12th Annual
**microRNA**
as Biomarkers and Diagnostics

2nd Annual
**Extracellular RNA** in Drug and Diagnostic Development

April 4 - 6, 2016 | Hyatt Regency Cambridge | Cambridge, MA

Featured Speakers:

- **Ajay Goel**
  Professor & Director,
  Baylor University

- **James Patton**
  Professor, Vanderbilt University

- **Molly Taylor**
  Senior Scientist, AstraZeneca

- **Peter Quesenberry**
  Professor, Brown University

- **Frank Slack**
  Professor & Director,
  Beth Israel Deaconess Medical Center

Dinner Courses:

- April 3: Data Normalization Challenges and Solutions
- April 4: microRNA-Based Therapeutics
- April 5: microRNAs in the Immune Response

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**Dinner Short Courses**

**SUNDAY, APRIL 3, 5:00-8:00 PM**

(SC1) Data Normalization Challenges and Solutions

Christos Argyropoulos, M.D., MS, Ph.D., Assistant Professor, Nephrology, Department of Internal Medicine, University of New Mexico School of Medicine

Matthew Roth, Ph.D., Assistant Professor & Co-Director, Bioinformatics Research Lab, Baylor College of Medicine; Data Management & Resource Repository of the Extracellular RNA Consortium (NIH)

Joel Rozowsky, Ph.D., Research Scientist, Molecular Biophysics & Biochemistry, Yale University

Robert Kitchen, Ph.D., Postdoctoral Associate, Bioinformatics, Yale University School of Medicine

Normalization is a critical step in the analyses of microRNA quantification profiles, since it guarantees statistically valid inferences. To date, a number of normalization approaches have been proposed, yet a comprehensive framework to put them on a sound footing is lacking. This workshop will provide an overview of statistical approaches to normalization of microarray, qPCR and NGS microRNA data for differential expression experimental designs. We will compare different normalization approaches on the multi-platform microRNA Quality Control (miRQC) dataset and explore the impact of different normalization methods on downstream inferences. Finally, we will present a case study in which the proposed framework facilitates the synthesis of multiplatform (qPCR, NGS) data in human renal disease.

*Separate registration required*
MicroRNAs as Non-Invasive Diagnostic and Predictive Biomarkers

8:10 Chairperson’s Opening Remarks
Ajay Goel, Ph.D., Professor and Director, Center for Gastrointestinal Research, and Director, Center for Epigenetics, Cancer Prevention and Cancer Genomics, Baylor Research Institute, Baylor University Medical Center

8:15 Non-Coding RNA Biomarkers in Colorectal Cancer
Ajay Goel, Ph.D., Professor and Director, Center for Gastrointestinal Research, and Director, Center for Epigenetics, Cancer Prevention and Cancer Genomics, Baylor Research Institute, Baylor University Medical Center

Non-coding RNAs (ncRNAs) are emerging as important regulators of gene expression in cancer. Overexpression of specific non-coding RNAs (including miRNAs, snoRNAs, piRNAs and circular RNAs) has been linked to the stepwise disease progression in colorectal cancer (CRC). Given their cancer-specific pattern of expression, remarkable stability and presence in blood and other body fluids, ncRNAs are considered to be highly promising cancer biomarkers. Accumulating evidence firmly supports the existence of unique ‘ncRNA signatures’ that can not only facilitate earlier detection of the tumor, but can also assist in predicting disease recurrence and therapeutic outcome to current treatment regimens.

8:45 Non-Invasive miRNA Biomarkers for Kidney Disease
Vishal S. Vaidya, Ph.D., Associate Professor, Medicine & Environmental Health, Harvard Medical School, Harvard T.H. Chan School of Public Health, Brigham and Women’s Hospital

miRNAs play a critical regulatory role in health and disease. Abundant expression, lower complexity, stability in various detection matrices and amplifiable signals are qualities that make extracellular miRNAs attractive as biomarkers reflecting a variety of pathophysiological conditions. We highlight the transformative potential of miRNAs as mechanistic biomarkers in translational medicine.

9:15 Circulating microRNAs in Cardiac Disease and Dysfunction
Yuri D’Alessandra, Ph.D., Senior Researcher, Immunology and Functional Genomics Unit, Centro Cardiologico Monzino

Circulating microRNAs are emerging as biomarkers of several heart-related diseases. We have conducted studies encompassing many different cardiac maladies and identified specific circulating miRNAs as potential diagnostic markers.

