



RNAi for Pathway Analysis 2006

January 31-February 2, 2006 • The Fairmont Hotel • San Francisco, California

This "end-users" meeting tackles the challenges of integrating RNAi technology into your functional genomics and target validation studies. If you are using RNAi as a research tool, this is one meeting you can't afford to miss!

SPEAKERS FROM:

Abbott
Boehringer Ingelheim
Cenix
Cornell
Eli Lilly
Exelixis
GNF
Harvard
Hoffmann-La Roche
Max Planck
Merck
NIST
Novartis
Pfizer
Tufts
Whitehead
Wyeth

CONFERENCE FEATURES:

- Pre-Conference Tutorial: More Effective RNAi Studies with High-Content Screening
- Post-Conference RNAi End-User Forum (open to end-users only)
- 2006 Highlight: Integrating siRNA and Compound Library Screening
- Expanded Coverage of High-Content Screening of siRNA
- Case Studies of Genome-Wide siRNA Screening, Pathway Analysis, and Target Validation
- Technology Showcase Highlighting Latest Tools
- Optional Access to Co-Located High-Content Analysis Sessions, Exhibits, and User Group Meetings

Executive Sponsor:

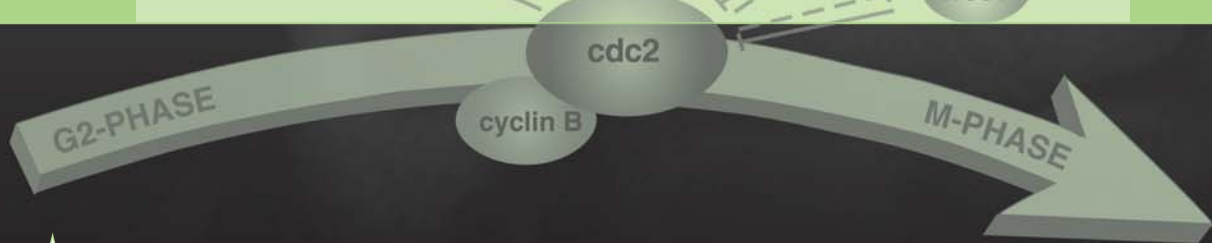


Premier Sponsor:

GE Healthcare



Corporate Sponsors:



CO-LOCATED Third Annual High-Content Analysis conference
 The most comprehensive and focused coverage of high-content cellular assays applications and technologies, including a 4-day scientific program, comprehensive trade show, technology showcases, and co-located user group meetings hosted by leading technology providers.
 Visit www.highcontentanalysis.com for complete details.

HOTEL INFORMATION

FAIRMONT HOTEL

950 Mason Street, San Francisco, CA 94108
Tel: 415-772-5000 • Fax: 415-391-4833
Room Rate: \$189 single/double
Cutoff: January 10, 2006



World-Renowned Fairmont San Francisco Hotel

Please call the hotel directly to make your room reservation. Identify yourself as a Cambridge Healthtech Institute conference attendee to receive the reduced room rate. Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space-and-rate-availability basis. Rooms are limited, so please book early.

For on-line reservations, please visit www.fairmont.com and be sure to enter the promotional code **GRHIG1** to obtain the group rate of \$189.

TRAVEL INFORMATION

Special Airline Discounts Available:

Discounts fares are available on United, United Express, United code share flights (UA*) operated by US Airways, and US Airways Express. You can receive up to a 15% discount off if you or your travel agent call United's toll-free number 1-800-521-4041 and refer to the Meeting ID Number 579YS.

PRESENT A POSTER

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference proceedings, your abstract must be submitted, accepted and registration paid in full by **January 11, 2006**. Register online to use the Poster Abstract Submission form. If you register by phone, fax, or mail, you will receive Poster Abstract Submission guidelines via email.

CONFERENCE SPONSORSHIPS

Luncheon Technology Showcases:

Present your technology, brand your company and generate sales leads with a corporate sponsorship (includes a 15-30 minute technology talk).

Focus Groups:

Sponsoring a "topic-specific" focus group allows you to get face-to-face with your target audience and share your expertise.

Additional Sponsorships:

- Badge Lanyards
- Travel Coffee Mugs
- Conference Tote Bags
- Conference Padfolios

...and more

Don't miss the opportunity for recognition during the conference and long after. High-quality promotional items with your corporate logo will be distributed to every delegate. For more information, please contact Carol Dinerstein at 617-630-1371 or dinerstein@healthtech.com.

DISTINGUISHED FACULTY:

