Register by January 6, 2012 and **Save up to $250!**

## EIGHTH ANNUAL microRNA

### IN HUMAN DISEASE AND DEVELOPMENT

**MARCH 12-13, 2012 | HYATT REGENCY CAMBRIDGE | CAMBRIDGE, MA**

---

**Track 1: microRNA in Diagnostic and Therapeutic Development**

**Track 2: microRNA Pathways in Disease and Development**

**COVERAGE INCLUDES:**

- microRNA as biomarkers and diagnostics
- microRNA and stem cells
- microRNA pathways in disease
- microRNA therapeutics: design and delivery
- Role of microRNA in viral infection
- Therapeutic potential of microRNA
- Role of microRNA in cancer mechanism
- microRNA as targets in therapeutic development

---

**Pre-Conference Web Symposia:**

- **Circulating microRNA as Biomarkers**
  - February 9, 2012
- **microRNA in Cancer**
  - February 15, 2012

---

**Corporate Sponsor**

**INGENUITY SYSTEMS**

---

*Healthtech.com/mrn*
**Track 1: microRNA in Diagnostic and Therapeutic Development**

**MONDAY, MARCH 12, 2012**

7:30-8:30 am Conference Registration and Morning Coffee
8:30-8:40 Welcoming Remarks from Conference Director

### microRNAs as Biomarkers and Diagnostics

**8:40-8:45 Chairperson’s Opening Remarks**

**8:45-9:15 microRNA Biomarkers for Cancer Treatment**

Glen J. Weiss, M.D., Co-Head, Lung Cancer Unit, The Translational Genomics Research Institute (TGen); Director, Thoracic Oncology, Virginia G. Piper Cancer Center Clinical Trials at Scottsdale Healthcare; CMO, CRAB-Clinical Trials Consortium

A single microRNA can impact hundreds of targets and can affect pathways controlling oncogenic processes. Data will be presented illustrating how using microRNA can impact cancer treatment decision making, validated microRNAs are associated with resistance and/or sensitivity to chemotherapy and targeted therapy, and how microRNAs could be used as therapeutics.

**9:15-9:45 Bridging Early Discovery Needs and Downstream Biomarker Requirements**

David von Schack, Ph.D., Senior Principal Research Scientist, Translational Immunology, Pfizer

miRNAs have been shown to be involved in a wide range of diseases and disease mechanisms and have become an integral component in building a complete understanding of molecular disease processes. Challenges remain in the interpretation of miRNA involvement in pathologic processes as they are predicted and shown to bind 10s or sometimes 100s of miRNA transcripts. While it is possible to show correlation of miRNA changes with disease processes, the understanding of these changes are hampered by our difficulties in assigning specific molecular functions to those regulated miRNAs. Target discovery efforts using miRNA profiling will be addressed and the potential for miRNA as mechanistic biomarkers of drug action or disease modulation discussed.

**9:45-10:15 Integrating Contextual microRNA and Protein Signatures for Diagnostic Applications in Cancer**

Lorenzo F. Sempere, Ph.D., Research Assistant Professor, Medicine, Dartmouth-Hitchcock/Norris Cotton Cancer Center

As each tumor lesion has a different ratio of cancer cells to reactive stroma and infiltrating immune cells, we implemented a multiplex tissue slide-based assay to measure miRNA expression levels at single cell resolution and to extract the contextual information embedded within these different cell types. We will present some salient examples that ascertain aberrant and dysfunctional miRNA-mediated pathways within cancer cells and other cellular compartments of the tumor microenvironment. We will also discuss a tissue slide-based strategy for integration of translational miRNA and well-established protein biomarkers to increase molecular characterization of tumors and enhance the diagnostic power of current clinical assays.

**10:15-11:15 Coffee Break in the Exhibit Hall with Poster Viewing**

**11:15-12:15 pm Sponsored Presentations**

**Technology Showcase**

**11:15-11:30 A Unique Biological Knowledge-Driven Method for Rapid microRNA Target Prioritization: Cancer Case Studies**

Aimee Jackson, Director, Product Management, Ingenuity Systems

microRNAs are a promising source of biomarkers. However, searching databases for predicted and observed targets yields thousands of potential targets and paring these down to a manageable number is a challenge. Case studies in which the number of potential targets was quickly reduced to just a few will be presented.

