2023 CONFERENCE
PROGRAMS

- ENGINEERING
- ONCOLOGY
- BISPECIFICS
- IMMUNOTHERAPY
- EXPRESSION
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The Essential Protein Engineering and Cell Therapy Summit

2023 PLENARY KEYNOTES

Carl June, MD,
Richard W. Vague Professor in Immunotherapy; Professor of Medicine; Director, Center for Cellular Immunotherapies; Director, Parker Institute for Cancer Immunotherapy, University of Pennsylvania Perelman School of Medicine

John C. Marioni, PhD
Senior Vice President and Head of Computation, Research and Early Development, Genentech

Rebecca A. Sendak, PhD
Global Head, Large Molecules Research Platform, Sanofi

YOUNG SCIENTIST KEYNOTE

Andrew Anzalone, MD, PhD
Head, Prime Editing Platform, Scientific Co-founder, Prime Medicine, Inc.

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PEGS BOSTON

Experience the Future of Biotherapeutic Drug Development at the World's Leading Biologics Event

The world's largest gathering of protein engineering and biotherapeutics experts is back in Boston! PEGS Boston Summit is the leading biologics event with comprehensive programming covering all aspects of biologic drug development with in-depth presentations on protein and antibody engineering, immunotherapy, oncology, expression, analytics, immunogenicity, and more.

Harness the power of in-person events, form genuine connections, create valuable relationships with peers, and become part of the PEGS community.

To provide maximum flexibility, CHI will present this event live in Boston as well as virtually for those unable to travel, forming one unique and valuable experience.

2023 CONFERENCE PROGRAMS

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SC SHORT COURSES

Training SEMINARS

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CONFERENCE AT-A-GLANCE

2023 PROGRAMS

- ENGINEERING
- ONCOLOGY
- BISPECIFIC
- IMMUNOTHERAPY
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- IMMUNOGENICITY
- THERAPEUTICS

SUNDAY MAY 14	TUESDAY MAY 16	MONDAY - TUESDAY AM (MAY 15-16)	TUESDAY PM - WEDNESDAY (MAY 16-17)	THURSDAY - FRIDAY AM (MAY 18-19)
AFTERNOON SHORT COURSES	DINNER SHORT COURSES	Display of Biologics	Engineering Antibodies	Machine Learning for Protein Engineering
		Antibodies for Cancer Therapy	Emerging Targets for Oncology & Beyond	Driving Clinical Success of Antibody-Drug Conjugates
		TRAINING SEMINAR: Introduction to Bispecific Antibodies	Advancing Bispecific Antibodies and Combination Therapy to the Clinic	Engineering Bispecific Antibodies
		Improving Immunotherapy Efficacy and Safety	Cell-Based Immunotherapies	Next-Generation Immunotherapies
		Difficult-to-Express Proteins	Optimizing Protein Expression	Maximizing Protein Production Workflows
		Digital Integration in Biotherapeutic Analytics	Biophysical Methods	Characterization for Novel Biotherapeutics
		TRAINING SEMINAR: Introduction to Immunogenicity	Immunogenicity Assessment and Management	TRAINING SEMINAR: Introduction to Bioassays
		Emerging Indications for Therapeutic Antibodies	mRNA Therapeutics	Next-Generation Immunotherapies

Training SEMINARS
By Cambridge Healthtech Institute

- Introduction to Bispecific Antibodies: History, Engineering, and Application
- Introduction to Immunogenicity
- Introduction to Protein Engineering
- Introduction to Machine Learning for Biologic Design
- Analysis and Interpretation of Antibody Deep Sequencing and Single Cell Analysis Data
- Introduction to Bioassays

PLENARY KEYNOTE SESSIONS

MONDAY, MAY 15 | 4:00 - 5:40 PM

Advances in CAR T Therapy

CARL JUNE, MD,
Richard W. Vague Professor & Director, Parker Institute for Cancer Immunotherapy at the University of Pennsylvania

The Next Frontier in Machine Learning and Biologics:

"Lab in a Loop" Large Molecule Drug Discovery, From Optimization to de novo Discovery

JOHN C. MARIONI, PhD, *Senior Vice President and Head of Computation, Research and Early Development, Genentech*

WEDNESDAY, MAY 17 | 11:20 AM – 1:00 PM

Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

REBECCA A. SENDAK, PhD,
Global Head, Large Molecules Research Platform, Sanofi

YOUNG SCIENTIST KEYNOTE

Engineering Prime Editor Proteins for Therapeutic Applications

ANDREW ANZALONE, PhD
Head, Prime Editing Platform, Scientific Co-founder, Prime Medicine, Inc.

SHORT COURSES*

IN-PERSON ONLY

*Separate registration required.

SUNDAY, MAY 14 2:00-5:00 PM

SC1: Antibody Drug Discovery: From Target to Lead

Instructor:

Zhiqiang An, PhD, Professor, Molecular Medicine, University of Texas Health Science Center at Houston

At least 100 antibody therapies have been approved for the treatment of cancer, immune disorders, metabolic, cardiovascular, and infectious diseases, and among the top 20 bestselling prescription medicines in 2020, 14 are antibody-based. This trend will continue as about 50% of the new drugs in various stages of clinical development are antibodies. This course will review state-of-the-art concepts, methodologies, and current trends in therapeutic antibody discovery.

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

Instructor:

Jan Jezek, CSO, Arecor, United Kingdom

With increasing focus on nucleic acid-based therapies, particularly mRNA, lipid nanoparticles are emerging as the non-viral vectors of choice for their efficient delivery. The short course will review the field of lipid nanoparticle formulation and characterization, including (a) lipid nanoparticles in the broader context of lipid nanocarriers, (b) key structural features, (c) stability, (d) characterization, (e) factors influencing transfection efficiency, (f) factors influencing tissue/cell targeting, (g) manufacture and (h) lessons from the COVID vaccines development. Recent developments in patent landscape will also be covered.

SC3: In silico and Machine Learning Tools for Antibody Design and Developability Predictions

Instructors:

Philip M. Kim, PhD, Professor, Molecular Genetics & Computer Science, University of Toronto

Vinodh B. Kurella, PhD, Biotherapeutic Computational Modeler, Takeda Pharmaceuticals, Inc.

Christopher J. Langmead, PhD, Director of Digital Biologics Discovery, Amgen

In silico developability predictive platforms offer promising screening support to identify optimal properties of a candidate biotherapeutic at early stages. Predicting your biologic's developability can help avoid instability problems during later development and impede significant economic consequences.

SC4: An Introduction to Protein Degraders: A Focus on PROTACs

Instructor:

John Erve, PhD, Senior Principal Scientist, Jerve Scientific Consulting

This seminar will give an overview of proteolysis targeting chimeras (PROTACs) and will introduce some important topics relevant to how they work as well as the challenges of developing them as oral therapeutics. Topics to be covered include examples of what they can accomplish that small molecules cannot, importance of ternary complex formation, and how proteomics is essential for their development. Strategies to increase their selectivity, such as antibody PROTACs, will be examined. PROTACs lie in Bro5 space, and we will cover the significance of this for developing them as oral drugs. Finally, the mechanism of action of PROTACs give rise to some unique drug safety issues which will also be discussed.

TUESDAY, MAY 16 6:30-9:00 PM

SC5: Introduction to Gene Therapy Product Manufacturing and Analytics

Instructors:

Claire Davies, PhD, Associate Vice President, Bioanalytics, Sanofi

Scott Dooley, Senior Scientist, Analytical Development, Sanofi

This short course introduces concepts that can be used to facilitate CMC development for gene therapy products. The instructors will review regulatory guidance and present phase-appropriate control strategies. Several CMC challenges unique to this modality will also be discussed, along with different manufacturing platforms. The workshop will include an interactive session on developing an integrated control strategy.

SC6: Developability of Bispecific Antibodies

Instructor:

Nimish Gera, PhD, Vice President, Biologics, Mythic Therapeutics

Bispecific antibodies are a rapidly growing and clinically validated class of antibodies with marketed drugs and multiple candidates in clinical trials. Targeting multiple antigens in a synergistic manner can confer enhanced therapeutic benefits and potentially uncover novel biological mechanisms. However, multiple formats and a tedious candidate selection process to select functional and developable bispecific antibodies make such programs cumbersome. This short course highlights the rapid growth in the field, therapeutic applications, and it focuses on challenges with discovery and development of bispecific antibodies. We will use an approved bispecific antibody as a case study to understand the varied aspects of discovery and development of bispecific antibody programs.

SC7: Use and Troubleshooting of Eukaryotic Expression Systems

Instructors:

Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

Henry C. Chiou, PhD, Senior Director General Manager, Biosciences, Thermo Fisher Scientific

Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory

Eukaryotic expression systems are extensively used for the generation of recombinant proteins thereby becoming an essential protein engineering tool. The choice of a suitable eukaryotic expression system depends mainly on the biological and biochemical properties of an individual protein. The course will focus on both the insect and mammalian expression systems, which have demonstrated the ability to express complex proteins for a wide variety of applications. We will discuss the concepts, uses, and optimization of these systems along with sharing experimental troubleshooting lessons learned. The course combines instruction and case studies in an interactive environment.

SC8: CAR T Cells: Improving Safety While Retaining Therapeutic Activity

Instructors:

Nasheed M. Hossain, MD, Assistant Professor of Medicine, University of Pennsylvania - Perelman School of Medicine, Department of Medicine - Division of Hematology/Oncology, Cell Therapy & Transplant Program

Michael I. Nishimura, PhD, Professor, Surgery, Loyola University Chicago

Rimas J. Orentas, PhD, Scientific Director, Caring Cross, Inc.; Professor, University of Washington School of Medicine

CD19 CAR T cells have revolutionized the treatment of B cell malignancies. However, CD19 CAR T cells have their drawbacks in that there can be serious adverse events and not all patients go into complete remission. Furthermore, CAR T cells have not as effective for other cancers, especially solid tumors. In this course, we will provide an overview of the current research/clinical landscape for CAR T cells will be reviewed, and next potential steps will be discussed.

