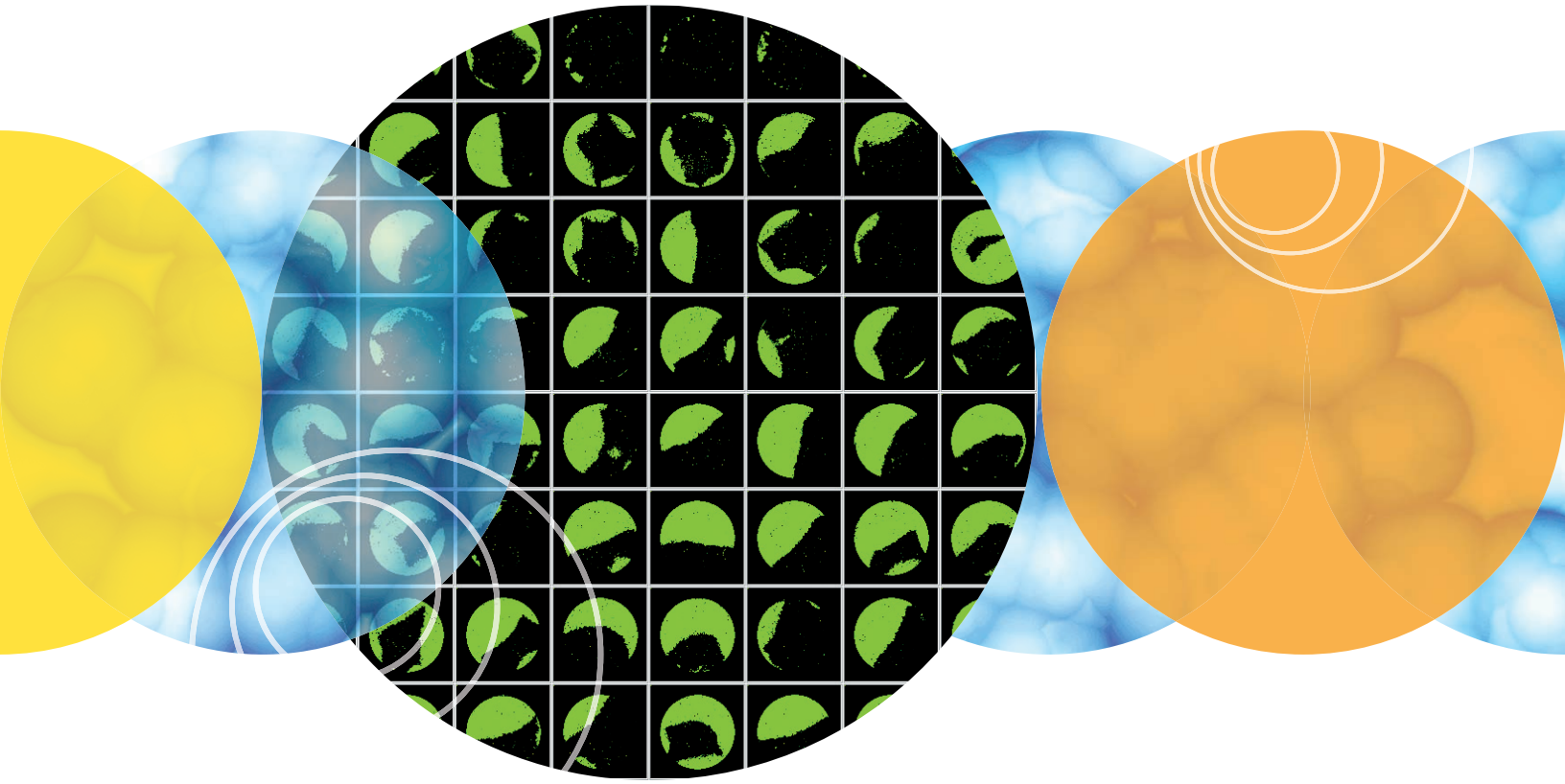
CloneSelect™ Imager

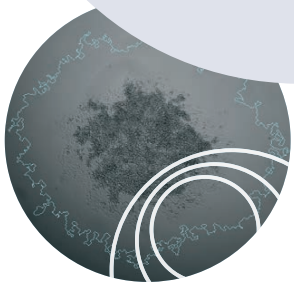


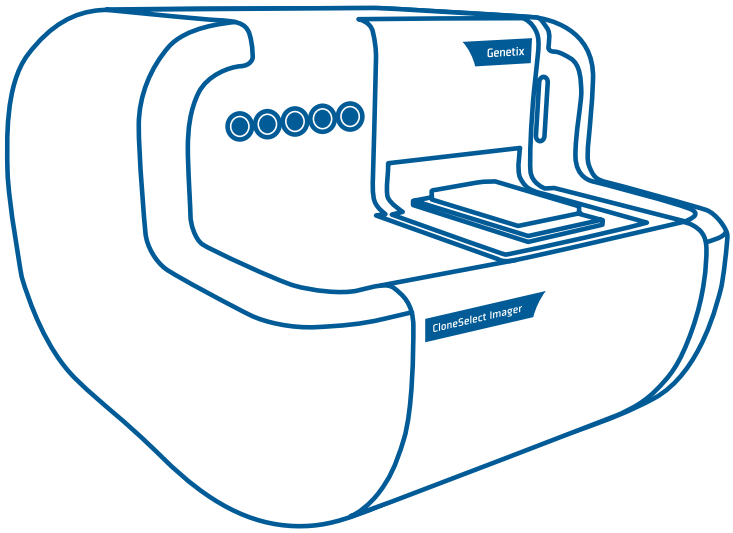
Objective, quantitative assessment of cell growth

MOLECULAR DEVICES

KEY BENEFITS

- Assess cell confluence objectively and quantitatively
- Streamline workflow: image, analyze, report
- Image every well anytime to track colony formation and verify monoclonality





Assess cell confluence objectively and quantitatively

Rapid determination of the growth of cell lines is important for a number of processes, such as optimization of cell culture conditions and verification of monoclonality.

