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June 8-10, 2009

The Fairmont Hotel
San Francisco, CA

**Conference Tracks:**

- **June 8 - 9**
  - Tackling RNAi Delivery
  - RNAi for Functional Screening

- **June 9 - 10**
  - RNAi for Therapeutic Indications
  - RNAi for Target Identification and Validation

**Pre-Conference Short Courses:**

- **June 7**
  - Strategies for Effective RNAi Screens
  - Strategies for Optimizing RNAi Delivery

**Executive Forum:**

- Surveying RNAi Opportunities: From Tools to Therapies

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**Sponsoring Publications:**

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(SC1) Strategies for Effective RNAi Screens
12:00-3:00 pm
The course is designed to provide in-depth information on how to go about setting up RNAi screening experiments and how to design assays for getting optimal results. The challenges working with different types of molecules i.e. siRNAs, shRNAs and the delivery systems to get them into the appropriate cells and tissues will be discussed. The instructors will also provide their input on best practices for the execution of experiments and interpretation of results when dealing with complex biology and informatics.

Topics to be covered:
- Overview of assay designs for siRNA and shRNA screens
- Testing and validating methods for RNA delivery
- Use of appropriate reagents and cell types
- Implementing proper quality control
- Minimizing cytotoxicity and off-target effects
- Data analysis and statistical considerations

Instructors:
Namjin Chung, Ph.D., Senior Research Investigator, Applied Genomics, Bristol-Myers Squibb
Christophe J. Echeverri, Ph. D., CEO/CSO, Cenix BioScience GmbH
Marc Ferrer, Ph.D., Senior Research Fellow, Automated Biotechnology, Merck & Co.

(SC2) Strategies for Optimizing RNAi Delivery
3:30-6:30 pm
The course is designed to provide both the beginner and the expert, with a comprehensive overview of current and emerging delivery systems and formulations facilitating RNAi delivery. Various methods for RNAi delivery such as viral vectors, liposomes, nanoparticles, chemical conjugates and other commonly used techniques will be compared and contrasted for different applications. The instructors will also discuss the challenges associated with RNAi delivery, both in vitro and in vivo, and offer guidance based on their knowledge and expertise in the field.

Topics to be covered:
- Testing and validating methods for delivery
- Overview of viral and non-viral vector systems
- Chemical methods of improving delivery
- New formulations to optimize delivery
- Minimizing cytotoxicity and off-target effects
- Examining tissue distribution and safety profiles

Instructors:
Muthiah Manoharan Ph.D., Vice President, Drug Discovery, Alnylam Pharmaceuticals
Roger Adami, Ph.D., Associate Director, Molecular Pharmaceutics, MDRNA Inc.
John Rossi, Ph.D., Professor and Chair, Molecular Biology, Beckman Research Institute of the City of Hope

TACKLING RNAi DELIVERY
EXPLORING VARIED DELIVERY SYSTEMS
8:30 Chairperson’s Remarks
C. Satishchandran, Ph.D., Chief Technology Officer, Research Technology Center, Pfizer Inc.

8:45 Delivering RNAi Therapeutics Using Chemistry
Muthiah Manoharan, Ph.D., Vice President, Drug Discovery, Alnylam Pharmaceuticals, Inc.

9:15 Systemic Delivery Against Multiple Liver Targets Using a DiLA2-Based Liposome
Roger Adami, Ph.D., Associate Director, Molecular Pharmaceutics, MDRNA Inc.
A novel class of modified amino acids has been developed for in vivo systemic delivery of siRNA. In vivo data using a DiLA2 based liposome and proprietary Dicer siRNAs demonstrating efficacy in the reduction of three liver targets; ApoB, DGAT2, and PCSK9, and the prevention of tumor growth in an orthotopic bladder cancer model will be presented.

9:45 Anti-HIV Aptamer Mediated Delivery of siRNAs to HIV Infected Cells

RNAi FOR FUNCTIONAL SCREENS
HARNESSING THE POWER OF GENOME-WIDE SCREENS
8:30 Chairperson’s Remarks
Anthony Orth, Ph.D., Associate Director, Head of Genomics Profiling, Genomics Institute of the Novartis Research Foundation

8:45 Development of a Flexible RNAi Screening Platform for Drug Discovery
Anthony Orth, Ph.D., Associate Director, Head of Genomics Profiling, Genomics Institute of the Novartis Research Foundation
Scanning the genome for druggable targets involved in therapeutically-relevant cellular models has become an increasingly important tool in the pre-clinical drug discovery process. We have developed an assay system permitting whole genome synthetic siRNA and druggome-scale lentiviral shRNA screening and describe its application, by way of example, to patient-derived glioblastoma.