TS3A: Introduction to Bispecific Antibodies: History, Engineering, and Application

Instructor:

G. Jonah Rainey, PhD, Senior Director, Protein Engineering, Eli Lilly and Company

Introduction to Bispecific Antibodies will be organized as an informative and practical guide to get up to speed on critical aspects of bispecific antibody therapeutics. Topics will include historical successes, failures, and lessons learned. Specific practical instruction will span mechanisms of action, engineering, developability, regulatory considerations, and translational guidelines. Perspectives on ideal implementation of bispecifics as targeted and immunomodulatory approaches will be discussed.

TS7A: Introduction to Immunogenicity

Instructors:

Chloé Ackaert, PhD, Senior Scientist, Immunogenicity, ImmunXperts, a Q2 Solutions Company

Sofie Pattijn, Founder & CTO, ImmunXperts, a Q2 Solutions Company

Bonnie Rup, PhD, Biotechnology Consultant, Bonnie Rup Consulting

This 1.5-day training seminar provides a practical, comprehensive overview of immunogenicity – the causes, how to assess, predict and prevent, and what to do if you observe immunogenicity during preclinical, clinical and post-market approval. The seminar begins by detailing the science behind immunogenicity, the latest international Guidance, followed by assay and bioanalytical assessment strategies for traditional and emerging biologics. Other topics include predictive models and reporting immunogenicity.

TS9A: Introduction to Protein Engineering

Instructor:

David Bramhill, PhD, Founder, Bramhill Biological Consulting LLC

CHI's Introduction to Protein Engineering training seminar offers a comprehensive tutorial in the concepts, strategies and tools of protein engineering – and explains the role of this discipline in the progression of biotherapeutic research and development. The class is directed at scientists new to the industry or working in support roles, academic scientists and career protein scientists wanting a detailed update on the current state of the field.

Today's wealth of knowledge of protein structures is reviewed, along with the genetics of diversity generation of antibodies, to give insights into the best strategies for improving protein function. There is particular emphasis on the selection of functional assays to monitor effectively the changes in desired properties.

Display technologies such as phage display and yeast display are described and the advantages and disadvantages of each compared. Design strategies are presented for constructing libraries of variant proteins for display, and panning strategies for enriching proteins with the desired properties considered.

The course details the engineering and enhancement of traditional antibodies and also cytokines, antibody fragments and emerging antibody-like scaffolds. Also included is a discussion of the roles of protein engineering in the discovery, design and development of new therapeutic modalities including antibody-drug conjugates (ADCs), bispecific antibodies and Chimeric Antigen Receptor (CAR) constructs.

This class will discuss the expression platforms used for producing proteins for testing and for manufacture, along with the rapidly emerging role of protein engineering in optimizing antibody and other protein therapeutics.

A background in biochemistry and molecular biology is useful, as the course is designed to progress rapidly from simple to advanced concepts. Links and references will be provided with the course materials to provide a glossary and other useful resources.

TS9B: Introduction to Machine Learning for Biologics Design

Instructors:

Christopher R. Corbeil, PhD, Research Officer, Human Health Therapeutics, National Research Council Canada

Francis Gaudreault, PhD, Research Officer, Human Health Therapeutics, National Research Council Canada

This course offers an introduction to concepts, strategies, and machine learning methods used for biologics design. It includes presentations and demonstrations of the methods used in the field, covering techniques such as triaging sequences, modulating affinity, and designing antibody libraries, along with increasing manufacturability. The course is directed at scientists new to the field and protein engineers wanting an introduction to how machine learning can aid in guiding biologics design.

TS10B: Analysis and Interpretation of Antibody Deep Sequencing and Single Cell Analysis Data

Instructors:

Brandon DeKosky, PhD, Phillip and Susan Ragon Career Development Professor of Chemical Engineering, MIT Core Member, The Ragon Institute of Massachusetts General Hospital, Massachusetts Institute of Technology, and Harvard

Matias Gutierrez-Gonzalez, PhD, Research Fellow, The Ragon Institute of MGH, MIT, and Harvard

In this training seminar, participants will learn about recently developed methods for Next-Generation Sequencing (NGS) and single-cell analysis of antibody repertoires. The course will be interactive with case studies, participants will be able to download data and examples. Please bring your computer.

TS7C: Introduction to Bioassay Design, Development, Analysis, Validation, and Monitoring

Instructor:

David Lansky, PhD, President, Precision Bioassay, Inc.

This course will build from an introduction to the statistical concepts needed for bioassays (all illustrated with useful and relevant examples) and some review of the properties of bioassays. These inform the choices we make in applying DOE to bioassay development, validation, and monitoring. We will cover ways that strategic assay design considerations support good assay monitoring with graphical and quantitative tools as part of a lifecycle approach.

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ENGINEERING STREAM
CONFERENCES

MAY 15-16

Display of Biologics

AGENDA

MAY 16-17

Engineering Antibodies

AGENDA

MAY 18-19

Machine Learning Approaches for Protein Engineering

AGENDA

ENGINEERING STREAM

The State of the Science in Biotherapeutics Research and Development

Antibody research in response to the COVID-19 pandemic has crash-tested new discovery technologies and caused the industry to find new ways of conducting discovery and development faster and more efficiently. With this as a foundation, the PEGS Engineering Stream examines the state of the science in biologics R&D, including smarter and higher throughput screening methods, creative engineering approaches for improving the precision and efficacy of therapeutic antibodies and the increasing role of machine learning in discovery and engineering.

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SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC4: An Introduction to Protein Degraders: A Focus on PROTACs
**Separate registration required. See short courses page for details.*

MONDAY, MAY 15

7:00 am Registration and Morning Coffee

CHALLENGES OF COMPUTATIONAL ANTIBODY DESIGN

8:20 Chairperson's Remarks
Andrew R.M. Bradbury, PhD, CSO, Specifica, Inc.

8:30 Opportunities & Challenges in Computational Antibody Design
Sarel J. Fleishman, PhD, Associate Professor, Biomolecular Sciences, Weizmann Institute of Science

Despite decades of research, the ability to generate effective antibodies completely on the computer is elusive, and antibody discovery and optimization continue to rely on iterative and time-consuming high-throughput screening. I will review the prerequisites for effective and universally applicable antibody design methods, the opportunities in developing methods for computational antibody optimization, and the underlying factors that explain why completely computational antibody design remains challenging.

9:00 Computational Design or *in vitro* Evolution… Better Together
Bruno Correia, PhD, Assistant Professor, Laboratory of Protein Design & Immunoengineering, University of Lausanne

Computational protein design has become a key tool in protein engineering. It is however clear that often computationally designed proteins are often suboptimal and require further optimization. During my talk, I will discuss the strengths and weaknesses of each approach and their synergistic usage to solve hard problems in protein engineering that become accessible by the use of hybrid approaches.

9:30 Disruptive Antibody Discovery & Development Solutions for Challenging Targets
Volker Lang, PhD, Managing Director, AbCheck s.r.o.

AbCheck has developed a number of technologies for efficiently discovering high-quality MAbs for next-generation protein therapeutics. Our drug discovery platform offers modular solutions to overcome target-specific challenges and improve success rates for drug discovery campaigns. Our proprietary microfluidics approach enables direct one-step sorting for function and/or other critical criteria with high throughput of millions of droplets per day for the discovery of antibodies to both known and emerging functional targets.

10:00 Networking Coffee Break

EMERGING PLATFORMS FOR PROTEIN DISCOVERY AND ENGINEERING

10:29 Chairperson's Remarks
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

10:30 Isolation of Binding Proteins Using Magnetized Yeast Cell Targets
Balaji M. Rao, PhD, Professor, Chemical & Biomolecular Engineering, North Carolina State University

The isolation of binding proteins from combinatorial libraries has typically relied on the use of a soluble, recombinantly expressed form of the target protein when performing magnetic selections or fluorescence-activated cell sorting. Appropriate target protein expression and subsequent purification represents a significant bottleneck in this process. As an alternative, the use of target proteins expressed on the surface of magnetized yeast cells in combinatorial library screening is discussed.

11:00 Systems Biologics: Large-Scale Engineering of Modulators of Protein Networks
Sachdev Sidhu, PhD, Research Professor; Entrepreneur in Residence, University of Waterloo

Systems biologics combines large-scale systems biology with the development of new antibody drugs. The efficient pipeline extends from basic research through translational science, and it constitutes a new model for research and drug development. Through this model, cutting-edge systems biology basic research can be seamlessly translated into systems biologics: novel, multi-functional drugs, and diagnostics that take advantage of the complexities of human biology revealed by genomics data.

11:30 Luncheon Presentation I to be Announced
Speaker to be Announced

12:00 pm Luncheon Presentation II to be Announced
Speaker to be Announced

12:30 Session Break

DESIGNING BIOLOGICS FOR NON-ONCOLOGY APPLICATIONS

12:34 Chairperson's Remarks
Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

12:35 Using Yeast Display for Non-Oncology Applications
Possu Huang, PhD, Assistant Professor, Bioengineering, Stanford University
The growing need for antibodies with customized specificity provides a rich environment for engineering efforts. By leveraging the unique properties of neural networks, we developed a generative model for immunoglobulin 3D structures, with which diverse structures can be modeled with unprecedented speed. This "Generative Design" strategy explores dynamic structures and our preliminary experimental results on multiple targets support the plausibility of *in silico* design of epitope-specific antibodies.

1:05 Designing Ultrapotent DARPins for Rapid Allergic Desensitization
Luke Pennington, PhD, CSO and Co-Founder, Excellergy
Using yeast display and structure-based engineering, we have generated potent IgE inhibitors built from designed ankyrin repeat proteins (DARPins). These fast-acting inhibitors employ multiple distinct anti-IgE domains to disrupt highly stable IgE receptor complexes at low nanomolar potencies. This dynamic mechanism of action desensitizes allergic effector cells in minutes by stripping allergen-reactive IgE from the high affinity IgE receptor and enables new therapeutic avenues for the anti-IgE inhibitor class.

1:35 Session Break

CHALLENGING TARGETS

1:45 Chairperson's Remarks
Gregory A. Weiss, PhD, Professor, Chemistry, Pharmaceutical Sciences, Molecular Biology & Biochemistry, University of California, Irvine

1:50 Phage-Displayed Noncanonical Amino Acids for Drug Discovery
Wenshe Ray Liu, PhD, Harry E. Bovay, Jr. Endowed Chair, Professor in Chemistry, Texas A&M University
As a powerful tool for drug discovery, the phage display technique is typically confined to 20 genetically encoded canonical amino acids. Using the amber suppression-based noncanonical amino acid mutagenesis technique, we showed that noncanonical amino acids can be genetically encoded in phage-displayed peptides. These genetically encoded noncanonical amino acids not only expand the chemical diversity of phage-displayed peptides but also allow multiple unique ways to facilitate the drug discovery process.