However, conventional techniques are time-consuming, subjective and may risk interference with cell growth:

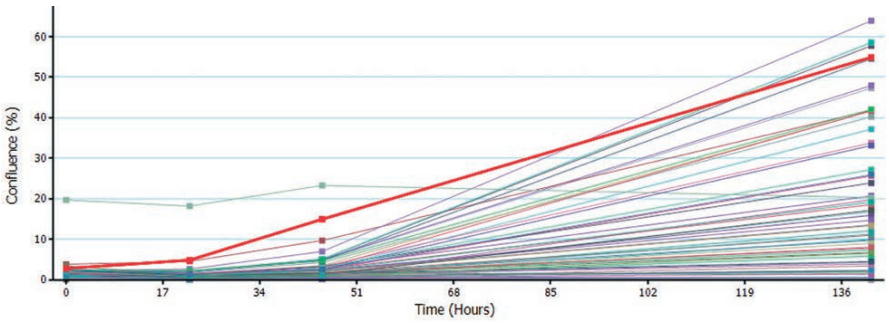
• Tracking cell growth in 96-well plates is challenging and labor-intensive

CONSISTENT RESULTS

Produce consistent results – in less time

Save time and produce objective, quantitative, and consistent results by using the CloneSelect™ Imager system to overcome the challenges associated with conventional techniques.

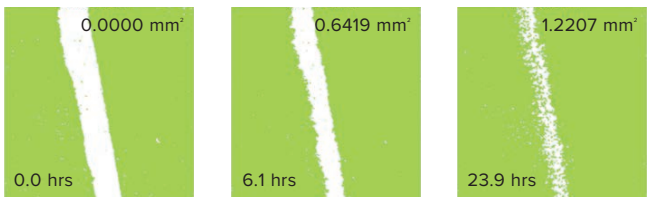
- Label-free white light imaging of living cells
- Suitable for adherent and settled suspension cells
- Growth rates accurately determined in every well of a 96-well plate



