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HIGH-CONTENT ANALYSIS

COVERAGE INCLUDES:

Compound Screening
HCA of Stem Cells
Data Analysis and Management
Image Analysis
Live-Cell Imaging
New Biological Models
Flow Cytometry
Novel Probes and Biosensors
siRNA Screening
Pathway Analysis
Toxicity Profiling
Neuronal Screening

THE ORIGINAL HCA EVENT

JANUARY 12-15, 2010

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CONFERENCE-AT-A-GLANCE

MONDAY, JANUARY 11			
8:30 - 9:00 am	Registration for the Advanced Course and Morning Coffee		
9:00 am - 5:00 pm	Pre-Conference Advanced High-Content Analysis Course (Separate Registration R0equired)		
TUESDAY, JANUARY 12			
7:45 am -2:00 pm	Thermo Scientific User Group Meeting		
2:30-6:30 pm	GE Healthcare User Group Meeting		
2:00-7:00 pm	Molecular Devices User Group Meeting		
5:00-7:00 pm	Conference Pre-Registration		
7:00-9:00 pm	Evening Reception in the Penthouse Suite	*Sponsored by* GE Healthcare	
WEDNESDAY, JANUARY 13			
7:00-8:00 am	Conference Registration and Morning Coffee		
8:00-8:10 am	Opening Remarks		
8:10-8:15 am	Introduction from Executive Sponsor Thermo Scientific		
8:15-9:15 am	Panel Discussion with End-Users and Vendors		
9:15-10:30 am	Coffee Break with Exhibit and Poster Viewing		
10:30 am -12:15 pm	HCA of Stem Cells	Image Analysis	Flow Cytometry
12:15-2:00 pm	Luncheon Technology Showcase: High-Content Screening	Luncheon Technology Showcase: High-Content Data Analysis	
2:15-3:35 pm	HCA for Compound Screening	Data Analysis and Management	Live-Cell Imaging
3:35-4:45 pm	Refreshment Break with Exhibit and Poster Viewing		
4:45-6:00 pm	HCA for Compound Screening	Data Analysis and Management	Live-Cell Imaging
6:00-7:00 pm	Reception with Exhibit and Poster Viewing		
THURSDAY, JANUARY 14			
7:30-8:15 am	Breakfast Presentation Sponsored by PerkinElmer	Breakfast Presentation (Sponsorship Available)	
8:30-9:30 am	ThinkTank Roundtable Discussions		
9:30-10:00 am	Reports from ThinkTank Roundtable Discussions		
10:00-10:30 am	Award Presentations		
10:30-11:30 am	Coffee Break with Exhibit and Poster Viewing		
11:30 am -1:10 pm	Novel Fluorescent Probes and Biosensors	New Biological Models for HCA	
1:10-2:00 pm	Lunch on Your Own		
2:00-6:00 pm	PerkinElmer User Group Meeting	BD Biosciences User Group Meeting	
FRIDAY, JANUARY 15			
7:30-8:15 am	Breakfast Presentation (Sponsorship Available) or Morning Coffee		
8:30-9:55 am	HCA for siRNA Screening	HCA for Toxicity Profiling	
9:55-10:20 am	Networking Coffee Break		
10:20-12:00 pm	HCA for Pathway Analysis	Neuronal Screening	
12:00 pm	Close of Conference		

MONDAY, JANUARY 11

Pre-Conference Advanced High-Content Analysis Course

(Separate Registration Required)

Visit www.HighContentAnalysis.com for more information.

8:30-9:00 **Registration for the Advanced High-Content Analysis Course and Morning Coffee**

9:00-10:00 **HCA Instrumentation: Planning, Procurement and Set-Up**
Anthony Davies, Ph.D., Director, High-Content Research Facility, Clinical Medicine, Trinity College, Ireland

10:00-10:30 **Assay Miniaturization Strategies: Smaller and Cheaper Cell-Based Assays for HCA**
Anthony Davies, Ph.D., Director, High-Content Research Facility, Clinical Medicine, Trinity College, Ireland

10:30-11:00 **Networking Coffee Break**

11:00-12:30 **Data Analysis and Management**
Karol Kozak, Ph.D., Head, Computation Analysis, HCA/HTS Informatics, LMC-RISC, Institute for Biochemistry

12:30-2:00 **Lunch on your own**

2:00-3:30 **HCA/HCS Assay Development**
Paul A. Johnston, Ph.D., Research Associate Professor, Pharmacology & Chemical Biology, University of Pittsburgh School of Medicine

3:30-4:00 **Networking Refreshment Break**

4:00-5:00 **Discussion with all Participants**
Moderator: Anthony Davies, Ph.D., Director, High-Content Research Facility, Clinical Medicine, Trinity College, Ireland

TUESDAY, JANUARY 12

7:45-2:00 **Thermo Scientific User Group Meeting**

Thermo SCIENTIFIC

2:30-6:30 **GE Healthcare User Group Meeting**

GE Healthcare

2:00-7:00 **Molecular Devices User Group Meeting**

Molecular Devices

Special User Forum – Flexibility and Speed: The MDS Analytical Technologies Complete Solution for Cellular Imaging

MDS Analytical Technologies will host a HCS/HCA imaging forum during the High-Content Analysis Conference on Tuesday, January 12, 2010. Attendees will get an in-depth look at MDS Analytical Technologies' Complete Imaging Solution. End-users and MDS experts will highlight recent developments in hardware and software components, illustrating how they improve application flexibility and total workflow speed. In addition, researchers will share their experiences with implementing these imaging technologies and our unique cellular informatics solutions. Finally, a series of presentations will showcase new applications as well as the integration of the imaging systems into their facilities and workflow. The forum is open to both existing and potential new users.

Reservations: There is no charge to attend the forum, but space is limited. To reserve your seat, please RSVP to Candace.Anderson@moldev.com who will be happy to register you for this event.

5:00-7:00 **Conference Pre-Registration**

7:00-9:00 **Evening Reception in the Penthouse Suite**

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WEDNESDAY, JANUARY 13

7:00-8:00 Conference Registration and Morning Coffee

8:00-8:10 Welcoming Remarks from Conference Director

Julia Boguslavsky, Cambridge Healthtech Institute

8:10-8:15 Introduction from Executive Sponsor Thermo SCIENTIFIC

Jeff Haskins, Ph.D., Product Line Director, Cellular Imaging & Analysis, Thermo Fisher Scientific

8:15-9:15 Panel Discussion with End-Users and Vendors

Discussion Questions Include:

- What new applications and image analysis tools are expected to be launched in 2010?
- What is the progress on imaging standards?
- How is the need for new probes and protein-protein interaction imaging tools addressed?
- What are the new application areas undergoing rapid adoption?

9:15-10:30 Coffee Break with Exhibit and Poster Viewing

HCA OF STEM CELLS

10:30-10:35 Chairperson's Opening Remarks

10:35-11:00 High-Content Imaging in Oncology Discovery: Identification and Characterization of Novel Targets in Cancer Stem Cells

Jonathan Low, Ph.D., Post-Doctoral Scientist, Cancer Cell Growth and Survival, Lilly Corporate Center

Although the cycling of eukaryotic cells has long been a primary focus for cancer therapeutics, recent advances in imaging and data analysis allow even further definition of cellular events as they occur in individual cells and cellular subpopulations in response to treatment. High-content imaging (HCI) has been an effective tool to elucidate cellular responses to a variety of agents, however, these data were most frequently observed as averages of the entire captured population, unnecessarily decreasing the resolution of each assay. Here we dissect the eukaryotic cellular subpopulations in response to treatment using HCI in conjunction with unsupervised K means clustering. We first generate distinct phenotypic fingerprints for each major cell cycle and mitotic compartment and use those fingerprints to characterize chemotherapeutic agents. We determine that the cell cycle arrest phenotypes caused by these agents are similar to, though distinct from, those found in untreated cells both *in vitro* and *in vivo*, and that these distinctions frequently suggest the mechanism of action. Further, we demonstrate the power of this technique to identify novel targets and detect the differential effects of target knockdown on cancer stem cells through the use of shRNA libraries. High-content data are then integrated with additional discovery tools to link phenotypic changes with cellular pathways. HCI analysis of imaging data, obtained from individual cells under all of these research conditions, grouped into cellular subpopulations, and multiplexed with additional tools represents a powerful method to discern both cellular events and treatment effects.

