Oligonucleotide & Precision Therapeutics

DISCOVERY, DEVELOPMENT AND DELIVERY

MARCH 16 - 19, 2020 | HYATT REGENCY CAMBRIDGE | CAMBRIDGE, MASSACHUSETTS

CONFERENCE PROGRAMS:
Oligonucleotide Discovery & Delivery
Oligonucleotide CMC and Regulatory Strategies
Symposium: AI for Drug Discovery & Development
Symposium: Rare Disease Drug Development

FEATURED SPEAKERS

Brett Monia, PhD
CEO, Ionis Pharmaceuticals
Edward Kaye, MD
CEO, Stoke Therapeutics
Ekkehard Leberer, PhD
Senior Director, R&D Alliance Management, Sanofi
Lubo Nechev, PhD
Vice President Process and Analytical Sciences, Alnylam Pharmaceuticals
Phil Baran, PhD
Professor, Department of Chemistry, Scripps Research

SHORT COURSES

SC1: Circular RNAs as a New Therapeutic Modality
SC2: Examining the Safety and Toxicity of Nucleic Acid Therapeutics
SC3: Oligonucleotides for Cancer Immunotherapy
SC4: Gene Editing for Targeted Therapies

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Oligo Factory

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For more information regarding exhibit and sponsorship, please contact:
Carolyn Cooke
Business Development Manager
781-972-5412 | c Cooke@healthtech.com

2019 Attendee Demographics

<table>
<thead>
<tr>
<th>COMPANY TYPE</th>
<th>TITLE</th>
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<tbody>
<tr>
<td>Biotech 66%</td>
<td>Executive/Director 47%</td>
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<tr>
<td>Pharmaceutical 15%</td>
<td>Scientist 32%</td>
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<tr>
<td>Academic 11%</td>
<td>Sales &amp; Marketing 12%</td>
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<td>Hospital/Healthcare 4%</td>
<td>Manager 7%</td>
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<td>Other 4%</td>
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WITH THANKS TO OUR EXECUTIVE ADVISORY BOARD

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Ekkehard Leberer, PhD, Senior Director, R&D Alliance Management, Sanofi
EVENT-AT-A-GLANCE

MONDAY, MARCH 16 | 3:00 – 6:00 PM

SC1: Circular RNAs as a New Therapeutic Modality
Circular RNA (circRNA) is a type of single-stranded RNA which forms a continuous loop due to the covalent binding of its 3′ and 5′ ends. They are naturally formed in the cell and found to play a role in cancer, CNS, cardiovascular and other diseases. The closed loop structure makes it less susceptible to exonuclease-mediated degradation and presumably more stable than most linear RNAs, which is appealing from a therapeutic standpoint. Studies involving the formation and function of circRNAs are still preliminary, however, there is a lot of interest in exploring its role in disease and how they can be used. This course aims to provide an introduction to circRNA biology, their function and how they can be used as a new therapeutic modality. The chemistry leading to design and manufacturing of circRNAs as potential therapeutics, and issues dealing with dosing, biodistribution, and immunogenicity will also be discussed.

Instructors:
Samie Jaffrey, MD, PhD, Department of Pharmacology, Weill Medical College, Cornell University
Bojan Losic, PhD, Associate Professor, Department of Genetics and Genomic Sciences, Icahn Institute for Data Science and Genomic Technology, Icahn School of Medicine at Mount Sinai
Additional Instructors to be Announced

MONDAY, MARCH 16 | 6:30 – 9:30 PM

SC2: Examining the Safety and Toxicity of Nucleic Acid Therapeutics
Nucleic acid drugs continue to deliver on their promise to become a third therapeutic modality, in addition to small molecules and biologics. Several antisense oligonucleotide drugs have been on the market for some time, while the first RNAi approval was granted in 2018. In addition, numerous mRNA and CRISPR therapeutic programs have entered clinical stages. Despite the common “nucleic acid” component, the mechanisms of action and of non-specific effects differ for each of these drug types.

Topics to be discussed include:
• Different types of nucleic acid-based drugs
• Mechanisms of actions and non-specific effects
• Current approaches to address non-specific and potentially toxic effects

Aimed at both novice and advanced nucleic drug developers, the course will:
• Introduce and explain the differences between various types of nucleic acid drugs
• Summarize our current understanding of the origins of non-specific and potentially toxic effects
• Provide direction on how to minimize the potential toxic effects of nucleic acids drugs

Instructors to be Announced

TUESDAY, MARCH 17, 2020 | 6:30 – 9:30 PM

SC3: Oligonucleotides for Cancer Immunotherapy
Oligonucleotide-based therapies are now gaining attention as an alternative to antibody and small molecule-based therapies for cancer immunotherapy. In cancers, where current treatment options are limited by efficacy and specificity, oligonucleotide-based drug modalities are offering a good alternative. This course will bring together experts who will share their perspectives on the opportunities and challenges underlying the generation of novel, more targeted and effective oligonucleotide-based drugs for cancer immunotherapy.