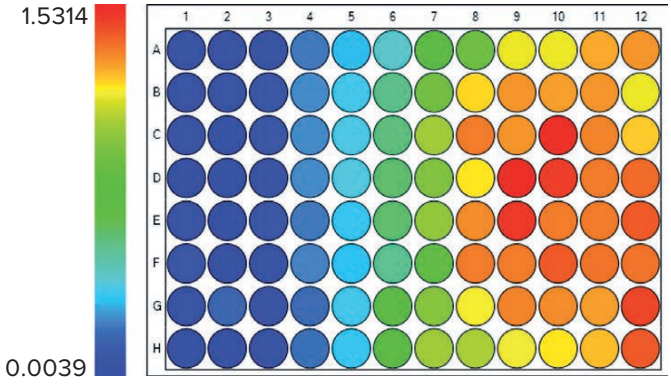
Consistent results

Visual readouts for label-free, cell migration assays

- Determine migration rates, maximum migration rate and total migration area
- Screen one microplate within 3 minutes
- Easy to read, numerical and graphical output



Wound healing time course



Wound healing heat map

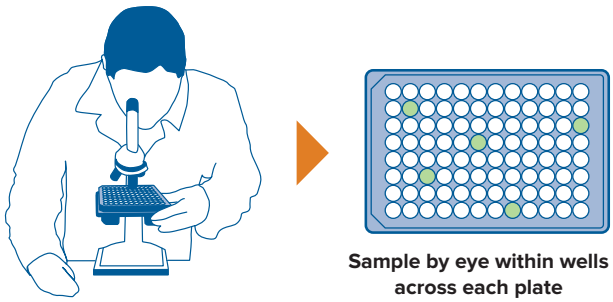
Track and record cell growth

CloneSelect Imager system estimates cell confluence and cell number

- Automatically scans every well in every plate
- Generates growth curves for each well
- Enables viewing and tracking of every well in every plate
- Reveals additional information on cellular morphology and an understanding of growth characteristics

Conventional technique: subjective, time-consuming

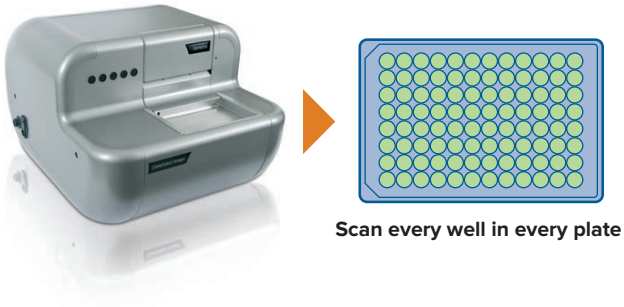
Inconsistent results: cannot determine whole well confluence – well after well