9:15 Meta-Analysis of Multiple Genome-Wide siRNA Screens
Renate König, PhD, Research Assistant Professor, Infectious & Inflammatory Disease Center, Burnham Institute for Medical Research
**TACKLING RNAi DELIVERY Continued**

John Rossi, Ph.D., Professor and Chair, Molecular Biology, Beckman Research Institute of the City of Hope

Dual inhibitory function anti-gp120 aptamer-siRNA chimeras have been developed in which both the aptamer and the siRNA portions have potent anti-HIV activities. This siRNA delivery system is specifically internalized into cells expressing gp160 and once internalized functional siRNAs are generated via Dicer processing of the siRNAs from the chimeric aptamer-siRNA constructs, resulting in RNAi mediated knockdown of target gene expression. The aptamersiRNA chimeras strongly suppressed HIV-1 infection in a RAG-hu mouse model infected with HIV.

**RNAi FOR FUNCTIONAL SCREENS Continued**

We have carried out a meta-analysis of host cell genes linked to HIV replication that were identified in several genome-wide studies, including three independent siRNA screens. The analysis of the overlaps between studies yielded a more extensively corroborated set of HIV host factors and led to refined networks of cellular subsystems recruited by HIV.

**10:15 Coffee Break**

**10:45 Peptide Transduction Domain Delivery of siRNAs**
Steven F. Dowdy, Ph.D., Investigator, Howard Hughes Medical Institute and Professor, Department of Cellular & Molecular Medicine, University of California-San Diego, School of Medicine

siRNA delivery remains the rate-limiting step for RNAi therapeutics development. We developed a Peptide Transduction Domain-siRNA Binding Domain (PTD-DRBD) fusion protein siRNA delivery approach. PTD-DRBD delivered siRNAs induced RNAi responses in the entire population of 30+ primary and transformed cell types in a non-cytotoxic fashion, including HUVECs, T cells and hESC. PTD-DRBD combinatorial in vivo delivery of EGFR and Akt2 siRNAs induced a synthetic lethal response that significantly increased survival of intracerebral glioblastoma pre-clinical models. Taken together, these observations demonstrate the ability of PTD-DRBD to efficiently deliver siRNAs in vitro and in vivo.

**11:15 Therapeutic AtuRNAi in the Pulmonary Vascular Endothelium Protects from Vascular Hyperpermeability**
Ansgar Santel, Ph.D., Senior Scientist, Silence Therapeutics AG

The AtuPLEX technology, a liposomal formulation of stabilized siRNA molecules (AtuRNAi), can be used systemically for RNAi-mediated therapeutic application in the vascular endothelium. The vascular endothelial cells contribute to the pathophysiology of many diseases. Here, we will discuss our approach of using a cationic liposomal formulation of siRNA molecules systemically for RNAi in the pulmonary vasculature. We characterized the involvement of particular target genes in the progression of vascular permeability in different murine models and analyzed their loss-of-function effect on improved vascular barrier function in vivo.

**11:45 Panel Discussion: RNAi Delivery: What Is the Progress and Where Are We Lacking?**

**12:15 pm Close of Morning of Session**
Tackling RNAi Delivery

The major hurdle for siRNA therapeutic is to deliver siRNA to the desired sites, and the solid tumor posts even a higher hurdle because of its anatomy. We have attacked the problem through various routes and investigated several critical aspects of siRNA therapy for cancer. We will discuss the lessons learned in the pre-clinical development of siRNA therapeutics and our evaluation of different delivery systems on the market.