Instructors:
Shanthi Ganesh, PhD, Associate Director, Preclinical Oncology, Dicerna Pharmaceuticals, Inc.
Weston Daniel, PhD, Senior Director Program Management, Exicure, Inc.
Additional Instructors to be Announced

MONDAY, MARCH 17 | 6:30 – 9:30 PM

SC4: Gene Editing for Targeted Therapies
While the challenges and risks associated with oligonucleotide therapies still remain, there is a new and better understanding of how DNA and RNA can be effectively manipulated and delivered. With the rise of gene editing tools and enhanced knowledge of targeted delivery, these therapeutic modalities are once again being embraced with renewed hope and enthusiasm. This course helps you understand how DNA and RNA editing – particularly the one enabled by the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas9 system – works, and how it can be used to help develop targeted therapies.

Instructors:
Clifford Steer, M.D., Professor of Medicine and, Genetics, Cell Biology, and Development, University of Minnesota Medical School
Branden Moriarity, PhD, Assistant Professor, Department of Pediatrics, University of Minnesota Medical School
Khali Shah, MS, PhD, Director, Center for Stem Cell Therapies and Imaging, Harvard Medical School; Vice Chair of Research, Brigham and Women's Hospital

WEDNESDAY, MARCH 18, 2020 | 5:30 – 8:30 PM

SC5: Oligonucleotide CMC & Regulatory Strategies

Instructors to be Announced

THURSDAY, MARCH 19, 2020

SYMPOSIUM: AI for Drug Discovery & Development

SYMPOSIUM: Rare Disease Drug Development
PRISM, we optimize stereopure oligonucleotides to meet pre-defined product profiles. We illustrate by example that optimized, stereopure oligonucleotides exhibit the desired activity across multiple modalities, for example those that depend on RNase H and those that promote exon skipping. We demonstrate that the potencies of stereopure oligonucleotides in cellular models under free-uptake conditions help predict their potencies in animal models. We also show that stereopure oligonucleotides can potently engage and durably impact the expression of their targets in animal models.

11:50 Learning from Failures: The Story of Drisapersen Exon Skipping Development for Duchenne Muscular Dystrophy
Annemieke Aartsma-Rus, PhD, Professor of Translational Genetics, Leiden University Medical Center
The aim of the antisense-mediated exon skipping therapy is to allow Duchenne patients to produce Becker-like dystrophins, hoping this will slow down disease progression. Antisense oligonucleotides (ASOs) will hide a target exon from the machinery, preventing its inclusion into mRNA. This restores the reading frame allowing the production of a partially functional dystrophin, as found in Becker muscular dystrophy patients. Currently, one exon skipping ASO has been approved for Duchenne therapy by the Food and Drug Administration, while another was not approved. The presentation will outline the development of this approach through proof-of-concept studies in cell and animal models, preclinical optimization studies and clinical trials, but also discuss the required multilateral education of stakeholders (patients, regulators and academics) to develop tools to measure clinical efficacy of the approach.

12:20 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch On Your Own
12:50 Session Break
2:00 Arrowhead TRiM Platform in the Clinic
Mark Yen, PhD, Director, Clinical Development, Arrowhead Pharmaceuticals
This presentation will describe the safety and clinical effect with Arrowhead’s siRNA molecules in ongoing trials.

2:30 Industry Case Study from Quark Pharmaceuticals
Elena Feinstein, MD, PhD, CSO, Quark Pharmaceuticals
3:00 Sponsored Presentation (Opportunity Available)
3:30 Refreshment Break in the Exhibit Hall with Poster Viewing
4:15 Next-Generation Oligonucleotide Therapy Candidates with Tunable Backbones
David Tabatadze, PhD, President, ZATA Pharmaceuticals
The ZON platform is a novel class of oligonucleotides synthesized via phosphoramidite chemistry that permits facile attachment to the internucleoside phosphate charge-neutralizing groups (CNG) bearing positive charges at their termini. ZONs have length optimized CNG branches, allowing these positive charges to reach their neighboring phosphate groups where they can neutralize negative charges. ZON technology can be equally applied to DNA and RNA derivatives and be applied in all oligotherapy approaches.