Sample by eye within wells across each plate

CloneSelect Imager: objective, automatic

Quantitative, whole well cell confluence for every well



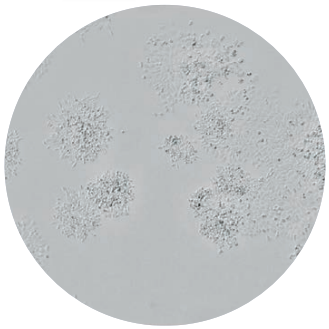
Scan every well in every plate

Streamlined workflow: images, analyzes, reports

Imaging

- Use adherent or settled suspension cells in microwell plate

CloneSelect Imager



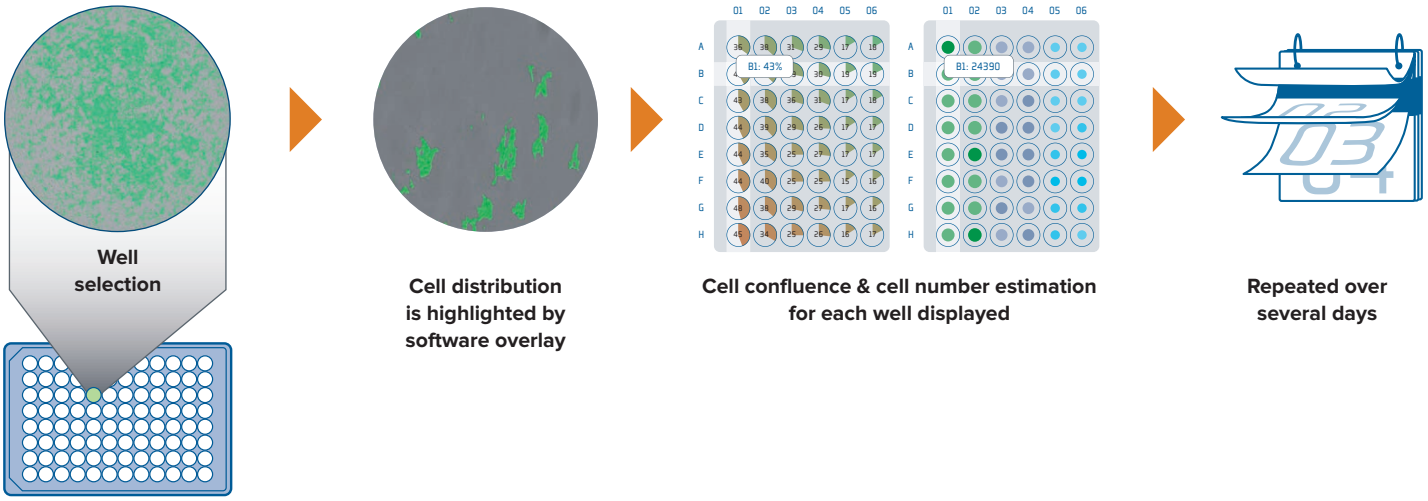
White light image

OPTIMIZE CLONAL OUTGROWTH

The system is particularly useful for optimizing clonal outgrowth strategies when platform approaches are not suitable e.g. when investigating new cell lines or variants.

Analysis

- Cell confluence and cell number estimation displayed for each well
- Growth curves calculated and displayed



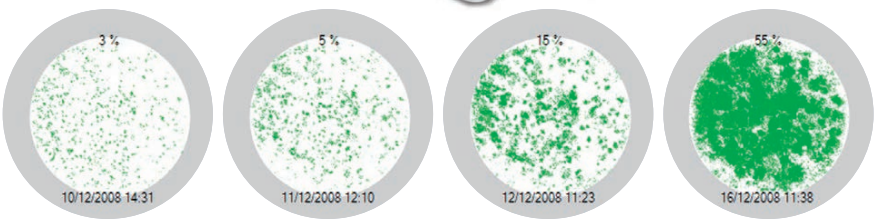
Report

- Make confident, image-driven decisions throughout plate history
- Track and view growth of every cell line

Growth curves calculated and displayed

- Electronically track and store plate data: cell confluence, cell number estimation, and growth curve

VIEW EVERY GROWTH CURVE IN EVERY WELL



3% Day 1 **5% Day 2** **15% Day 3** **55% Day 7**

Automate with robotic solutions

- Electronic data tracking ensures control of high throughput processes

CloneSelect Imager integrated with robotics from Beckman Coulter. Photo courtesy of Beckman Coulter Corp., shows first generation CloneSelect Imager system.

Process up to 75 lidded plates in a single run. *automate-it* scara robot is recommended and supplied through Molecular Devices – optimized for CloneSelect Imager.

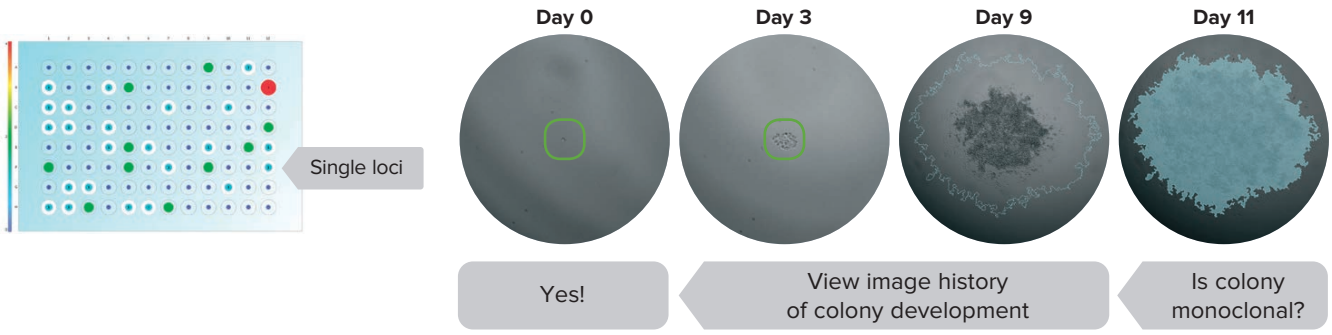
Verify monoclonality

After initial seeding, CloneSelect Imager system can image every well, at any time point, using a 'loci of growth' functionality to highlight those wells that contain a single colony.