9:45 Cell-Free Circulating microRNAs as a Reflection of Liver Disease
Steven Lockton, Ph.D., Senior Scientist, microMarkers, Regulus Therapeutics

MicroRNAs are stable in circulation and can be dysregulated with disease. Because microRNA expression is often organ-specific, cell-free circulating microRNA expression often reflects the diseased organ’s pathophysiology. To map microRNAs to organs we profiled microRNA expression in mouse tissues. In a transgenic mouse model of hepatocellular carcinoma this serum reflection of liver distress was clearly demonstrated upon inducing HRAS. Similarly, in HCV-infected patients, aberrant serum microRNA expression was restored to a healthy-like state after treatment.

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

Identifying microRNA Biomarkers in Tissue and Biofluids

10:45 Gender-Specific, Population-Specific, and Race-Specific Regulatory Non-Coding RNAs
Isidore Rigoutsos, Ph.D., Professor and Director, Computational Medicine Center, Sidney Kimmel Medical College, Thomas Jefferson University

By analyzing human transcriptomes from different people and different tissues, we found two types of short regulatory RNAs that are produced constitutively, and demonstrated that their composition and abundances depend on a person’s gender, population and race as well as on tissue, tissue state, and disease subtype. The first type of short RNAs comprises numerous isoforms of mature microRNAs (miRNAs) that arise from a very high number of miRNA precursors. The second type comprises fragments of nascent transfer RNAs (tRNAs). We also discovered a novel class of TRNA fragments, the i-tRFs, which are wholly internal to the span of the mature tRNA and contribute much of the observed difference across individuals and tissues. The findings have direct implications for Precision Medicine and our understanding of the mechanisms underlying the onset and progression of disease.

11:15 Identification of microRNA Signatures Predicting Survival and Treatment Response in Glioblastoma
Josie Hayes, Ph.D., Postdoctoral Fellow, Neurosurgery, Helen Diller Family Cancer Center, University of California, San Francisco

11:45 microRNA Signatures in Renal Disease: A Meta-Analysis of Tissue and Urine Datasets
Christos Argyropoulos, M.D., Ph.D., MS, Assistant Professor, Nephrology, Department of Internal Medicine, University of New Mexico School of Medicine

MicroRNA(miRNA) are negative regulators of gene translation and an emerging biomarker in a wide variety of diseases. Little is known about the ability of miRNA to correctly classify patients with clinically significant renal pathology. We undertook a meta-analysis of miRNA profiles from clinical samples (biopsy or biofluid) in Gene Expression Omnibus. MiRNA profiles from 31 urine samples and 117 biopsy samples were available for analyses. A short signature of 19 miRNAs achieved a superior classification performance for renal pathology (cross-validated AUC 0.96).

12:15 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

microRNAs in Drug Development

1:25 Chairperson’s Remarks

1:30 MicroRNA Profiling Identifies Potential Biomarkers of Hepatobiliary Injury Following Exposure to Several Toxicants in the Rat
Rachel J. Church, Ph.D., Director, Organ Injury Biomarker Core; Research Investigator, Institute for Drug Safety Sciences; Research Assistant Professor, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill

2:00 Evaluation of Noninvasive microRNAs as Biomarkers of Injury for Drug Safety
Xi Yang, Ph.D., Research Biologist, Systems Biology, National Center for Toxicological Research, FDA

Drug-induced liver injury is an important regulatory concern and a common reason for drug withdrawal. Acetaminophen (APAP) overdose is a major cause of acute liver failure in the Western world. Sensitive and specific biomarkers are required as diagnosis tools in the clinic and in screening assays during drug development stages. In our recent study, urinary miRNAs potential as diagnostic biomarkers has been explored.
2:30 Use of microRNAs to Understand Differential Signaling between Lung Tumor Subtypes and Predict Therapeutic Response
Molly A. Taylor, Ph.D., Senior Scientist, AstraZeneca
We have classified three novel subtypes of lung squamous cell carcinoma that each have unique microRNA expression and therapeutic response profiles. Combined analysis of activated pathways and microRNA promoters has identified transcription factors driven by activated pathways that drive differences in microRNA expression. Overall, these microRNAs and transcription factors may function as biomarkers of pathway activation and aid in distinguishing patient subtypes to predict response to therapy.