4:45 Divalent siRNA Scaffold for Robust Gene Modulation in the Central Nervous System
Chantal Ferguson, Senior PhD Student, RNA Therapeutic Institute, University of Massachusetts Medical School
We developed a divalent (Di)-siRNA scaffold that supports potent and sustained gene silencing in the CNS upon intra-cerebroventricular (ICV) injection. Di-siRNAs are stabilized by 2’ modifications on every ribose, phosphorothioate backbone modifications, and substitution of the 5’ phosphate with metabolically stable 5’-(E)-vinyl phosphate. In mice, di-siRNA silences target mRNA in mouse CNS for at least 6 months without detectable toxicity. In cynomologus macaques, a bolus injection of di-siRNA showed substantial uptake conditions help predict their potencies in animal models. We also show that stereopure oligonucleotides can potently engage and durably impact the expression of their targets in animal models.
action of miRNAs in cells is complex and must be justified with care. The process of natural RNAi in cells has remained obscure. Our results suggest that the successful drugs while endogenous miRNAs can control natural physiologic processes and disease. Despite two decades of study, however, the full scope of miRNA-21 as a therapeutic target in fibrosis up to the entry of the anti-miR-21 drug into Phase II clinical trial for a genetic fibrotic kidney disease called Alport Syndrome.

The non-coding genome makes up 98.8% of the human genome. Most of this non-coding genome is transcribed into non-coding RNAs that may play an important role in cellular regulation in health and disease; these non-coding RNAs could be novel targets for future medicines. MicroRNAs are short non-coding RNAs that regulate biochemical pathways and networks of pathways by the mechanism of RNA interference (RNAi). MicroRNA-21 has been implicated in multiple organs as a microRNA associated with fibrotic pathways by the mechanism of RNA interference (RNAi). MicroRNA-21 has been implicated in multiple organs as a microRNA associated with fibrotic diseases and cancer. The presentation will summarize the opportunities and challenges of developing microRNA-based drugs, discuss challenges and solutions for delivery to target tissues, and will illustrate the successful generation of an anti-fibrotic microRNA-based therapeutic approach by targeting microRNA-21 with an antisense oligonucleotide (anti-miR-21). The presentation will illustrate the drug development path from the identification of miRNA-21 as a therapeutic target in fibrosis up to the entry of the anti-miR-21 drug into Phase II clinical trial for a genetic fibrotic kidney disease called Alport Syndrome.

MACHINE LEARNING-GUIDED DRUG DESIGN

9:15 Chairperson's Remarks
Ekkehard Leberer, PhD, Senior Director, R&D Alliance Management, Sanofi; Scientific Managing Director, COMPACT Consortium

9:20 Machine Learning-Guided Design of Antisense Oligonucleotides
Peter Hagedorn, Senior Principal Scientist and Team Leader of Bioinformatics and RNA Biology, Roche Innovation Center Copenhagen

Antisense oligonucleotides are well-suited for machine learning-guided drug design. As oligomers, they can be represented digitally using well-established methods from biological sequence analysis, and any computationally predicted design is straightforward to synthesize using standard phosphoramidite building blocks. Recent examples of machine learning-guided drug design, enabled by careful organization and labeling of preclinical datasets across multiple discovery projects, as well as by investments in laboratory automation that allows cellular assays to be run in high-throughput, will be presented.

RECENT ADVANCES WITH RNAs

9:50 FEATURED PRESENTATION: MiRNA Therapeutics: From Bench to Bedside
Ekkehard Leberer, PhD, Senior Director, R&D Alliance Management, Sanofi; Scientific Managing Director, COMPACT Consortium

The non-coding genome makes up 98.8% of the human genome. Most of this non-coding genome is transcribed into non-coding RNAs that may play an important role in cellular regulation in health and disease; these non-coding RNAs could be novel targets for future medicines. MicroRNAs are short non-coding RNAs that regulate biochemical pathways and networks of pathways by the mechanism of RNA interference (RNAi). MicroRNA-21 has been implicated in multiple organs as a microRNA associated with fibrotic diseases and cancer. The presentation will summarize the opportunities and challenges of developing microRNA-based drugs, discuss challenges and solutions for delivery to target tissues, and will illustrate the successful generation of an anti-fibrotic microRNA-based therapeutic approach by targeting microRNA-21 with an antisense oligonucleotide (anti-miR-21). The presentation will illustrate the drug development path from the identification of miRNA-21 as a therapeutic target in fibrosis up to the entry of the anti-miR-21 drug into Phase II clinical trial for a genetic fibrotic kidney disease called Alport Syndrome.