2:35 Targeting T Cells for RNAi-Based HIV Therapy
Priti Kumar, Ph.D., Assistant Professor, Department of Internal Medicine/Section for Infectious Diseases, Yale University

Therapeutic application of siRNA requires delivery to the appropriate subcellular compartment, within the target cell, within the target tissue responsible for the pathology. The potency of RNAi as an HIV therapeutic has been largely restricted to in vitro demonstrations due to problems of siRNA delivery to the relevant HIV-infected immune cells in vivo. Novel antibody-based approaches for targeted delivery of antiviral siRNA into human T cells will be discussed.

3:05 Developing Immune Targeting Nanoparticles Containing siRNAs to Curtail Inflammatory Bowel Diseases
Dan Peer, Ph.D., Head, Laboratory of Nanomedicine, Department of Cell Research & Immunology, and the Center for Nanoscience and Nanotechnology, Tel Aviv University

We developed a strategy to target gut leukocytes and selectively silence genes in leukocytes in vivo using targeted, stabilized nanoparticles. This study revealed Cyclin D1 to be a potential anti-inflammatory target, and suggests that the application of similar modes of targeting by siRNA may be feasible in other therapeutic settings.

3:35 Targeted Nanoparticles for siRNA Delivery
Robert Lee, Ph.D., Associate Professor, Ohio State University

RNAi for Functional Screens

Continued

Pharmacology, The University of NC at Chapel Hill

2:35 Using HT Applications of RNAi to Drive Drug Discovery and Development
Christophe J. Echeverri, Ph.D., Chief Executive Officer and Chief Scientific Officer, Cenix BioScience GmbH

3:05 Probing the p53 Pathway
Laura Corson, Associate Scientist, Department of Cell Regulation, Genentech Inc.

A multi-parametric, high content siRNA screen of cells +/- p53 yielded insight into genes that impinge on the p53 tumor suppressor pathway. Identification of siRNAs that regulate the strength of the p53 response point to potential tumor suppressors, oncogenes, and possible drug targets.

3:35 siRNA Screening: Development of Hit Stratification Strategies
Louise Carr Baskin, Product Manager, Dharmacon Products, Thermo Fisher Scientific

While synthetic siRNA libraries are powerful tools for functional genomic screens, off-target effects mediated by siRNA seed interactions with the 3’UR of unintended targets can result in false positives. Given this potential, the development of effective hit validation/stratification strategies is imperative. We will present a study that compares two strategies for identification of high confidence hits, including a multiple-reagent approach where two or more individual siRNAs induce the same phenotype and a chemical modification approach where hit confirmation is achieved using pools of siRNAs that contain dual-strand specificity-enhancing modifications.

3:50 Refreshment Break

4:15 Targeted RNA Therapies for the Treatment of Prostate Cancer
Paloma H. Giangrande, Ph.D., Assistant Professor, Department of Internal Medicine, University of Iowa

The first generation aptamer-siRNA chimera can deliver siRNAs targeting cell-survival genes to PSMA-expressing cancer cells in vitro and in vivo. Here, we describe the development of chimeras with enhanced in vitro silencing activity and specificity over the first generation chimeras. In addition, these ‘optimized’ chimeras have been truncated to enable chemical synthesis for scale-up production. Importantly, when administered systemically to mice bearing PSMA-positive tumors, the ‘optimal’ chimeras resulted in pronounced tumor regression.

4:45 Dynamics of siRNA Glomerular Filtration and Proximal Tubule Handling in Vivo Using 2-Photon Microscopy
Bruce A. Molitoris, M.D., Director, Division of Nephrology and Professor of Medicine, Indiana University

Following intravenous injection Cy-3 labeled siRNA was rapidly filtered across the glomerulus and taken up selectively by proximal tubule cells. Total cellular and cytosolic accumulation in proximal tubule cells was quantified using threshold analysis and revealed a maximum at 120 minutes with a rapid decay over the next four hours. The biological activity of the siRNA correlated closely to the fluorescent half life.

4:15 High-Throughput RNAi-Based Cellular Pharmacogenomics Revealed Context of Vulnerabilities of Brostallicin
Holly Yin, Head of Cellular Genomics, Pharmaceutical Genomics Division (PGD), Translational Genomics Research Institute

We applied high-throughput RNA screen in the attempt to identify molecular determinants of Brostallicin, a minor groove DNA binding agent. From this, we identified two predominant concepts for brostallicin response, DNA repair and histone modification, on which additional studies were focused including confirmation, validation and in vitro drug combinations with Brostallicin. The combined results from this study can inform clinical development and rational drug combination strategies.