- Seed one cell per well and image at any point
- Focus on wells with a single loci of growth and view image history to verify monoclonality
- Verify colony origin by tracking image history of each well

"CLONESELECT IMAGER HAS BECOME AN ESSENTIAL SYSTEM FOR VERIFICATION OF MONOCLONALITY WITHIN OUR CELL LINE DEVELOPMENT WORKFLOW"

Dr. Howard Clarke, Senior Staff Scientist in Process Development, CMC ICOS Biologics Inc., USA



Colony forming assay

After seeding in a matrix that enhances colony formation, such as a semi-solid media, cells are typically incubated with compounds that may affect colony growth. The CloneSelect Imager system is used to image every well to count colony number, estimate colony area and track colony growth.

- Image every well at any time point
- Analyze wells of interest e.g. showing inhibition of colony growth
- Export colony number and colony area for each well

Colony counting and colony area

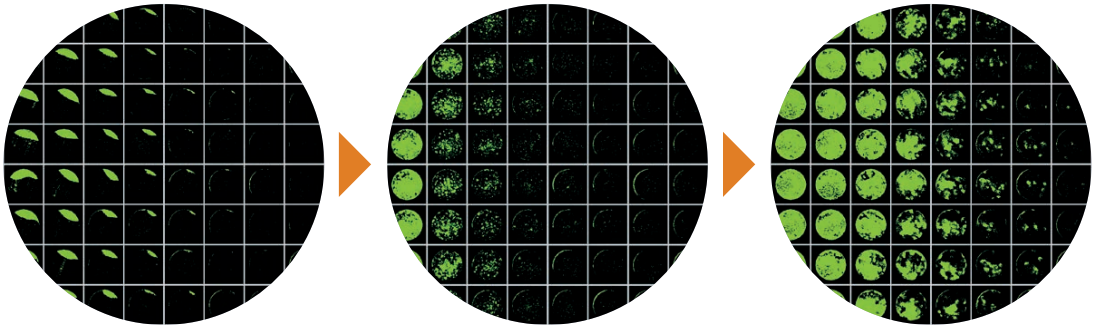
Optimize cell culture conditions

CloneSelect Imager has been used to rapidly screen culture variables to identify optimal culture conditions for low density or clonal outgrowth.

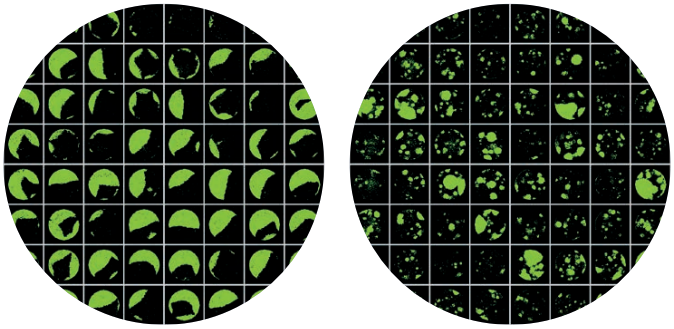
- Identify low-cell density growth conditions over a two-week period
- Achieve a robust and extended growth range over base-case data

"MAXIMIZE SUCCESS RATE FOR SERUM-FREE COLONY OUTGROWTH IN CHEMICALLY-DEFINED MEDIA BY PRIOR OPTIMIZATION OF GROWTH CONDITIONS"

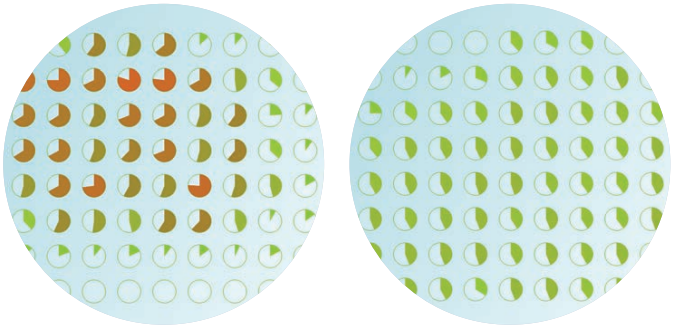
Ben Hughes, Senior Bioprocess Engineer, NCRIS Biologics Facility, Australian Institute for Bioengineering & Nanotechnology (AIBN), University of Queensland



Base-case – Day 7 data. Additional information gained on cellular morphology and understanding of growth characteristics.