10:20 Sponsored Presentation (Opportunity Available)

10:50 Coffee Break in the Exhibit Hall with Poster Viewing

11:35 How Do miRNAs and RNAi Function Inside Cells?
David Corey, PhD, Professor, Department of Pharmacology, UT Southwestern

RNA interference can be a potent regulatory mechanism in human cells. Synthetic RNAs can control gene expression and have been developed to be successful drugs while endogenous miRNAs can control natural physiologic processes and disease. Despite two decades of study, however, the full scope of natural RNAi in cells has remained obscure. Our results suggest that the action of miRNAs in cells is complex and must be justified with care.

12:05 pm Development of Lipid Nanoparticles for mRNA-Based Therapeutics
Kerry Benenato, PhD, Senior Director, Discovery Chemistry, Moderna

The development of mRNA delivery vehicles for therapeutics is challenging. To start, the delivery vehicle must be able to protect the mRNA from degradation, shield the mRNA from the immune system and release its cargo in a tissue and cell specific manner. We have found parallel optimization of the mRNA chemistry and the lipid nanoparticle delivery vehicle is integral to the solution to each challenge. This effort has resulted in a drug product which affords high level of protein expression with an optimized pharmacokinetics and a clean tolerability profile. This presentation will highlight some of the important structure activity relationships of the lipid nanoparticle chemistry and key factors in the design of a delivery system which enables safe repeat dosing in non-human primates.

12:35 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:05 Dessert Break in the Exhibit Hall with Poster Viewing

1:50 Advancing siRNA Drug Delivery to Enhance RNAi Cancer Therapy
Patrick Lu, PhD, President & CEO, Sirnaomics

2:20 PANEL DISCUSSION: Opportunities and Challenges with RNAs
Moderator: Ekkehard Leberer, PhD, Senior Director, R&D Alliance Management, Sanofi; Scientific Managing Director, COMPACT Consortium
Panelists: Patrick Lu, PhD, President & CEO, Sirnaomics
Kerry Benenato, PhD, Senior Director, Discovery Chemistry, Moderna
David Corey, PhD, Professor, Department of Pharmacology, UT Southwestern

3:05 Networking Refreshment Break

CLOSING PLENARY

3:35 Chairperson's Remarks
Chairperson to be Announced

3:40 Biological Activity of Thiomorpholino Oligonucleotides
Marvin Caruthers, PhD, Distinguished Professor, University of Colorado

Thiomorpholino oligonucleotides are analogues containing morpholino- and 2'deoxyribonucleosides joined through thiophosphor internucleotide linkages. These analogues stimulate biological activity in a dual luciferase assay, in exon skipping with Marfan Syndrome and Duschenne Muscular Dystrophy, and in regulating TUG 1 RNA. Current research includes regulating microRNA maturation, editing transcription termination, exon skipping of additional genetic diseases, and antisense experiments with RNase H.

4:10 Talk Title to be Announced
Speaker to be Announced, Alnylam Pharmaceuticals

4:40 Close of Oligonucleotide Discovery and Delivery

4:40 Dinner Short Course Registration*
6:00 completed its first process validation of a commercial oligonucleotide in 2019. The successful manufacture of several clinical oligonucleotides, Biogen has just begun construction of its first ASO manufacturing facility. After the successful manufacture of several clinical oligonucleotides, Biogen has just completed its first process validation of a commercial oligonucleotide in 2019.

This presentation will focus on key learnings from the process validation effort including process characterization, risk assessment, and platform strategies.

12:20 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:50 Session Break

2:00 Monte Carlo Simulations of Amidite Starting Material Impurity Incorporations for Drug Substance Specification Justifications
Francis Ring, Assistant Director, Manufacturing and Operations, Ionis Pharmaceuticals

For starting material-related product impurities, Ionis supplemented the product impurity data with Monte Carlo simulations of the corresponding starting material impurity. By building the Monte Carlo simulations from the entire amidite production history, significantly more historical variability was captured than any individual Ionis product experienced. The methodology for building the starting material impurity and product incorporation models will be discussed along with the Monte Carlo simulation results.