2:20 Reversible Covalent Ligand Discovery via Chemically Enhanced Phage-Display

Jianmin Gao, PhD, Associate Professor, Chemistry, Boston College

Chemoselective and site-selective modification of bacteriophage allows incorporation of designer functional groups into phage-displayed peptide libraries, which greatly expands the chemical space of phage display. Our laboratory has been developing and evaluating phage-display libraries that incorporate a reversible covalent warhead that target lysine residues. Screening of these libraries allows facile identification of reversible covalent ligands for difficult-to-inhibit proteins.

2:50 Talk Title to be Announced

Speaker to be Announced

BIO-RAD

3:20 Networking Refreshment Break

3:50 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

4:10 KEYNOTE PRESENTATION: Advances in CAR T Therapy

Carl H. June, MD, Richard W. Vague Professor in Immunotherapy; Professor of Medicine; Director, Center for Cellular Immunotherapies; Director, Parker Institute for Cancer Immunotherapy, University of Pennsylvania Perelman School of Medicine

Advances in the understanding of basic immunology have ushered in two major approaches for cancer therapy over the past 10 years. The first is checkpoint therapy to augment the function of the natural immune system. The second uses the emerging discipline of synthetic biology and the tools of molecular biology and genome engineering to create new forms of engineered cells with enhanced functionalities.

4:55 KEYNOTE PRESENTATION: The Next Frontier in Machine Learning and Biologics: "Lab in a Loop" Large Molecule Drug Discovery, From Optimization to *de novo* Discovery

John Marioni, PhD, Senior Vice President and Head of Computation, Research and Early Development, Genentech

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

TUESDAY, MAY 16

8:00 am Registration and Morning Coffee

BIOPROTACS

8:25 Chairperson's Remarks

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

8:30 KEYNOTE PRESENTATION: Pirating Biology to Degrade Extracellular Proteins

James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco

In contrast to intracellular PROTACs, approaches to degrade extracellular proteins are just emerging. I'll describe our recent progress to harness natural mechanisms such as transmembrane E3 ligases and chemokine receptors to degrade extracellular proteins using fully genetically encoded bi-specific antibodies we call AbTACs and KineTACs, respectively.

9:00 Biodegrader Optimization and Design Principles

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

9:30 Proteome-Scale Degrader Screens

Mikko Taipale, PhD, Assistant Professor, University of Toronto

Using Proteome-Scale Induced Proximity Screens to Identify Potent Protein Degraders and Stabilizers

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

ALTERNATIVE SCAFFOLDS

11:09 Chairperson's Remarks

E. Sally Ward, PhD, Director, Translational Immunology; Professor, Molecular Immunology, Centre for Cancer Immunology, University of Southampton

11:10 Targeting Tumors with Bicycle Conjugates

Mark Frigerio, PhD, MBA, Vice President, Chemistry, Bicycle Therapeutics

Bicycles have broad utility and may confer several advantages over existing modalities – namely their small size, modularity for conjugation, and favorable pharmacokinetics. Bicycles are currently being explored in the clinic as Bicycle toxin conjugates (BTCs) for targeted delivery of cytotoxic payloads into tumors, and Bicycle tumor-targeted immune cell agonists (Bicycle TICAs). In the talk, I will share our research progress in the development of Bicycle conjugates.

11:40 Therapeutic Applications Based on the DARPin Platform – From Small Size Single Domain to Hexavalent and Multi-Specific Binding Molecules

Christian Reichen, PhD, Associate Director, Oncology Research, Lead Generation, Molecular Partners AG

The DARPin technology enables the exploration of new therapeutic designs on multiple disease pathways. Based on DARPin properties (small size, high affinity, excellent stability), we can generate single-domain DARPin agents for fast-in/fast-out radio ligand therapies (RLT) with high tumor accumulation – OR – generate multi-specific DARPin therapeutics such as MP0533, a half-life extended CD3-based T cell engager targeting simultaneously CD33, CD123, and CD70 to selectively target malignant AML cancer cells.

12:10 pm Merck Synthetic Single-Domain Antibody Libraries and the Phage-to-Yeast Workflow for Rapid VHH Discovery and Affinity Maturation

Ming-Tang Chen, PhD, Principal Scientist, Biologics Discovery, Merck Research Labs

We describe the development of synthetic VHH libraries and phage-to-yeast affinity maturation workflow for rapid *in vitro* selection of high affinity single domain binders. The phage VHH libraries have 10^11 unique CDRH3 diversity. After 2 rounds of phage panning, the yeast display libraries are built to introduce additional CDRH1 and CDRH2 diversity. The platform is able to generate high affinity and potent antibodies with broad sequence diversity and epitope coverage.

12:40 LUNCHEON PRESENTATION I: Writing the Future of Biologics with an Integrated Offering of Immunization, Libraries, and Machine Learning

TWIST BIOSCIENCE

Aaron K. Sato, PhD, CSO, Twist Bioscience

Twist Biopharma, a division of Twist Bioscience, combines HT DNA synthesis technology with expertise in antibody engineering to provide antibody discovery solutions — from gene synthesis to antibody optimization. The result is a make-test cycle that yields better antibodies against challenging targets from immunization, libraries, and machine learning. We will continue to expand discovery, library synthesis and screening capabilities with others to further utilize their make-test cycle.

1:10 LUNCHEON PRESENTATION II: Luncheon Presentation II to be Announced

SPECIFICA

Speaker to be Announced

1:40 Close of Display of Biologics Conference

6:30 Recommended Dinner Short Course

SC6: Developability of Bispecific Antibodies

**Separate registration required. See short courses page for details.*

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SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC1: Antibody Drug Discovery: From Target to Lead
**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing

ENGINEERING FOR IMPROVED FC FUNCTION

2:15 Chairperson's Remarks

Katherine A. Vallis, PhD, Group Leader, Oxford Institute for Radiation Oncology; Professor, Experimental Radiotherapeutics, University of Oxford

2:20 Engineering the Antibody Fc for Conditional Activity in the Solid Tumor Microenvironment

Jennifer A. Maynard, PhD, Henry Beckman Professor, McKetta Department of Chemical Engineering, Cockrell School of Engineering, University of Texas Austin

Antibody-based therapeutics enjoy considerable successes as cancer treatments, but can cause serious toxicities due to recognition of tumor-associated antigens in non-cancerous tissues. We will discuss recent efforts to develop advanced antibody therapeutics with Fc-mediated activities that are restricted to the acidic solid tumor microenvironment. With the intent of decreasing toxicities and expanding therapeutic windows, protein engineering strategies can render antibody activity sensitive to multiple tumor-specific characteristics.

2:50 The Role of the Fc Domain in Immunity and Disease Outcomes

Bronwyn M. Gunn, PhD, Assistant Professor, Washington State University

The antibody Fc domain shapes protective immunity against many different viral pathogens. We will present a Systems Serology approach to define antibody Fc features associated with protection from Ebola virus and describe how we have used antibody engineering approach to validate and mechanistically dissect the role of distinct Fc-mediated functions in protection. Further, we will discuss how to translate these approaches to other pathogens, such as SARS-CoV-2.

3:20 Structure-Based Charge Calculations for Predicting Properties and Profiling Antibody Therapeutics

Nels Thorsteinson, Director of Biologics, Chemical Computing Group

We present a method for modeling antibodies and performing pH-dependent conformational sampling, which can enhance property calculations. Structure-based charge descriptors are evaluated for their predictive performance on recently published antibody pI, viscosity, and clearance data. From this, we devised four rules for therapeutic antibody profiling which address developability issues arising from hydrophobicity and charged-based solution behavior, PK, and the ability to enrich for those that are approved by the FDA.

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

CHALLENGING TARGETS

4:30 Identification of Rare Binders to Challenging Targets from a Phage Display Library Using Flow Cytometry and Biolayer Interferometry

Dong hee Chung, PhD, Postdoctoral Researcher, University of California, San Francisco

In vitro biopanning platforms have expanded the field of antibody identification beyond immunization. However, applying these strategies to identifying binders against challenging targets remains a critical challenge. Here, we present a new pipeline, RAPID (Rare Antibody Phage Isolation and Discrimination), for the identification of rare high-affinity antibodies against challenging targets. RAPID biopanning uses fluorescent-labeled phage-displayed libraries to isolate populations of promising binders which are subsequently screened in a discriminatory fashion.

5:00 Activating and Modulating Antibody Therapeutics for Difficult Membrane Protein Targets

Richard C. Yu, PhD, Co-Founder & CEO, Abalone Bio, Inc.

Antagonist antibodies for membrane protein targets like GPCRs and ion channels are difficult to discover. Agonist and modulating antibodies are even more challenging. Here I will discuss the challenges in the field and strategies for discovering and developing antibodies that access the full spectrum of activities against membrane protein targets.

5:30 Multi-Scale Simulations Reveal Antibody Reach and Energetics of Binding

Daniel Nissley, PhD, Florence Nightingale Bicentenary Research Fellow and Tutor in Bioinformatics, University of Oxford

Molecular simulation techniques can help solve the inverse problem of what antibody structures give rise to an experimental observable and provide valuable insight into the biophysical origin of antibody properties. Here, we use coarse-grain and all-atom molecular dynamics to accurately model how far antibodies can reach to bind antigens at both arms and to reveal differences in how TCR-mimetic antibodies bind pMHC targets in comparison to TCRs.

6:00 Close of Day

6:00 Dinner Short Course Registration

6:30 Recommended Dinner Short Course

SC6: Developability of Bispecific Antibodies
**Separate registration required. See short courses page for details.*

WEDNESDAY, MAY 17

7:30 am Registration and Morning Coffee

ENGINEERING FOR TARGETED DELIVERY AND IMPROVED SPECIFICITY

8:25 Chairperson's Remarks

Danielle DiCara, PhD, Principal Scientific Researcher, Antibody Engineering, Genentech, Inc.