**11:30-12:00 pm Translating miRNA Discovery in Biofluids into Robust Biomarkers for Disease**

Søren Jensby Nielsen, Ph.D., Head, Diagnostics, Exiqon A/S

Exiqon has developed a LNA™-based miRNA qPCR platform with unparalleled sensitivity and robustness to accelerate discovery and clinical development of miRNA-based biomarkers. We have profiled thousands of biofluid samples including plasma, serum and urine. To secure technical excellence and eliminate unwanted bias, an extensive

**Technology Showcase**

11:15-12:15 pm Sponsored Presentations (Opportunities available. Contact Ilana Quigley, Manager, Business Development, at 781-972-5457 or iquigley@healthtech.com.)

**Track 2: microRNA Pathways in Disease and Development**

### microRNA and Stem Cells

**8:40-8:45 Chairperson’s Opening Remarks**

**8:45-9:15 Talk Title to be Announced**

Richard J. Gregory, Ph.D., Children’s Hospital Boston, Harvard Stem Cell Institute (HSCI), Harvard Medical School

**9:15-9:45 microRNA Biomarkers Play an Important Role in Cortical Neural Stem Cell Development**

Tao Sun, Ph.D., Assistant Professor, Cell and Developmental Biology, Weill Medical College of Cornell University

Neural stem cells can self-renew and give rise to multiple cell types in the nervous system. We have identified some microRNAs that are expressed in neural stem cells derived from the cerebral cortex. We have found that microRNAs control self-renewal and differentiation of neural stem cells by regulating distinct targets. Our results have demonstrated the importance of microRNAs in neural stem cell development.

**9:45-10:15 Inducing Pluripotency by RNA**

Tariq M. Rana, Ph.D., Professor and Director, Program for RNA Biology, Sanford-Burnham Medical Research Institute

Although induced pluripotent stem cells (iPSCs) hold great promise for customized regenerative medicine, the molecular basis of reprogramming is largely unknown. Overcoming barriers that maintain cell identities is a critical step in the reprogramming of differentiated cells. Since microRNAs (miRNAs) modulate target genes tissue specifically, we reasoned that distinct fibroblast-enriched miRNAs post-transcriptionally modulate proteins that function as reprogramming barriers. We will present recent findings that cellular microRNAs regulate iPSC generation. Knockdown of key microRNA pathway proteins resulted in significant decreases in reprogramming efficiency. Three microRNA clusters, miR-17–92, 106b–25 and 106a–363, were shown to be highly induced during early reprogramming stages. Several microRNAs, including miR-93 and 106b, which have very similar seed regions, greatly enhanced iPSC induction and modulated the mesenchymal-to-epithelial transition step in the initiation stage of reprogramming, and inhibiting these microRNAs significantly decreased reprogramming efficiency. Moreover, miR-IPSC clones reached the fully reprogrammed state. Further analysis revealed that Tgfb2 and p21 are directly targeted by these microRNAs. Overall, our results demonstrate that microRNAs function in the reprogramming process and that iPSC induction efficiency can be greatly enhanced by modulating microRNA levels in cells. These studies should facilitate development of clinically-applicable reprogramming strategies.

**10:15-11:15 Coffee Break in the Exhibit Hall with Poster Viewing**

**11:15-12:00 pm Talk Title to be Announced**

Richard J. Gregory, Ph.D., Children’s Hospital Boston, Harvard Stem Cell Institute (HSCI), Harvard Medical School

**11:15-12:00 pm Translating miRNA Discovery in Biofluids into Robust Biomarkers for Disease**

Søren Jensby Nielsen, Ph.D., Head, Diagnostics, Exiqon A/S

Exiqon has developed a LNA™-based miRNA qPCR platform with unparalleled sensitivity and robustness to accelerate discovery and clinical development of miRNA-based biomarkers. We have profiled thousands of biofluid samples including plasma, serum and urine. To secure technical excellence and eliminate unwanted bias, an extensive
Disease and Development

Track 2: microRNA Pathways in Disease and Development

microRNAs as Biomarkers and Diagnostics

(continued)

1:45-1:50 Chairperson’s Opening Remarks

1:50-2:20 microRNAs as Potential Biomarkers for Non-Small Cell Lung Cancer
Feng Jiang, M.D., Ph.D., Associate Professor, Pathology, University of Maryland School of Medicine

We proposed to develop miRNAs as sensitive and specific sputum markers for early detection of NSCLC. From paired normal and tumor lung tissues from 20 patients with NSCLC using miRNA profiling, 7 miRNAs were found to have significantly altered expressions in tumors. On the sputum samples of 36 cancer patients and 36 healthy individuals, combination of the miRNAs produced 86.6% sensitivity and 91.7% specificity for lung cancer. Validation of the marker panel in an independent set confirmed the sensitivity and specificity. The sputum markers demonstrated the potential of translation to laboratory settings for improving the early detection of NSCLC.