2:30 Talk Title to be Announced
Speaker to be Announced

3:00 Sponsored Presentation (Opportunity Available)

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

4:15 CMC Case Study from ProQR Therapeutics
Vera Brinks, PhD, Director Pharmaceutics, ProQR Therapeutics

SAFETY AND TOXICITY OF OLIGONUCLEOTIDES

4:45 Oligonucleotides: Bioanalytical and DMPK Perspective Lessons Learned
Mary M. Sherman, PhD, Principal Consultant, Preclinical & Regulatory Consulting
Having worked with several small biotechs, focused on oligonucleotide research, I have seen a pattern emerging regarding their knowledge, their questions, their strategies, and the outcomes. A summary of some of those lessons will be presented during this presentation.

5:15 Welcome Reception in the Exhibit Hall with Poster Viewing

6:15 Dinner Short Course Registration*

3:00 - 9:30 SC3: Oligonucleotides for Cancer Immunotherapy

*Separate registration required. See page 3 for details.
Industry Case Study from Quark Pharmaceuticals
Vidhya Gopalakrishnan, PhD, Senior Vice President, Pharmaceutical Development, Quark Pharmaceuticals

9:50

Sponsored Presentation (Opportunity Available)

10:20

Coffee Break in the Exhibit Hall with Poster Viewing

CRITICAL FEEDBACK ON REGULATORY SUBMISSIONS

11:35 Practical, Quality and Regulatory CMC Considerations to Manufacture Clinical Trial Materials for Early Phase. What do you really need to do?
Kevin Fettes, PhD, Consultant and Founder, FTS Pharma Consulting
The complexity of oligonucleotide drug candidates being selected for clinical development has increased in recent years. These oligonucleotides often have significant chemical modifications requiring novel starting materials as well as technical innovations in process development, analytical chemistry, manufacturing and controls. This places extraordinary demands on both sponsor companies and contract manufacturing organizations to meet regulatory expectations under aggressive timelines.

12:05 pm Submitting Your First Investigational New Drug (IND) Application: A Roadmap of Key Activities
Paul Manley, President & Principal Consultant, Orvieto Consulting
An IND application can be daunting for a small company making such a submission for the first time. This presentation will discuss key activities to consider as you plan for this important FDA interaction, including: Pre-IND dialogue, project plans, use of internal and external resources, creation of your electronic submission and the IND review process.

12:35 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

1:05 Dessert Break in the Exhibit Hall with Poster Viewing

1:50 Rare Disease: CMC Regulatory Pathway
Kimberly Tyndall, Principal, CMC Tyndall Consultant
This talk will focus on CMC regulatory hurdles and pathways encountered when filing oligonucleotide drug substance and drug product. We will explore both hurdles that may be faced in the US as well as across the globe. How these can be overcome and how to streamline the process so as to ensure quality.

2:20 PANEL DISCUSSION: How to Successfully Prepare for a Regulatory Submission and Overcome Common Hurdles
Moderator: Kimberly Tyndall, Principal, CMC Tyndall Consultant
Panelists: Steven Kates, PhD, Vice President, Regulatory Affairs, Dicerna Pharmaceuticals
Paul Manley, President & Principal Consultant, Orvieto Consulting
Mary M. Sherman, PhD, Principal Consultant, Preclinical & Regulatory Consulting
- Challenges: Manufacturing development history for regulatory filings
- Global dossiers: FDA, EMA, Japan, Brazil and Canada
- Stability data: What was permitted and what was not?

3:05 Networking Refreshment Break

CLOSED PLENARY

3:35 Chairperson’s Remarks
Chairperson to be Announced

3:40 Biological Activity of Thiomorpholino Oligonucleotides
Marvin Caruthers, PhD, Distinguished Professor, University of Colorado
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4:10 Talk Title to be Announced
Speaker to be Announced, Alnylam Pharmaceuticals

4:40 Close of Oligonucleotide CMC and Regulatory Strategies

4:40 Dinner Short Course Registration*
5:00 - 8:00 SC4: Gene Editing for Targeted Therapies
*Separate registration required. See page 3 for details.

The scientific quality and value of the presentations was very high. The opportunities for networking have been excellent. I very much enjoyed attending the conference.

