



Flexibility and Speed for HCS: The Complete Imaging Solution From Molecular Devices

(Now part of MDS Analytical Technologies)

“Imaging with a Vision”

January 13, 2010

Michael Sjaastad, PhD.,
Director of Marketing Cellular Imaging
MDS Analytical Technologies



Why High Content Screening and Analysis?

- The promise of “High-content” screening:

HCS will deliver better hits and improve the quality of drug discovery...

Leverage...

Cell based assays

Automated Imaging and Image analysis

Multi-parametric data analysis

- What have we learned in a decade of advancing HCS?

HCS and HCA can deliver on the promise but...

To reach potential, acquisition and analysis must be flexible and scale

- ***Easy of use, flexibility in hardware***
- ***Efficiency for large libraries***
- ***Easily adapt to new assays***
- ***Infrastructure and support bottlenecks unique to imaging***

Agenda



- Molecular Devices Complete Imaging Solution
 - Flexibility
 - Hardware, Software and Applications
 - Ease of Use
 - Scalability
 - Acquisition and analysis speed
 - HCA
 - Address infrastructure bottlenecks
 - Data management
 - Shameless plugs to get you to drop by our booth...

Molecular Devices Complete Solution for HCS



A Turn-key solution for image acquisition, data mining & hit selection

Image Acquisition



ImageXpress® Micro System



ImageXpress® Ultra System



IsoCyte™ Cytometer

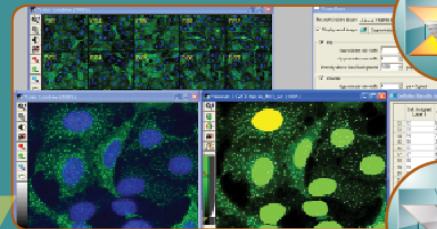
Data Management



MDCStore™ Data Management Solution

Autonomous Mode

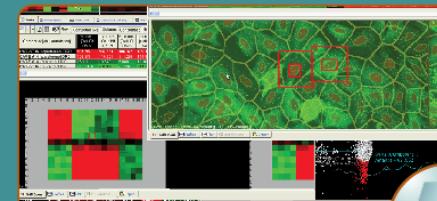
Image Analysis



MetaXpress® and
MetaXpress® PowerCore™ Software



Hit Selection

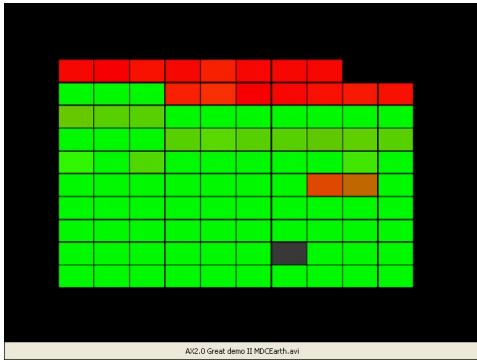


AcuityXpress™ Software



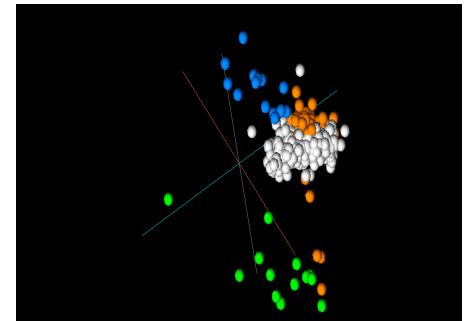
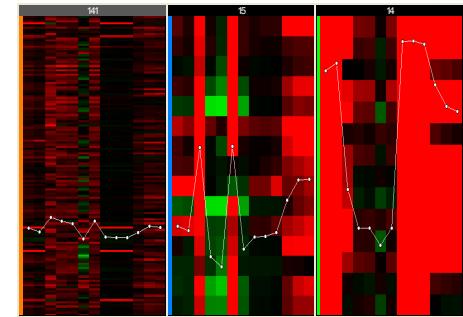
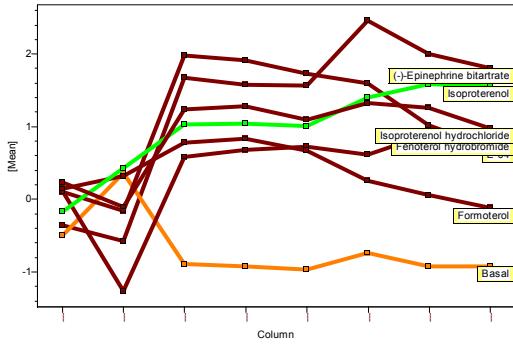
A turnkey solution: Image acquisition is integrated with the MDCStore Data Management Solution which works seamlessly with the image analysis and hit selection tools. In autonomous mode, the IsoCyte cytometer performs on-the-fly image acquisition and analysis.

Integrated HCA: AcuityXpress™ Software



Hit Selection

The AcuityXpress™ software interface is shown within a light blue rounded rectangle. It includes a logo with a stylized 'A' and 'X' inside a circle, a chromatogram with multiple peaks, a 3D surface plot, and several other data windows. The text "AcuityXpress™" is displayed at the bottom right of the interface.



AcuityXpress™ Software: Annotations and Weblinks

Compound [Well Annotation]	% G0/G1 (CellCycle) [Cell Measurement]	% S Phase (CellCycle) [Cell Measurement]	% G2 (CellCycle) [Cell Measurement]	% Early M (CellCycle) [Cell Measurement]	% Late M (CellCycle) [Cell Measurement]
AIDA	-0.319	0.385	-0.078	-0.0251	0.277
AL-8810	1.180	-1.444	0.693	-0.783	0.0357
Alaprocrate hydrochloride	0.262	0.262	0.262	0.262	0.262
Albuterol hemisulfate					
Allopurinol					
Alloxazine					
alpha,beta-Methylene adenosine					
alpha-Guanidino glutaric acid					
alpha-Lipoic Acid					
alpha-Lobeline hydrochloride					
alpha-Methyl-4-carboxyphenyl					
alpha-Methyl-5-hydroxytryptamine					
alpha-Methyl-DL-tyrosine methyl ester					
Alprenolol hydrochloride					
Alsterpaullone					
Altretamine					
Amantadine hydrochloride					
Amfotericin acid					
Amifostine					
Amiloride hydrochloride					
Aminobenzotropine					
Aminoquanidine hemisulfate					
Aminoquanidine hydrochloride					
Aminophylline ethylenediamine					
Aminopterin					
Amiodarone hydrochloride					
Amiprollose hydrochloride					
Amitriptyline hydrochloride					
Ammonium pyrrolidinedithiocarbamate					
Amoxapine					
AMPA hydrobromide					
Amperozide hydrochloride					
Amsacrine hydrochloride					
AMT hydrochloride					
Ancitabine hydrochloride					
Androsterone					
Aniracetam					
Antozoline hydrochloride					
Apigenin					
Apomorphine hydrochloride hemihydrate					
Arcaine sulfate					
Arecaidine propargyl ester hydrobromide					
Arecoline hydrobromide					
ARL 67156 trisodium salt					
Astaxanthin					
Atenolol					
ATPA					

EMBL-EBI EB-eye Search All Databases Enter Text Here Go Reset Advanced Search Give us feedback

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ChEBI

isoproterenol (ChEBI:6046)

Main Automatic Xrefs

ChEBI Name: isoproterenol
ChEBI ID: CHEBI:6046
Last Modified: 04 April 2007

Image
 Applet

Molfile

InChI: InChI=1/C11H17NO3/c1-7(2)12-6-11(15)8-3-4-9(13)10(14)5-8/h3-5,7,11-15H,6H2,1-2H3