IMAGE ANALYSIS

10:30-10:35 Chairperson's Opening Remarks

10:35-11:00 Quantifying Challenging Phenotypes in Images

Mark-Anthony Bray, Ph.D., Computational Biologist, Imaging Platform, Broad Institute

Many challenging image-based phenotypes have recently become quantifiable due to advances in image analysis and machine learning algorithms. Our recent work in the area has enabled high-content analysis of phenotypes relevant to multiple basic biological processes and clinically relevant diseases. For example, our recent work has enabled screens of phenotypes in physiologically relevant co-culture systems, where cell types with diverse morphologies are present in each sample. The variety of phenotypes that can be accurately quantified using software continues to grow.

11:00-11:25 Quantitative Analysis of High-Content Screens: How Can Machine Intelligence Help?

Peter Horvath, Ph.D., Image Processing Scientist, Light Microscopy Centre, ETH Zurich

Accurate quantitative analysis is essential for high-content screens. We will show cell-based classification with machine learning techniques. A novel semi-supervised learning-based method will be presented to speed up the learning process with orders of magnitude. Finally, we will present new machine intelligence methods for accurate quality control.

11:25-11:50 Application of Pattern Recognition to Image-Based Small Molecule Screening Data for Phenotypic Analysis

John McLaughlin, Ph.D., Scientist & Manager, Biology, Rigel Pharmaceuticals, Inc.

This presentation will describe an image based phenotypic screen for AuroraB Kinase inhibitors that we have developed, which lead to the discovery and subsequent development of a small molecule R763/AS703569 currently in clinical trials for cancer. This screen is a proliferation type

FLOW CYTOMETRY

10:30-10:35 Chairperson's Opening Remarks

10:35-11:00 Implications of High-Throughput Flow Cytometry on Drug Discovery

J. Paul Robinson, Ph.D., SVM, Professor, Cytomics & Deputy Director, Bindley Bioscience Center, Cytomics & Imaging, Purdue University

The time has come for high-content tools such as flow cytometry to also move into the high-throughput domain. This requires both hardware and software changes. It is not easy to move a technology that has a 40-year history of operating under the same conditions, to change its basic operational rationale. However, that is happening. One of the major changes is the radical change in analytical tools becoming available. This presentation will outline these recent tool-sets that will transform the field of flow cytometry.

11:00-11:25 Phospho Flow Cytometry in Drug Discovery: From Screening to Clinical Trials

Peter Krutzik, Ph.D., Senior Scientist, Baxter Lab in Genetics Pharmacology, Microbiology & Immunology, Stanford University

Flow cytometry is a powerful tool for analyzing 10 or more parameters at the single cell level. Recently, the use of phospho-specific antibodies has allowed us to measure intracellular signaling events in addition to classical surface markers. This enables us to analyze kinase signaling cascades in complex primary cell populations such as human peripheral blood. Using phospho flow, we performed a small molecule drug screen in primary cells, in both 96 and 384 well format, to search for inhibitors of immunological pathways. The screen yielded pathway- and novel cell type-specific inhibitors of cytokine-induced type-specific inhibitors of cytokine-induced Jak-Stat signaling. The method was used both *in vitro* and *in vivo* to confirm drug activity. To improve sample throughput, we employed Fluorescent Cell Barcoding (FCB), a multiplexing method that enables combination of samples prior to antibody staining. We will also discuss preliminary work in automating the phospho flow method for large scale screening projects.

11:00-11:25 Characteristics and Re-Programming of Breast Cancer Stem Cells

Fredika M. Robertson, Ph.D., Professor, Department of Experimental Therapeutics; Director, Translational Research, The Morgan Welch Inflammatory Breast Cancer Research Program, The University of Texas M.D. Anderson Cancer Center

Very aggressive tumor types contain a high percentage of cells defined as cancer stem cells (CSCs) with characteristics similar to those of embryonic stem cells including a slow turnover time that can be imaged and quantitated by their retention of the nucleoside analog ethynyl deoxyuridine (EDU). CSCs form 3-dimensional (3D) tumor spheroids that differentially express specific surface markers including stage specific embryonic antigens 1 and 4 (SSEA1/4), CD133, and CD44+/CD24-/low. CSCs have characteristic patterns of gene expression of molecules in signaling pathways that regulate survival, self-renewal, pleuripotency, and multi-drug resistance. Agents that can either stimulate the normally quiescent CSCs to re-enter the cell cycle or agents that target transcription factors regulating self renewal and survival result in re-programming CSCs for their elimination. The effects of exposure to these agents that can re-program activities of CSCs will be discussed in the context of image-based analysis.

11:25-11:40 Title to be Announced

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GE Healthcare

11:40-11:55 Technology Presentations

Sponsorships available. Contact Katelin Fitzgerald, Manager, Business Development, at 781-972-5458 or kfitzgerald@healthtech.com.

11:55-12:20 A Chemical Approach to Controlling Stem Cell Fate

Sheng Ding, Ph.D., Assistant Professor, Chemistry, Scripps Research Institute

Recent advances in stem cell biology may make possible new approaches for the treatment of a number of diseases. A better understanding of molecular mechanisms that control stem cell fate as well as an improved ability to manipulate them are required. Toward these goals, we have developed and implemented high throughput cell-based phenotypic screens of arrayed chemical and gene libraries to identify and further characterize small molecules and genes that can control stem cell fate in various systems. This talk will provide latest examples of discovery efforts in my lab that have advanced our ability and understanding toward controlling stem cell fate, including self-renewal, survival, differentiation and reprogramming of pluripotent stem cells.

assay in which cancer cell lines are treated with small molecules for 48hrs then fixed and stained for the presence of DNA and Actin. We create training sets from treatments with control compounds and use them to create support vector machine classifiers that are subsequently used to mine our data for interesting phenotypes in addition to AuroraB. Our large annotated data set with many well-characterized controls has provided an excellent opportunity to validate and improve the predictive capabilities of the classifiers. Various strategies for increasing training set robustness have demonstrated an impressive ability to productively mine screening data collected on a weekly basis over many years. We have found that pattern recognition can significantly enhance and speed attempts to quantify what are often overwhelmingly large and complex image data sets produced by image-based screening.

11:50-12:15 High-Performance Image Analysis for High-Content Screening

Dadong Wang, Ph.D., Stream Leader, Biotech Imaging, CSIRO

Large image datasets and fast turnaround requirements have made efficient High Content Screening (HCS) a challenging task. With the enormous progress in high performance computing, computers with multi-core CPUs have become standard and GPUs are being used more widely in data and compute-intensive environments. This talk will report some of our studies in high performance image.

11:25-11:50 High-Content High-Throughput Flow Cytometry for Small Molecule Discovery

Eric Prossnitz, Ph.D., Professor, Cell Biology and Physiology, University of New Mexico

The University of New Mexico Center for Molecule Discovery continues to innovate in the application of the HyperCyt flow cytometry platform for high-content high throughput small molecule discovery. The platform is evolving for 1536 well plates and direct sample delivery. Recently, we have demonstrated HTS applications with primary cells and yeast multiplex model systems for TOR pathway analysis, as well as innovative molecular assays for intracellular trafficking pathways. The flow cytometry platform is well-suited to fill a unique niche in small molecule identification for cell and molecular assays in suspension, especially in complex cell suspensions for primary cells, hematopoietic stem cells, and leukemia.