2:20-2:50 Blood Cell microRNAs: What Are They and What Future Do They Hold?
C.D. Atreya, Ph.D., Associate Director for Research, Office of Blood Research and Review, CBER, FDA

Storage of blood components has revolutionized health care by allowing for a managed supply of transfusion-quality blood products. During storage, blood components undergo a series of physiological changes that affect the product quality, which ultimately can interfere with the safety and efficacy of such products after transfusion. Despite continuous improvements in blood component quality and safety, it is still desirable to have in vitro standard markers of measurable characteristics that predict blood component safety and efficacy in vivo following their transfusion. There is potential for microRNAs to act as measurable characteristics (product biomarkers) for stored blood component quality and safety.

2:50-3:20 microRNAs as Effectors and Biomarkers in Cholestatic Liver Disease
Joshua Friedman, M.D., Ph.D., Assistant Professor, Pediatrics, Perelman School of Medicine, University of Pennsylvania

Consistent with their importance in many organ systems, microRNAs play critical roles in gastrointestinal development and differentiation. Using genetic tools, our laboratory has provided evidence of miRNA function in the developing and post-natal liver. Biliary atresia is a disease affecting infants in which the bile ducts are destroyed by a fibro-inflammatory process; it is the most common reason for liver transplantation in children. We have discovered that circulating miRNAs are biomarkers of the liver disease biliary atresia. In addition, we have identified a panel of miRNAs whose expression is altered in a variety of cholestatic disease models, and we have linked those miRNAs to several relevant regulatory pathways. These results will be reviewed in the context of growing evidence that microRNAs participate in the pathogenesis of digestive and liver diseases and make appealing therapeutic targets.

3:20-3:50 Circulating microRNAs as Biomarkers of Individual Sensitivity to Liver Injury in a Multistrain Panel of Inbred Mice
Igor Pognibny, M.D., Ph.D., Laboratory Director and Principal Research Investigator, Division of Biochemical Toxicology, National Center for Toxicological Research, U.S. Food and Drug Administration; Basic Science Professor, Pharmacology and Toxicology, University of Arkansas Medical Sciences

microRNAs (miRNAs) are a class of small, conserved, tissue-specific regulatory non-coding RNAs that modulate a variety of biological processes and play a fundamental role in pathogenesis of major human diseases, including nonalcoholic fatty liver disease (NAFLD), which is a major health problem and the leading cause of chronic liver disease in the United States and developed countries. In a relevant mouse model of human NAFLD, aberrant levels of several circulating miRNAs were highly correlated with a severity of liver injury.
Track 1: microRNA in Diagnostic and Therapeutic Development

NAFLD-associated pathomorphological changes in the livers. These changes correlated with an individual susceptibility to liver injury, suggesting that circulating miRNAs may be used as biomarkers of liver toxicity and, more importantly, as potential noninvasive indicators of susceptibility to NAFLD liver injury.

3:50-4:30 Refreshment Break in the Exhibit Hall with Poster Viewing

Role of microRNA in Viral Infection

4:45-5:15 Herpes Simplex Virus microRNAs and the Lytic-Latent Balance
Donald Coen, Ph.D., Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School

Herpes simplex viruses (HSV) 1 and 2 infect much of the human population. HSV-1 and -2 establish latent infections in sensory neurons from which the viruses can reactivate to cause recurrent disease and transmit to new hosts. During latency, expression of viral genes active during productive (“lytic”) infection is repressed. HSV-1 and -2 encode a score or more of microRNAs. There is increasing evidence that these microRNAs can tilt the outcome of infection either towards virus production or latency. The results have raised the possibility that latent HSV infections can be addressed by targeting HSV microRNAs.