8:30 Intracellular Delivery of Antibodies for Cancer Applications

Katherine A. Vallis, PhD, Group Leader, Oxford Institute for Radiation Oncology; Professor, Experimental Radiotherapeutics, University of Oxford

A significant barrier to cancer treatment is that although small molecule drugs easily enter cells, many intracellular oncoproteins lack suitable binding pockets, and so are unresponsive to them. Antibodies can act across a broad surface, so inhibit protein-protein interactions, but unfortunately do not naturally enter cells. We have developed multimeric, cyclised cell-penetrating peptides that transfer functional antibodies efficiently across the cell membrane, allowing the targeting of previously "undruggable" intracellular molecules.

9:00 Development of T Cell Engagers Selective for Cells Co-Expressing Two Antigens

Danielle DiCara, PhD, Principal Scientific Researcher, Antibody Engineering, Genentech, Inc.

For development of safe and effective T Cell Engagers (TCEs) for solid tumors, it is highly desirable to expand the number of available target antigens and to increase the precision with which a TCE can differentiate tumors from healthy tissue. I will present a strategy to reduce on-target, off-tumor TCE activity by targeting co-expression of two tumor-associated antigens and describe engineering of trispecific antibodies with this selectivity.

9:30 KEYNOTE PRESENTATION: Inhibition of Key Intracellular Targets via the Cytosolic Delivery of Antibodies and Proteins

Andrew Tsourkas, PhD, Co-Director, Center for Targeted Therapeutics and Translational Nanomedicine; Professor, Bioengineering, University of Pennsylvania

A limitation of biologics is their inability to cross the cell membrane. Conversely, small molecules readily cross cell membranes, but many intracellular proteins lack pockets for small molecule binding. We developed a method to deliver antibodies into the cytosol, which enabled us to inhibit the cancer-associated proteins, multidrug resistance Protein 1 and NFκB. We also delivered small, protein scaffolds intracellularly for therapeutic inhibition of conventionally-undruggable targets, Ras and Myc.

10:00 Targeting the High-Hanging Fruit - Icosagen Therapeutics Antibody Development Pipeline

Mart Ustav, Jr., CSO, Icosagen Therapeutics

Multi-pass integral membrane proteins compose the largest therapeutically relevant group of proteins that have so far not been effectively targeted with antibody-based molecules. Icosagen has developed a wide array of expertise and technologies in protein production, antibody development, protein engineering and analytics over the past 10 years and here we present the integration of these technologies by launching our therapeutic antibody development pipeline to specifically target those proteins.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

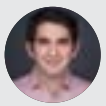
Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

11:30 KEYNOTE PRESENTATION: Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

Rebecca A. Sendak, PhD, Head, Global Large Molecules Research Platform, Sanofi

Addressing disease biology in the clinic with protein therapeutics has become increasingly complex. Turning to innovative and novel scaffolds offers opportunities to tailor therapeutics not previously possible due to advances in host cell engineering and protein design approaches. Designing and developing these modalities requires a next-generation approach as we exploit increased potential design space and also growing data sources to leverage as we invent the next wave of therapeutics.

YOUNG SCIENTIST KEYNOTE



12:15 pm KEYNOTE PRESENTATION: Engineering Prime Editor Proteins for Therapeutic Applications

Andrew V. Anzalone, PhD, Director & Head, Prime Editing Platform, Scientific Co-Founder, Prime Medicine, Inc.

Precision gene editing technologies have the potential to address a wide range of genetic diseases. Prime Editing is a recently developed "search-and-replace" gene editing approach that can precisely perform a wide variety of DNA sequence edits at programmed target sites in human genomes without requiring double-strand DNA breaks or donor DNA templates. I will describe advances to prime editing technology that improve its efficiency, specificity, and capabilities for therapeutic applications.

1:00 Session Break

1:10 LUNCHEON PRESENTATION: The Leap-in Transposase Platform: Past, Present, and Future

Claes Gustafsson, PhD, Chief Commercial Officer & Co-Founder, ATUM

Launched only a few years ago, the Leap-In Transposase platform has rapidly become an industry standard technology for the generation of CHO cells for the manufacturing of antibodies and other biologics. This presentation will highlight achievements and case studies of the platform including high titer mAb manufacturing, rapid anti-COVID responses, and some novel, next generation, applications.

1:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

2:10 Find Your Table and Meet Your Moderator

2:15 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

ACCELERATING AND OPTIMIZING PROTEIN ENGINEERING

3:00 Chairperson's Remarks

Daniel R. Woldring, PhD, Assistant Professor, Chemical Engineering & Materials Science, Michigan State University

3:05 Computational Methods to Complement, Enrich, and Accelerate Antibody Discovery Programs

Daphne Truan, PhD, Associate Director, Protein Design and Informatics, GlaxoSmithKline

In the eternal race to make better biotherapeutics faster, GSK Biopharm discovery pipelines are continuously revamped by a tight collaboration among different departments. This presentation will focus on the computational methods that help select better targets, design and enrich screening libraries, and accelerate the multiobjective optimization of lead candidates through the analysis of NGS data with developability criteria.

3:35 Achieving Functional Hits with Combination of Microfluidic Screening and Transgenic Animals

Shang-Pu Tsai, PhD, Senior Scientist, EMD Serono R&D

In this talk I will use a few case studies to highlight the combination of the Beacon microfluidics system and the humanized transgenic rats in our therapeutic antibody discovery in a pharmaceutical setting. I will also discuss the development of several new screening methods that enable us to rapidly discover functional hits on Beacon with high efficiency and accuracy.

4:05 Talk Title to be Announced

Speaker to be Announced

4:35 Ice Cream Break in the Exhibit Hall with Poster Viewing

5:10 Multiplexed *In Vivo* Drug Discovery Using a Novel Protein Barcoding Technology

Pierce J Ogden, PhD, Co Founder & CSO, Manifold Biotechnologies Inc.

When engineering therapeutics, *in vivo* validation remains the primary bottleneck to program advancement. We invented a novel method that enables multiplexed quantification of 100s of protein therapeutics *in vivo*. We have leveraged our *in vivo* data with machine learning to perform *in vivo* molecule design. Further, we show that *in vitro* assay results are often poorly predictive of downstream *in vivo* results, highlighting the importance of increased *in vivo* throughput.

STRUCTURAL MODELING IN ANTIBODY DISCOVERY AND ENGINEERING

5:40 GYST Platform: A Computational Sherpa for Augmented Exploration of Antibody Landscapes in Discovery and Engineering

Seth F. Harris, PhD, Director, Structural Biology, Genentech, Inc.

Effective navigation and distillation of large structural datasets necessitates programmatic approaches. We describe the custom structural informatics platform (GYST) we are developing and its application to study thousands of fab interfaces for opportunities to engineer novel polyvalent fab formats. This platform allows expansion to other protein families within and beyond large molecule drug discovery. We also discuss how the amassed, pre-computed annotations are suited for training deep learning models.

6:10 Modeling with Rosetta to Guide Library Design of Antibodies

Daniel R. Woldring, PhD, Assistant Professor, Chemical Engineering & Materials Science, Michigan State University

Therapeutic antibodies have played a critical role in healthcare for over three decades, yet the rate of discovering novel antibodies remains outpaced by the need for treatment options. This is particularly true for challenging glycan targets such as tumor-associated carbohydrate antigens (TACAs). In this work, we use Rosetta software to optimize affinity and specificity among a large collection of natively-paired, immune-evolved antibodies.

6:40 Networking Reception in the Exhibit Hall with Poster Viewing

7:40 Close of Engineering Antibodies Conference

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

6:00 Recommended Pre-Conference Short Course

SC3: In silico and Machine Learning Tools for Antibody Design and Developability Predictions

**Separate registration required. See short courses page for details.*

THURSDAY, MAY 18

7:30 am Registration and Morning Coffee

NEXT-GENERATION *IN SILICO* PROTEIN ENGINEERING AND *DE NOVO* DESIGN

8:25 Chairperson's Remarks

Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

8:30 KEYNOTE PRESENTATION: Recent Advances in Protein Engineering

Regina Barzilay, PhD, Delta Electronics Professor, Electrical Engineering & Computer Science, Massachusetts Institute of Technology

9:00 Surface ID: A Deep Learning-Based Molecular Descriptor and a Useful Tool for Drug Discovery

Yu Qiu, PhD, Senior Principal Scientist, Sanofi Genzyme R&D Center

"Surface ID" is a geometric deep learning system for high-throughput surface comparison based on geometric and chemical features. Surface ID offers a novel grouping and alignment algorithm useful for clustering proteins by function, visualization, and *in silico* screening of potential binding partners to a target molecule.

9:30 Talk Title to be Announced

Natalie Castellana, CEO, Abterra Biosciences

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

10:40 Accelerating Therapeutics Discovery with Disruptive Digital Innovation

Peter Clark, PhD, Director & Head, Data Science, Janssen Pharmaceuticals, Inc.

We are leveraging data from across the pharmaceutical value chain, manifested in a knowledge graph to inform novel computational, deep learning models to drive innovation and disrupt the therapeutic research and development lifecycle; building and leveraging our collective institutional knowledge across therapeutic programs and indications in order to inform novel AI/ML models to accelerate the development of lifesaving therapies for patients across the globe.

11:10 Addressing Real-World Challenges in AI-Guided Design and Optimization of Biologics

Christopher J. Langmead, PhD, Director of Digital Biologics Discovery, Amgen

This presentation will provide an overview of the key challenges faced when using AI/ML to guide the design and optimization of biologics, including multi-specifics. We will then discuss some of the techniques used within Amgen to address these issues. Finally, we will argue that certain challenges are best solved through collaborative mechanisms, such as federated learning.

11:40 Designing Highly Stable Protein Libraries by Interpreting Deep Learning Models Trained on Flow Cytometry-Based Assays

Andrew Chang, PhD, CEO, DeepSeq.AI; Individual Consultant

The deep learning model is no longer a 'black box'. This talk will explain how we design a high-throughput assay to generate a protein-stability dataset for the language model. Then we will demonstrate how we interpret the model weights to identify 'keywords' related to protein stability and expression.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing

MACHINE LEARNING FOR ANTIBODY DISCOVERY

1:15 Chairperson's Remarks

Victor Greiff, PhD, Associate Professor, Immunology, University of Oslo

1:20 Language Model-Driven Data Generation and Optimization of Ab and Nb Therapeutics

Tileli Amimeur, Machine Learning – Scientist II, Novo Nordisk

Recent advances in transformer-based language models have led to a variety of models and embeddings which can capture the sequence representation of Antibodies and Nanobodies from public repertoire. We use these models to guide data collection across a suite of assays and properties, and apply a multi-objective optimization of therapeutic properties – leading to next-generation design of Antibodies and Nanobodies.