InChIKey: InChIKey=JWZZKOKVBUJMES-UHFFFAOYAN

SMILES: CC(C)NCC(O)c1ccc(O)c(O)c1

Formula: C11H17NO3

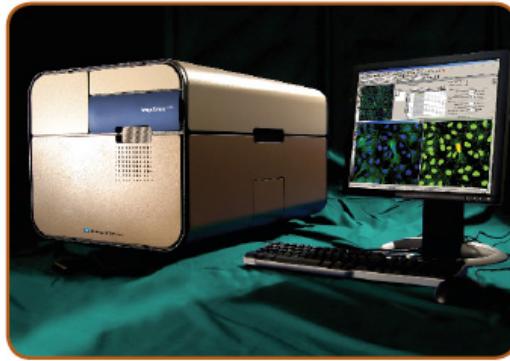
Flexibility: Choose the Appropriate Technology



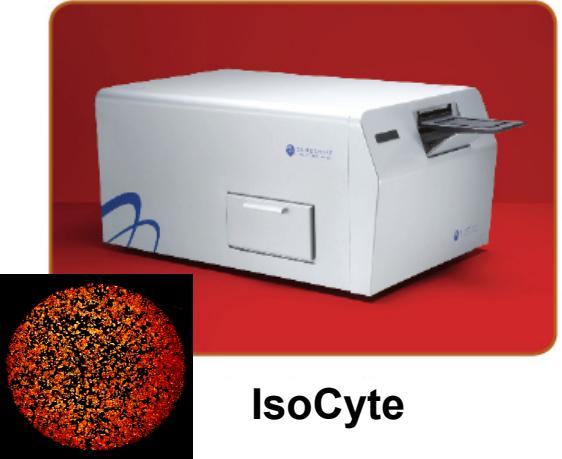
Match resolution, field of view, and speed to needs



ImageXpress^{MICRO}™



ImageXpress^{ULTRA}™



IsoCyte

Conventional Microscopy
CCD camera
Many Hardware options

True point scanning
Laser Confocal
(Adjustable Pinhole)

Laser Scanning Cytometry
Large Field of View
Stand Alone mode
FCS data Export

ImageXpress® Micro™

- Introduced in June 2005
- Third Generation Technology
- Modular Widefield Imaging System
 - 4 objectives (1x – 100xoil)
 - 5 filter cubes
 - high-speed laser auto-focus
 - 96 well plate, 1 λ , 3 minutes
 - 384 well plate, 2 λ , 12 minutes
 - linear encoded stage (100nm accuracy)
 - sample flexibility (slide to 1536 well plates)
 - Small footprint 18"W x 26.5"D
- Option Packages
 - bright field/phase illumination
 - environmental control (temp/CO₂/Humidity)
 - external Filter Wheel (10 position)
 - liquid handling
 - robotic plate handling
- Recommended for All Applications
 - Fixed and live HCS assays
 - 1° and 2° screening (high throughput)
 - multiplexed assays (7 wavelengths)
 - Time lapse, Stem Cells



ImageXpress® Ultra™



- **4- Channel Point Scanning Confocal**
- **Modular Confocal Imaging System**

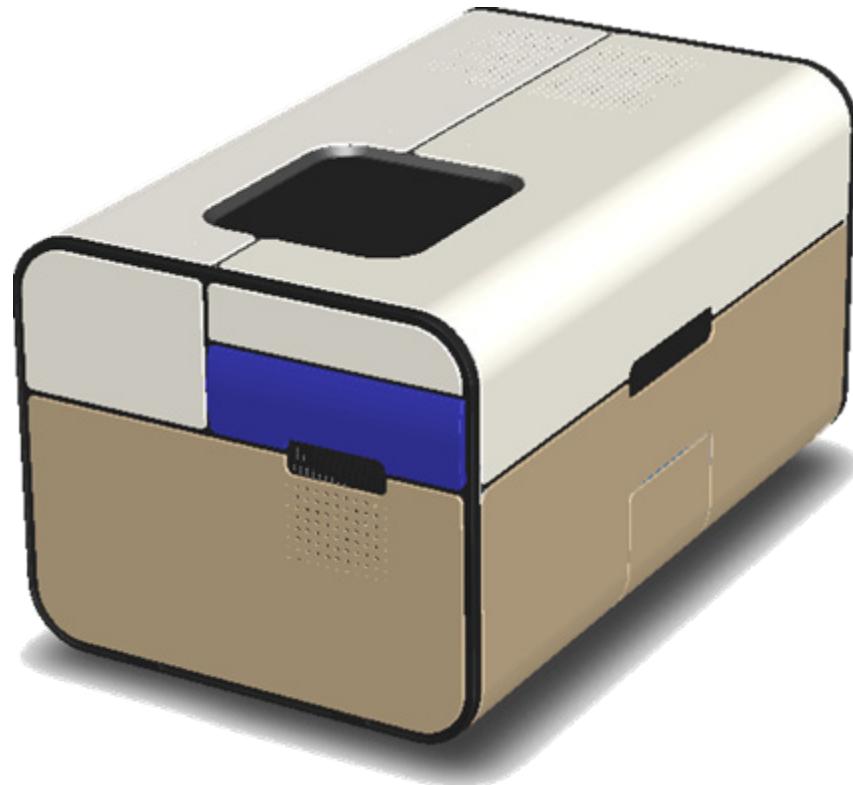
- 4 Nikon objectives (1x – 100oil)
- 4 Lasers with several different configurations
- high-speed laser auto-focus
- linear encoded stage (100nm accuracy)
- sample flexibility (slide to 1536 well plates)
- Bench-top footprint

- **The Confocal Advantage**

- Acquire several channels simultaneously, higher throughput
- Reject out of focus light, higher contrast
- **Configurable scan-length, fewer FOVs means higher throughput**
- **Adjustable pinhole, optimize light collection, higher contrast or higher throughput**