Identify multiple nucleation points versus "edge only" growth



Identify sub-optimal environmental conditions or "edge-effects"

ASSESS CELL VIABILITY

Replace cumbersome colorimetric MTT assays with a non-invasive technique that enables monitoring over time*

- Direct overview of initial results per well
- Screen one microplate within 3 minutes
- Avoid costly colorimetric kits – no staining required

* Accurate non-invasive image-based cytotoxicity assays for cultured cells, Marques-Gallego et al., BMC Biotechnology 2010, 10:43

ACCELERATE CELL LINE DEVELOPMENT

Monitor and evaluate outgrowth and productivity of cell lines that have been screened and selected using a ClonePix™ system.

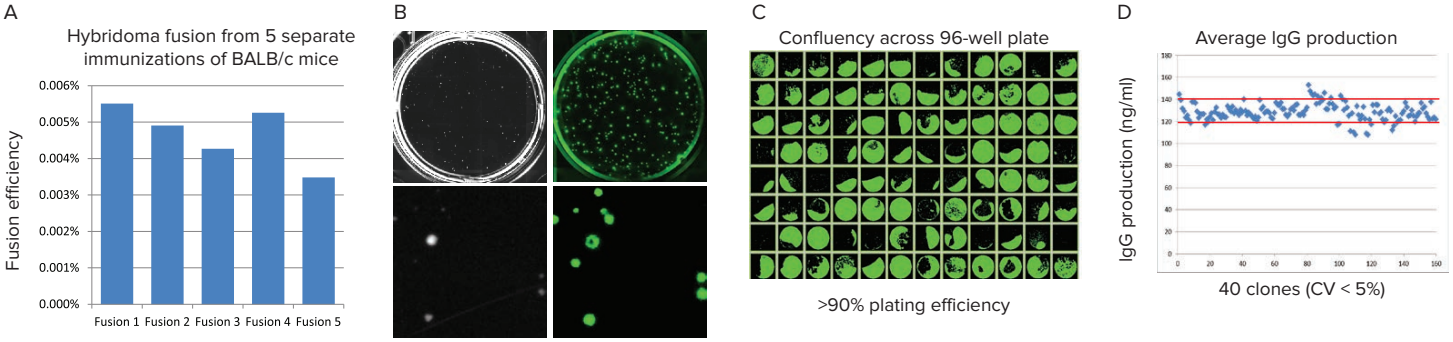
Maximize your hybridoma yield with our complete set of culture media

Culture media for every stage of hybridoma cell line generation

Stable hybridoma cell lines are critical for monoclonal antibody production. Our XP Media and CloneMedia portfolio of products is a complete solution that supports all stages of hybridoma cell line development from fusion to scale up. Optimized to support the selection and growth of hybridoma clones using our ClonePix 2 System, the kit is also compatible with other appropriate methods.

- HAT (hypoxanthine-aminopterin-thymidine) selection and cloning of hybridomas are accomplished in one step, which minimizes both time and materials required
- Not only does the semi-solid CloneMedia method eliminate the possible masking of potentially valuable slow-growing clones by fast-growing clones, but it also reduces or eliminates sub-cloning steps
- Reduce hands-on time when the workflow is combined with the ClonePix 2 System