1:50 Applications of Geometric Deep Learning Model with a Novel Coarse-Grained Protein Structure Representation

Jae Hyeon Lee, PhD, Machine Learning Scientist, Prescient Design

I will discuss a new protein structure prediction model based on a novel coarse-grained protein structure that achieves atomic accuracy on antibody structure prediction and is orders of magnitude faster than other state-of-the-art models. In addition, I'll describe its application in various antibody property prediction and design tasks.

2:20 Sponsored Presentation *(Opportunity Available)*

2:50 Networking Refreshment Break

3:20 Predicting Disposition: Progress towards Relevant Preclinical Models for the Pharmacokinetics of Biologics

Vanita D. Sood, PhD, Senior Vice President, Head of Drug Discovery Research Stealth Versant Ventures NewCo

The disposition of biologics (including clearance and immunogenicity) are key properties that influence efficacy (no exposure, no effect); tolerability/safety (neutralizing or clearing anti-drug antibodies); and commercial success (route of administration, patient convenience). Compared to small molecules, there is a dearth of predictive preclinical models of clinical pharmacokinetics. I will discuss recent progress and challenges in predicting human PK.

3:50 Antibody Profiling at Scale

H. Benjamin Larman, PhD, Associate Professor, Pathology, Johns Hopkins University

The Larman laboratory creates technologies for unbiased characterization of serum antibodies at cohort scale. This seminar will provide an overview of our current antibody profiling capabilities, recent findings, and ongoing developmental efforts that seek to overcome existing limitations of high-throughput antibody analyses.

4:20 Close of Day

FRIDAY, MAY 19

7:00 am Registration Open

INTERACTIVE DISCUSSIONS

7:30 Interactive Discussions with Continental Breakfast

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-

solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

RULES FOR DEVELOPABILITY

8:25 Chairperson's Remarks

M. Frank Erasmus, PhD, Head, Bioinformatics, Specifica, Inc.

8:30 Identifying Sequence and Structure Features for mAb Developability Assessment

Christopher Negron, PhD, Principal Research Scientist, AbbVie, Inc.

With over 100 approved antibody-based therapeutics, antibodies are a well-established starting point for drug discovery. Despite this success, lead antibodies may suffer from undesired drug-like properties. Thus, we present the Therapeutic Antibody Developability Analysis (TA-DA). A computational tool built by testing hundreds of sequence- and structure-based descriptors at differentiating clinical antibodies from non-natively paired human repertoire antibodies

9:00 Machine Learning Prediction of Methionine and Tryptophan Photooxidation Susceptibility

Jared Delmar, PhD, Associate Director, Biopharmaceutical Development, AstraZeneca

We applied the random forest machine learning algorithm to in-house liquid chromatography-tandem mass spectrometry (LC-MS/MS) datasets (Met, n = 421; Trp, n = 342) of tryptic therapeutic protein peptides to create computational models for Met and Trp photooxidation. We show that our machine learning models predict Met and Trp photooxidation likelihood with accuracy and further identify important physical, chemical, and formulation parameters that influence photooxidation.

9:30 Developability Profiling of Natural Antibody Repertoires.

Victor Greiff, PhD, Associate Professor, Immunology, University of Oslo

Developability, the set of physicochemical properties of an antibody relevant for manufacturing and success in clinical trials, is one of the key determinants for success during clinical testing and any developability parameters can be computed from the antibody sequence and structure. Exploiting the vast amount of available antibody high-throughput data will facilitate the derivation of the rules underlying developability profiles to guide antibody therapeutic discovery.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Networking Coffee Break

11:00 Predicting scFv Thermostability Using Machine Learning on Sequence and Structure Features

Kathy Y. Wei, PhD, Senior Scientist, Protein Design, Amgen, Inc.

Multi-specific biologics are of interest due to the advantage of engaging distinct targets. One important component is the scFv, but their relatively poor thermostability often hampers development. As experimental methods are laborious and expensive, computational methods are an attractive alternative. We show two machine learning approaches – one with pre-trained language models, and second, a supervised network trained with Rosetta energetics – to better classify thermostable scFv variants from sequence.

11:30 Development of Machine Learning Models for Prediction of Antibody Non-Specificity

Laila Sakhnini, PhD, Senior Research Scientist, Biophysics & Injectable Formulation, Novo Nordisk AS

Over the years, there has been an increased focus on decreasing non-specific binding during early-stage drug development. It has been recognized as a root cause for failure in many drug programs due to unexpected pharmacokinetics and elevated toxicity. From a computational design perspective, prediction has remained a challenge. Proposed work describes the development of sequence-based machine learning models for prediction of this property with accuracy of up to 74%.

12:00 pm Protein Design and Variant Prediction Using Autoregressive Generative Models

Deborah S. Marks, PhD, Associate Professor, Systems Biology, Harvard Medical School

12:30 Close of Machine Learning Approaches for Protein Engineering Conference

> **"Particularly exciting for me was this year's new conference stream on 'Machine Learning Approaches for Protein Engineering.' Spearheaded by last year's emergence of AlphaFold2, the field has seen tremendous progress in methods for structure prediction, antibody design, binder generation, etc. Super happy to work closely with our new colleagues in the Prescient Design team in this exciting area."**
>
> **Hubert K.**, Roche

ONCOLOGY STREAM
CONFERENCES

MAY 15-16

Antibodies for Cancer Therapy

AGENDA

MAY 16-17

Emerging Targets for Oncology

AGENDA

MAY 18-19

Antibody Drug Conjugates

AGENDA

ONCOLOGY STREAM

New Strategies for Targeting Solid Tumors and the Tumor Microenvironment

One of the biggest challenges for cancer therapeutics, is the targeting of solid tumors. Poor tumor tissue penetration and the heterogeneous distribution have limited the clinical efficacy of therapeutic antibodies. Striking advances in bispecific/multispecific antibodies, T cell engagers and antibody-drug conjugates are now leading the way in oncology discovery, with new strategies to target solid tumors and the tumor microenvironment. This year's PEGS Boston will present the latest and hottest in antibody-based therapies for cancer, highlight the emerging and new-again targets, as well as showcase the exciting resurgence of antibody-drug conjugates as a hot therapeutic modality. Together, the 3 conferences in this stream will present a comprehensive look at strategies driving toward clinical success.

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SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC3: *In silico* **and Machine Learning Tools for Antibody Design and Developability Predictions**

**Separate registration required. See short courses page for details.*

MONDAY, MAY 15

7:00 am Registration and Morning Coffee

ANTIBODIES IN DEVELOPMENT – WHAT'S HOT & PROMISING?

8:20 Chairperson's Opening Remarks

Daniel Chen, MD, PhD, Founder, Engenuity Life Sciences

8:30 KEYNOTE PRESENTATION: Antibody Therapeutics in Early Clinical Development: Format, Target, and Disease Trends

Janice M. Reichert, PhD, Executive Director, The Antibody Society

While trends in the global commercial late-stage clinical pipeline of antibody therapeutics are well documented, trends for the early-stage pipeline are difficult to ascertain because of the difference in scale – the late-stage and early-stage pipelines include ~150 and ~1100 molecules, respectively. This presentation will reveal recent trends in the formats and targets for antibody therapeutics in Phase I or II clinical studies, as well as the patient populations evaluated.

9:00 Cytotoxic PD-L1/PD-L2 Dual-Specific Antibodies Effectively Treat Both Immune "Hot" and "Cold" Cancers

Michael A. Curran, PhD, Founder and SAB Chairman, Immunogenesis; Associate Professor, Immunology, MD Anderson Cancer Center

We created novel fully human dual-specific antibodies that both block both PD-L1 and PD-L2 with high affinity and target PD-Ligand cells for depletion via ADCC and ADCP. The lead antibody outperforms PD-1 blockade across both "hot" and "cold" cancers through a unique combination of stromal depletion, complete PD-1 circuit blockade, and direct anti-tumor cytolysis. These antibodies appear safe in both mice and primates are moving into Phase I.

9:30 Combining Innovative Technologies to Overcome Multiple Challenges of Neutralizing Antibody Discovery in Cancer Therapy

Marcelo VIEGAS, PhD, MBA, Business Developer for Iberia, Italy, & UK, Business Development, ProteoGenix

Though Phage Display has been instrumental in therapeutic antibody development, new challenges have appeared. Neutralizing antibodies can be difficult to obtain from naïve human libraries due to lower affinity & self-tolerance. Combining innovative technologies such as Phage Display libraries supplemented with disease specific patient samples, NGS, AI & humanized mice for single B-cell sorting maximizes the chances of identifying neutralizing antibodies against any target, in particular for autoimmune disorders & cancer.

9:45 Sponsored Presentation *(Opportunity Available)*

10:00 Networking Coffee Break

10:30 Anti-CCR8 Mediated Treg Cell Depletion for the Treatment of Solid Tumor Indications: Preclinical PKPD and Translational Strategy

Gautham Gampa, PhD, Principal Scientist, Preclinical & Translational PKPD, Genentech, Inc.

Targeted depletion of tumor resident Treg cells can be a promising therapeutic approach to restore anti-tumor immunity. We have developed a human IgG1 antibody to preferentially eliminate CCR8-expressing Treg cells in tumor microenvironment through ADCC. The preclinical PK/PD findings and the methods used for translation to the clinic, including the selection of First-in-Human (FiH) dose, to inform the Phase I study design will be presented.

11:00 Targeting of a Cancer-Associated LYPD3 Glycoform for Tumor Therapy

Patrik Kehler, CSO, Glycotope GmbH

We have developed an antibody which binds to tumor-associated LYPD3 in an O-glycosylationdependent manner and shows superior tumor specificity compared to conventional protein-binding anti-LYPD3 antibodies. The specificity of our antibody for glycosylated LYPD3 was determined using differentially glycosylated proteins in an ELISA format and confirmed using cell lines with specific glycosylation patterns as well as tumor cell lines expressing varying levels of LYPD3.