- **Recommended for Speed and Specialized Applications**

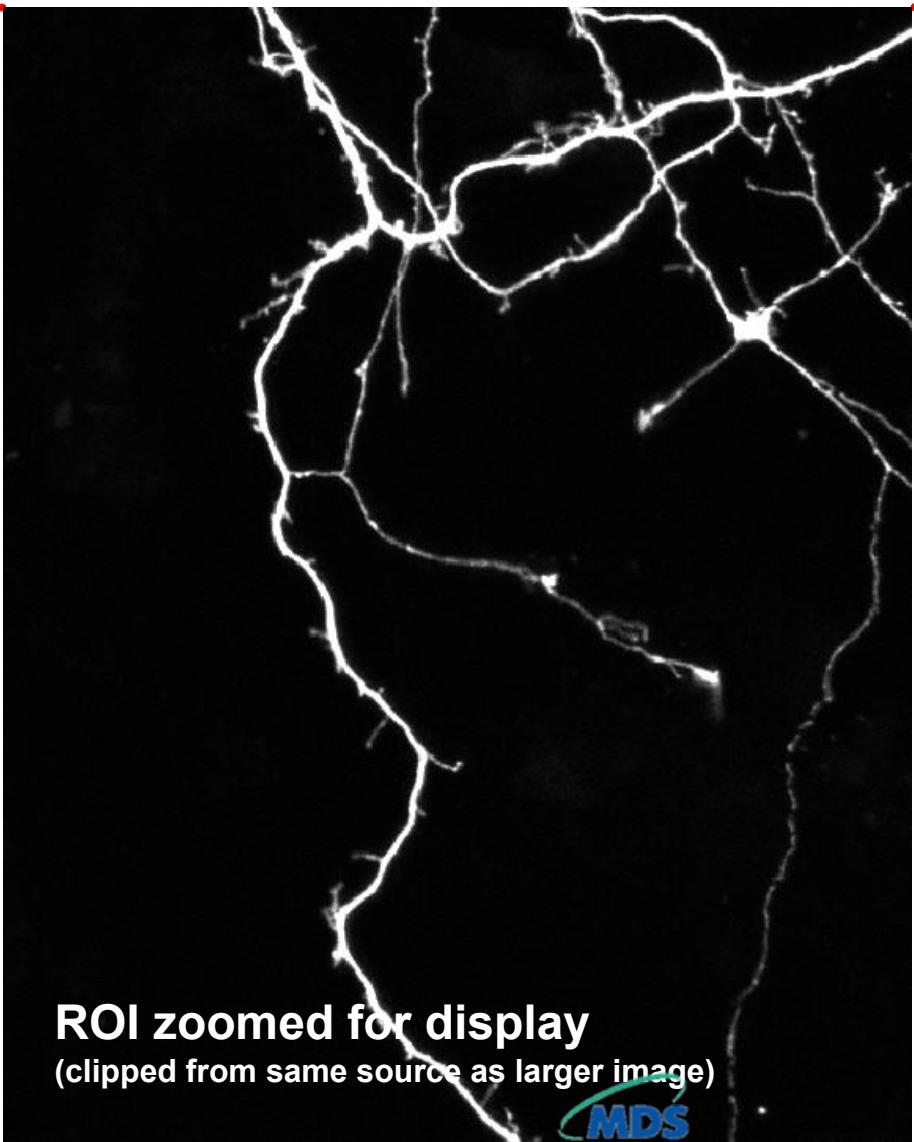
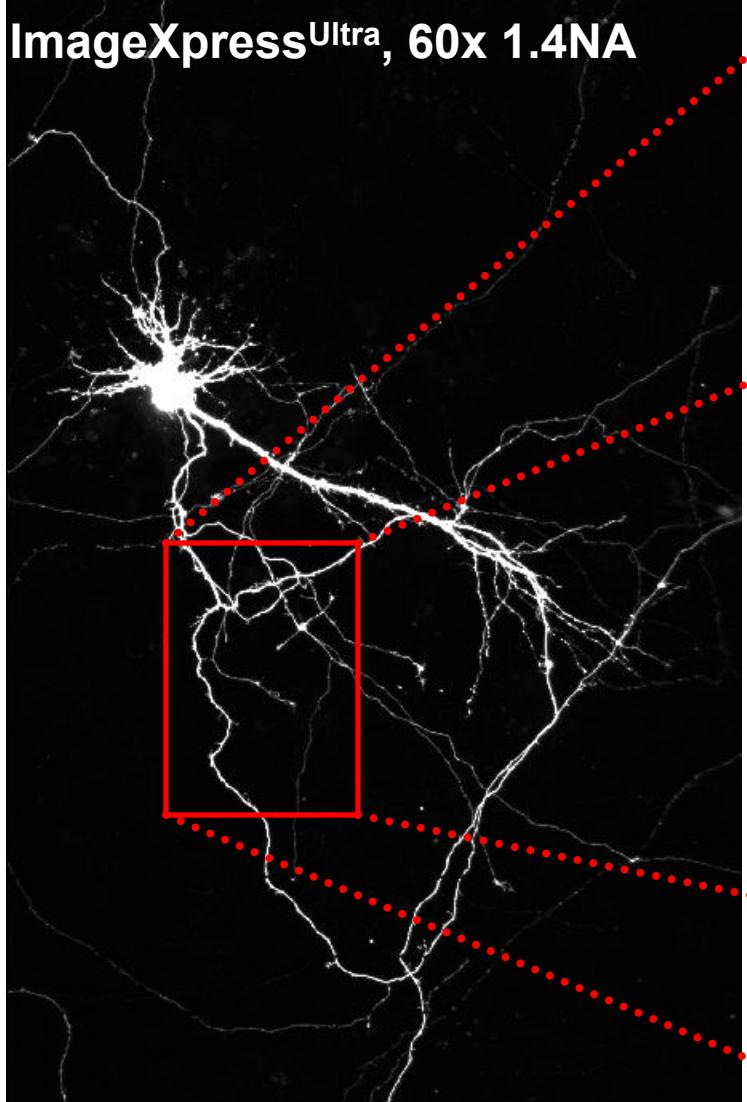
- 1° and 2° screening (high throughput)
- Simultaneous 4-channel scanning
- Thick samples – tissues, samples on feeder cells...
- High throughput imaging
- Homogeneous assays – remove rinsing steps from assay to increase throughput



ImageXpress® Ultra™



ImageXpress^{Ultra}, 60x 1.4NA



ROI zoomed for display
(clipped from same source as larger image)