- Dr. John Blenis, Professor of Cell Biology, Harvard Medical School
- Dr. Anne E. Carpenter, Novartis Fellow of the Life Sciences Research Foundation, Sabatini Laboratory, Whitehead Institute for Biomedical Research
- Dr. Namjin Chung, Senior Research Scientist, Automated Biotechnology, Merck Research Laboratories
- Dr. Robert Dullea, Principal Scientist, Genetic Technologies, Pfizer Inc.
- Dr. Christophe J. Echeverri, CEO/CSO, Cenix BioScience GmbH
- Dr. John Elliott, Research Scientist, Biotechnology, National Institute of Standards and Technology (NIST)
- Dr. Yan Feng, Lab Head, Genome and Proteome Sciences, Novartis Institute for BioMedical Research
- Mr. Ross Francis, Senior Scientist, Target Discovery, Exelixis, Inc.
- Dr. Steven Haney, Senior Scientist, Biological Technologies, Wyeth Research
- Dr. Eberhard Krausz, HT-Technology Development Studio, Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG)
- Dr. Siu Sylvia Lee, Assistant Professor, Department of Molecular Biology and Genetics, Cornell University
- Dr. Daniel R. Rines, Institute Fellow, Lead Discovery, Genomics Institute of the Novartis Research Foundation (GNF)
- Dr. Jörg F Rippmann, Head, Genomics Group, Boehringer Ingelheim Pharma GmbB & Co. KG
- Dr. Cristina M. Rondinone, Director of Research, Metabolic Diseases, Hoffmann-La Roche Inc.
- Dr. Yu Shen, Group Leader, Cancer Exploratory Biology, Abbott Laboratories
- Dr. Orian Shirihai, Professor, Pharmacology, Tufts University Medical School
- Dr. Louis Stancato, Principal Research Scientist, Cancer Growth and Translational Genetics, Eli Lilly and Company
- Mr. Joseph A. Zock, Senior Manager, HCS User Services, Cellomics, Inc.

RNAi for Pathway Analysis 2006

PRE-CONFERENCE EVENTS

Tuesday, January 31

3:30-6:00pm Tutorial (*separate registration is required*)

More Effective RNAi Studies with High-Content Screening

Mr. Joseph A. Zock, Senior Manager, HCS User Services, Cellomics, Inc.

The promise of using RNAi to deconvolve complex signaling pathways and cellular processes requires detection methods robust enough to deal with variability in transfection frequency and percent knockdown. High-Content Screening (HCS) technology is uniquely suited to this goal by quantitatively measuring multiple target intensity and morphology changes in individual cells of a given experimental population. The combination of HCS and RNAi provides a powerful platform for drug discovery. In this tutorial session you will learn the basics of HCS, how it works, and what unique features are being used to gather more effective data from RNAi experiments. We will also touch on analysis of RNAi effects, both primary and off-target, using multiple HCS endpoints.

Co-Located at High-Content Analysis 2006

8:00am-3:00pm Cellomics User Group Meeting

This user group meeting will be a forum for you to interact with other scientists who are using HCS as a tool for furthering their discovery efforts. Submit an abstract to present what your laboratory is doing with HCS, or attend to learn how your colleagues are optimizing their HCS experience. We will have oral and poster presentations by leading scientists in the industry. All Cellomics customers are welcome to attend. For more information on this event or to register to attend, please contact us at usergroup@cellomics.com or visit our User Group Web site at www.cellomics.com/usergroup/site/stf05_usergroup/index.html.



3:00-7:00pm High-Content Analysis End-User Forum*

OVERCOMING TECHNICAL CHALLENGES IN HCA IMPLEMENTATION

*Participation is limited to end-users only and subject to approval by conference organizers. Companies with HCA-related products or services on the market or in development (including sponsoring and exhibiting companies) will not receive access to the End-User Forum. Separate registration is required. Dinner is included.

For complete program and to register, please visit www.highcontentanalysis.com

RNAi for Pathway Analysis 2006

Tuesday, January 31

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

Wednesday, February 1

7:00-8:00 **Conference Registration**

8:00-8:15 **Chairperson's Opening Remarks**

RNAi FOR TARGET VALIDATION

8:15-8:45 **In Vivo Target Validation of Liver-X-Receptor Alpha with the Use of Adenoviral hsRNA Delivery**

Dr. Jörg F. Ripplmann, Head, Genomics Group, Boehringer Ingelheim Pharma GmbH & Co. KG

The presentation will briefly describe the RNAi portfolio for target validation at BI Germany and will further focus on the presentation of the experimental design and results of an *in vivo* target validation study with the use of adenovirus vectors delivered by Galadeno. The liver-X-receptor alpha is a liver specific member of the nuclear hormone receptor family and involved in the transcriptional control of lipid metabolism and transport. *In vitro* characterized knock-down vectors were injected into the mice at different dosages and the target gene expression as well as the physiological consequence was analyzed. The results will be critically discussed and future directions will be highlighted.

8:45-9:15 **siRNA Technology to Validate Novel Drug Targets from Genetics/Genomics Screens**

Dr. Cristina M. Rondinone, Director of Research, Metabolic Diseases, Hoffmann-La Roche Inc.

siRNA technology holds extraordinary promise for the identification of novel signal transduction pathways and potential drug targets. siRNAi can be useful to understand and infer the function of novel protein targets that can emerge from genetic linkage studies and genomics. This talk will cover the use of siRNA to validate, select and prioritize the hits from these genetic/genomic screens and obtained the best targets for metabolic diseases.

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

GENOME-WIDE siRNA HIGH-CONTENT SCREENING

10:15-10:45 **Statistical and Functional Analysis of a Genome-Wide siRNA Cell Cycle Screen**

Dr. Yan Feng, Lab Head, Genome and Proteome Sciences, Novartis Institutes for BioMedical Research

We used a multi-parameter imaging cytometry-based assay and genome-wide siRNA knockdown to characterize genes and pathways that regulate cell cycle progression. Cells from various cell cycle stages were categorized by a combination of clustering and machine learning algorithms. A multi-parameter cytometry fingerprint was then generated for each gene. System level analysis was performed by putting the cell cycle fingerprint into a function genomic context.