Ekkehard Leberer, PhD, Senior Director, R&D Alliance Management, Sanofi
Artificial Intelligence for Drug Discovery & Development
Applications from Drug Design to Clinical Trials

WEDNESDAY, MARCH 18

RECOMMENDED SHORT COURSE
4:40 pm Dinner Short Course Registration*
5:00 - 8:00 SC4: Gene Editing for Targeted Therapies
*Separate registration required. See page 3 for details

THURSDAY, MARCH 19

7:30 am Registration and Morning Coffee

AI FOR BETTER PREDICTIONS IN DRUG DEVELOPMENT

8:15 Welcome Remarks from Conference Director
Tanuja Koppal, PhD, Senior Conference Director, Cambridge Healthtech Institute

8:25 Chairperson’s Opening Remarks
Shruthi Bharadwaj, PhD, Senior Scientist, Novartis Oncology Precision Medicine

8:30 Bringing Precision Drugs to the Clinic Faster Using Artificial Intelligence and Data Science
Olivier Elemento, PhD, Director, The Caryl and Israel Englander Institute for Precision Medicine; Associate Director, Institute for Computational Biomedicine, Weill Cornell Medicine

We have developed novel genomic assays and analytical tools for precision medicine that are being used routinely for personalized medicine for a variety of Weill Cornell patients. We also have developed AI predictive models for improving how drugs are developed, from prediction of mechanisms-of-action to prediction of drug safety, prediction of indication for drug repositioning and predicting effective drug combinations.

9:00 Explainable AI for Data-Driven Medicine: From Data to Models and Treatments
Igor Jurisica, PhD, DrSc, Senior Scientist, Krembil Research Institute; Professor, Medical Biophysics, University of Toronto

To fathom complex diseases, we need to systematically integrate diverse data and link them using relevant annotations and relationships. Graph theory, data mining, machine learning and visualization enables data-driven modeling and precision medicine. Here, we highlight integrative computational biology and AI that help building explainable models, identifying prognostic and predictive signatures, re-positioning existing drugs for novel use, unraveling mechanism of action for therapeutics, and prioritizing them based on predicted toxicity.

9:30 Leveraging Image-Derived Phenotypic Measurements for Drug-Target Interaction Predictions
Arvind Rao, PhD, Associate Professor, Department of Computational Medicine and Bioinformatics, University of Michigan

We propose a novel in silico drug discovery approach to identify kinase targets that impinge on nuclear receptor signaling with data generated using high-content analysis (HCA). Using imaging-derived descriptors, we provide prediction results of drug-kinase-target interactions based on single-task learning, multi-task learning, and collaborative filtering methods. Our promising results suggest that imaging-based information can be used as an additional source of information to existing virtual screening methods, thereby making the drug discovery process more time and cost efficient.

10:00 Networking Coffee Break

10:30 AI-Based Method for Predicting and Validating Therapeutic Peptides
Paul Rohricht, MS, MBA, Chief Business Officer – Pharma, Nuritas Corporation

We are a drug discovery company that uses AI to accelerate the identification of bioactive peptides across multiple therapeutic areas. Whereas current pharma drug discovery takes years and has seen several late-stage failures in the clinic, Nuritas’ platform takes months to deliver molecules that have a high success rate (>60% predicted). We are currently addressing several indications across multiple therapeutic areas, including inflammation, diabetes, muscle health, anti-aging, hypertension, and anti-microbials. Efforts to expand into other therapeutic areas will continue, both internally and through external collaborations.

11:00 AI and ML Approaches for Clinical Trials
Shruthi Bharadwaj, PhD, Senior Scientist, Novartis Oncology Precision Medicine

With the increase in availability of clinical trial data, AI and machine learning approaches are becoming imperative in mining and finding clinically significant insights. In this talk, I will provide an overview of the various approaches currently used to tackle the big-data problem in pharma.

11:30 Sponsored Presentation (Opportunity Available)

12:00 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:30 Session Break
AI FOR DEVELOPING NEW THERAPIES

1:15 Chairperson’s Remarks
Barun Bhattarai, PhD, Investigator, Novartis Institute for Biomedical Research

1:20 PANEL DISCUSSION: How Is AI/ML Addressing Real-World Healthcare Problems?
Moderator: Michael Liebman, PhD, Managing Director, IPQ Analytics, LLC
Panelists:
Mary Jo Lamberti, PhD, Research Assistant Professor; Associate Director of Sponsored Research, Tufts Center for the Study of Drug Development
Debbie Lin, PhD, Executive Director, Venture Fund Digital Health, Boehringer-Ingelheim
Michael Montgomery, MD, Former Global Head of Medical Affairs, Incyte Pharmaceuticals

The methodologies of AI (e.g., machine learning, deep learning) are increasingly focused on healthcare to provide analysis with the goal of identifying critical relationships that can enhance clinical decision-making (e.g., diagnosis and treatment) and drug development. The availability of big data, however, may enable the application of these methods, but we must evaluate if the results actually address the clinical questions that exist in real-world medicine and in real-world patients.