11:30 LUNCHEON PRESENTATION: A Humanized Chicken Antibody Platform that Delivers Diverse and Developable Therapeutic Candidates

Ross Chambers, PhD, Vice President of Antibody Discovery, Integral Molecular

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

INTERACTIVE DISCUSSIONS

12:30 Find Your Table and Meet Your Moderator

12:45 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

INTERACTIVE DISCUSSION: How to Discover Antibodies Against Novel/Difficult Targets

Horacio G. Nastri, PhD, Associate Vice President, Biotherapeutics, Incyte Corporation

- What makes a target particularly difficult?
- How to evaluate the challenges
- Selection of therapeutic modality
- Selection of optimal discovery strategy
- Screening alternatives

INTERACTIVE DISCUSSION: Failures and Successes in TNFRSF Agonist Antibody Drugs, and Future Outlook

Jieyi Wang, PhD, Founder & CEO, Lyvgen Biopharma

- Mechanisms of action of TNFRSF agonistic antibodies
- Lessons learned in the clinic
- FcγR2B and tumor targeted conditional agonisms
- New clinical developments to watch

1:30 Session Break

ANTIBODIES IN DEVELOPMENT *(CONT.)*

1:45 Chairperson's Remarks

Horacio G. Nastri, PhD, Associate Vice President, Biotherapeutics, Incyte Corporation

1:50 INBRX-109: A Tetravalent Antibody Precisely Engineered for Optimal DR5 Agonism and Safety

Katelyn M. Willis, PhD, Associate Director, Biotherapeutics, Inhibrx, Inc.

INBRX-109 is a precisely engineered tetravalent agonist of death receptor 5. Designed to achieve a best-in-class therapeutic index, INBRX-109 induces robust apoptosis of cancer cells *in vitro* and *in vivo* while sparing healthy tissues. INBRX-109 was well tolerated and had anti-tumor activity in unresectable/metastatic conventional chondrosarcoma in a phase I study and is currently being evaluated in a blinded, placebo-controlled pivotal phase II trial.

2:20 Developing a CD8+ T Cell Epit

Yong-Sung Kim, PhD, Professor, Molecular Science & Technology, Ajou University, Korea

Redirecting preexisting virus-specific cytotoxic CD8+ T lymphocytes (CTLs) to tumors by simulating viral infection of the tumor cells has great potential for cancer immunotherapy. In this talk, I will present a CTL epitope-delivering antibody, termed a TEDbody, engineered to deliver a viral MHC-I epitope peptide into the cytosol of target tumor cells by fusion with a tumor-specific cytosol-penetrating antibody for the recognition and lysis by virus-specific CTLs.

2:50 Talk Title to be Announced

Speaker to be Announced

3:20 Networking Refreshment Break

3:50 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

4:10 KEYNOTE PRESENTATION: Advances in CAR T Therapy

Carl H. June, MD, Richard W. Vague Professor in Immunotherapy; Professor of Medicine; Director, Center for Cellular Immunotherapies; Director, Parker Institute for Cancer Immunotherapy, University of Pennsylvania Perelman School of Medicine

Advances in the understanding of basic immunology have ushered in two major approaches for cancer therapy over the past 10 years. The first is checkpoint therapy to augment the function of the natural immune system. The second uses the emerging discipline of synthetic biology and the tools of molecular biology and genome engineering to create new forms of engineered cells with enhanced functionalities.

4:55 KEYNOTE PRESENTATION: The Next Frontier in Machine Learning and Biologics: "Lab in a Loop" Large Molecule Drug Discovery, From Optimization to *de novo* Discovery

John Marioni, PhD, Senior Vice President and Head of Computation, Research and Early Development, Genentech

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

TUESDAY, MAY 16

8:00 am Registration and Morning Coffee

NON-TRADITIONAL ANTIBODY & BEYOND APPROACHES

8:25 Chairperson's Remarks

Daniel A. Vallera, PhD, Lion Scholar and Professor; Director, Section on Molecular Cancer Therapeutics; Professor, Therapeutic Radiology, University of Minnesota Masonic Cancer Center

8:30 Moxetumomab-Rituximab to Eliminate Minimal Residual Disease in Hairy Cell Leukemia

Robert J. Kreitman, MD, Chief Clinical Immunotherapy, Lab of Molecular Biology, NIH NCI

Complete remissions in hairy cell leukemia (HCL) with anti-CD22 recombinant immunotoxin Moxetumomab Pasudotox (Moxe) are more durable if minimal residual disease (MRD) negative, but anti-drug antibodies (ADA) can limit the effectiveness of the consolidation cycles needed to eliminate MRD. To prevent ADA, Rituximab or Ruxience was added to Moxe (MoxeR) and 9 (64%) of 14 evaluable patients so far achieved MRD-free CR. ADA was less frequent than Moxe alone historically.

9:00 NK Cell Therapy for Cancer, from Individual to Off-the-Shelf CAR-Targeted NK Cells

Jeffrey Miller, MD, Deputy Director, Masonic Cancer Center; Professor of Medicine, Division of Hematology, Oncology and Transplantation, University of Minnesota

Donor NK cells can induce complete remissions in patients with refractory leukemia. However, limitations include lack of persistence and specificity. Off-the-shelf NK cells from induced pluripotent stem cells (iPSC) containing multiple gene edits will promote specificity, persistence, and enhanced activity *in vivo* to enhance cancer therapy. While Chimeric Antigen Receptors (CARs) are best validated in B cell malignancies, strategies targeting B7-H3 in solid tumors will be discussed.

9:30 STK-012: An Engineered Selective IL2 Mutein That Promotes Anti-Tumor Responses without Related Toxicities

Patrick J. Lupardus, PhD, Vice President, Research & Head, Protein Sciences, Synthekine, Inc.

Interleukin-2 potently stimulates the proliferation, survival, and cytotoxicity of T and NK cells making it an attractive candidate for cancer immunotherapy. However, severe toxicities have limited its clinical utility. We have developed STK-012, an IL-2-agonist mutein selective for cells expressing high affinity, trimeric IL-2 receptor (IL-2Ra/b/g) such as activated T cells. STK-012 preferentially stimulates tumor-specific T cells without significantly activating NK cells thus facilitating prolonged treatment without acute toxicity.

10:00 Overcoming Challenge in Developing Full-Length Transmembrane Protein to Accelerate Development of Targeted Therapeutics

An Ouyang, PhD, Product Manager, Product Development, ACROBiosystems

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Stability-Engineered, Half-Life Extended IL-18 for Cancer Immunotherapy

Travis W. Bainbridge, Scientist 4, Large Molecule Drug Discovery, Genentech, Inc.

IL-18 is a pro-inflammatory cytokine that promotes CD8+ T cell and NK cell effector function, enhancing intratumoral cytotoxicity. To date, clinical trials of recombinant IL-18 have demonstrated safety, but a lack of efficacy alone, or in combination with anti-cancer agents. The wild-type cytokine is challenging to produce, unstable, and cleared rapidly from circulation. We engineered a stabilized, half-life extended version of IL-18 and will be sharing pre-clinical *in vivo* results.

11:40 XTEN Polypeptide-Masked Protease Activated T Cell Engagers: XPAT Proteins – A Novel Format to Mitigate On-Target, Off-Tumor Problem

Volker Schellenberger, PhD, President & CEO, Amunix

XPAT proteins are conditionally active T cell engagers (TCEs) designed to exploit the dysregulated protease activity in tumors. In preclinical studies across multiple tumor targets, XPAT proteins demonstrated 1) strong masking of *in vitro* cytotoxicity by up to 4 logs; 2) potent *in vivo* efficacy at doses similar to the efficacious doses of unmasked TCE controls; and 3) masking increases tolerated Cmax in NHP by greater than 400-fold for HER2-XPAT.

12:10 pm Designing Butyrophilin-Based Heterodimeric Gamma Delta T Cell Engagers for Immunotherapy

Suresh De Silva, PhD, Vice President Product Development, R&D, Shattuck Labs, Inc.

The ability to bridge the innate and adaptive arms of the immune system coupled with their capacity to recognize tumor cells independent of MHC makes gamma delta T cells an attractive target for cancer immunotherapy. The engineering and therapeutic potential of a butyrophilin 2A1 and 3A1 protein-based engager platform (GADLEN) that offers a novel approach to activate the Vg9Vd2 T cell subset for targeted killing of tumor cells will be presented.

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:40 Close of Antibodies for Cancer Therapy Conference

6:30 Recommended Dinner Short Course

SC6: Developability of Bispecific Antibodies

**Separate registration required. See short courses page for details.*

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC1: Antibody Drug Discovery: From Target to Lead

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing

TARGET DISCOVERY & VALIDATION

2:15 Chairperson's Opening Remarks

Mitchell Ho, PhD, Senior Investigator and Deputy Chief, Laboratory of Molecular Biology; Director, Antibody Engineering Program, National Cancer Institute (NCI), National Institutes of Health

2:20 First-in-Class: How the Unique, Multi-Drug Modality (ADC, IO, Bispecifics, CAR T) Oncology Target Discovery Platform OGAP Results in Novel Antibody Cancer Therapeutics

Ben Thomas, Senior Director, External Innovations and Operations, Oxford Biotherapeutics

Oxford Biotherapeutics developed a novel proteomics target discovery platform (OGAP) for identifying cancer unique proteins/isoforms, with minimal expression in normal/NAT tissues. Plasma membrane protein abundance is directly measured in patient cancer and normal tissues, circumventing inaccurate RNA-based predictions. This approach has led to the development of a unique set of antibody-based drug programs including ADCs, IO agonists, & bispecifics eg., 076 ADC targeting DEC205, 003R a novel checkpoint agonist.

2:50 TCR-Based Therapeutics against Known and Novel pHLA Targets in Solid Tumors

Marvin Gee, PhD, Co-Founder & Vice President, Target Discovery, 3T Biosciences

T cells recognize intracellular targets presented by HLA to enable potent anti-tumor immune responses, and these targets can be leveraged to generate off-the-shelf therapeutics using T cell bispecific engagers to treat a broad patient population. We've developed 3T-TRACE to rapidly identify the antigens of orphan T cells from patient tumors and a TCR mimetic platform to rapidly generate potent and specific binders for therapeutic development.