10:45-11:15 **Genome-Wide RNAi Screen Identifying Novel Cell Cycle and Cancer Targets**

Dr. Daniel R. Rines, Institute Fellow, Lead Discovery, Genomics Institute of the Novartis Research Foundation (GNF)

The application of highly parallelized methods to examine cellular phenotypes can enable the study of gene activities at the level of the genome. Toward this end, we have assembled genome-wide collections of siRNAs and cDNAs. Combining these libraries with high-throughput methodologies for parallel transduction of various cell-types and high speed microscopy platforms, we have executed cell-based assays to examine a diverse range of activities. In particular, we have recently used a RNA library of 49,000 double-stranded (ds)RNAs, targeting approximately 24,000 genes, in a genome-wide loss-of-function screen for essential mitotic chromosome segregation genes. Multi-parametric quantitative analysis of the image-based data has allowed us to isolate over 200 known and novel genes. The application of this functional profiling technology has led to the elucidation of several novel gene activities, and will likely play an integral role in the understanding of gene function on a global scale.

11:15-11:45 **Genome-Wide High-Content RNAi Screening to Identify Regulators of Endocytotic Pathways**

Dr. Eberhard Krausz, HT-Technology Development Studio, Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG)

We are applying siRNA libraries to multi-parametric high-content assays using an automated high-throughput microscope. In primary viral infection screens, kinases were identified to regulate two independent endocytotic pathways each specifically hijacked by a virus. Primary 'hits' were further characterized in a set of six secondary assays that allow pathway dissection. Complex regulative networks were discovered. A subsequent genome-wide screen has been implemented.

11:45-12:15 **Rapid, High-Content Genome-Wide Assays Using Cell Microarrays**

Dr. Anne E. Carpenter, Novartis Fellow of the Life Sciences Research Foundation, Sabatini Laboratory, Whitehead Institute for Biomedical Research

Cell-based microarrays allow the preparation of thousands of individual cell samples on a single microscope slide using conventional microarrays. This allows testing an entire genome for high-content phenotypes on 4-8 slides. Each spot on the slide is a cluster of several hundred cells that are perturbed by a single gene expression plasmid, small molecule, or RNA interference reagent (RNAi), and can be imaged using high resolution microscopy. Because existing commercial software had limitations, we developed CellProfiler cell image analysis software to measure a variety of interesting phenotypes of cells on these arrays. By knocking down each gene in *Drosophila* by RNAi and analyzing cells with CellProfiler, we are obtaining a high-quality, high-content readout of the effects of knocking down each gene on a variety of cellular phenotypes.

LEAD SPONSORING PUBLICATIONS

Cell

Science
MAAS

Molecular Cell

SPONSORING PUBLICATIONS

Current Biology

Drug Discovery
& Development

Cover artwork courtesy of Cellomics and Cell Signaling Technology

**12:30-12:45 Adenoviral Vectors in Pathway Analysis and Target Validation**

Dr. Stephen Game, Department Director, Molecular and Cell Biology, GE Healthcare

The new Adenoviral Vector Gene Delivery System from GE Healthcare expands the possibilities for drug target validation by enabling the development of cellular assays that can greatly aid secondary screening and early-stage drug discovery. The system includes a range of ready-to-use recombinant adenoviral preparations and data will be presented of a range of assay targets and applications.

12:45-1:00 Recent Developments in siRNA-Based RNA Interference

Mr. Kirk Brown, Territory Manager, Dharmacon



One of the keys to achieving potent gene silencing is the selection of well-designed, highly functional siRNAs. We have identified thermodynamic and sequence-related characteristics that affect key steps in RISC-mediated mRNA degradation. These parameters have been combined into a weighted rational design SMARTselection™ algorithm for the identification of highly functional siRNAs. Silencing efficiency is further improved by pooling selected siRNA duplexes into one SMARTpool reagent. Together, SMARTselection design and SMARTpool technologies enable functional siRNAs to be designed against any gene target.

Recently, Dharmacon introduced ON-TARGET™ siRNA which further increases the specificity of RNAi by introducing modifications to the siRNA sense strand that eliminate sense strand mediated off-target effects as determined by microarray-based genome wide expression profiling. Continuing innovations at Dharmacon are directed toward enabling researchers to expand studies beyond cultured cells to whole animal systems. In particular, Dharmacon developed siSTABLE™, a chemical modification strategy that increases siRNA half-life in serum from minutes to days, increases the duration of silencing after a single treatment and increases the specificity of certain siRNA sequences. Rational siRNA design and the use of stabilized duplexes provide a generally useful mechanism for reducing expression of any target gene in biological systems and accelerates critical investigations across a broad range of biomedical and biological research.

1:00- 1:30 Application of Ingenuity Pathways Analysis and RNAi technology in drug discovery programs

Dr. Keith Joho, Senior Vice President Research and Product Management, Ingenuity Systems, Inc

Ingenuity Pathways Analysis (IPA) enables biologists and bioinformaticians to model, analyze and understand the complex biological systems at the core of life science research. IPA 3.1 allows scientists to elucidate and customize biological pathways for particular targets, biomarkers, disease areas, and processes, leveraging Ingenuity's broad knowledge base of biological relationships between genes and proteins, cells, tissues, and diseases. This web-delivered application enables effective interpretation of critical pathways that are activated or disrupted upon RNAi knockdown. Target identification studies in which Ingenuity Pathways Analysis has been used in conjunction with RNAi to elucidate pathways for potential drug targets and to assess genome-wide effects of a knockdown of that target will be presented.