11:50-12:15 SERS Cytometry for High Content Analysis: More Parameters for Less

John P. Nolan, Ph.D., Professor, La Jolla Bioengineering Institute

Fluorescence methods dominate the field of cytometry, providing sensitive and quantitative measurements of molecules, cells, and other particles. In flow cytometry especially, multiple light sources, filters and detectors enable as many as 20 different fluorescence probes to be detected and measured simultaneously and rapidly on individual cells. However, this requires the use of multiple lasers and fluorophores with emission spectra that fill the optical spectrum from the UV to the near IR, and significant increases in this number are unlikely with existing light sources, fluorophores, and detectors. To make more efficient use of this spectral range, we have developed instruments and probes that take advantage of surface-enhanced Raman scattering (SERS). SERS occurs at the surface of metal nanoparticles and offers sensitivity comparable to fluorescence, but with much more efficient use of the optical spectrum, providing the potential of hundreds of tags to be resolved with a single laser line and less than 100 nm of spectral space. We use nanoparticle probes with distinctive SERS spectra functionalized with antibodies or other targeting molecules to measure multiple targets simultaneously. Raman flow cytometers use spectrographs and array detectors to measure high resolution SERS spectra from hundreds of individual particles per second. Simultaneous Raman and fluorescence flow cytometry provide the best of both worlds, with fluorescence measurements of both functionally and antigenic markers combined with very highly multiparameter measurements of antigens or other targets.

LUNCHEON TECHNOLOGY SHOWCASE: HIGH-CONTENT SCREENING

12:30-1:00 Improved Speed and Applications Flexibility for High-Content Screening: The MDS Complete Imaging Solution for HCS

Sponsored by Molecular Devices

Michael Sjaastad, Ph.D., Director, Marketing, Cellular Imaging, MDS Analytical Technologies

Speed and application flexibility allow researchers to process more compounds in high-content screens while maintaining the data quality and content achieved using traditional microscopy. MDS Analytical Technologies offers a Complete Imaging Solution for HCS to seamlessly acquire, analyze and identify compounds for hit selection. Three choices in instrumentation provide a range of image resolution and speed for all HCS applications. Turnkey image analysis modules enable hundreds of specific assays while proprietary parallel processing software now accelerates image analysis many fold. These new capabilities improve workflow and accelerate hit identification. We will present examples of the Complete Imaging Solution for HTS used for confocal imaging campaigns, object based image screens at 5 minutes per 1536 well plate, and large organism screening of Zebrafish.

1:00-2:00 Technology Short Talks

Sponsorship available. Contact Katelin Fitzgerald, Manager, Business Development, at 781-972-5458 or kfitzgerald@healthtech.com.

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NEW DVD

ADVANCED HIGH-CONTENT ANALYSIS COURSE

Recorded at High-Content Analysis East, September 22, 2009

Part 1: Setting up the HCA Lab
Anthony Davies, Ph.D., Director, High-Content Research Facility, Clinical Medicine, Trinity College, Ireland

Part 2: Instrumentation: Choosing the Right Platform
Anthony Davies, Ph.D., Director, High-Content Research Facility, Clinical Medicine, Trinity College, Ireland

Part 3: Assay Development
Ann F. Hoffman, Senior Principal Scientist, Roche Discovery Technologies

Part 4: Data Analysis and Management
Karol Kozak, Ph.D., Head, Computation Analysis, HCA/HTS Informatics, LMC-RISC, Institute for Biochemistry

NEW HCA WEB SYMPOSIA

1. PRE-CONFERENCE HCA WEB SYMPOSIUM Sponsored by Molecular Devices

2. CHARACTERIZATION OF STEM CELLS USING HIGH-CONTENT IMAGING AND FLOW CYTOMETRY

Visit HighContentAnalysis.com for program details and additional Web Symposia.

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Program Suggestions: Contact Julia Boguslavsky, Executive Director, Conferences, at juliab@healthtech.com.

LUNCHEON TECHNOLOGY SHOWCASE: HIGH-CONTENT DATA ANALYSIS

12:30-12:45 Intelligent Assay Development: Removing the Bottlenecks Using iDEV™ Software

Sponsored by Thermo Scientific

Scott Keefer, MBA, Product Manager, Thermo Fisher Scientific

Rapid, robust, in depth image analysis is the key to researchers productivity in high content., yet developing assays for vast range of biologies, from simple translocations, through complex morphological phenotypes to whole organisms such as Zebrafish, remains a bottleneck for many researchers. The Thermo Scientific iDEV software combines our BioApplication image analysis power with the latest innovations in software to provide a simple workflow that guides assay development in the most efficient manner possible, even for someone new to image analysis and high content. We will demonstrate this new innovation and show how even the most complex biologies can be quickly and comprehensively analyzed, in minutes

Sponsored by GE Healthcare

12:45-1:00 Title to be Announced

1:00-1:15 Beyond Basic HCS Data Management: Learning, Modeling, and Advanced Data Analysis using Pipeline Pilot

Sponsored by accelrys®

Kurt Scudder, Ph.D., Solution Scientist, Accelrys

Accelrys' Pipeline Pilot has found a place in the labs of many HCA practitioners, taking advantage of the image analysis, statistics, and plate data handling collections in the product. The toolbox approach allows developers and users to envision a way to analyze or visualize data, then rapidly construct one or more protocols to enable that vision. This approach complements and extends the HCS instrument vendors' data management and analysis software. Accelrys has facilitated this by building into Pipeline Pilot connectivity to the data management systems from most major HCA vendors such as Cellomics, GE Healthcare, BD Bioscience, PE, Molecular Devices, and Beckman-Coulter. This capability can now be combined with the learning and advanced data modeling capabilities in Pipeline Pilot to move beyond simple HCS analysis and data management into more detailed examination of images and extracted data, and examination of the data for latent patterns or characteristics which can give new insights. All of this can be done while remaining within the Pipeline Pilot environment. Examples of the application of advanced data modeling with images and image objects will be presented.

1:15-1:30 High-Content Hit Selection Based on Single-Cell Data–Leveraging Rich Biological Outcomes with Extreme Efficiency

Sponsored by Genedata

Stephan Heyse, Ph.D., Head, Genedata Screener, Genedata AG

High-content screening experiments produce rich information on phenotypic changes of individual cells when subjected to treatment with compounds, siRNAs, or other inducers. While the management of the resulting microscope images is the current concern, upcoming challenges are the biologically meaningful representation and quantification of HCS outcomes. This includes distinguishing cell sub-populations of differential response, statistically aggregating them across wells and replicates, normalizing signals and eliminating errors, separating and quantifying phenotypes and effects. Leveraging this information from the complex single-cell data sets, with millions of data points per plate, requires a scalable framework with automated data processing and intelligent management functions, including scientists' review at any stage of the process. Taking examples from large siRNA and compound screens, we show how such systematic in-depth analysis of high content screens can be accomplished routinely, passing from single-cell data to hit selection in a highly efficient workflow.

1:30-2:00 Technology Short Talks

Sponsorship available. Contact Katelin Fitzgerald, Manager, Business Development, at 781-972-5458 or kfitzgerald@healthtech.com.

HCA FOR COMPOUND SCREENING

2:15-2:40 Whole Library Screen by Utilizing Fully Automated High-Content Analysis Approach

Stefan Prechtl, Ph.D., Team Leader, High-Content Analysis, Bayer Schering Pharma AG

HCA technology has extended the ability of researchers to identify and quantify compound effects on a number of cellular events allowing the rapid screening of chemical libraries. The recent developments have enabled scientists to analyze intracellular signaling pathways and physiologically relevant events using fully automated approaches. In this way, High-Content Screening represents drug screening in a more appropriate physiologically context. Here, we present data from our whole library screen that we have performed with optimally selected HCA tools providing a reliable environment to perform a primary Ultra-HCS campaign.

2:40-3:10 Phenotypic High-Content Screens Utilizing Multi-Parametric Data Analysis for Novel Lead Identification

Daniela Gabriel, Ph.D., Associate Director, Lead Finding Platform, Novartis Institutes for Biomedical Research

High-content screening (HCS) applications allow the characterization of novel compounds in a cellular environment. Generally compound dependent effects are analyzed with regard to target specificity whereas a great potential of HCS is the analysis of cellular phenotypes by generation of multidimensional readouts of cellular effects in response to compound treatment. Multivariate statistics provide a range of data reduction and classification tools to not only identify hits but also to classify the compound's effect and to consider different responses in subpopulations. Utilizing multivariate analysis of phenotypic profiles enhances the potential of hit discovery in small molecule screening and help classifying hits for target identification. The rationale behind this strategy will be illustrated with screening examples.