3:20 Sponsored Presentation *(Opportunity Available)*

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

RE-EMERGING TARGETS FOR SOLID TUMORS

4:30 Glypicans as Emerging Therapeutic Targets in Solid Tumors: GPC3, GPC2, and GPC1

Mitchell Ho, PhD, Senior Investigator and Deputy Chief, Laboratory of Molecular Biology; Director, Antibody Engineering Program, National Cancer Institute (NCI), National Institutes of Health

My laboratory research has been focused on the validation of GPC3 as an immunotherapeutic target in liver cancer. In the present lecture, I will discuss our recent work on characterizing GPC2 and GPC1 as new cancer targets and engineering CAR T cells for treating solid tumors such as neuroblastoma and pancreatic cancer. I will also discuss the use of nanobody technology to improve efficacy of CAR T cells.

5:00 IL15.GPC4-CAR T Cells to Treat Solid Tumors

Andras A. Heczey, MD, Assistant Professor & Director, Pediatrics & Oncology, Texas Children's Hospital

Glypican 3 (GPC3) is an attractive immunotherapeutic target given its preferential expression in several solid cancers. In pre-clinical studies, co-expression of IL15 enhances the antitumor properties of GPC3-CAR T cells (15.GPC3-CAR T cells). I will discuss the results emerging from two first-in-human, Phase I studies evaluating 15.GPC3-CAR T cells focused on safety, expansions, and antitumor responses in adults and children.

5:30 B7-H3, an Attractive Target of Antibody-Based Immunotherapy for Solid Tumors

Soldano Ferrone, PhD, Professor-in-Residence, Surgery, Massachusetts General Hospital

The characteristics of the tumor antigen B7-H3, B7-H3, a member of the B7 superfamily of ligands, will be described. The use of B7-H3 as a target of antibody-based immunotherapeutic strategies for the treatment of solid tumors will be discussed. Information about clinical trials targeting B7-H3 for the treatment of solid tumors will be summarized.

6:00 Close of Day

6:00 Dinner Short Course Registration

6:30 Recommended Dinner Short Course

SC8: CAR T Cells: Improving Safety While Retaining Therapeutic Activity

**Separate registration required. See short courses page for details.*

WEDNESDAY, MAY 17

7:30 am Registration and Morning Coffee

RE-EMERGING TARGETS FOR SOLID TUMORS II

8:25 Chairperson's Remarks

Horacio G. Nastri, PhD, Associate Vice President, Biotherapeutics, Incyte Corporation

8:30 KEYNOTE PRESENTATION: Targeting ROR1 with Antibody-Based Cancer Therapy

Christoph Rader, PhD, Professor, Immunology and Microbiology, UF Scripps Biomedical Research, University of Florida

In embryogenesis and oncogenesis, the receptor tyrosine kinase ROR1 activates cell signaling events to promote cell proliferation, survival, and migration. Undetectable in adult vital organs and most healthy tissues, ROR1 is generally considered a safe target for antibody-based cancer therapy. We report on our progress with targeting ROR1 with novel T cell recruiting and activating bispecific antibodies (T-biAbs) and CAR T cells for treating hematologic and solid malignancies.

9:00 Autonomous IL-36R Signaling in Neutrophils Activates Potent Anti-Tumor Effector Functions

Rajkumar Noubade, PhD, Senior Scientist, Amgen, Inc.

We report that IL-36 signaling can modulate neutrophils in a cell-intrinsic manner to greatly enhance their ability to directly kill tumor cells and to promote T cell proliferation. While poor prognostic outcomes are typically associated with neutrophil enrichment in the TME, our results highlight the therapeutic potential of IL-36 to modify tumor-infiltrating neutrophils into potent effector cells and engage both innate and adaptive immune system to achieve durable anti-tumor responses.

9:30 Conformational Stabilization and Use of CCR8 Purified Protein for the Discovery of High-Affinity Antibodies Binding to the Core Transmembrane Domain

Mauro Mileni, PhD, Founder & CEO, Abilita Bio

Discovering therapeutic-quality antibodies for integral membrane protein targets is still a formidable challenge. To address this challenge, Abilita has developed the EMP technology, which dramatically improves target properties without impacting physiological relevance. Using CCR8, an immuno-oncology GPCR target, as a case study, we enabled protein-based approaches that led to the isolation of large families of antagonistic VHH antibodies binding to transmembrane epitopes.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

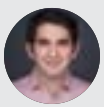
Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

11:30 KEYNOTE PRESENTATION: Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

Rebecca A. Sendak, PhD, Head, Global Large Molecules Research Platform, Sanofi

Addressing disease biology in the clinic with protein therapeutics has become increasingly complex. Turning to innovative and novel scaffolds offers opportunities to tailor therapeutics not previously possible due to advances in host cell engineering and protein design approaches. Designing and developing these modalities requires a next-generation approach as we exploit increased potential design space and also growing data sources to leverage as we invent the next wave of therapeutics.

YOUNG SCIENTIST KEYNOTE



12:15 pm KEYNOTE PRESENTATION: Engineering Prime Editor Proteins for Therapeutic Applications

Andrew V. Anzalone, PhD, Director & Head, Prime Editing Platform, Scientific Co-Founder, Prime Medicine, Inc.

Precision gene editing technologies have the potential to address a wide range of genetic diseases. Prime Editing is a recently developed "search-and-replace" gene editing approach that can precisely perform a wide variety of DNA sequence edits at programmed target sites in human genomes without requiring double-strand DNA breaks or donor DNA templates. I will describe advances to prime editing technology that improve its efficiency, specificity, and capabilities for therapeutic applications.

1:00 Session Break

1:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

2:10 Find Your Table and Meet Your Moderator

2:15 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

INTERACTIVE DISCUSSION: Pros and Cons for Alternatives to Current Standard of Autologous CAR T Cells

Andras A. Heczey, MD, Assistant Professor & Director, Pediatrics & Oncology, Texas Children's Hospital

- Rapid, point of care manufacturing
- Off-the-shelf, ***in vivo*** engineering
- How generalizable are the findings from CAR T cell studies treated leukemia to solid tumors?

INTERACTIVE DISCUSSION: CAR-Ts for Solid Tumor

Mitchell Ho, PhD, Senior Investigator and Deputy Chief, Laboratory of Molecular Biology; Director, Antibody Engineering Program, National Cancer Institute (NCI), National Institutes of Health

My laboratory has characterized GPC3 as an immunotherapeutic target in liver cancer. In the present talk, I will discuss our recent advances in studying GPC2 and GPC1 as new targets in solid tumors and engineering CAR T cells for treating neuroblastoma and pancreatic cancer. I will also discuss new strategies using camel nanobodies to improve efficacy of CAR T cells.

TUMORS IN THE MICRO-ENVIRONMENT

3:00 Chairperson's Remarks

Jaime Modiano, PhD, Perlman Professor, Oncology & Comparative Medicine, Veterinary Clinical Sciences, University of Minnesota, Twin Cities

3:05 Modulating the Tumor Immune Microenvironment with ONIx, a Peptide for Dual Immune Checkpoint Blockade

Jaime Modiano, PhD, Perlman Professor, Oncology & Comparative Medicine, Veterinary Clinical Sciences, University of Minnesota, Twin Cities

ONix (oncoimmuneaccelerator) is a novel peptide that includes a variant of the SIRP-gamma extracellular domain (GV3) and a high-affinity construct (HAC) of the soluble PD-1 extracellular domain. ONIx binds CD47 and PD-L1 in human, mouse, and dog cells, effectively displacing antibodies against these receptors. ONIx is safe and effective in mouse models and is currently being evaluated in two independent clinical studies of dogs with naturally occurring tumors.

3:35 Novel Myeloid Checkpoint Inhibitors Targeting the LILRB Family Members

Charlene Liao, PhD, President & CEO, Immune-Onc Therapeutics, Inc.

Immune-Onc Therapeutics' differentiated pipeline with a current focus on targeting the Leukocyte Immunoglobulin-Like Receptor subfamily B (LILRB) of myeloid checkpoints will be presented. These include IO-108, an antagonist antibody targeting LILRB2 (ILT4), in Phase I clinical development for solid tumors and IO-202, an antagonist antibody targeting LILRB4 (ILT3), in Phase I clinical development for the treatment of acute myeloid leukemia (AML), chronic myelomonocytic leukemia (CMML), and solid tumors.

4:05 Sponsored Presentation *(Opportunity Available)*

4:35 Ice Cream Break in the Exhibit Hall with Poster Viewing

5:10 Targeting Macrophage Immune Checkpoints in Lung Cancer

Kipp Weiskopf, MD, PhD, Whitehead Fellow, Whitehead Institute for Biomedical Research

Macrophages are often the most common infiltrating immune cell in tumors. New therapies that target macrophage immune checkpoints, such as CD47/SIRPa, show promise in clinical trials for solid and hematologic malignancies. These drugs may work best when used with other anti-cancer agents, but the optimal combination strategies have not been determined. Here, we present unbiased screening efforts to identify novel small molecules and biologics that enhance macrophage anti-tumor function.

5:40 Taking Clues from Patients to Target TAMS

Myriam N. Bouchlaka, PhD, Associate Director, Immuno-Oncology, OncoResponse, Inc.

Resistance to checkpoint inhibitor (CPI) therapy is in part due to immunosuppression created by tumor-associated macrophages (TAMs). OncoResponse uses a proprietary B cell screening platform to identify autoantibodies from patient with excellent response to CPI therapy that may reverse immunosuppression caused by TAMs. OR2805 is a first-in-class mAb directed against CD163 that reverses immunosuppression caused by TAMs and restores T cell function, both *in vitro* and *in vivo*.

6:10 Engaging FLT3 to Promote Dendritic Cell Expansion and Drive the Adaptive Anti-Tumor Immune Response

Michelle R. Kuhne, PhD, Senior Scientist II, Gilead Sciences, Inc.