5:15-5:45 Promoting hepatitis C Virus Replication through miR-122 Manipulation
Matthew J. Evans, Ph.D., Assistant Professor, Microbiology, Mount Sinai School of Medicine

The hepatitis C virus (HCV) is a major cause of chronic hepatitis, affecting approximately 170 million people worldwide. HCV replication requires a direct interaction with the liver-specific microRNA miR-122, and the few cell lines that support the HCV life cycle

SPONSORSHIP AND EXHIBIT INFORMATION

Sponsors and Exhibitors will enjoy facilitated networking opportunities with over 200 international scientists and executives. Enhance business development and lead generation initiatives by presenting and exhibiting your expertise to this hard-to-reach market.

Sponsored Presentations
Showcase your technology to a guaranteed, highly-targeted audience. Package includes a 15- or 30-minute podium presentation within the scientific agenda, exhibit space, on-site branding and access to cooperative marketing efforts by CHI.

Breakfast Presentations
Opportunity includes a 20-minute podium presentation with a 10-minute Q&A session. A limited number of presentations are available for sponsorship and they will sell out quickly. Sign on early to secure your talk!

Invitation-Only VIP Dinner/Hospitality Suite
Sponsor will hand-pick their top prospects from the conference pre-registration list for an evening of networking at the hotel or at a top local venue. CHI will extend invitations and deliver prospects. Evening will be customized according to sponsor’s objectives (i.e. purely social, focus group, reception style or plated dinner, plated dinner with specific conversation focus).

For Sponsor & Exhibitor information, please contact: Ilana Quigley, Manager, Business Development | 781-972-5457 | iquigley@healthtech.com
Disease and Development

Track 2: microRNA Pathways in Disease and Development

express high levels of this microRNA. Here we show that overexpression of miR-122 in the normally HCV-nonpermissive and miR-122-deficient hepatocyte-derived HepG2 cell line renders these cells able to support the entire HCV life cycle. Thus HepG2 cells represent a novel HCV cell culture system that is particularly useful for exploring the mechanism by which this microRNA enhances HCV replication.

TUESDAY, MARCH 13, 2012

7:30-8:15 am Breakfast Presentation: A Novel Experimental Method for miRNA Target Identification and Validation
Abhishek Saharia, Ph.D., Global Product Manager, Sigma Life Science

A monumental challenge for miRNA researchers is the experimental identification and validation of functional gene sequences that bind miRNAs. A need exists for assays that provide experimental ease-of-use as well as consistent results for miRNA target identification and validation. The MISSION® Target ID Library enables bench-top transcriptome-wide human miRNA target identification. The Lenti GoClone™ delivers human 3'UTRs fused to a novel Renilla Luciferase reporter, enabling you to easily and experimentally validate these miRNA targets.

Role of microRNA in Cancer Mechanism

10:25-10:30 Chairperson's Opening Remarks

10:30-11:00 HNF4a-miRNA Circuit in Hepatocellular Oncogenesis
Maria Hatzipostolou, Ph.D., Research Fellow, Cancer Immunology and AIDS, Dana Farber Cancer Institute, Harvard Medical School, Department of Microbiology and Immunobiology

11:00-11:30 Impact of Non-Coding miRNAs in Chemoresistance, EMT and Cancer Stem Cells
Jingfang Ju, Ph.D., Professor and Co-Director, Translational Research Laboratory, Pathology, State University of New York at Stony Brook
Our laboratory first discovered that a number of miRNAs were regulated by tumor suppressor p53. Such regulatory mechanism was important in regulating cell proliferation and cell cycle control. To investigate the impact of miRNA in chemoresistance to fluoropyrimidines and antifolates, we discovered that miR-215 suppresses the expression of both thymidylate synthase and dihydrofolate reductase. In addition, the expression of miR-215 was directly regulated by p53. The expression of miR-215 was significantly associated with colorectal cancer patient survival. miR-140 modulates chemosensitivity by suppressing HDAC4 expression, and the levels of miR-140 and miR-215 were elevated in colon cancer stem cells. Our recent studies have shown that miR-194 was directly involved in epithelial-to-mesenchymal (EMT) transition, a critical event for tumor progression and metastasis. The expression of Bmi-1 protein was suppressed by miR-194 directly at the 3'-UTR region of Bmi-1 miRNA. Given the significant role of miRNAs in many aspects of tumor development such as proliferation, cell cycle control, invasion, EMT and maintained tumor stem cell phenotype, we remain hopeful that miRNA based therapeutics, diagnostics and prognosis may emerge in the near future to benefit patients.