3:10-3:35 Combining High-Content and High-Throughput Screening

Claudine Grepin, Ph.D., Head, Lead Discovery Technology, Sanofi-Aventis Pharma R&D, France

Accurate prediction of human responses to potential drugs is often unreliable and leads to a high attrition rate in development. One of the strategies implemented to increase the chance of isolating the best chemical matter as early as possible during the drug discovery process is to implement cell-based screens, which address targets and compounds in a more physiological context. High-Content Analysis assay formats are examples of those cellular assays that provide accurate and relevant multiple parameter information from a unique experiment. The presentation will focus on a few selected examples where High-Content Screening has been scaled up to High-Throughput Screening to facilitate the decision on compound progression thanks to the wealth of data generated. The added value and lessons learned will be discussed.

DATA ANALYSIS AND MANAGEMENT

2:15-2:40 Patches and Batches: New Approaches to Analyzing Drug Effects on Subcellular Patterns

Robert F. Murphy, Ph.D., Professor, Departments of Biological Sciences and Biomedical Engineering, Carnegie Mellon University

A critical task that is addressed by high-content screening and analysis is learning the effects of compounds (e.g., drug candidates) on the localization of targets (e.g., proteins). This is usually performed by exhaustive analysis of many compounds on one protein, a process that is repeated for the next drug. I will describe methods for learning the dependency of many proteins on many compounds without such exhaustive analysis.

2:40-3:10 Multivariate Characterization of High-Content Data for Relevant Phenotypic Change in Type II Diabetes Screening

Sponsored by BD

Jonathan Z. Sexton, Ph.D., Assistant Professor, Biomanufacturing Research Institute and Technology Enterprise (BRITE), North Carolina Central University

Current fluorescent probe technology and increased multiplexation in HCS can result in an overwhelming array of cellular data. The characterization of subtle phenotypic changes can be challenging and resulting phenotypic endpoints are often non-obvious. Phenotypic change must then be reported back to an information management system for registration of biological data with chemical structures. Here we present an automated method for the discovery of relevant phenotypic change through multivariate analysis of preliminary HCA data in the assay development phase to guide discovery in large scale screening efforts, including (1) How to use multivariate techniques to discover meaningful phenotypic change; (2) Reduction of primary screening data to facilitate the merging of biological data with chemical information for hit triage and prioritization in data management systems; (3) Tools for developing a high content screening information pipeline.

3:10-3:35 Multilayered Analysis of HCS Data: An Integrated Approach to Scientific Insight

Ansuman Bagchi, Ph.D., Director, Applied Computer Science & Mathematics, Merck & Co.

LIVE-CELL IMAGING

2:15-2:40 Quantitative 4D Live-Cell Imaging Reveals Regulation of Kinetochore Alignment within the Metaphase Plate

Jason Swedlow, Ph.D., Senior Research Fellow & Reader, Gene Regulation & Expression, University of Dundee

A hallmark of mitosis in most eukaryotic cells is the formation of a metaphase plate half-way between the spindle poles, about which chromosomes exhibit oscillatory movements. These movements are accompanied by changes in the distance between sister kinetochores, commonly referred to as 'breathing'. The relationships between oscillations, breathing, and formation of the metaphase plate, and the molecular components that regulate these processes, are poorly understood. We developed a four-dimensional imaging assay combined with computational image analysis that identifies and tracks sister kinetochores over time, classifies kinetochores as aligned or unaligned, and determines the mitotic phase of the cell. Our assay shows that late prometaphase and metaphase oscillation and breathing speeds are most sensitive to depletion of microtubule depolymerases, while oscillation and breathing periods are most sensitive to perturbations that alter the stiffness of the mechanical linkage between sisters. It also reveals that metaphase plates become thinner as cells progress towards anaphase, due to a progressive reduction in oscillation speed at constant oscillation period.

2:40-3:10 Technology Presentations

Sponsorships available. Contact Katelin Fitzgerald, Manager, Business Development, at 781-972-5458 or kfitzgerald@healthtech.com.

3:10-3:35 Live-Cell Imaging of Caspase Activation for High-Content Screening

Hakim Djaballah, Ph.D., Director, HTS Core Facility, Memorial Sloan Kettering Cancer Center

Caspases are central to the execution of programmed cell death and their activation constitutes the biochemical hallmark of apoptosis. No method currently available that allows continuous live-cell monitoring of caspase activation in high-content assays; which require amenability to high-density plate formats, live and continuous monitoring, and the fluorogenic reporter to be non-toxic and does not interfere with nor stimulate induction of apoptosis. My talk will focus on the adaptation of a high-content assay method utilizing the DEVD-NucView™ 488fluorogenic substrate that meet the required criteria, and for the first time, we show caspase activation in live cells induced either by chemicals or RNAi. I will present data on the adaptation, optimization and validation of the use of this substrate as a homogeneous, live assay reporter for monitoring real-time kinetics of induction of apoptosis in 384-well plates, and discuss its advantages for use in real time screening of chemical and RNAi libraries for the rapid identification of novel modulators of apoptosis; and discuss the merits of using this new high-content live cell assay to screen chemical or RNAi libraries.

3:35-4:45 Refreshment Break with Exhibit and Poster Viewing

4:45-5:10 HCS as a Key Technology in Primary and Secondary Screening

Oliver Poeschke, Ph.D., Senior Scientist, Assay Development, Biomolecular Pharmacology Lead Discovery, Merck Serono

HCS has evolved from a new technology into a powerful compound screening platform over the last years in our company. This is documented by a number of success stories, of which two case studies will be presented. I will describe how HCS enables the identification, characterization and chemical optimization of small molecules leading to *in-vivo* active compounds in the early drug discovery phase.

5:10-5:35 High-Content Screening of the NIH MLSMR Library

Susanne Heynen-Genel, Ph.D., Director, High-Content Screening Systems, Conrad Prebys Center for Chemical Genomics, Burnham Institute for Medical Research

The Conrad Prebys Center for Chemical Genomics (CPCCG) at the Burnham Institute for Medical Research is one of four comprehensive screening centers for the NIH Molecular Libraries Probe Production Centers Network (MLPCN, http://mli.nih.gov). While these comprehensive screening centers cover all aspects of small molecule library screening and probe development, CPCCG also specializes in high-content analysis and screening. Thus high-content assays against very diverse targets are being developed and screened at CPCCG. This presentation will describe some examples of the image-based assays and screens run against the NIH Molecular Libraries Small Molecule Repository (MLSMR) library including recently performed GPCR and lipid screens.

5:35-6:00 Automated High-Content Screening for Compounds That Disassemble the Perinucleolar Compartment (PNC)

Steve Titus, Ph.D., Staff Scientist, Biology, NIH Chemical Genomics Center

We have conducted an automated high-content screen using a collection of 140,000 small molecules to look for compounds which disassemble the PNC. The assay was conducted on an InCell 1000 imager in 1536 well format. From the 140,000 compounds screened, 120 hits were identified and ordered, and 91 confirmed activity. I will discuss the assay optimization, screen, and hit confirmation processes in detail.

4:45-5:10 The Role of Open Source in High-Content Screening Informatics

Karol Kozak, Ph.D., Head, Computation Analysis, HCA/HTS Informatics, LMC-RISC, Institute for Biochemistry

Its main strength – the high information content of the delivered data (images) – means at the same time a considerable challenge on the IT side. The aim of this presentation is to describe an open-source informatics platform for integrating, sharing and processing HCS data using a workflow-oriented architecture. This talk will focus on a platform that covers the whole process of a HCS screen, from the basic compound management through the image processing and data handling, up to the analysis of the screens. The platform offers not only standard/routine functions but also integrates the newest, state-of-the-art algorithms related to machine learning, data mining, standards and knowledge management. A further specialty of this platform is that we want to actively make use of its open source nature by creating an international development community through which one can reach not only new informatics solutions but broaden the application areas and accelerate the development speed.

