessel: 100 mm culture dish  
 Magnification: 2x  
 Culture period: 3 weeks  
 Imaging interval: 4 hours  
 Courtesy of Dr. Hidemasa Kato, Saitama Medical University



### Cancer and other researches Image analysis software CL-Quant (optional)

#### Scratch assay

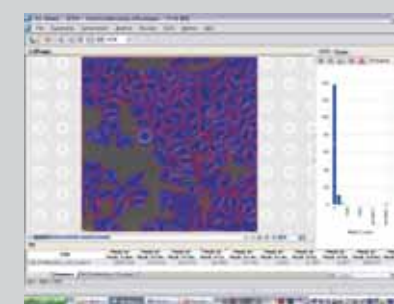
The acellular areas are extracted from captured images, and the time course is quantified. This enables comparative analysis of cells' metastatic ability.

Inhibition of cell migration by the anti-cancer drug sunitinib (Sutent®) added to clear cell renal carcinoma cell line (KMRC-1) was quantified by scratch assay. Cellular areas in the images captured in three-hour-interval time-lapse observation by BioStation CT were quantified by image analysis software CL-Quant.  
 Courtesy of Dr. Naohisa Tomosugi and Dr. Shintaro Maru, Division of Nephrology, Kanazawa Medical University



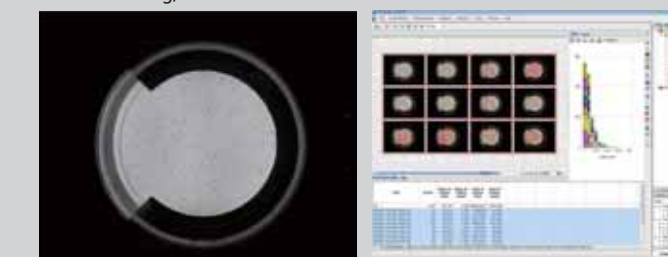
#### Cell counting

Cell counting is possible with phase contrast images.



#### Alkaline phosphatase (AP)-positive colony counting

BioStation CT offers alkaline phosphatase-positive colony counting in macro images captured after AP staining, which enables valuation of the undifferentiated stem cell state.



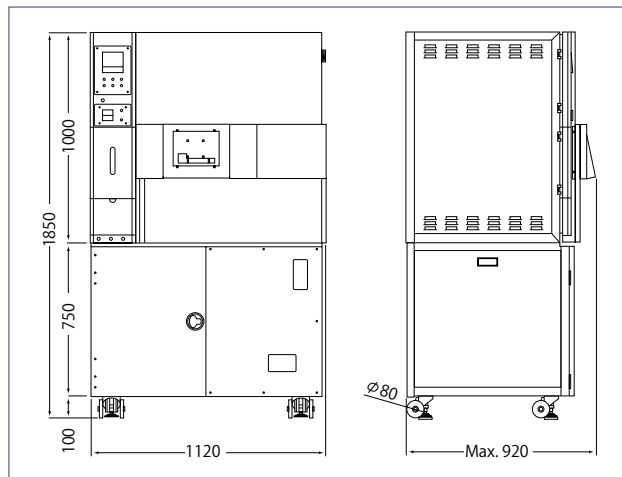
AP-positive colony area comparison in 12 100 mm culture dishes  
 Courtesy of Dr. Kazutoshi Takahashi and Mr. Koji Tanabe, Department of Reprogramming Science, Center for iPS Cell Research and Application (CIRA), Kyoto University