9:00 microRNA Expression in Bronchial Epithelium for Lung Cancer Detection
Ana Brandusa Pavel, Ph.D., Researcher, Computational Biomedicine, Boston University School of Medicine
Using bronchial brushings from current and former smokers undergoing bronchoscopy for suspect lung cancer, we profiled microRNA expression via small RNAseq on the Illumina HiSeq 2000 platform. We found microRNA expression profiles significantly associated with lung cancer and that these microRNAs target miRNA whose expression was previously reported to be associated with lung cancer. Importantly, we show that integrating microRNA expression together with a gene-expression lung cancer biomarker increases performance.

9:30 Reducing Bias and Improving Small RNA-Seqing
Adam Morris, Ph.D., Senior Scientist, Bioo Scientific
Small RNA sequencing has typically suffered from three major drawbacks: 1) severe bias, such that sequencing data does not reflect original miRNA abundances, 2) the need to gel-purify final libraries, and 3) lack of low-input protocols. Here we present a method combining reduced bias with gel-free or low-input protocols.

4:45 Coffee Break in the Exhibit Hall with Poster Viewing

Role of microRNAs in Cancer Pathways
10:25 Chairperson's Remarks
Richard I. Gregory, Ph.D., Associate Professor, Department of Biological Chemistry and Molecular Pharmacology, Department of Pediatrics, Harvard Medical School, Harvard Stem Cell Institute, The Stem Cell Program at Boston Children's Hospital

10:30 Predictive and Functional Roles of miRNA in Metastatic Melanoma
Eva Hernandez, Ph.D., Associate Professor and Vice Chair for Science, Department of Pathology, Co-Leader, Melanoma Program, NYU Langone Medical Center
Our laboratory has identified a miRNA signature in primary melanomas predictive of recurrence and metastasis. We have also demonstrated that some components of that signature which are lost in aggressive primary tumors act as metastasis suppressors. Our data supports that a miRNA-based prognostic assay could identify patients at higher risk of developing metastatic disease who could be subjected to increased surveillance or adjuvant therapies. Moreover our results support that miRNA changes can capture the molecular heterogeneity that dictates metastatic behavior since early tumor stages.

11:00 microRNA Biogenesis Pathways in Cancer
Richard I. Gregory, Ph.D., Associate Professor, Department of Biological Chemistry and Molecular Pharmacology, Department of Pediatrics, Harvard Medical School, Harvard Stem Cell Institute, The Stem Cell Program at Boston Children's Hospital
Amplification and overexpression of individual 'oncomiRs' or genetic loss of tumor suppressor miRNAs promotes tumorigenesis. Furthermore, global miRNA depletion caused by genetic and epigenetic alterations in components of the miRNA biogenesis machinery is oncogenic. This, together with the recent identification of novel miRNA regulatory factors and pathways, highlights the importance of miRNA dysregulation in cancer.

11:30 Elimination of Colon Cancer Stem Cells by miR-140 through SMAD2 and Autophagy
Jingfang Ju, Ph.D., Associate Professor and Co-Director, Translational Research, Pathology, Stony Brook University
Colorectal cancer (CRC) is the third highest mortality cancer in the US and frequently metastasizes to liver and lung. Smad2 is a key element downstream of the TGFβ signaling pathway to regulate cancer metastasis by promoting epithelial to mesenchymal transition and maintaining the cancer stem cell (CSC) phenotype. In this study, we show that hsa-mir-140-5p directly targets Smad2 and overexpression of hsa-mir-140-5p in CRC cell lines decreases Smad2 expression levels, leading to decreased cell invasion and proliferation, and increased cell cycle arrest. The functional and clinical significance of hsa-mir-140-5p suggests that it is a key regulator in CRC progression and metastasis, and may have potential as a novel therapeutic molecule to treat CRC.

12:00 pm Close of Conference
1:25 Chairperson’s Opening Remarks
Frank Slack, Ph.D., Director, Institute for RNA Medicine, Department of Pathology, BIDMC Cancer Center, Harvard Medical School

1:30 OncomiRs as Functional Biomarkers for Cancer
Frank Slack, Ph.D., Director, Institute for RNA Medicine, Department of Pathology, BIDMC Cancer Center, Harvard Medical School
MicroRNAs are excellent candidates for human biomarker studies because their signature short sequences can be easily identified, they are stable in tissue and body fluids, and their expression patterns can be rigorously detected and quantified without harm to the individual. MicroRNAs have been found in multiple body fluids, such as serum and plasma, making them an attractive option for studying non-invasive, blood-based biomarkers. These circulating miRNAs are resistant to RNases and are in fact very stable in an extracellular environment, as they can be packaged in microvesicles, exosomes, or apoptotic bodies. Indeed, profiles of plasma and serum miRNAs have been linked to numerous cancers, and diabetes, indicating that miRNAs are a new class of blood-based biomarkers of human diseases.