4:30 To Be Announced
Dr. Albert Seymour, Director Biological Profiling & Human Genetics, Pfizer

4:45 RNAi Screens Reveal a Conserved Damage Survival Network
Alexander J. R. Bishop, D.Phil Assistant Professor Cellular and Structural Biology, The University of Texas Health Science Center

DNA damage initiates a pleiotropic response aimed at cellular survival. However, survival pathway dysregulation may produce chemoresistant cancer cells. A cell-based Drosophila RNAi survival screen was used for damaging agents. Bioinformatics mapping to the protein interactome revealed a damage survival network that is conserved across species. These studies provide novel rationale for therapeutic strategies.

5:15 Welcoming Reception in the Exhibit Hall
6:30 End of Day
OPTIMIZING RNAi DELIVERY FOR IN VITRO APPLICATIONS [Shared Session]

In this session the speakers will each present case studies to elaborate on the do’s and don’ts for testing and validating various RNAi delivery systems, specifically for in vitro applications.

Participants:
Paul Kassner, Ph.D., Principal Scientist, Amgen Inc.
Shane Marine, Ph.D., Automated Biotechnology, Merck & Co., Inc.
Namjin Chung, Ph.D., Senior Research Investigator, Applied Genomics, Bristol-Myers Squibb Co.
David Davis, Ph.D., Scientist, Molecular Biology, Genentech Inc.

9:50 Networking Coffee Break Poster and Exhibit Viewing
11:15 Panel Discussion: Criteria for Testing and Validating Systems for RNAi Delivery
12:15 pm Close of Morning Session

SPONSORED LUNCHEON PRESENTATIONS

12:30 pm Next-Generation siRNAs: Combining Support Vector Machine Learning With Novel Chemical Modifications for More Consistent siRNA Performance in High-Content Screens

Susan Magdaleno, Ph.D., Senior Manager, Scientists, Applied Biosystems

Current RNAi technologies often yield confusing results in siRNA screens due to inconsistent or incomplete knock-down of the intended mRNA target, knock-down of unintended mRNAs and/or siRNA toxicity. Our newest siRNA technology alleviates these problems by developing an innovative algorithm for greater predictability and by incorporating chemical modifications to enhance specific properties of the siRNAs on a genome-wide level. A classification strategy using support vector machine (SVM) was developed to improve the ability to predict the highest potency siRNAs. A second SVM classifier was developed to predict and eliminate 80% of the potentially toxic siRNA. This new algorithm can identify siRNAs that can produce maximum mRNA knock-down at 5-100x lower siRNA concentration than previous siRNAs technologies. The algorithm was used as a foundation for screening and identifying the optimal chemical modification to enhance siRNA specificity and performance in cell based assays. Greater than 20 siRNA modification patterns were screened with three different chemistries in two high-content microscopy-based cell assays. The optimal modification gave the most benefit by removing the off-target phenotypes from a previously identified collection of “problematic” siRNAs while maintaining the desired expected phenotype in the two cell-based assays. The new SVM algorithm combined with the chemical modifications was developed into a genome-wide collection of siRNAs called Silencer® Select. Using Silencer® Select, RNAi screens can be performed at lower concentrations while maintaining potency and the enhanced specificity will provide greater confidence in screening results.

1:00 pm Presentation 2 (Opportunity Available) or Lunch on Your Own
TUESDAY, JUNE 9

12:00 - 2:00 pm Registration for RNAi for Therapeutic Indications and RNAi for Target Identification and Validation Conferences

MAKING RNAi THERAPIES A REALITY

8:15 Chairperson’s Remarks
Christina Rondinone, Ph.D., Director, Research, Metabolic Diseases, Hoffmann-La Roche Inc.

8:20 Development of an RNAi Therapeutic for Colon Polyposis
Johannes Fruehauf M.D., Ph.D., Vice President, Research, Cequent Pharmaceuticals Inc.