5:10-5:35 The Open Microscopy Environment: Image Informatics for Biological Microscopy and HCAs

Jason Swedlow, Ph.D., Senior Research Fellow & Reader, Gene Regulation & Expression, University of Dundee

We have developed an open-source software framework to address the needs for image data integration and interoperability known as the Open Microscopy Environment (OME). OME has three components—an open data model for biological imaging, standardized file formats and software libraries for data file conversion and software tools for image data management and analysis. The OME Data Model has recently been updated to more fully support fluorescence filter sets, the requirement for unique identifiers, including LSIDs, and screening experiments using multi-well plates. The OME-TIFF file format and the Bio-Formats file format library provide an easy-to-use set of tools for converting data from proprietary file formats. These resources enable access to data by different processing and visualization applications, and sharing of data between scientific collaborators. The Java-based OMERO platform includes server and client applications that combine an image metadata database, a binary image data repository and high performance visualization and analysis. The current release of OMERO includes interfaces for C/C++ and Python to support a wide variety of client applications and support for Matlab-based applications like Cellprofiler. For computational analysis of images, this standardized interface provides a single mechanism for accessing image data of all types– regardless of the original file format. Moreover, a compute distribution facility is included, to support multi-cpu computing installations.

4:45-5:10 Using FLIM to Analyze 2-Way and 3-Way Protein:Protein Interaction and Caspase Activation in Live Cells

David Andrews, Ph.D., Professor, Biochemistry and Biomedical Sciences, Canada Research Chair in Membrane Biogenesis, McMaster University

We have been using Fluorescence Lifetime IMaging (FLIM) to measure protein:protein interactions in live cells by Fluorescence Resonance Energy Transfer (FRET) between fluorescence proteins. Methods to measure caspase activity in live cells using a single molecule consisting of a CFP donor linked via a caspase site to an YFP acceptor are well established. We have successfully automated this assay for high throughput using the FLIM Opera. To examine interactions crucial for regulation of apoptosis by interactions between different Bcl-2 family proteins is more challenging because the relative concentration of the two proteins varies in different areas of the cell. Because fluorescence lifetime is independent of concentration we used FLIM FRET to measure 3-way interactions between the anti-apoptotic protein Bcl-XL with the pro-apoptotic proteins Bid, Bad and Bim. In a single cell it was possible to examine drug induced FRET between CFP-Bid and YFP-Bcl-XL as well as FRET between YFP-Bcl-XL and RFP-Bad or RFP-Bim on mitochondria. Currently we are using this approach to examine in live cells the molecular mechanism of drugs such as ABT-737 that are designed to disrupt the interactions between Bcl-XL and its binding partners.

5:10-5:35 Live-Cell Imaging of Specific RNAs Using Fluorescent Probes

Gang Bao, Ph.D., Professor, Robert A. Milton Chair in Biomedical Engineering, College of Engineering Distinguished Professor, Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University

With the recent development of novel techniques for imaging RNA in living cells, it is now possible to study the dynamics of RNA expression and regulation. In this presentation I will review the application of fluorescent probes, especially molecular beacons, in live-cell RNA detection, viral infection studies, and the isolation of stem cells. Common challenges faced by fluorescent probes, such as probe design, delivery, and target accessibility, are also discussed. It is expected that continued advancements in live-cell imaging of RNA will open new and exciting opportunities in a wide range of biological and medical applications.

WEDNESDAY, JANUARY 13

5:35-6:00 Bioassay Ontology and Software Tools to Integrate and Analyze Diverse Data Sets

Stephan C. Schurer, Ph.D., Research Assistant Professor, Pharmacology, Center for Computational Science, University of Miami Miller School of Medicine

The primary goal of the project is the development of a content and software framework to enable systematic mining and analysis of large screening data sets from diverse biological assays, including HCA studies. Currently, bioassay experiments and their endpoints are described primarily as free text. Formalizing this knowledge is required for any computational analysis that involves multiple assay data sets. It is also required to integrate these data with existing bioinformatics resources, such as pathway and interaction databases. A framework to enable researchers to exploit these enormous resources will improve the efficiency of chemical biology research projects, and will lead to the discovery of treatments, usually compounds, that may not emerge from individual screening campaigns.

5:35-6:00 Quantitative Molecular Imaging in Living Cells via FLIM

Mary-Ann Mycek, Ph.D., Associate Professor & Associate Chair, Biomedical Engineering; Faculty Member, Applied Physics Program; Core Member, Comprehensive Cancer Center, University of Michigan

Fluorescence lifetime imaging microscopy (FLIM) employs fluorophore lifetime, rather than fluorescence intensity, for image contrast. Compared to intensity-based methods, lifetime imaging requires less calibration and/or correction for fluorophore concentration, photobleaching, and other artifacts that affect intensity measurements. FLIM has been employed to probe the microenvironments of endogenous and exogenous fluorophores, including measurements of cellular metabolic co-factors, pH, dissolved gas concentration, and molecular interactions via FRET. Several applications of FLIM for quantitative, live cell imaging will be described, including studies of cellular metabolic pathways, improved FRET detection of oncogene association, microfluidic bioreactor characterization for continuous cell culture, and improved precision for low-light FLIM imaging.

6:00-7:00 Reception with Exhibit and Poster Viewing

HOTEL & TRAVEL INFORMATION

Conference Venue and Hotel:

The Fairmont Hotel
950 Mason Street, San Francisco, CA 94108
Tel: 415-772-5000 • Fax: 415-391-4833
Reservations Direct Line: 415-772-5147

Discounted Room Rate: $199 s/d
Discounted Reservation Cut-off Date: December 16, 2009

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Car Rental Discounts:

Special discount rentals have been established with AVIS for this conference. Please call AVIS directly at 800-331-1600 and reference our Avis Worldwide Discount (AWD) Number J868190.

THURSDAY, JANUARY 14

7:30-8:15 Breakfast Presentation

Sponsored by PerkinElmer For the Better

Imaging Infection: An Impetus to Technology Innovation in High-Content Analysis

Spencer Shorte, Plateforme d'Imagerie Dynamique (PFID), Imagopole, Institut Pasteur, Paris

A wealth of celluloid evidence details "high-content analysis" (HCA) of living microbiology using a microscope and cinema camera as early as 1907. However, these remarkable records were lost for decades as an historic artifact. Today, a variety of technologies including imaging & flow cytometry, multi-dimensional dynamic imaging, ultra-structural microscopy and intravital imaging facilitate analysis of infectious disease processes at sub-cellular, cellular, tissue and whole organism levels providing rich information content. Using malaria as a disease model, this lecture will describe multi-facetted visualization of the disease process, including high-resolution intravital multi-dimensional dynamic imaging that ultimately helped the scientific animation filmmaker Drew Berry to complete his magnificent animated description of the malaria life cycle. In perspective, studies on infectious biology require relevant, high-fidelity experimental paradigms, and improved HCA approaches will better ensure fragile host-pathogen interactions are analyzed *in situ* without compromise.

8:30-9:30 ThinkTank Roundtable Discussions

Roundtable discussions, led by expert facilitators, are open to all delegates.

Topics include:

- Compound Screening
- HCA of Stem Cells
- Data Analysis and Management
- Image Analysis
- Live-Cell Imaging
- New Biological Models
- Flow Cytometry
- Novel Probes and Biosensors
- siRNA Screening and Pathway Analysis
- Toxicity Profiling
- Neuronal Screening

9:30-10:00 Reports from ThinkTank Roundtable Discussions

10:00-10:30 Award Presentations

- Poster Competition Awards, Sponsored by Thermo Scientific.
- Best Publication Awards, Sponsored by Thermo Scientific.
- Image Competition Awards, Sponsored by GE Healthcare.