## Specifications

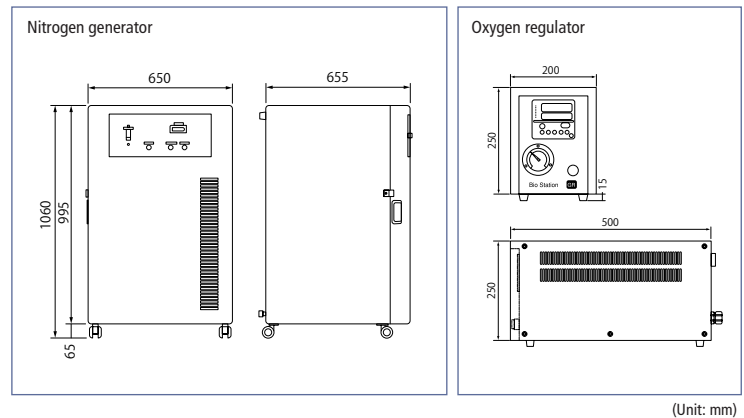
Operation	With touchscreen LCD Controllable via a network-linked PC (with Internet Explorer® web browser)
Incubator volume	460 L
Temperature control	Direct control via heater panels Range: room temperature + 5 °C to 42 °C (max.), 0.1 °C increments
Humidity control	Via aerosol spray humidifier Range: 70% to 95%, 1% increments
CO <sub>2</sub> concentration control	CO <sub>2</sub> supply: by external CO <sub>2</sub> gas cylinder connection Range: 0% to 20%, 0.1% increments
O <sub>2</sub> concentration control (optional)	Via optional nitrogen gas generator Range: 0% to 20%, 1% increments
Compatible culture vessels	Culture dish: ø35 mm, ø60 mm, ø100 mm Well plate: 4-well, 6-well, 12-well, 24-well, 48-well, 96-well Culture flask: 25 cm <sup>2</sup> , 75 cm <sup>2</sup> (cannot be installed in optional storage rack drawer)
Specimen storage rack	3 rows x 10 tiers (autoclave sterilizable)
Macro observation	Image capture of whole vessel with dedicated camera (bird's-eye view) Camera head: color CCD camera (1280 x 960 pixels) Brightfield: backlight illumination

Micro observation	Magnification: 2x, 4x, 10x, 20x, 40x Intermediate magnification: 0.5x, 1x, 2x, 4x Objective: 4x (Plan Apo DLL), 10x (Plan Fluor ADL) Camera head: 2/3-inch cooled CCD camera (1M pixels) Phase contrast: high-intensity red LED illumination, automatic phase ring changeover Epi-fluorescence (optional): LED 438 nm, 472 nm, white light illumination (up to 5 fluorescence filter cubes mountable)
Observation range	X-Y: 120 x 90 mm Z: 4 mm
Z-axis focusing	Z-focus point is automatically detected by image contrast detection through Z-axis scanning
Observation	With touchscreen LCD or via network-linked PC
Power source	Voltage: 115, 230 VAC ± 10% Power consumption: 1300 VA (max.)
Weight	Approx. 470 kg
Operating environment	Temperature: 15 °C to 28 °C Humidity: max. 60% relative humidity (noncondensing)

## Dimensional diagram



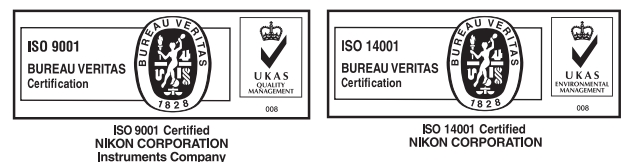
## Hypoxic culture units dimensional diagrams



Cover image: courtesy of Dr. Ronald McKay, NIH  
Specifications and equipment are subject to change without any notice or obligation on the part of the manufacturer. May 2011 ©2007-11 NIKON CORPORATION

	<b>WARNING</b> TO ENSURE CORRECT USAGE, READ THE CORRESPONDING MANUALS CAREFULLY BEFORE USING YOUR EQUIPMENT.
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Depending on the vessel used, the BioStation CT may not be able to focus on some areas.  
External PC for data download is not included.  
Repair of the machine under definite conditions is guaranteed by Nikon, but Nikon is not responsible for specimen and reagents. Monitor images are simulated.  
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