Indications in the gastrointestinal tract (GIT) pose particular challenges to the delivery of therapeutic RNAi. Cequent’s lead candidate CEQ508 is a non-pathogenic E.Coli equipped to produce and deliver shRNA against beta-catenin for the indication of Familial Adenomatous Polyposis. Treatment leads to the silencing of beta-catenin in the epithelial cells of the mucosa, this has been shown to result in reduction of polyp formation and polyp dysplasia in a mouse model of polyposis. Extensive toxicology testing performed in rodents and non-human primates has demonstrated the efficacy and safety of this technology and Cequent is planning to initiate Phase I testing for Familial Polyposis in late-2009.

WEDNESDAY, JUNE 10

7:00 am – 4:00 pm Executive Forum – A Shared Session

RNA INTERFERENCE SUMMIT

7:00- 8:00 am Facilitated Break-Out Discussion Groups and Continental Breakfast

I. Surveying RNAi Opportunities: From Tools to Therapies
Participants:
Arthur M. Krieg, M.D., Chief Scientific Officer, Research Technology Center, Pfizer Inc.
Elena Feinstein, M.D., Chief Scientific Officer, Quark Pharmaceuticals Inc.
Klaus Giese, Ph.D., Chief Scientific Officer, Silence Therapeutics PLC
Thomas Singer D.A.B.T. Global Head of Non-Clinical Safety, F Hoffmann-La Roche AG

3:35 Sponsored Presentation (Opportunity Available)
3:50 Networking Refreshment Break Poster and Exhibit Viewing

II. Navigating the Intellectual Property Landscape
Participants:
Kathleen M. Williams, Ph.D., J.D., Intellectual Property Attorney, Partner, Edwards Angell Palmer & Dodge LLP
Rochelle K. Seide, Ph.D., Senior Counsel, Schwegman, Lundberg & Woessner, PA.
Steven L. Highlander, Ph.D., Partner, Intellectual Property, Fulbright & Jaworski LLP

5:45 End of Day
**RNAi FOR THERAPEUTIC INDICATIONS** Continued

significant inhibition of tumor growth and lymph node metastasis formation. A prospective, open label, single-centre, dose finding Phase I study with Atu027 in subjects with advanced solid tumours will commence in 2009.

**RNAi FOR TARGET IDENTIFICATION AND VALIDATION** Continued

9:50 Networking Coffee Break Poster and Exhibit Viewing

10:45 Delivery of shRNA and Other Anti-HIV RNAs by Autologous Transplantation of Lentivirus-Transduced CD34+ Cells: A Feasibility Trial
John Zaia, M.D., Chairman, Department of Virology and Director of the General Clinical Research Center, Beckman Research Institute, City of Hope

A lentivirus encoding three anti-HIV RNAs was used for the first time in a clinical trial. The problems and approaches to design of such a vector, the large-scale packaging of a lentivirus encoding inhibitory packaging elements, and the issue of manufacture and release testing of the final cell product will be discussed. The study has completed enrollment and the study status will be updated at the time of the presentation.

11:15 Bringing up CALAA-01: The First Nanoparticle-Formulated siRNA for Cancer in the Clinic
Bob D. Brown, Ph.D., Senior Vice President, Research, Dicerna Pharmaceuticals

A lentivirus encoding three anti-HIV RNAs was used for the first time in a clinical trial. The problems and approaches to design of such a vector, the large-scale packaging of a lentivirus encoding inhibitory packaging elements, and the issue of manufacture and release testing of the final cell product will be discussed. The study has completed enrollment and the study status will be updated at the time of the presentation.

11:45 siRNA Therapeutics for Ocular Angiogenesis and Ocular Neuroprotection
Elena Feinstein, CSO, Quark Pharmaceuticals

Efficient siRNA delivery to target cells remains the main challenge in the field of siRNA therapeutics. It turns out that siRNA delivered topically to the eye, inner ear or lungs (including tumors residing in the lungs) can efficiently reach its target cells, exert target gene knockdown and pharmacological effect.

12:15 pm Conception of Circular Interfering RNA and Production’s Strategy
Guillaume Plane, Ph.D., CEO, MitoProd SA

Circular Interfering RNAs represent a powerful tool for the Pharmaceutical Industry. The discovery of the basic mechanism of RNA Interference was made by Andrew Fire and Craig Mello, who won the Nobel Prize in Medicine in 2006. Indeed, the stability, quality, in vivo efficiency, and delivery of these molecules represent major challenges for their development. Basically, by circularizing the primary transcript and thus removing extremities, MitoProd brings an innovative solution to face most of these challenges. In association with MitoProd’s innovative technology for RNA manufacturing, based on the fermentation of Saccharomyces cerevisiae yeast, Circular Interfering RNAs (ciRNA®s) offer some major advantages for the development of siRNA-based drugs.