1:30-1:45 RNAi Goes Genomic: Elucidating Gene Function with siRNA Libraries

Dr. David Dorris, Vice President RNAi Technologies, Ambion, Inc

Four keys to successful RNAi screens in human cells are: using highly effective siRNAs, reproducibly and efficiently delivering those siRNAs, ascertaining RNAi effects with a robust assay, and carefully controlling experiments. We will discuss the latest developments in siRNA design and delivery as they relate to RNAi screening, and present data from experiments using siRNA libraries to identify genes involved in apoptosis, cell proliferation and cell cycle progression. We will also present data on use of siRNA pools versus multiple individual siRNAs, as well as data illustrating the need for multiple carefully chosen siRNA controls for siRNA screening experiments.

145:2:00 Technology Short Talks

Additional Sponsorship Available. Contact: Carol Dinerstein at 617-630-1371 or dinerstein@healthtech.com.

RNAi AND HIGH-CONTENT CELLULAR ASSAYS FOR PATHWAY ANALYSIS**2:15-2:45 Phenotypic Fingerprinting of shRNA Effects on Mitotic Progression Using High-Content Imaging**

To Be Announced

Successful application of RNAi at scale combined with high-content imaging has the potential to greatly increase our understanding of a wide range of cellular processes. Lentiviral-based shRNA delivery is a particularly effective method that allows for RNAi evaluation in a wide range of cell types, including non-dividing primary cells. This presentation focuses on high-content analysis of both on and off targets effects of lentiviral delivered shRNAs on mitotic progression in human cells with the aim of identifying phenotypic fingerprints derived from protein knockdown. Analysis of high-content data captured using Cellomics VTI technology, with an emphasis on the mitotic markers cyclinB1 and phospho-histoneH3, will be presented. RNAi technology comparison data (shRNA vs. siRNA) will also be included.

2:45-3:15 RNAi-Based Pathway Analysis Using HCA of Non-Adherent Primary Cells

Dr. Orian Shirihai, Professor, Pharmacology, Tufts University Medical School

To study cellular functions in heterogeneous populations of cells, such as tissue-derived cells, there is a need to continuously monitor functional parameters at a single cell resolution in a large number of cells. This is becoming a unique challenge when the cells of interest are non-adherent, as in the case of blood or bone marrow samples. To overcome this limitation, we used Molecular Cytomics' Optical LiveCell™ Array, a device containing a densely packed array of transparent micron-sized wells. This technology enables real-time, ongoing observation of cellular events from thousands of individual adherent or non-adherent living cells, followed by structural and post-fixation studies on the same cells, using bright field and fluorescent microscopy. We employed this technology for investigating mitochondrial proteins involved in the heme biosynthetic pathway during differentiation of hematopoietic cells. We suggest this approach as a robust tool for HCA studies in heterogeneous populations of cells and as a revolutionary platform for imaging non-adherent cells.

3:15-3:45 Cytoskeletal and Cell Viability Assays for RNAi-Based Validation of Oncology Targets Associated with Rho/Rac Signaling

Mr. Ross Francis, Senior Scientist, Target Discovery, Exelixis, Inc.

Conserved members of the Ras super-family Rho, Rac, and CDC42 are key regulators of the cytoskeleton that have roles in promoting cellular proliferation and are implicated in tumorigenesis. We have combined RNAi knockdown techniques and automated fluorescence imaging of cytoskeletal organization, cellular apoptosis and proliferation to investigate the role of candidate genes in these pathways. Knockdown analysis of Rho/Rac/CDC42 proteins or known pathway regulators / effectors, supports the view that Rho and Rac signaling are necessary for cell viability and proliferation and that knockdown of specific pathway components leads to well-defined cytoskeletal alterations. For example RhoA siRNA is associated with reduced myosin light chain phosphorylation. siRNAi of Rac1 or -3, or CDC42 is generally associated with increased actin content and in some cases with reduced cell/matrix adhesion. We discuss assay development for siRNA screens and target validation, and efforts to distinguish primary cytoskeletal alterations from those arising more indirectly from apoptosis or perturbations in other cellular processes.

3:45-5:00 Refreshment Break with Exhibit and Poster Viewing**STANDARDS FOR HIGH-CONTENT CELLULAR ASSAYS****5:00-5:30 Controlling the Extracellular Matrix for Standardizing Cell Environment**

Dr. John Elliott, Research Scientist, Biotechnology, National Institute of Standards and Technology (NIST)

Extracellular matrix (ECM) proteins provide adhesion sites and signaling cues to cells in culture. Even cells cultured on polystyrene are responding to ECM proteins adsorbed to the substrate surface. Since the molecular features of the adsorbed extracellular matrix proteins can have a dramatic effect on the adhesion and phenotype of adherent cells, it is important to control the tissue culture substrate for optimal intra-experimental and intra-laboratory comparison of high-content assay data. Self assembly of ECM protein, such as collagen, into films on alkanethiol monolayers is a controllable process that provides a highly reproducible, highly homogeneous matrix environment for cells, which can be independently validated by surface chemistry analytical techniques. Using this approach, we have studied how subtle variations in ECM preparations can alter cell phenotypic response in dramatic ways. Thus, control of the ECM environment is also critical for assuring the appropriateness of cell response in pharmacological screening, and for allowing correct interpretation of the assay results in terms of signaling pathways. This approach to fabricating ECM substrates can be used to benchmark cell response and may aid in the standardization of data that is available from high-content analysis.