2:00 Circulating miRNA as a Disease Marker in Multiple Sclerosis
Roopali Gandhi, Ph.D., Assistant Professor, Neurology, Harvard Medical School; Head, MS Biomarkers, Brigham & Women’s Hospital

2:30 microRNAs in Cerebrospinal Fluid as Biomarkers for Alzheimer’s Disease
Julie Saugstad, Ph.D., Associate Professor, Anesthesiology & Perioperative Medicine, Oregon Health & Science University
Alzheimer’s disease (AD) is the most common form of dementia. There are currently no clinical biomarkers to confirm the onset of AD, but such a tool would allow earlier initiation of treatments that can slow disease progression. Here, we describe our efforts to identify extracellular microRNAs circulating in cerebrospinal fluid obtained from living donors to serve as biomarkers for AD using quantitative RT-PCR platforms for discovery and validation studies.

3:00 Refreshment Break in the Exhibit Hall with Poster Viewing

3:45 The NIH Extracellular RNA Communication Program: exRNA for Therapy and Biomarker Development
Tania Lombo, Ph.D., Scientific Program Manager, National Center for Advancing Translational Sciences, National Institutes of Health
Extracellular RNA (exRNA) can act as endocrine signals to alter the phenotypes of target cells, and represents a novel paradigm in intercellular signaling. RNAseq analyses have identified a diverse population of exRNA that have been linked to regulation of the epigenome which could have profound implications for a wide range of physiologic and pathologic processes. The NIH Extracellular RNA Communication program supports research in exRNA-based biomarker and therapy development, as well as understanding fundamental principles of their biogenesis, distribution, uptake and function.

5:15 Exploring exRNA Function via RNA-Seq Pipelines, Pathway Analysis Tools, and Data Resources Developed by the exRNA Communication Consortium (ERCC)
Matthew Roth, Ph.D., Assistant Professor & Co-Director, Bioinformatics Research Lab, Baylor College of Medicine; Data Management & Resource Repository of the Extracellular RNA Consortium (NIH)
The NIH funded extracellular RNA Communication Consortium (ERCC) brings together experts in exRNA biology, human disease, bioinformatics, biomarker discovery, and therapeutic development to better understand exRNA biology and potential clinical applications. A key ERCC mission is the development of analytical pipelines and data resources for the broader scientific community. A description of these resources and their application to exRNA analyses will be presented.

5:45 Close of Day One

WEDNESDAY, APRIL 6

7:45 am Breakfast Presentation (Sponsorship Opportunity Available) or Morning Coffee

Potential of Extracellular Vesicles as Biomarkers and Therapeutics

8:25 Chairperson’s Remarks
Peter J. Quesenberry, M.D., Professor, Medicine, Brown University

8:30 miRNA as a Vesicular Therapeutic
Peter J. Quesenberry, M.D., Professor, Medicine, Brown University
Extracellular vesicles represent a new mode of intercellular communication. We have studies showing that “toxic” endothelial progenitors induced by vesicle exposure can induce pulmonary hypertension (PH) and that mesenchymal stem cell (MSC) derived vesicles can reverse PH. Similarly, normal or MSC vesicles can reverse ischemia-reperfusion renal injury and radiation injury to murine narrow stem cells. MSC or normal vesicles can also reverse the malignant phenotype of prostate and colorectal cancer.
9:00 Oncogene Patterning of the Tumor Microenvironment via exRNA and Exosomes
James G. Patton, Ph.D., Professor, Biological Sciences, Vanderbilt University
Mutant KRAS induces trafficking of EGF receptor (EGFR) and the EGFR ligand amphiregulin to exosomes and drastically changes exosomal protein content, leading to activities that can alter the tumor microenvironment. We characterized small RNAs from cells and matched exosomes that differ only in KRAS status. Exosomal small RNA profiles were distinct from cellular profiles, and mutant KRAS exosomes clustered separately from wild-type KRAS exosomes. miR-100 levels were increased in mutant KRAS cell-derived exosomes and deliver exosomes with miR-100 downregulated mTOR in recipient cells. Selective trafficking of miRNAs into exosomes appears to be dependent on KRAS-MEK signaling effects on Argonaute 2, a key component of RNA-Induced Silencing Complexes. Besides extracellular RNA transfer, we find that mutant KRAS derived exosomes confer metabolic-altering activity to cells in vitro and in vivo. These findings have implications for non-cell autonomous effects of cancer on the tumor microenvironment and the cancer field effect.