10:45 Unlocking the Genome with Pooled shRNA Screens
David Davis, Ph.D., Scientist, Molecular Biology, Genentech Inc.

Genome-wide shRNA libraries are a revolutionary tool for reverse genetic screens. The ability to pool large numbers of independent constructs has been shown to be an efficient screening approach. We have applied this technology to identify novel regulators of oncogenic signaling pathways. The advantages and considerations in the application and deconvolution of pooled shRNA libraries will be presented.

11:15 Panel Discussion: How Far Have We Progressed with the Targets Identified from RNAi Screens?

12:15 pm Close of Morning Session

**POSTER SUBMISSION INFORMATION**

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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 May 1, 2009. 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.

**SPONSORED LUNCHEON PRESENTATIONS**

12:30 pm Presentation 1 (Opportunity Available) or Lunch on Your Own
1:00 Session Break

**ADDRESSING SPECIFICITY AND SAFETY CONCERNS**

1:45 Chairperson’s Remarks
Arthur M. Krieg, M.D., Chief Scientific Officer, Research Technology Center, Pfizer Inc.

1:50 Understanding the Immune Effects of RNA
Arthur M. Krieg, M.D., Chief Scientific Officer, Research Technology Center, Pfizer Inc.

Natural or synthetic RNA can stimulate several innate immune receptors, resulting in distinct patterns of cytokine and cellular responses. This innate immune ac-

**TARGET VALIDATION: EXPERIMENTAL DESIGN AND FOLLOW-THROUGH**

1:45 Chairperson’s Remarks
Albert B. Seymour, Ph.D., Director of Biological Profiling, Target Generation Unit, Biotherapeutics and Bioinnovation Center, Pfizer, Inc.

1:50 Cancer Target Identification and Validation by siRNA Library Screening
Xiaoyu Lin, Ph.D., Associate Research Investigator, siRNA therapeutics, Abbott Laboratories
RNAi FOR THERAPEUTIC INDICATION Continued

**2:20**  
**Non-Clinical Safety Assessment of siRNA-Based Therapeutics**  
Thomas Singer, D.A.B.T., Global Head of Non-Clinical Safety, F. Hoffmann-La Roche AG  
siRNA-based therapeutics represent a new class of molecules in addition to small molecules and biologicals. They offer the unique opportunity to target virtually any gene of the human genome leading to a significant extension of therapeutic opportunities. However, there are no guidelines addressing siRNA safety yet and there is little information available in the public domain. It is assumed that the safety assessment of siRNAs is more complex as with classical drugs because the delivery vehicle and the double stranded RNA trigger independent responses such as immune system or transcriptome interference. Strategies to address these interactions will be presented together with a panel of standard assays we consider important to enable siRNAs to enter clinical development.

**2:50**  
**Networking Refreshment Break (Last Chance for Poster and Exhibit Viewing)**

**3:30**  
**Optimization of shRNA Features for Targeting Hepatitis C Virus**  
Qing Ge, Ph.D., Director, Viral Therapeutics, Somagenics Inc.  
Short hairpin RNAs (shRNAs) targeting the highly conserved internal ribosome entry site (IRES) of HCV were designed and tested for their capabilities to silence gene expression. Comparison of shRNA and siRNA of the same sequence showed that shRNAs are of similar or greater potency than the corresponding siRNAs. No type I interferon-induction and cytotoxicity was found with lead shRNAs. The results indicate that shRNAs, delivered as chemically synthesized, may be effective agents for the control of HCV.