2:20 Networking Refreshment Break

2:40 ML and AI on ADME/Tox-Accelerating Drug Discovery
Barun Bhattarai, PhD, Investigator, Novartis Institute for Biomedical Research

This talk will focus on the application of ML and AI approaches to accelerate drug discovery in ADME/Tox with some case studies and the spirited path traditional pharma has to navigate aiming towards the end goal.

3:10 Key Elements of a Digital Strategy for Nucleic Acid based Medicines
Peter Hagedorn, Senior Principal Scientist and Team Leader of Bioinformatics and RNA Biology, Roche Innovation Center Copenhagen

For drug discovery of small molecule compounds, examples leveraging AI methods have started to appear, although major breakthroughs have yet to be seen. For nucleic-acid based medicines that target RNA, an analysis of the opportunities and pitfalls for using AI methods will be presented. For this modality, there is a high pace of technology innovations and new fundamental insights, and key elements of a general digital strategy that takes this into account will be discussed.

3:40 Accelerating Research in Rare Disease through Patient-Partnered Collaborations
Ryan Leung, Vice President, Strategy & Corporate Development, Research to the People

Patient-centricity is becoming increasingly important in all areas of healthcare, particularly in rare diseases. With so few patients, it is critical that we make the most out of every patients’ story and experience, engaging them at every point of research, development, care, and treatment. Leveraging advances in -omics, bioinformatics, deep learning, and cloud computing, we partner with patients directly to help them access and understand their health data while creating new opportunities for rare disease research. With 5 successful collaborations to date, we’ll share our thoughts on the impact and potential of patient-partnered research.

4:10 Close of Symposium
**Rare Disease Drug Development**

**New Drug Modalities and Emerging Trends**

**WEDNESDAY, MARCH 18**

**RECOMMENDED SHORT COURSE**

4:40 pm Dinner Short Course Registration*

5:00 - 8:00 SC4: Gene Editing for Targeted Therapies

*Separate registration required. See page 3 for details.

**THURSDAY, MARCH 19**

7:30 am Registration and Morning Coffee

**EMERGING DRUG MODALITIES FOR ORPHAN DRUGS**

8:15 Welcome Remarks from Conference Director
Tanuja Koppal, PhD, Senior Conference Director, Cambridge Healthtech Institute

8:25 Chairperson’s Opening Remarks
David Erbe, PhD, Distinguished Investigator, Alnylam Pharmaceuticals

8:30 Delivering on the Promise of RNAi Therapeutics
David Erbe, PhD, Distinguished Investigator, Alnylam Pharmaceuticals

RNAi (RNA interference) is a natural cellular process of gene silencing that represents one of the most promising and rapidly advancing frontiers in biology and drug development today. By harnessing this process, a new class of medicines, known as RNAi therapeutics, is now a reality with the potential to transform the care of patients with genetic and other diseases.

9:00 Novel STING Antagonists for Interferonopathies and Autoimmune Diseases
Radhakrishnan P. Iyer, PhD, Co-Founder and CSO, Spring Bank Pharmaceuticals

Cellular immune responses to double-stranded DNA result in the activation of the cGAS-STING pathway for IFN production; however, aberrant activation of the STING pathway has been hypothesized to cause autoimmune diseases. Reported here is the discovery of small molecule STING antagonists that broadly inhibit aberrant STING-signaling with potential therapeutic applications in inflammatory diseases including systemic lupus erythematosus (SLE), and rare diseases including Aicardi-Goutières Syndrome, Sjogren’s syndrome, SAVI, familial chilblain lupus and so on.

9:30 Protein Replacement with mRNA for Inherited Metabolic Diseases
Paloma H. Giangrande, PhD, Director, Research, Rare Diseases, Moderna Therapeutics

Many rare inherited metabolic disorders are caused by deficiency of essential intracellular proteins responsible for maintaining proper homeostasis. Conventional protein replacement (e.g., enzyme replacement therapy or ERT) and gene therapy-based approaches are not an option for treating these disorders due to drug-delivery and efficacy/safety considerations. To develop new treatments for these diseases, we encapsulated nucleoside-modified, codon-optimized mRNAs encoding these genes in lipid nanoparticles. Preclinical data demonstrating the efficacy and safety of our mRNA-LNP therapy for several rare metabolic disorders will be presented.