Analytical Technologies

ImageXpress® Ultra™—Long Scan



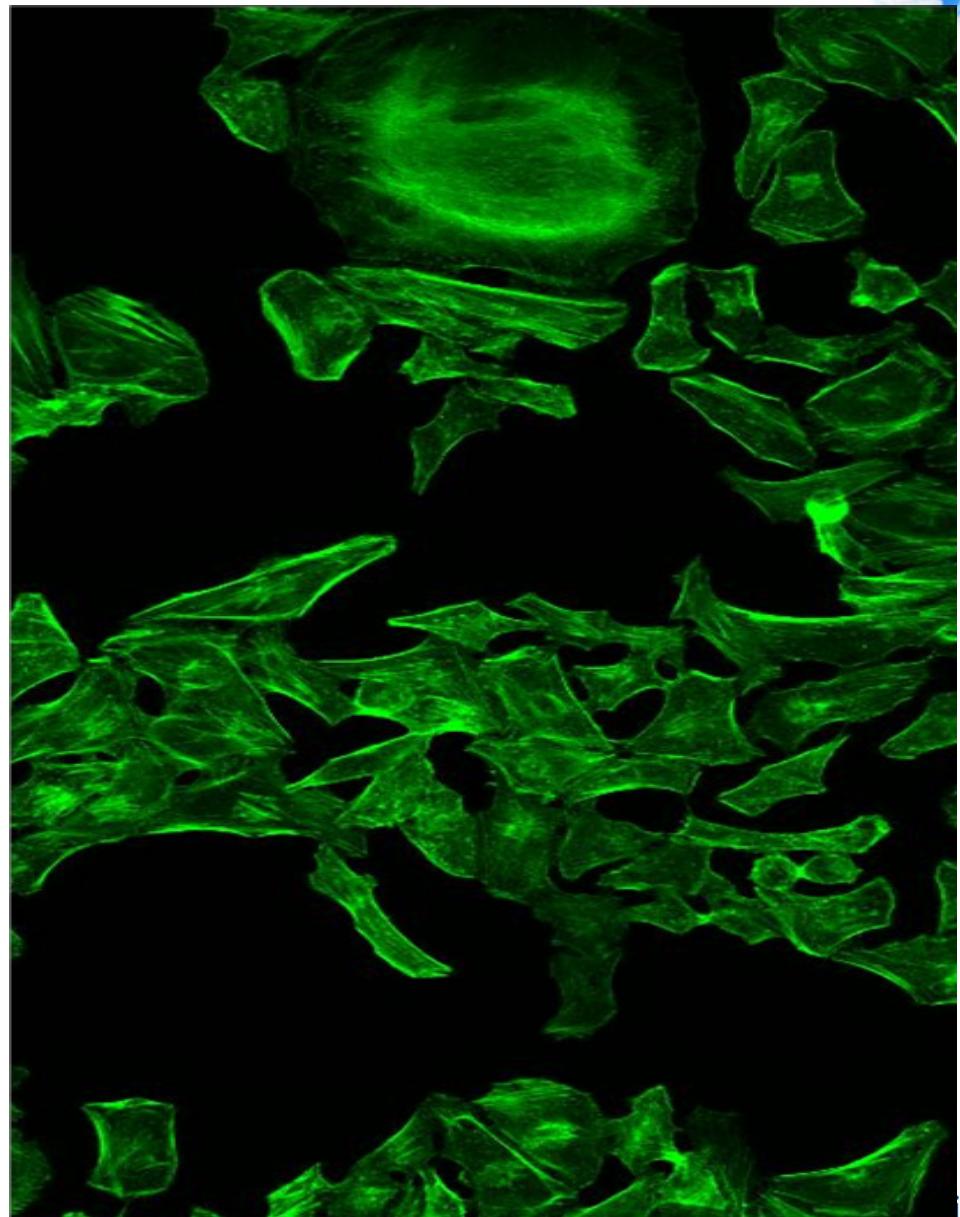
User-Configurable Scan Length

Up to 1:32 aspect ratio

Optimize speed

Rare events requiring high cell count

Imaging of large structures or networks



IsoCyt^e



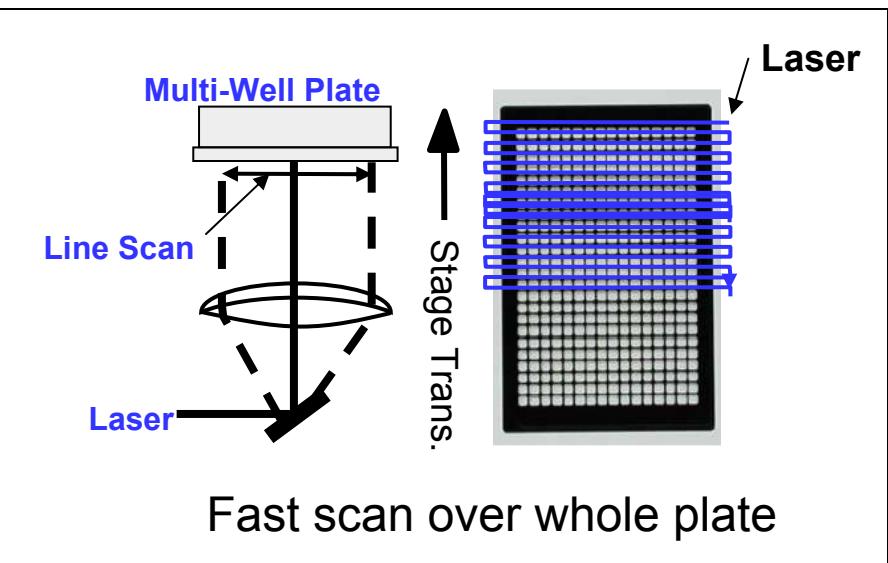
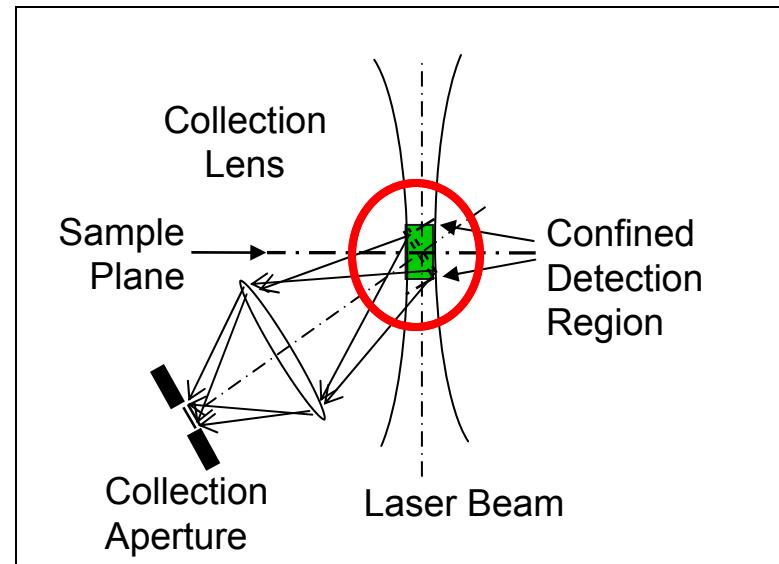
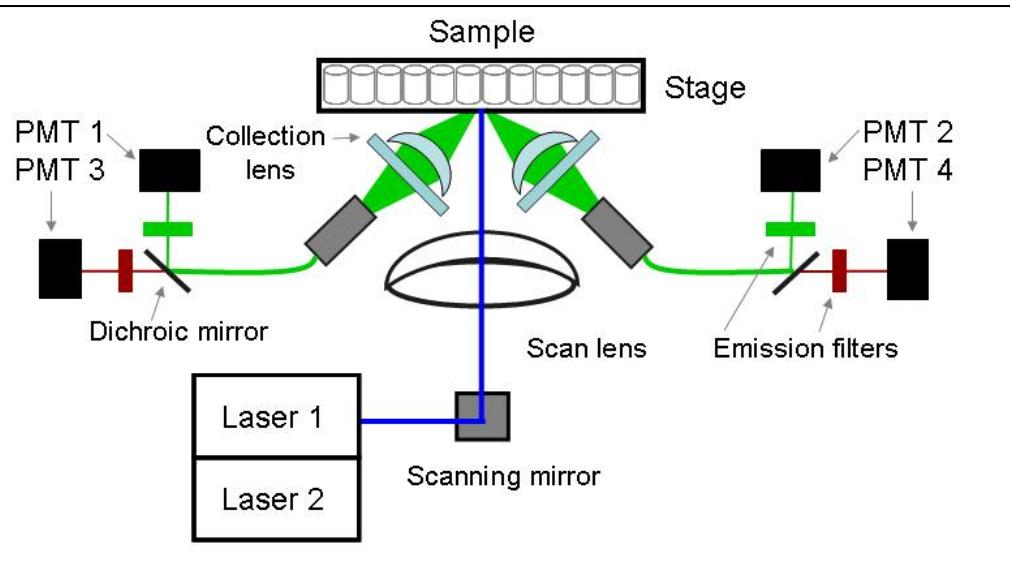
- 4 Channel Laser Scanning Cytometer
 - 1 or 2 excitation lasers
 - 4 detection PMTs
 - Laser scatter (grayscale)
- Large Field of View:
 - Scans the entire SBS plate format
 - Whole-well imaging
 - 200micron Z-section
- Fast: Scan in 2-10 minutes
 - (depends on resolution)
- Simultaneous acquisition and analysis
 - Autonomous mode
 - Import data into MDCStore
- Expansion of HCS:
 - From intracellular to cellular
 - Multi-cellular and macro models
 - Whole organism: (Zebrafish)



IsoCyt^e

- Export data in FCS (Flow cytometry) format
- Additional image analysis and visualization via MetaXpress and AcuityXpress