**4:00**  
**Applying Locked Nucleic Acid (LNA)-based RNA Antagonist Therapy for Cancer Therapy: Preclinical and Clinical Experience**  
Lee Greenberger, Ph.D., Vice President, Research, Enzon Pharmaceuticals, Inc.  
LNA-based antisense oligonucleotides (LNA-ONs) demonstrate extraordinary potency, stability in vitro, and long tissue half-life. They are being utilized to inhibit the expression of four key cancer targets: hypoxia inducible factor-1alpha (HIF-1alpha), survivin, human epidermal growth factor 3 (HER3) and the androgen receptor. Pre-clinical data indicates that LNA-ONs, given without assisted delivery (e.g. transfection agents) get into the nucleus of certain tumor cells, silence mRNA, down regulate protein expression, and inhibit tumor growth. Tumor and liver mRNA silencing associated with inhibition of tumor growth in vivo has been demonstrated in xenograft models. Evaluation of an anti-HIF-1alpha LNA-ON in patients with advanced malignancies demonstrates that the molecule is well-tolerated, produces stable disease, and is associated with tumor shrinkage in some patients.

**4:30**  
**Developing Multi-Targeted siRNA Therapeutics for Treatment of Critical Human Diseases**  
David Evans Ph.D., Vice President, Discovery Research, Sirnaomics  
Using siRNA cocktail to silence multiple disease genes is truly realizing the advantage of small interfering RNA (siRNA)-based drugs. We have developed a set of siRNA cocktails using proprietary algorithm and “Tri-Blocker™” platform, delivered with optimized nanoparticle formulations locally and systemically for treatment of various human diseases.

**5:00**  
**U1 Adaptors: A Novel Gene Silencing Technology**  
Mark Behlke, M.D., Ph.D., Chief Scientific Officer, Integrated DNA Technologies  
U1 Adaptors represent a novel gene silencing method where a bi-functional synthetic oligonucleotide recruits action of the U1 snRNP complex in the terminal exon of a targeted gene. Tethering of U1 snRNP inhibits 3’ end processing (polyA tail addition) leading to degradation of that RNA species within the nucleus. Adaptors work via different mechanisms of action at different sub-cellular locations; the methods can be combined to increase the level of knockdown achieved using lower doses of both reagents.

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RNAi FOR TARGET IDENTIFICATION AND VALIDATION Continued

**2:20**  
**Establishing a siRNA Pipeline: From in vivo Target Validation to Use as a RNA Therapeutic**  
Steven Bartz, Ph.D., Director, Lead Development, Sirna Therapeutics (A wholly owned subsidiary of Merck & Co.)  
A process has been established to enable use of siRNAs for in vivo target validation through rapid testing of candidate targets. Targets validated using siRNAs in animal models proceed to populate a pipeline for development of RNA therapeutics. This target validation to clinical development process has generated large amounts of in vivo data that drives continued improvement in siRNA lead development.

**3:30**  
**A Framework for the Analysis of RNAi Phenotypes as Quantitative Traits**  
Kim Quon, Ph.D., Principal Scientist, Amgen Inc.  
siRNA phenotypes are usually interpreted like genetic knockout experiments: a gene’s normal function is inferred from its knockdown phenotype. However, because individual siRNAs against a given gene have differing knockdown efficiencies, a spectrum of quantitative phenotypes is typically obtained. We propose that siRNAs should therefore be treated analogously to hypomorphic allelic series rather than to knockouts. Using such a framework, we have developed rigorous methods for inferring true gene function from siRNA data, treating phenotypes as quantitative traits. We show that such a framework can be critical for properly interpreting siRNA screening and validation experiments, particularly when cell viability is a critical phenotype of interest as for oncology targets.

**4:00**  
**High-Throughput RNAi Genetic Screens for Drug Discovery and Development**  
Attila A. Seyhan, Ph.D., Head of RNAi and Compound Delivery and Screens Systems Biology Technologies, Wyeth Research  
We have employed RNAi-based gene function analysis which has been recognized as a powerful approach when combined with high-content screening involving different parameters for defining a specific target. Using HeLa cells as model, we have screened 280 known cell cycle and 280 randomly selected genes from a custom pooled druggable genome siRNA library, demonstrating the utility of integrating the liquid handling workstation automation format with the endpoint readout of gene knockdown by high content screening for RNAi genetic screens. From this pilot study, we now are now expanding the RNAi gene targeting scale of this concept to include a larger “druggable-genome” or “genome-wide” RNAi library screens in arrayed (synthetic siRNA or Lentiviral-shRNA) or pooled (Lentiviral-shRNA) formats.