5:30-6:00 Panel Discussion: Developing Standards for Cellular Assays: Reagents, Cells, Plateware, and Informatics

6:00-7:00 ThinkTank Roundtable Discussions

The concurrent roundtable discussions (open to all delegates) provide a small-circle forum for discussing key issues and meeting potential partners. During the networking session, you are welcome to move freely between the roundtables. The discussion facilitators will present an update the following morning. (You must be a registered attendee to participate.)

Discussion Topics Include:

- RNAi Validation and Off-Target Effects
- Genome-Wide siRNA Screening
- High-Content Cellular Assays for siRNA Screening
- RNAi for Pathway Analysis
- siRNA Delivery and Assay Development
- Integrating siRNA and Compound Library Screening



Thursday, February 2

7:30-8:15 Technology Workshop

Sponsorship Available. Contact: Carol Dinerstein at 617-630-1371 or dinerstein@healthtech.com.

GENOME-WIDE RNAi SCREENING FOR TARGET IDENTIFICATION

8:30 Chairperson's Opening Remarks

8:30-9:00 Sensitized RNAi Screen of Human Kinases and Phosphatases Identifies Novel Regulators of Apoptosis and Chemoresistance

Dr. John Blenis, Professor of Cell Biology, Harvard Medical School

Given the adaptability of tumor cells, drug resistance is a major cause of failure in conventional chemotherapy. Tilting the cellular balance towards apoptosis by activating cell death signals with conventional chemotherapeutic agents, combined with inhibiting tumor-specific survival signals, may be crucial in determining the fate of cancer cells. The combination of targeted and conventional therapies has the potential to maximize efficacy, while minimizing toxicity. Using large-scale RNAi-based screens, we report the identification of known and novel human kinases and phosphatases that promote cell survival, and a new group of phosphatases with tumor-suppressor-like activity. In addition, functional screens in the presence of low dose apoptosis-inducing chemotherapeutic agents has identified a group of kinases whose loss of function sensitizes cells to undergo cell death, highlighting their importance as potential drug targets.

9:00-9:30 Fast siRNA Transfection Method for Automated High-Throughput Screen of Genome-Scale siRNA Libraries

Dr. Namjin Chung, Senior Research Scientist, Automated Biotechnology, Merck Research Laboratories

By understanding the efficacy, stability, and toxicity of lipid-based transfection reagents, we developed a fast and efficient method for transfecting siRNA into cultured mammalian cells. Transfection throughput is only limited by the speed of liquid and microplate handling on the robotic platform, and triplicate transfections of a genome-scale siRNA library of more than 20,000 genes can be completed in 16 hours. Transfection efficiency, behaviors of various control siRNAs, and other quality metrics were comparable to or better than conventional, low-throughput methods, while the cost of screening was significantly lower. The current method provides an efficient means for investigating gene functions in the large scale.

9:30-10:00 A Systematic RNAi Screen for C. Elegans Longevity Genes

Dr. Siu Sylvia Lee, Assistant Professor, Department of Molecular Biology and Genetics, Cornell University

We are using genome-wide RNAi screenings to identify C. elegans longevity genes. We have screened over 16,000 RNAi clones, and identified about 90 RNAi inactivations that reproducibly extended C. elegans lifespan. These RNAi clones correspond to 90 distinct C. elegans genes. The candidate longevity genes we identified participate in a wide variety of cellular processes, indicating that diverse biological functions can influence longevity in C. elegans.

10:00-10:30 HT RNAi Screen and Analysis of Cholesterol Synthesis Pathway in Human Hepatoma Cells

Dr. Christophe J. Echeverri, CEO/CSO, Cenix BioScience GmbH

The talk will describe a recently-completed RNAi screen of over 5,000 therapeutically-relevant genes for new atherosclerosis targets, conducted in collaboration with Bayer Healthcare. The screening assay was further refined to identify genes whose inhibition caused an increase in LDL uptake, as a direct consequence of inhibiting cholesterol synthesis. Genes that were thereby newly implicated in this complex pathway were further analyzed using a titration approach known as Pathway Titration™. I will particularly focus on the range of scientific and strategic decisions that led us through the many challenges of this large study.



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

INTEGRATING siRNA- AND COMPOUND-LIBRARY SCREENING

11:30-12:00 Targeting the HIF-1 Pathway: An Experience with siRNA and Small Molecule Screens

Dr. Yu Shen, Group Leader, Cancer Exploratory Biology, Abbott Laboratories

HIF-1 emerges as an attractive target for cancer therapy. However, the lack of apparent "druggable" targets in the pathway hinders the development of small molecule inhibitors targeting HIF-1. In order to identify "druggable" targets in the HIF-1 pathway, we carried out an HIF-1 reporter screen using both a siRNA library against the "druggable genome" and a compound library consisting of 800,000 small molecule compounds. The siRNA library screen resulted in overwhelming "off-target hits." An analysis of some of the off-target hits revealed that siRNA-mediated off-target gene silencing could be triggered by as low as 7-nt complementation between a siRNA and an mRNA. In contrast, screening of the compound library using the HIF-1 reporter assay resulted in the identification of a class of HIF-1 inhibitors with sub-nanomolar cellular activity. Further analysis of this class of compounds highlights the importance of an often-overlooked mechanism in HIF-1 regulation.