10:30-11:30 Coffee Break with Exhibit and Poster Viewing

7:30-8:15 Breakfast Presentation

Sponsorship available. Contact Katelin Fitzgerald, Manager, Business Development, at 781-972-5458 or kfitzgerald@healthtech.com

NOVEL FLUORESCENT PROBES AND BIOSENSORS

11:30-11:55 Development and Characterization of a Novel AR -TIF2 Protein-Protein Interaction Biosensor HCS Assay to Measure Co-Activator Recruitment Interactions

Paul A. Johnston, Ph.D., Research Associate Professor, Pharmacology & Chemical Biology, University of Pittsburgh School of Medicine

The AR-TIF2 protein-protein interaction biosensor (PPIB) was developed to measure the interactions between the p160 steroid receptor coactivators (SRC) with nuclear hormone receptors (NRs). Researchers at Cellumen Inc. have generated recombinant adenovirus (R-AV) constructs of the nuclear anchored Transcription Initiation Factor-2 (TIF2-GFP) and the nuclear-cytoplasmic Androgen receptor (AR-RFP) shuttling components of the PPIB. We have characterized the responses of the AR-TIF2 PPIB to androgens and developed a HCS assay that is sufficiently robust and reproducible to be compatible with screening large compound libraries. We have utilized the AR-TIF2 PPIB to characterize and quantify the phenotypes of AR anti-androgens (Biclautamide & Flutamide) that have been used in the clinic to treat prostate cancer. We have also characterized and quantified the phenotype produced by the Hsp90 ATPase inhibitor 17-AAG.

NEW BIOLOGICAL MODELS FOR HCA

11:30-11:55 High-Content Screen for Compounds that Modulate Misfolded Protein Aggregation in *C. elegans*

Stephen Pak, Ph.D., Research Assistant Professor, Pediatrics, University of Pittsburgh

C. elegans is a powerful genetic organism useful for the study of human diseases. Recently, we developed a *C. elegans* model of a human misfolded protein accumulation disorder, a1-antitrypsin-deficiency. To facilitate the identification of therapeutic compounds, we developed a fully automated, whole organism-based assay for the high content screening of small molecules. Initial screens identified hit compounds that significantly reduce the accumulation of protein aggregates. Characterization of these compounds should provide valuable insight into pathways responsible for the disposition of protein aggregates. These results demonstrate the utility of *C. elegans* in drug discovery and provide a stepping-stone for future *C. elegans*-based drug screens.

11:55-12:20 Structure-Guided Improvements to Fluorescent Proteins

Mark Rizzo, Ph.D., Assistant Professor, Department of Physiology, University of Maryland School of Medicine

A full complement of colors for genetically-encoded fluorescent proteins has nearly been achieved. However, the far majority of these proteins are less than ideal probes for live cell microscopy because of problems with overall brightness when observed with existing imaging technology. Limited brightness, and in particular, low quantum yields are particularly important for cyan fluorescent proteins because they are widely used as donors in Förster resonance energy transfer (FRET) assays and energy transfer efficiency is directly related to the donor quantum yield. To improve the quantum yield of Cerulean fluorescent protein, we used site-directed mutagenesis to optimize residues surrounding the chromophore. This new variant, mCerulean2, has a greatly improved quantum yield of 0.78, is 50% brighter than mCerulean in cells, and is a superior donor for FRET experiments. In an *in vitro* assay, FRET with mCerulean2: mVenus can be detected with 7.5-fold less protein than for mCerulean. With increased brightness and performance for FRET experiments, mCerulean2 is well suited for FRET experiments in living cells.

12:20-12:45 Multidimensional Fluorescence Imaging for Cell Biology, High-Content Analysis and Label-Free Tissue Analysis

Sunil Kumar, Ph.D., Research Associate, Photonics Group, Physics Department, Imperial College London

This talk will review our development and application of multidimensional fluorescence imaging (MDFI) technology, with an emphasis on fluorescence lifetime imaging (FLIM), implemented in microscopy, endoscopy and tomography. Applied to autofluorescence, MDFI can provide label-free molecular contrast in biological tissue for *ex vivo* and *in vivo* applications. For cell biology, high speed FLIM can be used to image the spatio-temporal organisation of proteins and their interactions, including via FRET, for which we are working to improve the imaging speed and spatial resolution. For high content analysis, we have developed an automated high-speed optically-sectioned FLIM multiwell plate reader applicable to fixed and live cells. We have also developed a multiplexed FRET microscope capable of simultaneously imaging two different protein-protein interactions in a cell signalling network. For 3-D imaging of embryos and small organisms, we have developed a FLIM optical projection tomography (OPT) system and are working towards tomographic FLIM and FRET of cleared samples and of live animals for dynamic studies *in vivo*.

12:45-1:10 Controlling the Signaling Dynamics of Rho GTPases and Cell Motility Using Genetically Encoded Photoactivatable Proteins

Yi Wu, Ph.D., Assistant Professor, Department of Pharmacology, University of North Carolina

For many highly dynamic cell behaviors such as cell migration, signaling occurs transiently at specific locations, with subsecond and submicron precision. Study of such rapid dynamics has been hindered by our inability to manipulate protein activities with precise spatio-temporal control in living cells and animals. Here we describe the engineering of several genetically-encoded photoactivatable Rho GTPases using a light-responsive protein domain (LOV) derived from plant phototropin, enabling reversible and repeatable control of cell signaling in living systems.

11:55-12:20 Quantitation of Fibroblast Growth Factor (FGF) Signaling by High-Content Analysis in Transgenic Zebrafish

Andreas Vogt, Ph.D., Research Assistant Professor, Pharmacology, University of Pittsburgh

The zebrafish is one of few multicellular organisms compatible with compound screening in multiwell plates. The zebrafish embryo is particularly suited for image based screens due to its small size and optical transparency. We have developed an image analysis method to quantify activation of fibroblast growth factor (FGF) signaling in a transgenic zebrafish reporter line that expresses green fluorescent protein (GFP) in particular regions of the brain. The system delivers graded responses and quantified the activity of a novel small molecule inhibitor of the dual specificity phosphatase DUSP6 (MKP-3).

12:20-12:45 High-Content Imaging Approaches to Interrogate *in vitro* and *in vivo* Tumor Angiogenesis

Mark Uhlik, Ph.D., Senior Research Scientist, Angiogenesis & Tumor Microenvironment DHT, Eli Lilly & Co.

Solid tumors require the development of new blood vessels via angiogenesis for their continued growth and metastasis. Tumor angiogenesis is a complex biological process involving multiple cell types, soluble factors, microenvironmental cues, and cell-cell interactions. In order to enable the discovery of anti-angiogenic compounds that interfere with these biological processes we are pursuing a phenotypic drug discovery approach driven predominately by cell-based high-content assays. This high content-enabled paradigm of phenotypic drug discovery provides an avenue to 1) identify compounds that modulate molecular targets from a variety of functional classes, 2) identify compounds that modulate pathways not previously identified as having roles in angiogenesis, 3) screen compounds in complex biological systems composed of multiple cell types, and 4) recognize and filter out compounds that may be overtly cytotoxic. Using an endothelial/mesenchymal stem cell co-culture model of cord formation and assays to assess endothelial migration, proliferation, and apoptosis we are able to bin compounds into discrete phenotypic activity classes. Compounds are further tested in tumor xenograft models for *in vivo* angiogenesis and tumor growth properties using quantitative multiplexed fluorescence tissue imaging.

12:45-1:10 From Cilia to Schistosomes: High-Content Analysis for Unusual Targets

Michelle Arkin, Ph.D., Assistant Adjunct Professor, Pharmaceutical Chemistry, University of California, San Francisco

The Small Molecule Discovery Center is a high-throughput screening and probe-discovery facility at UCSF. The SMDC works with 12 - 20 groups per year, developing and running screens against unusual and challenging targets. This seminar will highlight some of these off-the-beaten track systems, including whole organisms, parasites, and organelles.

1:10-2:00 Lunch on Your Own

2:00-6:00 PerkinElmer User Group Meeting

Easy, Efficient, and Fast - HCS Solutions from PerkinElmer

PerkinElmer cordially invites you to hear top scientists discuss their work in high-throughput, high-content screening processes. With the emphasis on ease-of-use, talks will include case studies on the use of our HCS solutions and news of our latest product developments.