9:30 Extracellular Vesicles in Cancer Diagnosis, Prognosis and Epidemiology: Are We Ready for the PrimeTime?
Mukesh Verma, Ph.D., Chief, Methods and Technologies Branch, National Cancer Institute, National Institutes of Health
Both normal and diseased cells continuously shed extracellular vesicles (EVs) into extracellular space, and the EVs carry molecular signatures and effectors of both health and disease. EVs reflect dynamic changes that are occurring in cells and tissue microenvironment in health and at a different stage of a disease. EVs are capable of altering the function of the recipient cells. Trafficking and reciprocal exchange of molecular information by EVs among different organs and cell types have been shown to contribute to horizontal cellular transformation, cellular reprogramming, functional alterations, and metastasis. EV contents may include tumor suppressors, phosphoproteins, proteases, growth factors, bioactive lipids, mutant oncoproteins, oncogenic transcripts, microRNAs, and DNA sequences. Therefore, the EVs present in biofluids offer unprecedented, remote, and non-invasive access to crucial molecular information about the health status of cells, including their driver mutations, classifiers, molecular subtypes, therapeutic targets, and biomarkers of drug resistance. In addition, EVs may offer a non-invasive means to assess cancer initiation, progression, risk, survival, and treatment outcomes. The goal of this review is to highlight the current status of information on the role of EVs in cancer, and to explore the utility of EVs for cancer diagnosis, prognosis and epidemiology.

10:00 Networking Coffee Break

10:30 Large Oncosomes: New Frontiers for Cell-to-Cell Communication in Cancer
Dolores Di Vizio, M.D., Ph.D., Associate Professor, Surgery, Biomedical Sciences, Pathology & Laboratory Medicine, Cedars-Sinai Medical Center; Associate Professor, Medicine, University California, Los Angeles; Assistant Professor, Boston Children’s Hospital, Harvard Medical School
Our team recently reported that highly metastatic cells export large (1-10 µm diameter) bioactive EVs (large oncosomes) that originate from the shedding of bulky membrane protrusions from the plasma membrane. We have demonstrated that the abundance of large oncosomes in the circulation and in tissues correlate with advanced disease in mouse models and human subjects. Large-scale profile analyses demonstrate that large oncosomes represent a novel population of EVs enriched in tumor-derived molecules. Large oncosomes are thus valuable candidates for new biomarker profiles to be developed using tissue- and blood-based assays in combination.

11:00 Clinical Evaluation of Circulating Biomarkers in Precision Medicine
Shidong Jia, Ph.D., Founder & CEO, Predicine
The enumeration and characterization of circulating tumor cells (CTCs), exosomes and circulating tumor-free DNA (ctDNA) in the peripheral blood provide important prognostic and diagnostic information in personalized cancer care. Specific examples will be shown to demonstrate the opportunities and challenges for the development of circulating biomarkers in cancer.

12:00 MicroRNAs and the Immunometabolic Response to Viral Infection
John Paul Pezacki, Ph.D., Professor, Chemistry & Biomolecular Science, University of California, Los Angeles; Assistant Professor, Medicine, University California, Los Angeles; Associate Professor, Surgery, Biomedical Sciences, Pathology & Laboratory Medicine, Cedars-Sinai Medical Center; Associate Professor, Medicine, University California, Los Angeles; Assistant Professor, Boston Children’s Hospital, Harvard Medical School
Mutant KRAS induces trafficking of EGF receptor (EGFR) and the EGFR ligand amphiregulin to exosomes and drastically changes exosomal protein content, leading to activities that can alter the tumor microenvironment. We characterized small RNAs from cells and matched exosomes that differ only in KRAS status. Exosomal small RNA profiles were distinct from cellular profiles, and mutant KRAS exosomes clustered separately from wild-type KRAS exosomes. miR-100 levels were increased in mutant KRAS cell-derived exosomes and deliver exosomes with miR-100 downregulated mTOR in recipient cells. Selective trafficking of miRNAs into exosomes appears to be dependent on KRAS-MEK signaling effects on Argonaute 2, a key component of RNA-Induced Silencing Complexes. Besides extracellular RNA transfer, we find that mutant KRAS derived exosomes confer metabolic-altering activity to cells in vitro and in vivo. These findings have implications for non-cell autonomous effects of cancer on the tumor microenvironment and the cancer field effect.