11:30-12:00 pm microRNAs and Tumor Angiogenesis
Andrei Thomas-Tikhonenko, Ph.D., Chief, Division of Cancer Pathobiology, The Children's Hospital of Philadelphia
Thrombospondin-1 is an inhibitor of angiogenesis encoded by the THBS1 gene. THBS1 promoter is activated by p53, and its RNA is downregulated by Myc via the miR-17-92 cluster. Additionally, it responds to TGFbeta signaling, which is also inhibited by miR-17-92. Yet in advanced colorectal cancers, THBS1 expression is sustained despite frequent loss of p53, overexpression of miR-17-92, and loss of TGFbeta signaling. We discovered that this is because the loss of p53 also brings down miR-194 levels, which is the key microRNA limiting THBS1 expression. Moreover, stable overexpression of miR-194 in murine colon carcinomas yields increased microvascular densities and vessel sizes, attesting to its pro-angiogenic properties.

12:00-12:30 pm ThinkTank Roundtable Discussions
Roundtable discussions, led by expert facilitators, are open to all delegates.

12:00-12:30 Activation of miR-31 Function in Already-Established Metastases Elicits Metastatic Regression
Scott J. Valastyan, Ph.D., Research Fellow, Cell Biology, Harvard Medical School

Distant metastases, rather than the primary tumors from which these lesions arise, are responsible for >90% of carcinoma-associated mortality. Many patients already harbor disseminated tumor cells in their bloodstream, bone marrow and distant organs when they initially present with cancer. Hence, truly effective anti-metastatic therapeutics are needed that prevent primary tumors from generating disseminated tumor cells in their bloodstream, bone marrow and distant organs. miR-31 has been found to be a marker for pre-invasive lesions, and we found that miR-31 expression levels are decreased in human breast carcinomas compared to adjacent normal tissues. We have also found that miR-31 expression is repressed in breast cancer cells in culture by E2F1 and that miR-31 re-expression is accompanied by reduced cell motility. By re-expressing miR-31 in breast cancer cells, we directly demonstrated that miR-31 can prevent tumor cell invasion and metastatic colonization in vivo. In a metastatic model, miR-31 re-expression in metastatic mammary cells was accompanied by a striking reduction in metastasis. We also showed that miR-31 is able to elicit metastatic regression in already-established metastases in vivo, and we found that this effect is accompanied by a reduction in tumor progression and a downregulation of steps in the canonical EMT pathway such as Vimentin, N-cadherin, and Slug. These results demonstrate that miR-31 is a potent therapeutic target in breast cancer and may represent a novel treatment option for patients with metastatic breast cancer.

10:25-10:30 Chairperson's Opening Remarks

10:30-11:00 Therapeutic Gene Silencing Using RNA Interference
Bulent Ozpolat, M.D., Ph.D., Assistant Professor, Experimental Therapeutics, University of Texas MD Anderson Cancer Center

Using a KrasG12D/+;p53R172H/+ mouse model of aggressive lung cancer, we show that miR-34 can prevent tumors from forming. Untreated animals have high-grade adenocarcinomas leading to macrophage infiltration and death, while miR-34 treated mice have limited-to-no tumor growth. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis. We also show a synergistic effect between let-7 and miR-34 for the treatment of lung cancer in the same model. miRNAs in these mice have limited-to-no tumorigenesis.

11:00-11:30 Impact of Non-Coding miRNAs in Chemoresistance, EMT and Cancer Stem Cells
Jingfang Ju, Ph.D., Professor and Co-Director, Translational Research Laboratory, Pathology, State University of New York at Stony Brook

Our laboratory first discovered that a number of miRNAs were regulated by tumor suppressor p53. Such regulatory mechanism was important in regulating cell proliferation and cell cycle control. To investigate the impact of miRNA in chemoresistance to fluoropyrimidines and antifolates, we discovered that miR-215 suppresses the expression of both thymidylate synthase and dihydrofolate reductase. In addition, the expression of miR-215 was directly regulated by p53. The expression of miR-215 was significantly associated with colorectal cancer patient survival. miR-140 modulates chemosensitivity by suppressing HDAC4 expression, and the levels of miR-140 and miR-215 were elevated in colon cancer stem cells. Our recent studies have shown that miR-194 was directly involved in epithelial-to-mesenchymal (EMT) transition, a critical event for tumor progression and metastasis. The expression of Bmi-1 protein was suppressed by miR-194 directly at the 3'-UTR region of Bmi-1 miRNA. Given the significant role of miRNAs in many aspects of tumor development such as proliferation, cell cycle control, invasion, EMT and maintained tumor stem cell phenotype, we remain hopeful that miRNA based therapeutics, diagnostics and prognosis may emerge in the near future to benefit patients.