For further information about speakers and topics, please visit www.perkinelmer.com/hcawest

2:00-6:00 BD Biosciences User Group Meeting

FRIDAY, JANUARY 15

7:30-8:15 Breakfast Presentation or Morning Coffee

Sponsorship available. Contact Katelin Fitzgerald, Manager, Business Development, at 781-972-5458 or kfitzgerald@healthtech.com

HCA FOR siRNA SCREENING

8:30-8:35 Chairperson's Opening Remarks

8:35-9:00 The Pros and Cons of siRNA Use in HCS

Eugenio Fava, Ph.D., Director, Services and Facilities, German Centre for Neurodegenerative Diseases

The use of siRNA in high-content screens (HCS) in mammalian cells has become a valuable method to identify and describe genetic relationships in both basic biology and disease mechanisms. However, the use of siRNAs in HCS has been hampered by an inherent problem of siRNA, namely off target. Off target is the phenomenon that takes place when genes with incomplete complementarity are downregulated by the siRNA. This leads to problems in data interpretation and overall difficulties in the determination of hits. Although there are different strategies to reduce siRNA target, ranging from design to chemical modification, avoiding it is very difficult if not impossible. Here we analyze and discuss a complementary method approach that allows us to evaluate the siRNA off target from the HCS data. We used this method to compare and contrast different siRNA technologies and the results will be discussed.

9:00-9:30 Technology Presentations

Sponsorships available. Contact Katelin Fitzgerald, Manager, Business Development, at 781-972-5458 or kfitzgerald@healthtech.com.

9:30-9:55 A High-Content Assay to Screen for Modulators of the miRNA Machinery

David Shum, Ph.D., Assay Development Specialist, HTS Core Facility, Memorial Sloan Kettering

MicroRNAs are small non-coding regulatory RNAs reducing stability and/or translation of fully or partially sequence-complementary target mRNAs in plants and animals. Their upregulation has been reported in many malignancies and proposed to regulate several tumor suppressor pathways; the understanding of their biogenesis may offer novel therapeutic approaches and intervention. There are no well documented modulators to help us study the pathway and unravel its biological significance; for this purpose, we set out to develop a high-content assay using a stably transfected HeLa S3 cells expressing EGFP under miR-21 regulation as the reporter gene carries a sequence with perfect complementarity to miR-21 in its 3' UTR region, thus decrease in miR-21 levels would induce increase in the expression and maturation of the EGFP reporter which can easily be imaged using automated microscopy. We will present and discuss our assay development and validation against both a pilot chemical library and a custom siRNA library targeting known genes of the miRNA pathway together with few essential housekeeping genes to assess transfection efficiencies. Our high-content assay and its dual adaptation would allow screening and discovery of novel modulators of the miRNA pathway and a better understanding of the regulatory components of its maturation machinery.

HCA FOR TOXICITY PROFILING

8:30-8:35 Chairperson's Opening Remarks

8:35-9:00 Refinement of Predictive Cytotoxicity Assays Using High-Content Analysis and Extension into Different Cell Lines

Peter O'Brien, D.V.M., Ph.D., Veterinary Clinical Pathologist, Pathology, University College Dublin, Ireland

Our HepG2 predictive cytotoxicity assay using HCA was refined, along with the associated process and data analysis and applied in new capacities, including screening in academic "drug discovery" activities. It was streamlined and made more user-friendly, reproducible, and cost-effective at the biological reagents, assaying, and data reduction and analysis ends. Its effective application was extended into several other cell lines, including lymphoid, monocytic, and intestinal, and into other programs and disciplines, including in cancer drug evaluation, food health, and environmental monitoring.

9:00-9:15 Use More Cells! High-Content Alternatives for In Vitro Toxicity Assessment

Sponsored by Thermo SCIENTIFIC

Mark A. Collins Ph.D., Director, Marketing, Thermo Fisher Scientific

9:15-9:30 Title to be Announced

Sponsored by GE Healthcare

9:30-9:55 *In-vitro* Toxicity Profiling in Non-Adherent Cells by Automated High-Content Microscopy

Michael Prummer, Ph.D., Scientist, High-Content Screening, Discovery Technologies, Pharma Research, F. Hoffmann-La Roche Ltd.

Most High-Content Screening assays are run with adherent cells and not with suspension cells due to practical limitations. However, there are established cellular models for conventional microscopy in which suspension cells are used. We are presenting here a novel and universal approach to immobilize non-adherent cells in multi-well format for automated microscopy that fills this gap. As a first application we report on a high-content toxicity assay at the single-cell level using an innovative new preparation tool. For image segmentation and object classification we have developed an adaptive and iterative algorithm in collaboration with Definiens AG. To extract a toxicity score from the derived data, non-parametric statistical methods were employed. Taken together, these developments open up new routes for high-content screening with suspension cells.

9:55-10:20 Networking Coffee Break

HCA FOR PATHWAY ANALYSIS

10:20-10:45 Phenotypic Drug Discovery to Identify Novel Oncolytics using High-Content Fingerprinting

Louis Stancato, Ph.D., Principal Research Scientist, Cancer Growth & Translational Genetics, Eli Lilly & Co.

The development of high-content imaging subpopulation analysis tools has enabled a high resolution look into cancer cell function, and as a result is now an integral technology in Lilly Oncology. One area in particular that has experienced a renaissance is phenotypic drug discovery, a discipline ideally suited to the application of HCI. By incorporating custom in-house informatics tools we are able to advance molecules with novel mechanisms of action through the lead generation process, in particular chemical series previously discarded due to perceived failure in conventional "targeted" approaches. This presentation will focus on how the HCI informatics tools are used to identify, phenotypically fingerprint and subsequently advance *in vivo*, novel anti-cancer molecules using both cultured cell and cancer stem cell models.

10:45-11:10 Targeting Cytokine Receptor-JAK-STAT Signaling Pathways - Development of an HCS Assay to Identify Selective Inhibitors of STAT-3 Phosphorylation and Nuclear Translocation

Paul A. Johnston, Ph.D., Research Associate Professor, Pharmacology & Chemical Biology, University of Pittsburgh School of Medicine

The Signal Transducers and Activators of Transcription (STATs) are transcription factors that mediate the effects of growth factors and cytokines to regulate the expression of genes involved in cell proliferation, differentiation, inflammation, migration, and apoptosis. Activated STAT3 is an oncogene that directs tumor cells toward proliferation and survival, induces angiogenesis and alters the tumor microenvironment, and promotes tumor metastases through its effects on cell migration and invasion. In sharp contrast activated STAT1 is considered a tumor suppressor because it is a potent inhibitor of tumor growth, promotes tumor cell apoptosis, and enhances tumor immunity. Consequently, the discovery of a STAT3 selective inhibitor would be a highly desirable goal for the development of an anti-cancer drug. The development of an HCS assay to identify selective inhibitors of STAT-3 phosphorylation and nuclear translocation will be described.

11:10-11:35 Development of a Multiparametric Assay to Measure Cell Phenotypic and Pathway Parameters Indicative of ROCK Activity

Danli L. Towne, Scientist II, High-Content Screening, Lead Discovery, Abbott Laboratories

11:35-12:00 High-Content Cellomics Cell Cycle Analysis of the Effects of HSP90 Inhibition

Susan Lyman, Ph.D., Research Scientist, Exelixis, Inc.

Cell cycle analysis has traditionally been carried out by FACS – or more recently, by combining a measurement of DNA content with imaging of one or more phase-specific readouts, such as phospho-histone H3. We have used the latter approach to develop a novel and robust high-throughput Cellomics-based cell cycle assay that accurately reports the phase status of a cell (G1, S, G2, or M) as well as its DNA content (2n, 4n, >4n). We have applied this technique to examine the cell cycle perturbations caused by inhibition of HSP90, a molecular chaperone that enhances the stability of a wide spectrum of client proteins. HSP90 clients include cell cycle proteins such as PLK1 and CDC2 as well as cancer-associated proteins such as EGFR, ERBB2, and MET, making it an attractive cancer target. This presentation will illustrate the Cellomics cell cycle technique and will highlight the strikingly similar complex cell cycle perturbations induced by 3 different small-molecule HSP90 inhibitors in a large panel of immortalized cancer cell lines.

NEURONAL SCREENING

10:20-10:45 Using HCA to Identify a Transcription Factor Family that Regulates the Intrinsic Ability of Neurons to Extend Axons

Vance Lemmon, Ph.D., Professor, Neurological Surgery, Miami Project to Cure Paralysis, University of Miami Miller School of Medicine

As neurons age, they lose the ability to extend axons, resulting in failure of regeneration after injury to the central nervous system. We used HCA to screen genes that were differentially expressed during development in retinal neurons and cortical neurons. We identified a family of transcription factors that regulate axon growth *in vitro* and *in vivo*. In the course of these studies we found that some types of primary neurons are more suitable for detecting increases in neurite growth than other types of neurons.