Crash Course on IsoCyte Technology



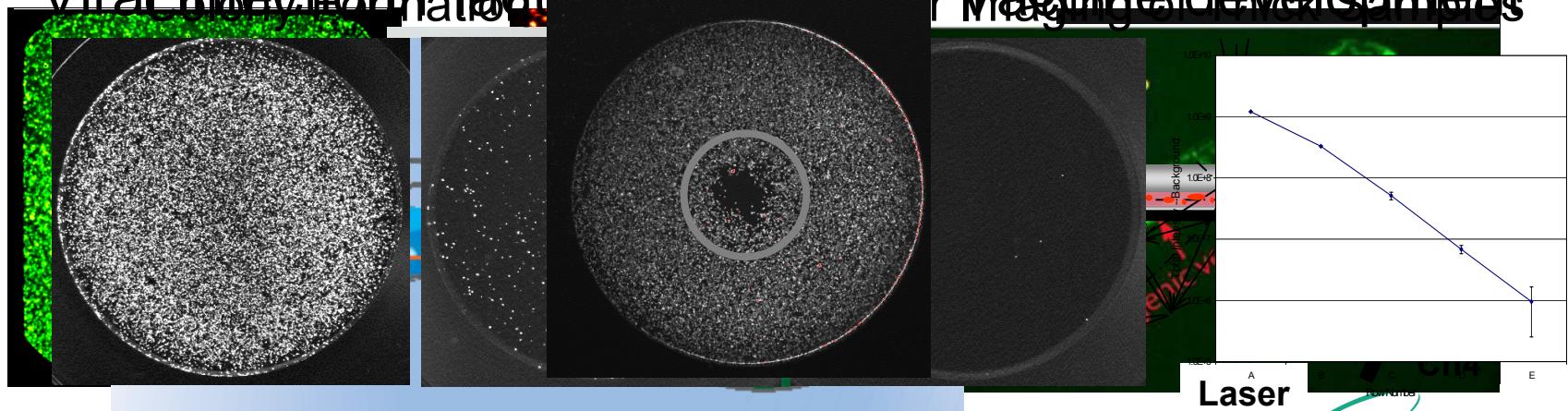
- Unique optics
 - Large depth of field
 - Image entire plate in 2-10 minutes
- Eliminates auto focusing steps
 - Works with all plates
 - Images 3D cell colonies
- Confined detection region reduces background
- On-the-fly object based image analysis

IsoCyte: Broader HCS Application Capability



- Many common HCS assays easily migrate to IsoCyte for HTS speeds
- New applications enabled with a large field of view and “whole well” imaging
- Run in “Autonomous Mode”, export to excel, FCS, or import images in MDCStore Data Management Solution and use MetaXpress® software
- Easy transition from Flow Cytometry, HTS plate reading or High Resolution HCS Applications

Antibody Binding Whole-Well Migration Cell Migration Cell Screening Cell Morphology



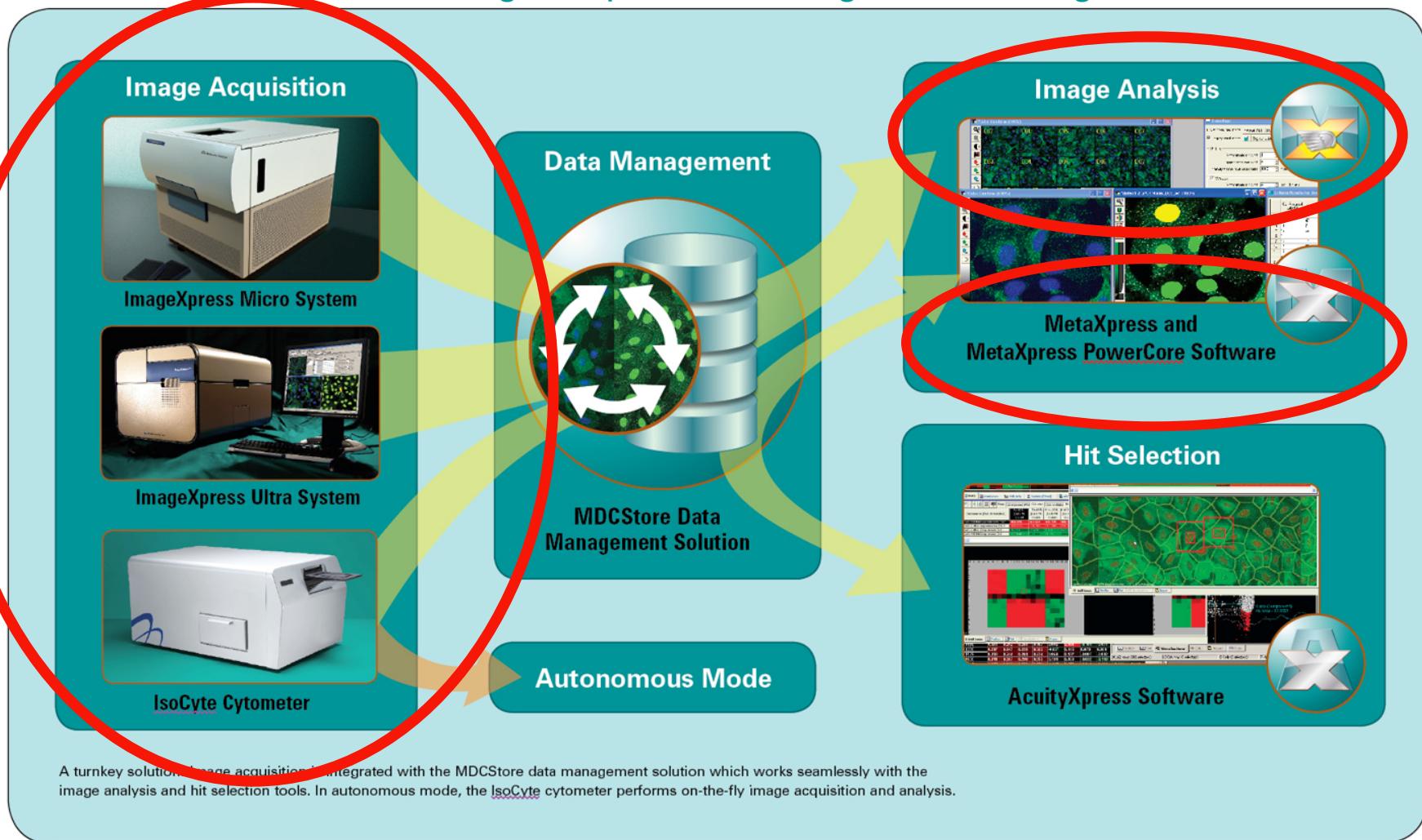
MDS

Analytical Technologies

The MDS-AT Complete Solution for HCS



Turn-key solution for image acquisition through data mining & hit selection



Superior Micronuclei Detection



- Introducing the Micronuclei application module from MDS Analytical Technologies
- One of the most challenging HCS applications
 - Wide range of phenotypes
 - Rare events, requires many images (Long Scans)
 - Early drug discovery, large compound libraries
- Capabilities needed
 - Superior segmentation algorithms
 - “on the fly” cell counting
 - Fast acquisition and analysis
 - Simple set-up



Micronuclei Application Module



Nuclei

Approximate min width: 12 <input type="button" value=""/>	μm
Approximate max width: 20 <input type="button" value=""/>	μm
Intensity above local background: 400 <input type="button" value=""/>	graylevels
Max distance of nuclei in polynucleated cells: 6.3 <input type="button" value=""/>	μm
Mitotic cell min intensity: 1000 <input type="button" value=""/>	graylevels
Mitotic cell min coverage: 50 <input type="button" value=""/>	%