11:30-12:00 pm microRNAs and Tumor Angiogenesis
Andrei Thomas-Tikhonenko, Ph.D., Chief, Division of Cancer Pathobiology, The Children's Hospital of Philadelphia

Thrombospondin-1 is an inhibitor of angiogenesis encoded by the THBS1 gene. THBS1 promoter is activated by p53, and its RNA is downregulated by Myc via the miR-17-92 cluster. Additionally, it responds to TGFbeta signaling, which is also inhibited by miR-17-92. Yet in advanced colorectal cancers, THBS1 expression is sustained despite frequent loss of p53, overexpression of miR-17-92, and loss of TGFbeta signaling. We discovered that this is because the loss of p53 also brings down miR-194 levels, which is the key microRNA limiting THBS1 expression. Moreover, stable overexpression of miR-194 in murine colon carcinomas yields increased microvascular densities and vessel sizes, attesting to its pro-angiogenic properties.

12:00-12:30 pm microRNAs and Tumor Angiogenesis
Lin He, Ph.D., Assistant Professor, Cell and Developmental Biology, University of California Berkeley

Malignant transformation represents the endpoint of successive genetic lesions that confer uncontrolled proliferation and survival, unlimited replicative potential, and invasive growth. Emerging evidence has suggested that ncRNAs, particularly microRNAs (miRNAs), are essential regulators for gene expression in diverse
12:30-2:00 Enjoy Lunch on Your Own

Track 1: microRNA in Diagnostic and Therapeutic Development

**microRNA as Targets in Therapeutic Development**

2:00-2:05 Chairperson’s Opening Remarks

2:05-2:35 miRNAs as Targets for Overcoming Therapeutic Resistance

Fazil H. Sarkar, Ph.D., Professor of Pathology, Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine

Emerging evidence clearly suggests the important roles of microRNAs (miRNAs) in the regulation of genes that are critical for cancer cells but most importantly for those cancer cells that are highly resistant to conventional therapeutics. Since therapeutic resistance is the cause of treatment failure, novel approaches must be discovered for overcoming such resistance in order to improve the overall survival of patients diagnosed with cancer. This presentation will focus on the mechanistic role of miRNAs in therapeutic resistance and will also provide examples of novel avenues for targeting miRNAs in overcoming therapeutic resistance of pancreas, prostate, breast and lung cancer cells.

2:35-3:05 microRNA Binding Site Disruption in Cancer

Joanne Weidhaas, M.D., Ph.D., Assistant Professor, Therapeutic Radiology, Yale University School of Medicine

The importance of variants in microRNA binding sites in the 3’ untranslated region of miRNAs as biomarkers of disease risk has been indisputably shown over the last 5 years. However, new insight into the potential of these variants to act as biomarkers of tumor biology as well as to act as potential future targets for treatment is a novel area that is quickly evolving. These topics will be discussed.

3:05-3:35 microRNAs as Therapeutic Targets in Cardiovascular Disease

Eva van Rooij, Ph.D., Senior Director of Biology, Miragen Therapeutics

Chronic and acute stress to the heart results in a pathological remodeling response accompanied by hypertrophy, fibrosis, myocyte apoptosis and eventual death from pump failure and arrhythmias. We have identified signature expression patterns of miRNAs accompanied by hypertrophy, fibrosis, myocyte apoptosis and eventual death in the absence of functional p53. Through expression profiling of p53-deleted miRNAs we identified multiple miR-dependent pathways important for tumor progression; for instance, we identified a new and physiologically important miRNA-dependent network that maintains p53 homeostasis and controls p53-independent survival and chemosensitivity in squamous cell carcinoma. This network involves a subset of miRs that target miRNAs in overcoming therapeutic resistance of pancreas, prostate, breast and lung cancer cells.