12:15 Extracellular RNA Profiles Predictive of Human Allograft Status
Manikkam Suthanthiran, M.D., Stanton Griffis Distinguished Professor, Medicine; Chief, Division of Nephrology and Hypertension, Weill Cornell Medical College
Liver transplantation is the only lifesaving therapy for patients with irreversible liver failure. A frequent post-transplant complication is acute rejection, currently diagnosed by invasive needle biopsy of the liver allograft. Because miRNAs may serve as biomarkers of clinical disease, we investigated whether circulating extracellular miRNAs in the serum of liver transplant recipients predict human liver transplant status. Our findings support the hypothesis that measurement of circulating levels of extracellular miRNAs offers a noninvasive means of monitoring lifesaving liver transplants.

12:30 pm Enjoy Lunch on Your Own

Intracellular RNA and the Promise of ncRNAs

1:55 Chairperson’s Remarks
Da-Zhi Wang, Ph.D., Associate Professor, Cardiovascular Research Division, Department of Cardiology, Boston Children’s Hospital, Harvard Medical School

2:00 ncRNAs in Cardiovascular Diseases
Da-Zhi Wang, Ph.D., Associate Professor, Cardiovascular Research Division, Department of Cardiology, Boston Children’s Hospital, Harvard Medical School
Thousands of long non-coding RNAs (lncRNAs) have been discovered; however, the role of most lncRNAs in heart failure remains largely unknown. We performed RNA deep sequencing from cardiac samples of patients with ICM and controls. Expression correlation coefficient analyses revealed a strong association between lncRNAs and extracellular matrix (ECM) protein-coding genes. Gain- and loss-of-function studies demonstrate that lncRNAs are important regulators of fibrosis. Our results indicate that lncRNAs may represent novel regulators of heart function and cardiac disorders, including ischemic cardiomyopathy.

2:30 Long Non-Coding RNAs and Tumor Suppression
Nadya Dimitrova, Ph.D., Assistant Professor, Molecular, Cellular, and Developmental Biology, Yale University
There is an unmet need to gain a deeper understanding of the in vivo biology of lncRNAs that are deregulated in disease states, such as cancer. Our laboratory uses genetic approaches to study a subset of lncRNAs that are directly regulated by the important tumor suppressor protein, p53. Our analyses reveal that lncRNAs influence the expression of proteins in the p53 pathway and play key roles in the physiological response to stress and in tumor suppression.

3:00 Using ncRNAs to Identify Cancer Cell Vulnerabilities
Alexander Pertsinidis, Ph.D., Associate Professor, Pediatrics and Cellular & Structural Biology, University of Texas Health Science Center at San Antonio
To identify miRNAs that regulate tumor cell viability, we have combined a high-throughput screening platform with libraries of chemically synthesized ncRNA mimics and inhibitors. Candidate targets are validated using qRT-PCR, protein quantification, and luciferase reporter assays. The response of cancer cells to perturbations in candidate ncRNA levels is assessed through flow cytometric analysis of cell cycle phase distribution and through colony formation and caspase activation assays, and validated in mouse xenograft models. We have identified ncRNA mimics and inhibitors that have significant effects on cell viability and drug response. While these ncRNAs may have intrinsic value as biomarkers or therapeutic agents, the vulnerabilities that they uncover are also of value, in that they can be targeted directly with pathway-specific perturbations.

3:30 Close of Conference
### Pricing and Registration Information

#### CONFERENCE PRICING

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#### BEST VALUE PACKAGE (Includes access to both microRNA and Extracellular RNA entire 3-day event. *Excludes access to short course)*

| Advance Registration by March 4, 2016 | $2249 | $1129 |
| Late Registration after March 4, 2016 | $2449 | $1199 |

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| Advance Registration by March 4, 2016 | $1649 | $759 |
| Late Registration after March 4, 2016 | $1849 | $829 |

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#### CONFERENCE DISCOUNTS

**Poster Submission - Discount ($50 Off)**: Poster abstracts are due by February 28, 2016. 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 jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

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