12:00-12:30 Advanced Analytical Approaches to Small Molecule and RNAi Studies Using High-Content Screening and Informatics

Dr. Steven Haney, Senior Scientist, Biological Technologies, Wyeth Research

High-Content Screening is a powerful technology for studying effects of small molecule compounds and RNAi on cells. In fact, it is a challenge to integrate all of the data that is available. We have been interested in leveraging these data, and have begun to develop methods for extracting and analyzing these complex data sets. Our goal is to be able to identify responses of cells in an unbiased approach that will maximize our understanding of how gene and target perturbations affect signaling pathways.

12:30-1:00 High-Content Functional Genomics Screening to Enhance Target Confidence in Safety and Mechanism

To Be Announced

A limited understanding of genes' mechanistic properties is a major factors contributing to the unacceptably high attrition rate observed for many drug targets. Current cell-based screening assays typically measure a discrete event and not the cause, as such a negative result does not distinguish between a target or compound driven response. Here we describe a molecular genetics screening approach incorporating siRNA duplexes as a tool to modulate the expression of molecules within "druggable" target space. The Cellomics ArrayScan platform is subsequently utilized to monitor and evaluate multiple functional endpoints. The integration of these phenotypic measurements with existing chemical and informatics data will enhance the understanding of target mechanism and secondary pharmacology enabling better decision making within a therapeutic program.

1:00-2:30 Lunch with Exhibit and Poster Viewing (last chance to view)

2:30 Close of Main Conference

2:30-6:00

RNAi End-User Forum*

* *Separate registration is required. Participation is limited to end-users only and subject to approval by conference organizers. Companies with RNAi-related products or services on the market or in development (including sponsoring and exhibiting companies) will not receive access to the End-User Forum.*

2:30-3:00

Participant Introductions

3:00-4:20

Discussion I: Strategies to Validate RNAi Data and Minimize Off-Target Effects

Discussion Leader: To Be Announced

Discussion Topics Include:

- How to increase specificity by using multiple siRNAs for each target and designing siRNAs with multiple mismatches with off-target genes?
- How to choose siRNA delivery methods to maximize transfection, while minimizing toxicity and off-target effects?
- How to use scrambled siRNA as negative controls to account for siRNA delivery effects?
- How to "rescue" RNAi effect by expressing siRNA-resistant form of the gene?
- How to confirm siRNA specificity by monitoring global gene expression patterns?
- How to validate knockdown by monitoring mRNA and protein levels?

4:20-4:40

Networking Refreshment Break

4:40-6:00

Discussion II: Overcoming Challenges in Applying RNAi for Target Identification and Validation

Discussion Leader: To Be Announced

Discussion Topics Include:

- Do RNAi technologies offer sufficient gene silencing specificity for target validation?
- What are the limitations in using siRNA for target validation given that it has a different mechanism of action than a small molecule?
- What are participants' experiences in comparing siRNA and small molecule library screening?
- What other technologies should be combined with RNAi to increase confidence in "validated" targets?
- Do *in vitro* RNAi experiments provide a sufficiently good prediction of *in vivo* effect?
- What experimental design features increase confidence in siRNA-based target validation?

6:00

Close of RNAi End-User Forum



**High-Content Analysis 2005
End-User Forum**

2:00-7:00

CONCURRENT USER GROUP MEETINGS

For more information or to register please visit www.highcontentanalysis.com.

GE Healthcare - CHI IN Cell User Group Meeting

The GE Healthcare IN Cell user day will provide a stimulating forum for our IN Cell customers to present and discuss their work. Customers will get an insight into future plans and directions for the IN Cell platform and there will be open discussion sessions to capture any issues and new ideas.

More Imaging: New Options for the MDC Total Imaging Solution

Attend the First Annual MDC Imaging User Forum! At this user forum Molecular Devices will introduce the components of our Total High-content Imaging solution and announce several new developments! The forum will also include in-depth discussions of image acquisition and analysis software, imaging hardware options and turnkey assay-specific analysis modules from both end-users and MDC experts. High-content screening with fixed and live cell-based assays provides extensive multiparametric cellular data. However, successful implementation of HCS requires a complete, turnkey environment from image acquisition through to data management. This forum will give attendees a complete perspective of HCS implementation. www.moleculardevices.com

Advanced Biological Exploration and Screening Using the BD Pathway Bioimager

This workshop will allow both users of the BD Pathway Bioimager and those interested in high content imaging to gather and discuss new applications and methods in imaging. The workshop will explore current topics in high content imaging and will introduce users to recent advances in hardware, software and reagents. A special emphasis will be given to assay development and advanced imaging techniques (e.g. kinetic and confocal imaging) to get the most out of automated imaging instrumentation.

**Co-Located
at High-
Content
Analysis
2006**

GE Healthcare



 **Molecular Devices**



SPONSOR BIOGRAPHIES



Cellomics, Inc. is automating drug discovery through a unique, cell-based assay platform that addresses the needs of Drug Discovery and Systems Biology groups by offering complete systems for High-Content Screening (HCS). The platform includes HCS instrumentation (both fixed end-point and kinetic systems), informatics, cellular image analysis software (BioApplications), fluorescent reagents, kits, cell lines, and multiparametric assays. When applied to early drug discovery, this platform is proving to reduce the 'idea-to-discovery' cycle time in drug discovery, while increasing the probability of the therapeutic success of leads as well as enhancing throughput in systems biology

Dharmacon is the world's leading provider of RNA oligonucleotides, siRNA, and related RNAi products and technologies. Dharmacon has pioneered a custom siRNA design service that employs its proprietary technologies for maximizing the efficiency of gene silencing across a broad range of research. Dharmacon is a subsidiary of Fisher Scientific International Inc.