Optimized growth conditions result in stable antibody production

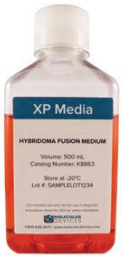


Hybridomas were generated, selected, and screened using our XP Media and CloneMedia suite of hybridoma media. (A) 5 individual hybridoma fusion experiments were conducted on BALB/c mice, immunized to the same antigen, to assess reproducibility of fusions in XP Media suite of products. Fusion efficiency was calculated by dividing the number of hybridoma colonies detected on the ClonePix 2 System by the number of splenocytes grown in XP Media Pre-Fusion Myeloma Growth Medium and Hybridoma Expansion Medium (without HT). **(B)** Images of hybridomas were captured with the ClonePix 2 System in white light (left panel) and FITC (right panel), after 7 days growth, to determine growth and expression of IgGs, respectively. Colonies grown in the presence of CloneDetect were ranked according to their FITC intensity (indicating total IgG production), with the highest producers picked for further characterization. **(C)** Software detection of cell confluency, indicated by the green overlay, across a 96-well plate allowing for a quick visualization of plating efficiency. Images were collected on the CloneSelect Imager. 87 out of 96 wells grew to a confluency >5% after 7 days (the initial confluency of all wells was <1%) for a >90% plating efficiency. The real plating efficiency may be even higher because slow growing clones may be classified as non-growing using the >5% confluency criteria. **(D)** IgG production plotted per well (show in blue) with red lines indicating 2 s.d. away from the mean. Because these are stable hybridomas, we don't expect a large variation in the total amount of IgG produced per cell, which is confirmed by <5% CV across all clones tested.

The full kit contains*:

XP Media Pre-Fusion Myeloma Growth Medium and Hybridoma Expansion Medium (without HT), P/N K8862

Used to support the growth of myeloma cells before fusion. Also supports expansion of hybridoma clones. Does not contain hypoxanthine or thymidine (HT).



XP Media Hybridoma Fusion Medium, P/N K8863

Used to wash cells before fusion and during fusion process. Does not contain supplements to support growth.

XP Media Hybridoma Fusion Recovery Medium, P/N K8864

Used to promote hybridoma viability after the fusion process but before clone selection. Does not contain hypoxanthine, aminopterin, and thymidine (HAT).

CloneMedia Hybridoma Semi-Solid Selection and Cloning Medium (with HAT), P/N K8865

Used after fusion of splenocytes and myeloma cells to select and clone hybridomas in one step. Optimized for colony formation. Equally suitable for fresh fusions and for stable hybridoma cell lines.

XP Media Hybridoma Growth Medium (with HT), P/N K8866

Optimized for hybridoma expansion following clone selection and colony picking. Contains hypoxanthine and thymidine (HT) and is used to wean hybridomas off aminopterin from the selection process.

Hybridoma Polyethylene Glycol (PEG) for Cell Fusion, P/N K8868

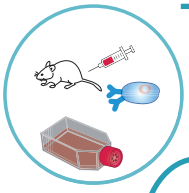
Used for the fusion of mouse splenocytes and parental myeloma cells to generate hybridomas. PEG is present as a 50% solution in DMEM.

CloneMedia Hybridoma Semi-Solid Selection and Cloning Medium (without HAT), P/N K8867

Does not contain any selection reagents. If appropriate selective reagent has been added, then the medium can be used after fusion to select and clone hybridomas in one step. Optimized for colony formation.

*Components can be ordered separately. If you are using alternate hybridoma selection methods, then CloneMedia Hybridoma Semi-Solid Selection and Cloning Medium (without HAT) (P/N K8867) is available. You must add agents for hybridoma selection to this medium before use.

Accelerate your hybridoma cell line development with a complete set of platforms and culture media



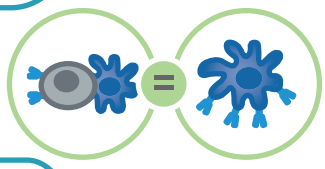
Pre-Fusion

Culture myeloma cells in pre-fusion growth medium. Prepare splenocytes for fusion.

Expansion Medium without HT (K8862), Fusion Medium (K8863)

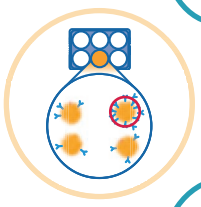
Fuse splenocytes and myeloma cells.

Fusion



Hybridoma fusion

Fusion Medium (K8863), Polyethylene Glycol (K8868), Fusion Recovery Medium (K8864)



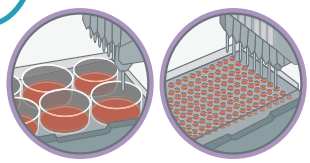
Clone Selection

Clone screening and selection in semi-solid medium.