**4:30**  
**Human Genetic Approaches to Target Discovery and Validation: Starting With the Clinical Endpoint of Interest**  
Albert B. Seymour, Ph.D., Director of Biological Profiling, Target Generation Unit, Biotherapeutics and Bioinnovation Center, Pfizer, Inc.

**5:00**  
**Panel Discussion: Identifying the Bottlenecks in Target Validation**

**5:30**  
**Close of RNAi for Target Identification and Validation Conference**
RNA INTERFERENCE SUMMIT

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The Fairmont Hotel
950 Mason Street
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For more information, please contact:
Jon Stroup – Manager, Business Development
781-972-5483 • jstroup@healthtech.com

Conference Tracks Include:
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The Business of Genomics June 8-9, 2009
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Advance Registration until May 1, 2009
$1,195
$1,895
Commercial
Academic, Government, Hospital-affiliated
June 9-10
$775
$845

Select the conferences you will most likely attend. Please CHOOSE TWO only - one from each column

June 8-10
AND
June 9-10

- RNAi for Functional Screens
- Tackling RNA Delivery
- Genotyping Tools (co-located)
- The Business of Genomics (co-located)

One Conference Only:
June 8-9 OR June 9-10
Advance Registration until May 1, 2009
$1,145
$1,395
Commercial
Academic, Government, Hospital-affiliated

Select the conference you will most likely attend. Please CHOOSE ONE only
June 8-9
OR
June 9-10

- RNAi for Functional Screens
- Tackling RNA Delivery
- Genotyping Tools (co-located)
- The Business of Genomics (co-located)

SHORT COURSE PRICING
Includes access to the short course(s) ONLY

June 7

- (SC 1) Strategies for Effective RNAi Screens (Sun. 12:30-3:00 pm)
- (SC 2) Strategies for Optimizing RNAi Delivery (Sun. 3:30-6:30 pm)

One Short Course
$595
$295

Two Short Courses
$895
$495
$50 off
$50 off

POSTER DISCOUNT

REGISTER 3 - 4TH IS FREE

Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply. Please reproduce this registration form as needed.

For more information on group discounts contact David Cunningham at 781-972-5472

I cannot attend but would like to purchase the RNA interference Summit conference CD for $350 (plus shipping).

Massachusetts delivery will include 5% sales tax

Please send information on exhibiting and opportunities to present workshops.

PAYMENT INFORMATION

Enclosed is a check or money order payable to Cambridge Healthtech Institute, drawn on a U.S. bank, in U.S. currency.

Please note, however that my space with credit card information listed below. Invoices unpaid two weeks prior to conference will be billed to my 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.

Card #
Cardholder
Signature
Cardholder’s Address (if different from above)
City/State/Postal Code
Country

Please refer to the Registration Code below:

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 May 1, 2009. 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
RNA Interference Summit and will submit a completed one-page abstract by May 1, 2009

(Please Note: Registration must be paid in full to present poster. After submitting your registration, a form will appear allowing you to submit your poster abstract information)

Title

Cambridge Healthtech Institute
620 First Avenue, Suite 300, Needham, MA 02494
Toll-free in the U.S. 888.999.6288
Fax: 781-972-5425
www.healthtech.com

CHI Insight Pharma Reports
A series of diverse reports designed to keep life science professionals informed of the salient trends in pharmaceutical technology, business, clinical development, and therapeutic disease markets. For a detailed list of reports, visit InsightPharmaReports.com, or contact Rose LaRaia, rlaraia@healthtech.com, 781-972-5444.

Barnett Educational Services
Barnett is a recognized leader in clinical education, training, and reference guides for life science professionals involved in the drug development process. For more information, visit www.barnettinternational.com.

Additional Registration Details
Each registration includes all conference sessions, posters and exhibits, food functions, and a copy of the conference CD.

Group Discounts
Special rates are available for multiple attendees from the same organization. Contact David Cunningham at 781-972-5472
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 ($350 of ordering a copy of the CD)

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

Program and speaker changes are subject to change.

Fax or Mail Registration to:
Cambridge Healthtech Institute
620 First Avenue, Suite 300, Needham, MA 02494
T: 781.972.5400 F: 781.972.5425 www.healthtech.com

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