10:45-11:10 High-Content Analysis of Synapse Formation in Primary Neuronal Cultures for Developmental Neurotoxicity Screening

William R. Mundy, Ph.D., Integrated Systems Toxicology Division, U.S. Environmental Protection Agency

Cell-based assays can model neurodevelopmental processes including neurite growth and synaptogenesis, and may be useful for screening and evaluation of large numbers of chemicals for developmental neurotoxicity. This work describes the use of HCA to detect chemical effects on synaptogenesis *in vitro*. Pre-synaptic puncta were associated with the cell body and dendrites of primary cortical neurons, and increased over several weeks in culture. Several chemicals were identified that decreased synapse number during development *in vitro*.

11:10-11:35 Screening Neuronal Pattern Formation *in vivo*

Sebastian Munck, Ph.D., Coordinator, Light Microscopy and Imaging Network LiMoNe, Department of Molecular and Developmental Genetics, VIB, K.U. Leuven

We would like to describe an assay for imaging-based high-content analysis of the network formation ***in vivo***. The neurons in the optic lobe of Drosophila melanogaster form a stereotypical pattern. In the optical system neuronal / electrical activity is believed to be a crucial part in the pattern formation process. We want to dissect the genetic and activity depended processes. The aim of the project is to identify the key players of the pattern formation and to modulate them by combining the power of a genetic screen in drosophila with the imaging based read out of the formed pattern.

11:35-12:00 Title to be Announced

Oscar Joseph Trask, Jr., Ph.D., Associate in Research, Neurobiology, Duke University (tentative)

12:00 Close of Conference

DISTINGUISHED FACULTY

David Andrews, Ph.D., Professor, Biochemistry and Biomedical Sciences, Canada Research Chair in Membrane Biogenesis, McMaster University

Michelle Arkin, Ph.D., Assistant Adjunct Professor, Pharmaceutical Chemistry, University of California, San Francisco

Ansuman Bagchi, Ph.D., Director, Applied Computer Science & Mathematics, Merck & Co.

Gang Bao, Ph.D., Professor, Robert A. Milton Chair in Biomedical Engineering, College of Engineering Distinguished Professor, Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University

Mark-Anthony Bray, Ph.D., Computational Biologist, Imaging Platform, Broad Institute

Sheng Ding, Ph.D., Assistant Professor, Chemistry, Scripps Research Institute

Hakim Djaballah, Ph.D., Director, HTS Core Facility, Memorial Sloan Kettering Cancer Center

Eugenio Fava, Ph.D., Director, Services and Facilities, German Centre for Neurodegenerative Diseases

Daniela Gabriel, Ph.D., Associate Director, Lead Finding Platform, Novartis Institutes for Biomedical Research

Claudine Grepin, Ph.D., Head, Lead Discovery Technology, Sanofi-Aventis Pharma R&D, France

Susanne Heynen-Genel, Ph.D., Director, High-Content Screening Systems, Conrad Prebys Center for Chemical Genomics, Burnham Institute for Medical Research

Peter Horvath, Ph.D., Image Processing Scientist, Light Microscopy Centre, ETH Zurich

Paul A. Johnston, Ph.D., Research Associate Professor, Pharmacology & Chemical Biology, University of Pittsburgh School of Medicine

Karol Kozak, Ph.D., Head, Computation Analysis, HCA/HTS Informatics, LMC-RISC, Institute for Biochemistry

Peter Krutzik, Ph.D., Senior Scientist, Baxter Lab in Genetics Pharmacology, Microbiology & Immunology, Stanford University

Sunil Kumar, Ph.D., Research Associate, Photonics Group, Physics Department, Imperial College London

Vance Lemmon, Ph.D., Professor, Neurological Surgery, Miami Project to Cure Paralysis, University of Miami Miller School of Medicine

Jonathan Low, Ph.D., Post-Doctoral Scientist, Cancer Cell Growth and Survival, Lilly Corporate Center

Susan Lyman, Ph.D., Research Scientist, Exelixis, Inc.

John McLaughlin, Ph.D., Scientist & Manager, Biology, Rigel Pharmaceuticals, Inc.

Sebastian Munck, Ph.D., Coordinator Light Microscopy and Imaging Network LiMoNe, Department of Molecular and Developmental Genetics, VIB, K.U. Leuven

William R. Mundy, Ph.D., Integrated Systems Toxicology Division, U.S. Environmental Protection Agency

Robert F. Murphy, Ph.D., Professor, Departments of Biological Sciences and Biomedical Engineering, Carnegie Mellon University

Mary-Ann Mycek, Ph.D., Associate Professor & Associate Chair, Biomedical Engineering; Faculty Member, Applied Physics Program; Core Member, Comprehensive Cancer Center, University of Michigan

John P. Nolan, Ph.D., Professor, La Jolla Bioengineering Institute

Peter O'Brien, D.V.M., Ph.D., Veterinary Clinical Pathologist, Pathology, University College Dublin, Ireland

Stephen Pak, Ph.D., Research Assistant Professor, Pediatrics, University of Pittsburgh

Oliver Poeschke, Ph.D., Senior Scientist, Assay Development, Biomolecular Pharmacology Lead Discovery, Merck Serono

Stefan Prechtl, Ph.D., Team Leader, High-Content Analysis, Bayer Schering Pharma AG

Eric Prossnitz, Ph.D., Professor, Cell Biology and Physiology, University of New Mexico

Michael Prummer, Ph.D., Scientist, High-Content Screening, Discovery Technologies, Pharma Research, F. Hoffmann-La Roche Ltd.

Mark Rizzo, Ph.D., Assistant Professor, Department of Physiology, University of Maryland School of Medicine

Fredika M. Robertson, Ph.D., Professor, Department of Experimental Therapeutics; Director, Translational Research, The Morgan Welch Inflammatory Breast Cancer Research Program, The University of Texas M.D. Anderson Cancer Center

J. Paul Robinson, Ph.D., SVM Professor, Cytomics & Deputy Director, Bindley Bioscience Center, Cytomics & Imaging, Purdue University

Stephan C. Schurer, Ph.D., Research Assistant Professor, Pharmacology, Center for Computational Science, University of Miami Miller School of Medicine

David Shum, Ph.D., Assay Development Specialist, HTS Core Facility, Memorial Sloan Kettering

Louis Stancato, Ph.D., Principal Research Scientist, Cancer Growth & Translational Genetics, Eli Lilly & Co.

Jason Swedlow, Ph.D., Senior Research Fellow & Reader, Gene Regulation & Expression, University of Dundee

Steve Titus, Ph.D., Staff Scientist, Biology, NIH Chemical Genomics Center

Danli L. Towne, Scientist II, High-Content Screening, Lead Discovery, Abbott Laboratories

Oscar Joseph Trask, Jr., Ph.D., Associate in Research, Neurobiology, Duke University

Mark Uhlik, Ph.D., Senior Research Scientist, Angiogenesis & Tumor Microenvironment DHT, Eli Lilly & Co.

Andreas Vogt, Ph.D., Research Assistant Professor, Pharmacology, University of Pittsburgh

Dadong Wang, Ph.D., Stream Leader, Biotech Imaging, CSIRO

Yi Wu, Ph.D., Assistant Professor, Department of Pharmacology, University of North Carolina

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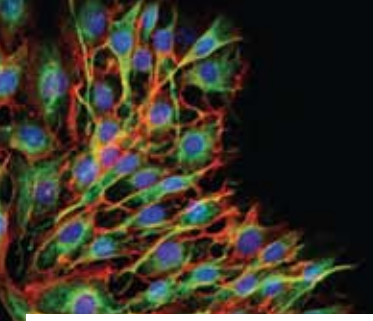

Cambridge Healthtech Institute's Seventh Annual

HIGH-CONTENT ANALYSIS

JANUARY 12-15, 2010

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HOW TO REGISTER: Online: www.highcontentanalysis.com

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❑ **Yes! Please register me for High-Content Analysis 2010** **Key Code 008F**

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