ClonePix 2 System, CloneDetect, CloneMedia Selection and Cloning Medium with and without HAT (K8865, K8867)

Pick selected, high-producing clones from semi-solid medium and transfer to liquid medium.

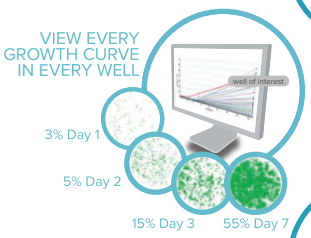
Clone Picking



Accurate and gentle picking

Transfer of colony to destination plates

ClonePix 2 System, Growth Medium with HT (K8866)



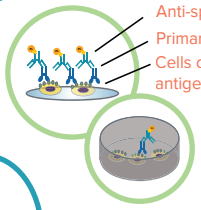
Clone Stability

Monitor growth of picked clones.

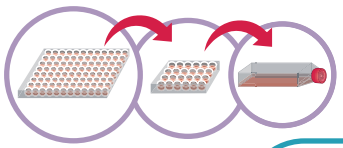
CloneSelect Imager

Functional Characterization

Perform secondary screening on clone supernatants (e.g. ELISA).



SpectraMax i3x or other Molecular Devices microplate readers



Scale-Up and Wean

Scale up clones producing desired antibodies and wean off HT selection.

Growth Medium with HT (K8866) and Expansion Medium without HT (K8862) at 1:1 ratio

Expand clones producing desired antibodies.

Expansion

Expansion Medium without HT (K8862)

Accelerate cell line development with a range of Molecular Devices platforms

ClonePix 2 Mammlian Colony Picker

Automatically screen more clones in less time than conventional techniques, select cells with optimal expression levels, and pick colonies with accuracy with the ClonePix™ 2 System. ClonePix systems are now used in over 100 laboratories around the world to increase workflow productivity, leaving more time to better characterize target proteins and run new projects.

QPix 400 Series Microbial Colony Picker

The QPix™ 400 series of microbial colony pickers offer you the unique option to simultaneously detect colonies and quantify fluorescent markers in a pre-screening step before picking. Our QPix systems are used worldwide in over 600 installations in research institutes, biotech, and pharmaceutical companies. QPix robotics developed a famous reputation for reliability and accuracy in sequencing centers during the Human Genome project.

SpectraMax i3x Multi-Mode Microplate Reader

The SpectraMax® i3x multi-Mode microplate reader measures spectral-based absorbance, fluorescence, and luminescence with the added functionality of modular upgrades for western blot, imaging, and fast kinetics with injectors.

Unrivalled solutions based on excellent imaging and intelligent image analysis

Products from Molecular Devices offer scientists unrivalled solutions that utilize imaging and intelligent image analysis to support basic research, pharmaceutical and biotherapeutic development. The company's systems continue to establish industry standards in areas such as picking microbial colonies for genomic studies or screening and selection of mammalian cell lines. Other systems use imaging platforms to monitor cell growth, evaluate cellular responses and quantify protein production. Through its expertise in robotics, cell and molecular biology, image analysis and interpretation, supported by a strong IP portfolio, the company is committed to the continual development of innovative solutions for life science applications.

CloneSelect Imager - System Specifications	
Imaging	
Software	Dedicated imaging software pre-installed on a high specification PC, Microsoft Windows 7
White light imaging	Trans-illumination
Data tracking	1 x internal barcode reader for data tracking of each plate
Camera	High-resolution CCD camera
Imaging speed	96-well microplate: 90 sec
Objective	4x
Resolution	Standard: 3.6 micron; Maximum: 1.8 micron
Instrumentation	
Source plate type	Range of 6-, 12-, 24-, 96-well SBS microplates
Source plate capacity	1 x plates
Instrument dimensions	720 mm (width) x 428 mm (height) x 575 mm (depth)
Instrument weight	45 kg
Regulatory approval	
Compliance	CE
Quality	ISO9001:2008 certified
Automation compatibility	
API suite available for robotic integration. Please contact us for details.	

For more information, visit **www.moleculardevices.com**

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