10:00 Networking Coffee Break

**TACKLING TRANSLATIONAL CHALLENGES**

10:30 PANEL DISCUSSION: Rare, Ultra-Rare, and the Impact of Precision Medicine
Moderator: Michael Liebman, PhD, Managing Director, IPQ Analytics, LLC
Panelists: Michael Montgomery, MD, Former Global Head of Medical Affairs, Incyte Pharmaceuticals
E. Michael D. (“Mike”) Scott, Founding Partner and Executive Rebel, Ex Archa

Much of current rare disease research and practice targets the potential that genetics is the major driver of these conditions and while this is likely an important factor, it may not be the sole driver. Rare disease diagnosis is complicated as these diseases are complex even though small population numbers limit the potential for adequate stratification. Additionally, other factors that may arise during fetal development, beyond epigenetics, may have a causal relationship.

11:30 Sponsored Presentation (Opportunity Available)

12:00 pm Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

12:30 Session Break

**HOTEL & TRAVEL**

**CONFERENCE VENUE AND HOTEL:**
Hyatt Regency Cambridge
575 Memorial Drive
Cambridge, MA 02142
Phone: 617-492-1234

Discounted Room Rate: $219 s/d
Discounted Room Rate Cut-off Date: February 18, 2020

Reservation: Go to the travel page of OPTCongress.com
TECHNOLOGIES ENABLING RARE DISEASE DRUG DISCOVERY

1:15 Chairperson’s Remarks
Anthony Hicks, PhD, Director, UNC Catalyst for Rare Diseases, University of North Carolina, Eshelman School of Pharmacy

1:20 Down to the Last Base: Genetic Screens for Variant-to-Function
John Doench, PhD, Director R&D, Genetic Perturbation Platform, Broad Institute of Harvard and MIT

Genome-wide CRISPR screens have revitalized functional genomics. Large-scale data sets enable rapid hypothesis generation, and focused screening efforts can provide detailed mechanistic insights into the function of any gene of interest. Here I will discuss how CRISPR screens are being employed in gene function discovery projects, with an emphasis on the latest technological advances.

1:50 Correction of a Progeriod Mouse Model with Optimized Base Editors
Luke Koblan, Graduate Student, Laboratory of Dr. David Liu, Department of Chemistry and Chemical Biology, Harvard University

Base editors are genome-editing reagents capable of installing directed single nucleotide conversions in genomic DNA. We have developed a split-intein AAV system for in vivo delivery of these tools and have used these reagents for the correction of the c.1824T mutation that drives the majority of Hutchinson-Gilford Progeria Syndrome (HGPS) cases.

2:20 Networking Refreshment Break

2:40 Modifier Genes: En Route to Identify Compensatory Mechanisms to Improve Rare Disease Outcomes
Maja Tarailo-Graovac, PhD, Assistant Professor, Departments of Medical Genetics and Biochemistry & Molecular Biology, Alberta Children’s Hospital Research Institute (ACHRI), Cumming School of Medicine, University of Calgary

Advances in high-throughput sequencing have revolutionized diagnosis and discovery in rare diseases by enabling the entire genome of an individual to be read in a single test. Importantly, genome sequencing allows testing of how variants within a genome interact to modify the effect of the primary disease-causing variant. My interdisciplinary research team combines human and model organism genomics in order to accelerate discovery of compensatory mechanisms in rare disease via modifiers known as suppressors.

3:10 A Multidisciplinary Approach to Discovery and Development of Rare Disease Therapy
Anthony Hicks, PhD, Director, UNC Catalyst for Rare Diseases, University of North Carolina, Eshelman School of Pharmacy

Rare disease research and development requires urgent interfacing of a range of disciplines to bring forward new therapies due to the severity of disease, poor quality of life and mortality associated with many disorders. Catalyzing parallel interactions between subject matter experts across disciplines facilitates the rapid identification of targets and development of therapeutic strategies to address unmet medical needs.

3:40 Accelerating Research in Rare Disease through Patient-Partnered Collaborations
Ryan Leung, Vice President, Strategy & Corporate Development, Research to the People

Patient-centricity is becoming increasingly important in all areas of healthcare, particularly in rare diseases. With so few patients, it is critical that we make the most out of every patients’ story and experience, engaging them at every point of research, development, care, and treatment. Leveraging advances in -omics, bioinformatics, deep learning, and cloud computing, we partner with patients directly to help them access and understand their health data while creating new opportunities for rare disease research. With 5 successful collaborations to date, we’ll share our thoughts on the impact and potential of patient-partnered research.

4:10 Close of Symposium