Reasons you should present your research poster at this conference:

- Your poster will be exposed to our international delegation
- Receive $50 off your registration
- Your poster abstract will be published in our conference materials
- Your research will be seen by leaders from top pharmaceutical, biotech, academic and government institutes

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 materials, your abstract must be submitted, approved and your registration paid in full by February 15, 2012.

Register online, or by phone, fax or mail. Please indicate that you would like to present a poster. Once your registration has been fully processed, we will send an email with a unique link and instructions for submitting your abstract using our online abstract submission tool.
Track 1: microRNA in Diagnostic and Therapeutic Development

3:35-4:00 Networking Refreshment Break

4:00-4:30 Discovery of Novel APP and BACE-specific microRNAs Important for Alzheimer’s Disease
Debomoy K. Lahir, Ph.D., Professor of Neuroscience, Departments of Psychiatry and Medical and Molecular Genetics; Member, Stark Neurosciences Research Institute, Indiana University School of Medicine

Aberrations in Alzheimer’s disease are believed to result, in part, from the over-production of amyloid-beta peptide (Aβ), a product of Aβ precursor protein (APP). Expression studies suggest that dysregulation of proteins involved in Aβ production, such as APP and beta-secretase, or BACE1, contribute to excess Aβ deposition. Elucidating how expression of these proteins is regulated will ultimately reveal new drug targets. We study the regulation of gene products by microRNA, an abundant class of small RNAs with inhibitory effects on gene expression. Our results reveal a novel regulatory interaction between two important AD-related genes (APP and BACE1) and specific endogenously-expressed miRNA species. These regulatory interactions may serve as novel therapeutic targets and enable the development of treatment strategies beneficial for AD.

4:30-5:00 Sensing Global microRNA Activity
Brian D. Brown, Ph.D., Assistant Professor, Genetics and Genomic Sciences, Mount Sinai School of Medicine

microRNAs have emerged as important regulators of gene expression. More than 800 different microRNAs are encoded in the human genome, and each cell type and even cell state appears to express a unique battery of microRNAs. One open question about microRNA regulation is how microRNA concentration relates to target suppression. To gain insight into this process, we generated a panel of microRNA sensors, which enabled us to compare a microRNAs abundance to its activity. Our results provide interesting new insights into microRNA function which are particularly relevant for microRNA profiling.

Track 2: microRNA Pathways in Disease and Development

worse 5-year survival rates of 62% and 16% in those with regional lymph node involvement and distal metastasis, respectively. Identifying functionally relevant molecular events that occur early in melanoma development may inform clinical decision-making, and uncover novel therapeutic targets. We found that microRNA alterations that confer increased metastatic potential can be captured at early stages of melanoma development. Our study supports that molecular defects occurring during melanogenesis simultaneously impact the progression from a treatable primary tumor to an invasive and ultimately metastatic disease.

4:00-4:30 microRNAs and Melanoma
Prasun J. Mishra, Ph.D., Laboratory of Cancer Biology and Genetics, National Cancer Institute, NIH

Melanoma is a genetically complex and often highly aggressive disease, notorious both for its ability to metastasize and for its poor response to currently available therapeutic approaches. The incidence of melanoma has steadily increased over the last 40 years, and continues to rise at a time when the incidence of other cancers is falling, accounting for 75% of all deaths associated with skin cancer. Moreover, melanoma’s propensity to metastasize, even many years after removal of the primary tumor, makes this cancer especially deadly. In this study, using an integrated approach, we have identified and characterized genes and microRNAs associated with melanogenesis.

4:30-5:00 Hypoxia Induces hESC-Enriched microRNAs in Normal and Cancer Cells
Julie Mathieu, Ph.D., Postdoctoral Fellow, Biochemistry, University of Washington