Micronuclei

Approximate min width: 1 <input type="button" value=""/>	μm
Approximate max width: 10 <input type="button" value=""/>	μm
Intensity above local background: 100 <input type="button" value=""/>	graylevels
Min distance from main nucleus: 5 <input type="button" value=""/>	μm
Max distance from main nucleus: 10 <input type="button" value=""/>	μm

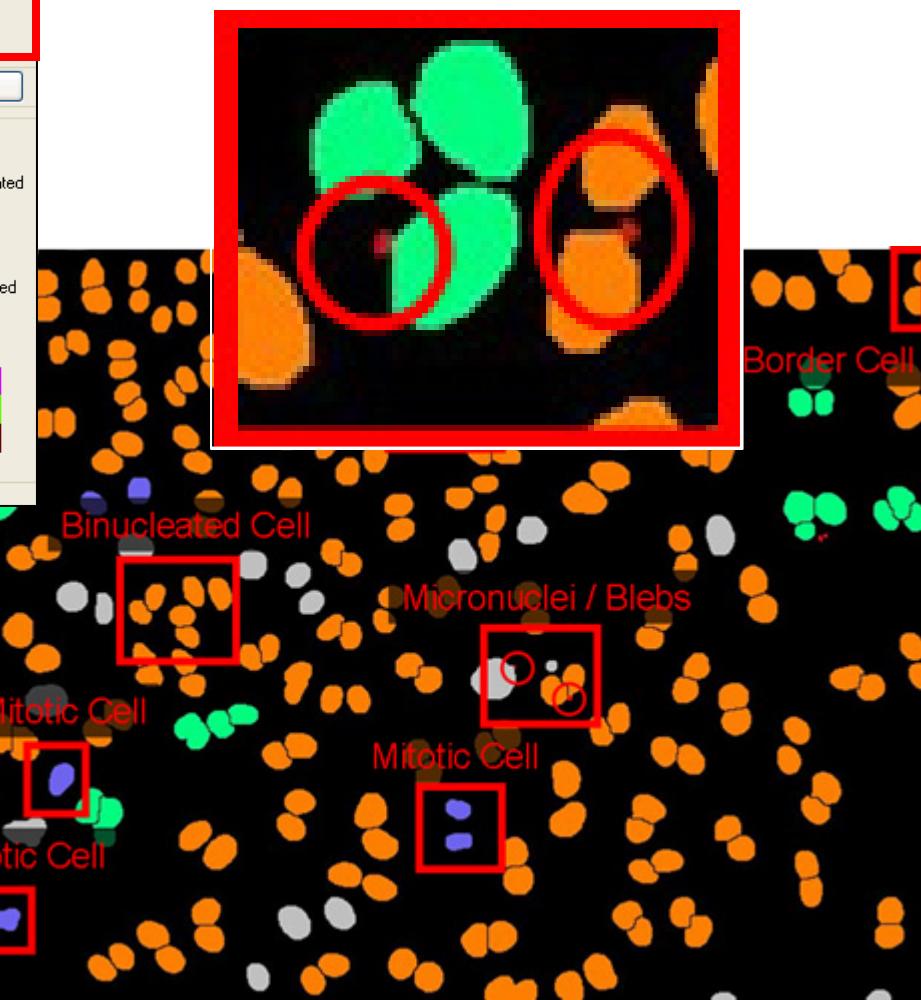
Exclude border nuclei

Apoptotic-specific staining (optional)
Source image: [None]

Necrotic-specific staining (optional)
Source image: [None]

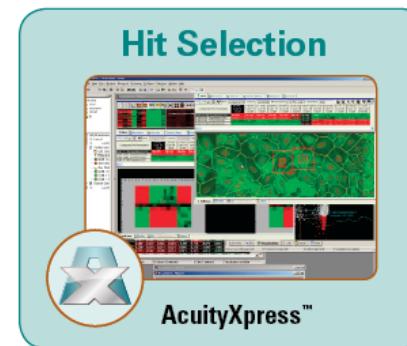
Probe A (optional)
Source image: [None]

Probe B (optional)
Source image: [None]



Superior Segmentation / Multiple Detection Channels

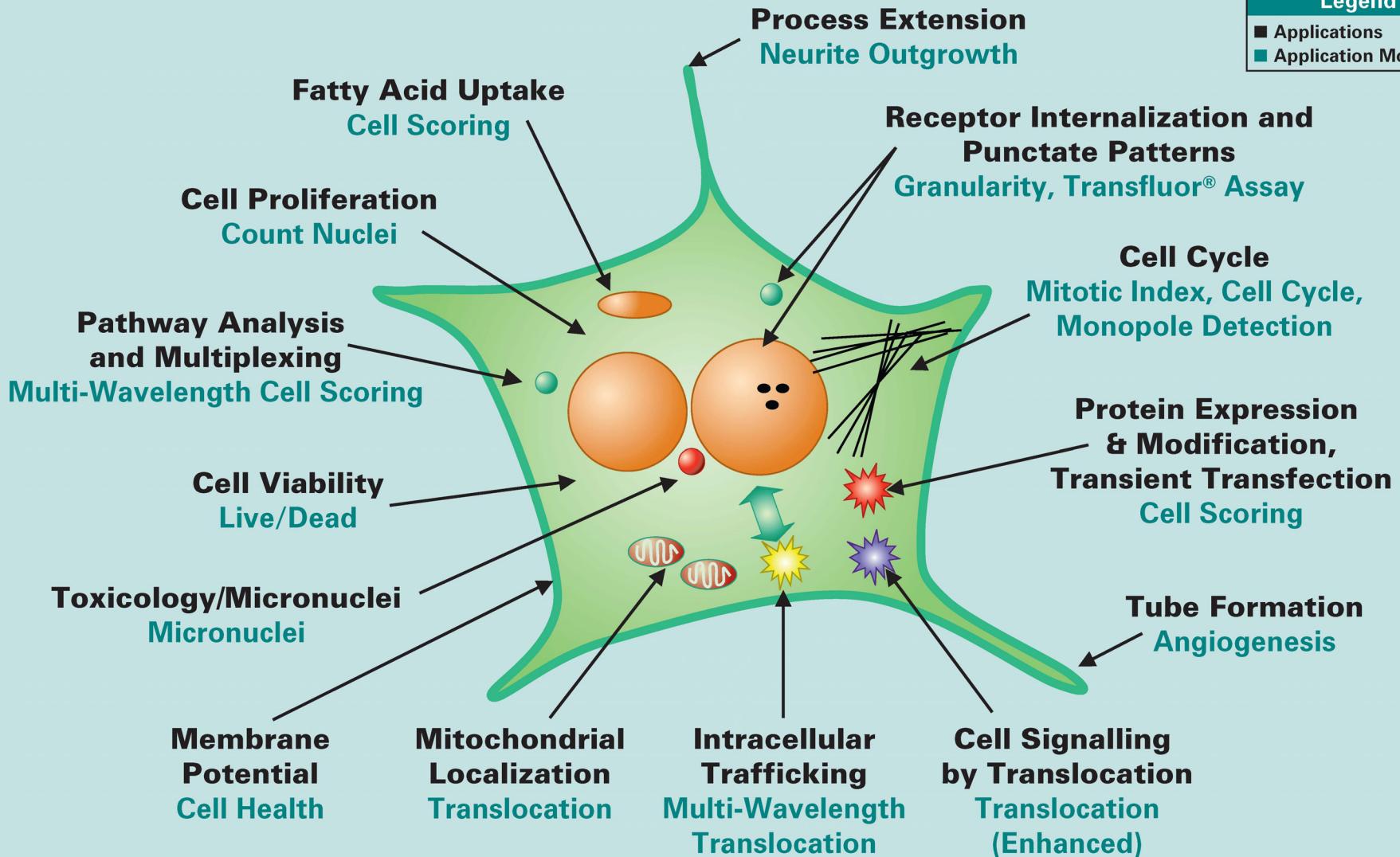
- Only requires one wavelength (nuclear stain)
 - Reduces sample preparation, image acquisition and analysis time
 - 4 additional probes (Apoptosis, Necrosis, and +2 custom)
- Segmentation and classification of multi-nucleated cells is highly accurate
 - Proprietary algorithm
 - Discriminate phenotypes based on Cell Morphology, Mono-nucleated, Bi-nucleated or Multi-Nucleated Cells, Distance of Micronuclei from Nucleus, Micronuclei vs. “Blebs” or “buds”
 - Area and intensities for all probes
- Run analysis
 - On-the-fly cell counting
 - MetaXpress® PowerCore™ compatible
- Multi-parametric analysis, data mining and QC performed with AcuityXpress
 - 68 parameters per image
 - 30 parameters per cell