GE Healthcare provides transformational medical technologies that are shaping a new age of patient care. GE Healthcare's expertise in medical imaging and information technologies, medical diagnostics, patient monitoring systems, disease research, drug discovery and biopharmaceuticals is dedicated to detecting disease earlier and tailoring treatment for individual patients.

GE Healthcare



Extend your conference experience by adding on an extra day of the co-located High-Content Analysis 2006 program.*

*Additional registration fee applies.

Friday, February 3

Visit www.highcontentanalysis.com for more information.

7:30-8:15 Technology Workshop

Sponsorship Available. Contact: Carol Dinerstein at 617-630-1371 or dinerstein@healthtech.com.

ASSAY DESIGN FOR HCA

CONCURRENT SESSIONS

NEURONAL SCREENING

8:30-9:00

A Comparison of Different High-Content Methodologies as Applied to Lead Discovery and Target Validation

Mrs. Judy Dziuba, Senior Scientist, Lead Discovery, Bayer Healthcare AG

9:00-9:30

Assay Development for the Targeting of Distinct Cellular Phenotypes

Dr. Oliver Poeschke, Scientist, Central Assay Development & Screening, Merck KGaA

9:30-10:00

An Integrated Robotic Platform for High-Content Screening: Analysis of GPCR Internalization and Cellular Signaling

Dr. Ralf Heilker, Senior Scientist, Integrated Lead Discovery, Boehringer Ingelheim Pharma GmbH & Co. KG

8:30-9:00

Applying the Power of HCA to Neuronal Screening

Dr. John Dunlop, Director, Discovery Neuroscience, Wyeth Research

9:00-9:30

Screening Chemical Libraries to Identify Regulators of CNS Axon Growth and Branching

Dr. John Bixby, Professor, Pharmacology/Miami Project, University of Miami Miller School of Medicine

9:30-10:00

Technologically Integrated Assay Approaches to Complex Signaling Events

Dr. Vahri Beaumont, Senior Research Biologist, Automated Imaging and Electrophysiology, Merck Sharp and Dohme

10:00-10:30

Coffee Break

10:30-11:00

Phenotypic Assays for Oncology Drug Discovery

Dr. Bonnie Howell, Senior Research Biochemist, Cancer Research, Merck & Co., Inc.

11:00-11:30

Developing and Validating a High-Content Screen for Intracellular Cholesterol Distribution

Dr. Fred Maxfield, Professor and Chairman, Department of Biochemistry, Weill Medical College of Cornell University

11:30-12:00

High-Content Analysis for DNA Content

Mr. Aidas Kriauciunas, Research Scientist, Integrative Biology, Eli Lilly and Company

12:00-12:30

Finding Content in High-Content Data: Two Case Studies for Target-Specific and Phenotypic HCS Assays

Dr. Andreas Vogt, Research Assistant Professor, Pharmacology, University of Pittsburgh

10:30-11:00

High-Content Secondary Screening of Apoptosis in Neuronal Cell Lines

Dr. Dorothea Haasen, Research Scientist, Integrated Lead Discovery, Boehringer Ingelheim Pharma GmbH&Co. KG

11:00-11:30

High-Content Analysis of Human Embryonic Stem Cell Growth and Pluripotency

Dr. Paul Sammak, Associate Professor, Pittsburgh Development Center at the Magee Women's Research Institute, Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh

11:30-12:00

Development of an *In Vitro* Model for Nerve Injury on the Discovery-1 Platform

Dr. Mark Schurdak, Group Leader, Biological Screening, Abbott Laboratories

12:00-12:30

Automated Fluorescent Imaging in Live Brain Tissue Explants: Challenges for Ultra-High-Content Screening (HCS) in Drug Discovery for Neurodegenerative Diseases

Mr. Oscar Trask, Associate in Research, Center for Drug Discovery, Duke University Medical Center

12:30-2:00 Lunch (on your own) or Technology Workshop

Additional Sponsorship Available. Contact: Carol Dinerstein at 617-630-1371 or dinerstein@healthtech.com.

LIVE-CELL IMAGING

2:00-2:30

Utilizing Live-Cell Imaging for Target Validation and Lead Optimization

Dr. Stefan Prechtel, HCA Group Leader, Enabling Technologies / AD-HTS, Schering AG

2:30-3:00

Improving Performance of High-Content Assays by Using Division-Arrested Cell Reagents

Dr. Zhong Zhong, Vice President, Drug Discovery Technologies, Cell & Molecular Technologies, Inc.

3:00-3:30

Refreshment Break

3:30-4:00

Advances in Live-Cell imaging: New Tools for Kinetic Analysis

Dr. Robert Graves, Senior Scientist, GE Healthcare

4:00-4:30

Novel Multifunctional Reporter Protein for High-Content Cell Analysis

Dr. Georgyi V. Los, Senior Scientist, Imaging Group Leader, Promega Corporation

4:30

Close of Conference

Register by November 11th and Save up to \$400!



Cambridge Healthtech Institute's Third Annual

RNAi for Pathway Analysis 2006

January 31-February 2, 2006 • The Fairmont Hotel • San Francisco, California

Register 3 – 4th is Free:
Individuals must register for the same conference or conference combination and submit completed registration forms together for discount to apply. Please reproduce this registration form as needed.