microRNAs are important new actors in stem cell development by regulating differentiation and maintenance of stem cells. We and others have shown that human embryonic stem cells (hESCs) display a specific microRNA signature and that microRNAs are critical for hESC self-renewal and proliferation. hESCs are derived from the low oxygen environment that characterizes the inner cell mass of blastocysts. However, hESCs are able to self-renew in normoxia or hypoxia. We now show that hypoxia is involved specifically in the acquisition of “stemness” since hypoxia alone can reprogram differentiated hESCs back to a stem-cell-like state. Hypoxia-induced de-differentiated cells also mimic hESCs in their morphology, cell surface markers expression, genome-wide mRNA profile, and capacity to form teratomas. In addition, the set of up-regulated miRNAs in hypoxia de-differentiated cells was highly similar to those enriched in undifferentiated hESCs. These data suggest that hypoxia is sufficient to induce human pluripotent stem cells from committed cells. In cancer, we showed that hypoxia can induce hESC markers in cancer cells, correlating with tumor aggressiveness. Cancer cells cultured under hypoxia also expressed a higher level of hESC-enriched miRNAs compared to cancer cells cultured under normoxia. Hypoxia may therefore induce acquisition of stemness both in normal and cancer cells. Several groups have demonstrated that microRNAs can reprogram somatic cells into pluripotent stem cells, underlying their fundamental role in cell fate decision. We are now investigating whether the effect of hypoxia on the acquisition of stem cell properties is mediated by hESC microRNAs.

5:00 Close of Conference

HOTEL & TRAVEL INFORMATION

Conference Venue and Hotel:
Hyatt Regency Cambridge
575 Memorial Drive
Cambridge, MA 02139
Phone: 617-492-1234

Discounted Room Rate: $149 s/d
Discounted Room Cut-off Date: February 13, 2012

Please visit the conference website to book your room online, or call the hotel directly to reserve your sleeping accommodations. You will need to identify yourself as a Cambridge Healthtech Institute (CHI) conference attendee to receive the discounted room rate with the host hotel. 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.

We understand that you have many choices when making your travel arrangements, and may ultimately decide to stay at another hotel. Please understand that reserving your room in the CHI room block allows you to take full advantage of the conference sessions, events and networking opportunities, and ensures that our staff will be available to help should you have any issues with your accommodations.

Flight Discounts:
Special discount rates have been established with American Airlines for this conference.
• Call American Airlines Directly at 1-800-433-1790 use Conference code 1732AZ.
• Go to www.aa.com enter Conference code 1732AZ in promotion discount box.
• Contact our designated travel agents at 1-877-559-5549 or chi@protravelinc.com.

Car Rental Discounts:
Special discount rentals have been established with Hertz for this conference.
• Visit www.hertz.com to make your reservation and use our Hertz Convention Number (CV) 04KL0003
• Call Hertz directly at 1-800-654-3131 and reference our Hertz Convention Number(CV) 04KL0003

•  Visit www.aa.com enter Conference code 1732AZ in promotion discount box.
•  Contact our designated travel agents at 1-877-559-5549 or chi@protravelinc.com.
How to Register: healthtech.com/MRN
T: 781.972.5400 or Toll-free in the U.S. 888.999.6288 | reg@healthtech.com

PRICING AND REGISTRATION INFORMATION

<table>
<thead>
<tr>
<th>Conference Pricing (March 12-13)</th>
<th>Commercial</th>
<th>Academic, Government, Hospital-Affiliated</th>
<th>Group* (Over 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Registration until January 6, 2012</td>
<td>$1595</td>
<td>$695</td>
<td></td>
</tr>
<tr>
<td>Advance Registration until February 3, 2012</td>
<td>$1695</td>
<td>$795</td>
<td></td>
</tr>
<tr>
<td>Registration after February 3, 2012 and on-site</td>
<td>$1845</td>
<td>$895</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pre-Conference Web Symposia Pricing Only:</th>
</tr>
</thead>
<tbody>
<tr>
<td>One Web Symposium</td>
</tr>
<tr>
<td>Two Web Symposia</td>
</tr>
</tbody>
</table>

Attend the microRNA Conference & the Web Symposia and Receive a 50% Discount off the Webinar!

| One Web Symposium | $245 | $125 | $495 |
| Two Web Symposia | $445 | $195 | $895 |

Visit www.healthtech.com/MRN/websymposia for updated information

*Group registrations provide only one set of log-in information for the whole group. All group members must participate from the same location.

CONFERENCE DISCOUNTS

Poster Submission-Discount ($50 Off)
Poster abstracts are due by February 15, 2012. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact iring@healthtech.com. * CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

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.

Additional discounts are available for multiple attendees from the same organization. For more information on group rates contact David Cunningham at +1-781-972-5472

15% discount for SAPA Members

If you are unable to attend but would like to purchase the microRNA in Human Disease and Development CD for $350 (plus shipping), please visit healthtech.com/MRN.
Massachusetts delivery will include sales tax.

Please use keycode MRN F when registering