Application Modules for Hundreds of Assays

Easy Custom Analysis with Journaling

Legend
■ Applications
■ Application Modules



The Solution for High-speed Image Analysis



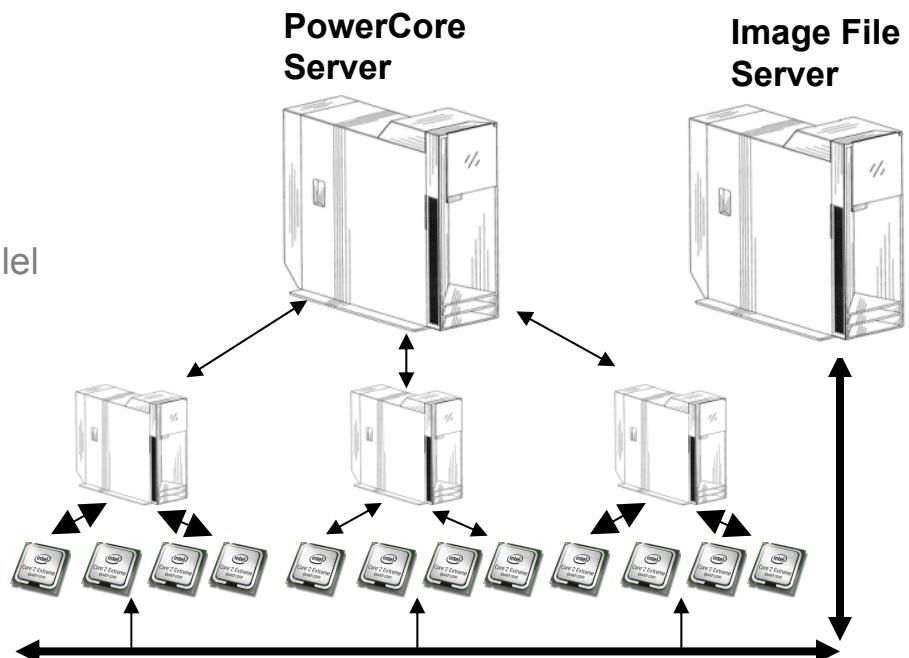
- MetaXpress® PowerCore™ Software
- Integrates seamlessly into existing environment
- The Power of Parallel Processing
 - Remove analysis bottleneck: Faster than image acquisition
 - License the power required
 - Process data in minutes a plate
 - Modified Analysis Settings? Quickly reanalyze entire screens



MetaXpress® PowerCore™



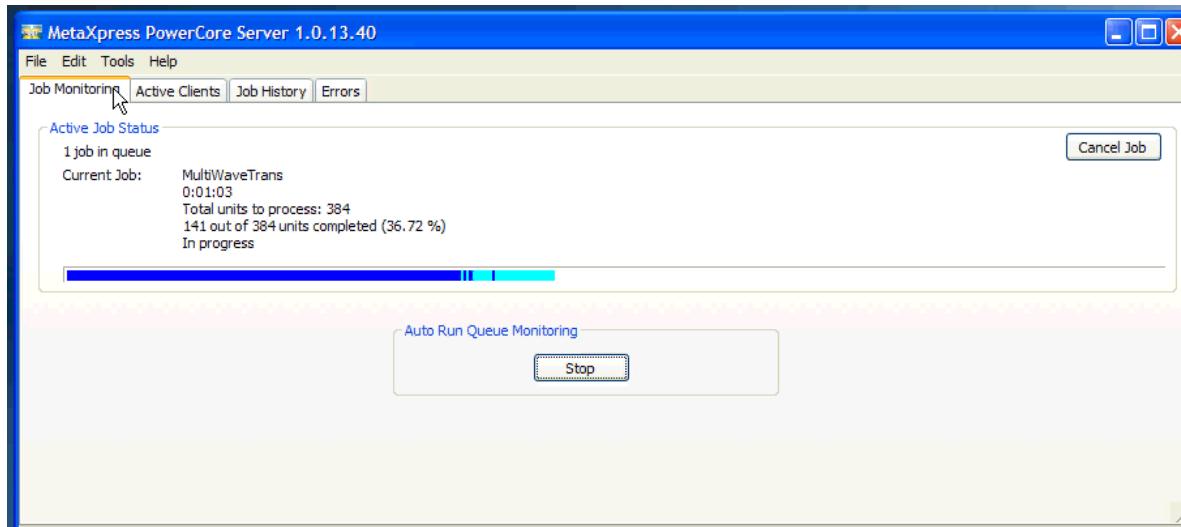
- MetaXpress application modules are intuitive and easy to use
- Increasing 5-10 times the speed of analysis with MetaXpress
 - Analysis speed ~ acquisition speed
- Increasing 10-50 times
 - Enables High-throughput Imaging (HTI)
 - Multiple ImageXpress® systems in parallel



High Throughput Image Analysis



- High Throughput Imaging
 - Image analysis faster than acquisition
- 3 color HCS assay: 1,152 images (384 wells)
 - ~ 25 minutes on ImageXpress (Micro/Ultra)
 - Multi wavelength Translocation Application module
- MetaXpress® PowerCore™ distributed analysis to multiple CPUs
 - ~ 1 hour on a single copy of MetaXpress
 - ~ 2 minutes with 32 CPUs and MetaXpress® PowerCore™
 - ~ 4 min with 16 CPUs
 - ~ 8 min with 4 CPUs



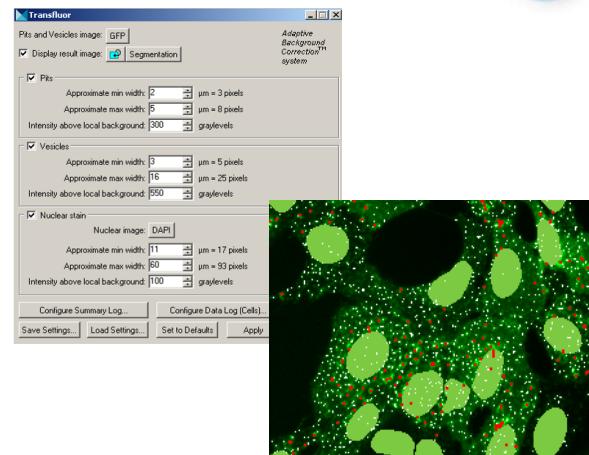
New for 2010

- Hardware

- ImageXpress® Micro External Filter Wheel
 - Expand number of filter combinations and probes
 - Ratio Imaging
 - Multi-pass filters for speed and image registration