TO REGISTER: WEB: www.healthtech.com • PHONE: 617-630-1300 or toll-free in the U.S. 888-999-6288 • FAX: 617-630-1325 • MAIL: 1037 Chestnut Street, Newton Upper Falls, MA 02464 USA

YES! Register me for RNAi for Pathway Analysis 2006

628 F

Mr. Ms. Mrs. Dr. Prof.

Name _____

Job Title _____ Div./Dept. _____

Company _____

Address _____

City/State/Postal Code _____ Country _____

Telephone _____

Would you like to receive CHI event updates via fax? Yes No Fax _____

Email _____

*Email is not a mandatory field. However by excluding your email you will not receive notification about online access to pre-conference presenter materials, conference updates and networking opportunities.

PRICING INFORMATION

	Commercial	Academic, Govt., Hospital-Affiliated
Conference: Access to the main conference (February 1-2, 2006)		
Early Registration Discount until November 11, 2005	<input type="checkbox"/> \$1,095	<input type="checkbox"/> \$495
Advance Registration Discount until December 16, 2005	<input type="checkbox"/> \$1,295	<input type="checkbox"/> \$595
Registrations after December 16, 2005, and on-site	<input type="checkbox"/> \$1,495	<input type="checkbox"/> \$695
Poster Discount	<input type="checkbox"/> \$50 off	<input type="checkbox"/> \$50 off
Add-on Options		
High-Content Analysis End-User Forum: Tuesday, January 31, 3:00-7:00pm <i>(Participation is limited to end-users only and subject to approval by conference organizers.)</i>	<input type="checkbox"/> \$295	<input type="checkbox"/> \$145
Tutorial: Tuesday, January 31, 3:30-6:30pm More Effective RNAi Studies with High-Content Screening	<input type="checkbox"/> \$295	<input type="checkbox"/> \$145
RNAi End-User Forum: Thursday, February 2, 2:30-6:00pm <i>(Participation is limited to end-users only and subject to approval by conference organizers.)</i>	<input type="checkbox"/> \$295	<input type="checkbox"/> \$145
Add-on Day at High-Content Analysis: Friday, February 3	<input type="checkbox"/> \$695	<input type="checkbox"/> \$345

- Please send information on exhibiting and opportunities to present workshops.
- I am interested in presenting a poster at **RNAi for Pathway Analysis 2006** and will submit a completed one-page abstract by **January 11, 2006**. Registration must be paid in full to present poster.
- I cannot attend but would like to purchase conference proceedings for \$400 plus shipping. Massachusetts delivery will include 5% sales tax.

PAYMENT INFORMATION

- Enclosed is a check or money order payable to Cambridge Healthtech Institute, drawn on a U.S. bank, in U.S. currency.
 - Invoice me, but reserve my space with credit card information listed below. Invoices unpaid two weeks prior to conference will be billed to credit card at full registration rate. Invoices must be paid in full and checks received by the deadline date to retain registration discount. If you plan to register on site, please check with CHI beforehand for space availability.
- Please charge: AMEX (15 digits) Visa (13-16 digits) MasterCard (16 digits) Diners Club (14 digits)

Card # _____ Exp. Date _____

Cardholder _____ Signature _____

Cardholder's Address (if different from above) _____

City/State/Postal Code _____ Country _____

Please refer to the Keycode below:

IHD

Please send information about related CHI conferences:
 Beyond Genome (BYG)
 Molecular Medicine Tri-Conference (MMTC)
 Discovery on Target (DOT)

PRESENT A POSTER AND SAVE \$50

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference CD, your abstract must be submitted, accepted and registration paid in full by January 11, 2006. Register online to use the Poster Abstract Submission form or, if you register by phone, fax, or mail, you will receive Poster Abstract Submission guidelines via email.

I am interested in presenting a poster at **RNAi for Pathway Analysis 2006** and will submit a completed one-page abstract by **January 11, 2006** (Please Note: Registration must be paid in full to present poster.)

Title _____

CHA ADVANCES LIFE SCIENCES REPORTS:

Affiliate authors collaborate with CHA experts to provide a series of reports that evaluate the salient trends in pharmaceutical technology, business, and therapy markets. For more information, visit www.chadvisors.com, or contact Cindy Ohlman at cohlman@chadvisors.com or 781-547-0202.

ADDITIONAL REGISTRATION DETAILS:

Each registration includes all conference sessions, posters and exhibits, food functions, and a copy of one conference CD.

GROUP DISCOUNTS:

Special rates are available for multiple attendees from the same organization. Contact David Cunningham at 617-630-1372 to discuss your options and take advantage of the savings.

HANDICAPPED EQUAL ACCESS:

In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

SUBSTITUTION/CANCELLATION POLICY:

In the event that you need to cancel a registration, you may:

- Transfer your registration to a colleague within your organization
- Credit your registration to another Cambridge Healthtech Institute program
- Request a refund minus a \$100 processing fee per conference
- Request a refund minus the cost of ordering a copy of the CD

NOTE: Cancellations will only be accepted up to two weeks prior to the conference.

Program and speakers are subject to change.

FAX OR MAIL YOUR REGISTRATION TO:

Cambridge Healthtech Institute
1037 Chestnut Street
Newton Upper Falls, MA 02464
Phone: 617-630-1300 or toll-free in the U.S. 888-999-6288
Fax: 617-630-1325 • www.healthtech.com