- Software

- ImageXpress® PowerCore™ Image Processing software
 - Dramatically improved image analysis speed
 - Improves workflow for large screens
 - Re-analyze large datasets easily
 - MetaXpress® 3.0/3.1
 - Laser Autofocus Wizard
 - Micronuclei Application Module
 - Many new features from MetaMorph 7.6 backbone
 - MDCStore Tools Database Utility
 - Vista 64-bit Support (Offline only)
Significant performance boost



New for 2010

- Complete Solution Collaborations

- Third Party “Inter-operability”
- Customer driven
- MDCStore™ API Access and Licensing
- De Novo FCS Express Software
 - Analysis and reporting for IsoCyté data
- Adtech Global Solutions
 - Compute, Storage and IT Professional Services



Introduction to Adtech Global Solutions



- **Company Overview**

- Founded: 1999
- Global Sales: Over \$50 million
- Headquarters: Atlanta, Georgia
- 45,000 Square Foot Facility
- Employees: 125 worldwide
- Locations: Atlanta, Hong Kong, London, Sydney
- Long-Term Partnerships; First customers still with AGS.
- Over 1500 customers in 20 countries
- Privately held, profitable since inception.



*Large enough to be a major player in the industry,
small enough to roll out the red carpet to our
partners.*



Global Presence: Locations



World Headquarters - Atlanta



International Headquarters - London



Hong Kong



Sydney

Adtech Global Solutions & Molecular Devices

- Enhance Complete Solution with a Global Service Partnership
- Compute, Storage, Integration, and Support Options
 - Existing and new customers
 - Consulting
 - Facilities infrastructure design
 - Database installation and optimization
 - MetaXpress® PowerCore™ Software installations
 - Hardware configurations validated for Molecular Devices HCS Software
 - Global coverage



Atlanta Hong Kong London Sydney



now part of MDS Analytical Technologies

- More information available at the Molecular Devices Booth
 - Hardware Configurations
 - Support Options
 - MetaXpress® PowerCore™ Software Demo



Base Hardware Configurations



➤ HCS Quest 32/64

The ideal image and **data analysis workstation for the scientist or lab manager** wishing to take full advantage of the functionality of the MetaXpress® and AcuityXpress™ software.

- Single workstation validated for optimal performance of the MetaXpress and AcuityXpress software.
- Includes latest computing technologies such as Intel© Xeon© 3400 Series Processor, up to 8 GB of DDR3 Memory, and up to 4 hot-swappable hard drive disks.



➤ HCS Research 10 (Small Research / Screening lab)

- 1 Imaging System
- Mostly research
- 500GB/year

Designed for the **integration in a small research HCS lab with limited IT and database administration** capabilities, HCS Research 10 is about focusing on the biology and enjoying the speed of analysis and solution reliability without the issues of a complex infrastructure.

- Complete hardware solution for image analysis and image data management.
- Validated for optimal performance of the MetaXpress software, the MetaXpress® PowerCore™ software and the MDCStore™ database and file storage solution.
- Extensive support options and database services to help simplify your analysis
- Features include the latest computing technologies such as Intel© Xeon© 5500 Series Processor, up to 16 GB, DDR3 Memory, and up to 8 hot-swappable hard drive disks .
- *Also available in a rack mounted or desktop version.*



Base Hardware Configurations



➤ HCS Screen 10 (Small Screening lab)

- 1 Imaging System
- 2-3 Screens/year
- 1-5 TB/year



Tailored with speed of analysis ***HCS Screen 10 is the perfect solution for HCS screening labs generating 5 to 10TB of data from several 10-20,000 compounds/treatment screens per year.***

With HCS Screen 10 quickly implement your HCS environment and run your screens without worrying about downtime

- Turnkey appliance for HCS at medium throughput
- Easy to install and integrate
- Validated for best performance of the MetaXpress software, the MetaXpress® PowerCore™ software and the MDCStore™ database and file storage solution.
- Extensive support and training options
- Features include the latest computing technologies such as the Intel© Xeon© 5500 Series Processor, up to 16 GB, DDR3 Memory, and up to 8 hot-swappable hard drive disks.

Base Hardware Configurations



➤ HCS Core 10 (Core Facility lab)

- 2 Imaging Systems
- Multiple screens/ year
- Generate 100 GB/day 5 days a week (500 GB/week; ~10-20 screens)
- Multiple databases and file storage locations



HCS Core 10 is designed for the life sciences research organization that serves multiple users, and desires scalability, efficiency and ultimate flexibility in applications. ***Best suited for high capacity or multi-user core lab environment, HCS Core 10 is the ultimate tool for HCS Research and screens.***

➤ HCS HTI 10 (High Throughput Screening facility)

- 2+ Imaging Systems in screening mode
- Large number of screens /year
- Generate 200GB/day 5 days a week (1 TB/week; ~ 50 TB/year)
- Few databases and file storage locations



The ultimate, customizable solution when speed of analysis, scalability are critical to an entire organization. Designed for High Throughput Imaging (HTI), that the HCS HTI 10 solution is ideal for organizations undertaking large screening campaigns under pressure to move from one screen to the next. Rapid escalation and troubleshooting procedures are key elements of this solution that moves beyond powerful hardware with the ultimate level of service.

Summary



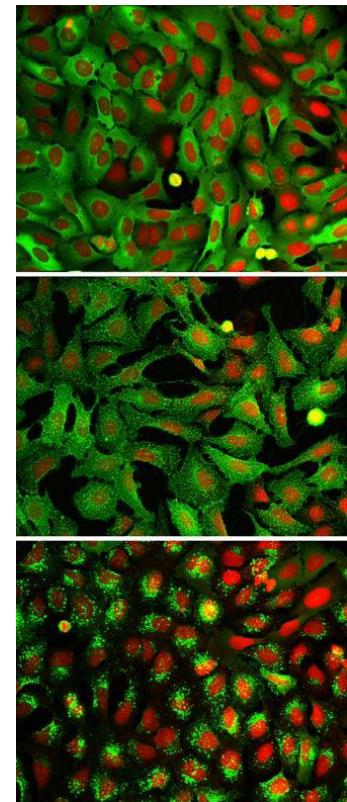
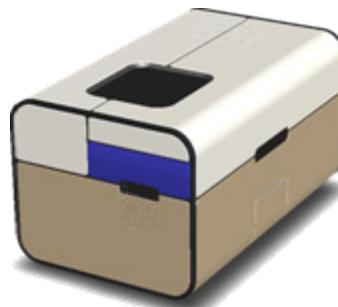
- Molecular Devices Complete Imaging Solution Platform
 - Flexible
 - Multiple imaging modalities with many additional options
 - Turn-key and customer image analysis
 - Ease of Use
 - MetaXpress® with Application Modules and Macro capability
 - Stand alone capability of IsoCyte
 - Third party analysis software access
 - Scalable
 - MDCStore Data Management Solution
 - Multiple instrument configurations
 - MetaXpress® PowerCore™ Software
 - Addressing infrastructure bottlenecks
 - Compute, Storage and Data management partnerships
 - Adtech Global Solutions

HIGH-CONTENT ANALYSIS

JANUARY 11-15, 2010 THE FAIRMONT HOTEL • SAN FRANCISCO, CALIFORNIA

Thank-you!

- Enjoy the Meeting!
- Molecular Devices Booth
 - ImageXpress® Ultra
 - ImageXpress® PowerCore with Adtech Hardware
 - Adtech Global Team
 - Sales, Marketing and FAS to answer questions



END