The ligand for the receptor tyrosine kinase FMS-like tyrosine kinase 3 (FLT3) plays an important role in hematopoiesis. FLT3 signaling is required for the differentiation and expansion of dendritic cells. GS-3583 is a fusion protein composed of human FLT3 ligand (FLT3L) combined with a modified Fc region of human IgG4. GS-3583 was designed to induce cDC1 expansion and subsequently promote tumor-reactive T cell priming and activation in the tumor microenvironment.

6:40 Networking Reception in the Exhibit Hall with Poster Viewing

7:40 Close of Emerging Targets for Oncology and Beyond Conference

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

6:00 Recommended Pre-Conference Short Course

SC4: An Introduction to Protein Degraders: A Focus on PROTACs

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

6:30 pm Recommended Dinner Short Course

SC8: CAR T Cells: Improving Safety While Retaining Therapeutic Activity

**Separate registration required. See short courses page for details.*

THURSDAY, MAY 18

7:30 am Registration and Morning Coffee

OPENING KEYNOTES

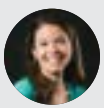
8:25 Chairperson's Opening Remarks

John M. Lambert, PhD, Consultant

8:30 Trastuzumab Deruxtecan – Successful ADC Development from Payload Selection to Multi-Indication Approval

Gerold Meinhardt, MD, PhD, Vice President – Asset & Portfolio Management, Global Team Lead, DS-8201/ ENHERTU, Daiichi Sankyo, Inc.

Trastuzumab Deruxtecan (T-DXd; ENHERTU) is a HER2-directed ADC, consisting of a HER2 monoclonal antibody attached to a potent topoisomerase I inhibitor payload. Remarkable features include a stable cleavable linker and a bystander effect in tumor tissue. T-DXd has demonstrated superior efficacy compared to standard-of-care therapies in different tumor types and lines of therapy. This presentation will provide an overview of the development of T-DXd including recent data.



9:00 Mirvetuximab Soravtansine: A Novel FR Alpha-Targeted ADC for Platinum-Resistant Ovarian Cancer

Elisabeth Diver, MD, Medical Director, ImmunoGen

Mirvetuximab soravtansine (MIRV) is a novel antibody-drug conjugate targeting folate receptor alpha. This talk will review clinical safety and efficacy data of MIRV monotherapy in platinum-resistant ovarian cancer from the pivotal SORAYA and MIRASOL trials that led to submission to the FDA. Efficacy and safety data of MIRV with bevacizumab from the FORWARD II trial will be reviewed, leading to a discussion of next steps in clinical development for MIRV.

9:30 Talk Title to be Announced

Catalent BIOLOGICS

Speaker to be Announced

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

CYTOTOXIC PAYLOADS

10:35 Chairperson's Opening Remarks

David Thurston, PhD, Professor, Drug Discovery, Institute of Pharmaceutical Sciences, King's College London

10:40 The Current Landscape of DNA Damaging ADC Payloads: Which Mechanism of Action Works the Best?

David Thurston, PhD, Professor, Drug Discovery, Institute of Pharmaceutical Sciences, King's College London

Many ADCs contain DNA-interactive payloads with different mechanisms of action including DNA cleavage, G/G-crosslinking, mono-G-alkylating, mono-A-alkylating, and topoisomerase inhibition. A number of ADCs with DNA-cleaving and topoisomerase inhibiting payloads have been approved, and two with mono-G-alkylating and mono-A-alkylating payloads are in late-stage clinical trials. This presentation will discuss the advantages and disadvantages of the various mechanisms, with a focus on efficacy and side effects.

11:10 Improved Therapeutic Index with Novel Tumor-Selective Linker Technologies

Robert J. Lutz, PhD, CSO, Iksuda Therapeutics

While ADCs are designed to improve the therapeutic index (TI) compared to traditional chemotherapeutic agents, toxicities remain a challenge in developing ADCs as effective cancer therapies. One emerging approach to improve the TI of ADCs is to incorporate tumor-selective chemistries for the release and/or activation of the payload. These innovative designs have been shown to improve both the MTD and toxicity profile in preclinical models, and recently, in the clinic.

11:40 Antibody Targeted Amanitin Conjugates (ATAC): A New Payload Provides New Options for Cancer Therapy

Andreas Pahl, PhD, CSO & Executive Board Member, Heidelberg Pharma AG

ATACs comprise a new class of antibody-drug conjugates (ADCs) using amanitin as toxic payload. Amanitin binds to the eukaryotic RNA polymerase II and thereby efficiently inhibits the cellular transcription process. Non-dividing as well as antigen low expressing cells can also be targeted. First ATACs entered Phase I/IIa clinical trials in 2022. HDP-101 is directed against BCMA for the treatment of relapsed and refractory Multiple Myeloma patients.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing

IMMUNE-STIMULATORY PAYLOADS

1:15 Chairperson's Remarks

Mahendra P. Deonarain, PhD, Chief Executive and Science Officer, Antikor Biopharma Ltd.

1:20 Tumor-Targeted Activation of the STING Pathway with Immunosynthen ADCs

Marc I. Damelin, PhD, Vice President Biology, Mersana Therapeutics

Activating an innate anti-tumor immune response could be an effective therapeutic strategy in oncology, and an ADC could enable this approach by localizing activation to the tumor microenvironment. Tumor-targeted Immunosynthen ADCs activate STING in tumor-resident immune cells and in tumor cells ("the 1-2 punch"). XMT-2056 is a HER2-targeted Immunosynthen ADC that binds a novel HER2 epitope and has entered clinical development. The mechanistic translational studies presented could guide clinical development.

1:50 TPD2 Conjugates – Antibody-Enabled Dual Precision Targeted Protein Degraders

Peter Park, PhD, CSO, Orum Therapeutics

TPD², dual precision-targeted protein degradation merges the power of targeted protein degraders with the precision of antibodies to deliver molecular glues or bifunctional degraders intracellularly with cell-specificity and increases the therapeutic index of degraders. Using TPD² approach, highly specific GSPT1 degrader platform was developed that shows promising efficacy against tumors. Two TPD² GSPT1 degraders in clinical/late preclinical testing, ORM-5029 for breast cancer and ORM-6151 for AML will be discussed.

2:20 Sponsored Presentation *(Opportunity Available)*

2:50 Networking Refreshment Break

3:20 Targeting STING to CCR2+ Cells via an Immune Stimulating Antibody Conjugate

Victoria A. Appleman, PhD, Scientist, Takeda Oncology

Myeloid cells are present in most human solid tumors and they exert local immunomodulatory functions. STING signaling in intratumor myeloid cells can enhance interferon (IFN) production, boost local adaptive anti-tumor immunity, and could synergize with other anti-

cancer therapies. We discuss nonclinical data for a novel iADC, TAK-500, which selectively activates STING in CCR2-expressing cells to enable systemic delivery, favor intratumor accumulation of the active compound, and achieve anti-tumor immunity.

3:50 Developing an Immunostimulatory Antibody Drug Conjugate with Optimized Linker and Payload Components

Kung-Pern Wang, PhD, Principal Scientist, Chemistry, Seagen, Inc.

TLR 7/8 agonists can stimulate innate immune functions and prime downstream T cell activation to drive profound anti-tumor immunity. However, systemic administration of TLR 7/8 agonists in cancer therapy has been limited by toxicities. Antibody-drug conjugates are a clinically validated platform to improve drug tolerability and efficacy. We have developed ADCs comprising an optimized TLR agonist-linker design. Our ADCs demonstrate potent and durable anti-tumor activity in several tumor models.

4:20 Close of Day

FRIDAY, MAY 19

7:00 am Registration Open

INTERACTIVE DISCUSSIONS

7:30 Interactive Discussions with Continental Breakfast

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

INTERACTIVE DISCUSSION: Next-Generation Antibody Drug Conjugates: What Do We Need to Do for the Next Major Step Up?

Mahendra P. Deonarain, PhD, Chief Executive and Science Officer, Antikor Biopharma Ltd.

There are many emerging innovations in the Antibody-Drug Conjugate (ADC) space, some radical and some incremental. This roundtable discussion will highlight some of the more radical innovations (e.g. novel formats, conditional activation, unconventional targets or payloads) and debate which ones could make a real impact in the treatment of solid tumours.

INTERACTIVE DISCUSSION: ADCs in the Era of Immunotherapy - Their Current Roles and Potential Future

Greg M. Thurber, PhD, Associate Professor, Chemical Engineering & Biomedical Engineering, University of Michigan

- Antibody-drug conjugates (ADCs) have achieved 8 new approvals in the past 5 years.
- ADCs can initiate immunogenic cell death without the broad immunosuppression of small molecule chemotherapy and interact via their Fc-domain.
- Discussion on current therapeutics that are being combined with checkpoint inhibitors, anti-VEGF therapy, and other treatments to potentially increase the immune response.
- Conversation about new avenues that are being developed to maximum the immune response with these novel therapeutics.

NON-ANTIBODY BINDERS

8:25 Chairperson's Remarks

Philipp Spycher, PhD, CEO, Araris Biotech AG

8:30 CDoT-Targeted Nanoparticle-Drug Conjugates for Platinum Resistant Ovarian Cancer

Gregory P. Adams, PhD, CSO, Elucida Oncology, Inc.

ELU001 is an anti-FRa CDC targeted by 13 folic acid moieties and delivering 21 exatecan payloads. Preclinically ELU001 penetrates into and is retained by tumors including brain tumors and efficiently targets and kills tumor cells *in vitro* and *in vivo* that express low, moderate, and high levels of FRa. Non-clinical toxicity studies of ELU001 revealed a lack of the common ADC-related toxicities. ELU001 is currently being evaluated in clinical trials.

9:00 Exploiting Novel Protein Domain Architectures to Deliver Next-Generation Mono- and Bispecific Protein-Drug Conjugates Targeting ROR1

Graham Cotton, PhD, Head, Protein Therapeutics, Almac Discovery

A novel PDC platform has been developed, which exploits small protein domain binders to deliver homogenous conjugates in monospecific, biparatopic, and bispecific formats. This approach has delivered development candidate ADP-c389, a differentiated VNAR-based PDC for the treatment of ROR1-positive solid tumours. Capitalising on the co-expression pattern of ROR1 and EGFR, bispecific PDCs have been developed, which are highly promising next-generation agents for the treatment of additional oncology indications.

9:30 The Influence of DM1, MMAE, and MMAF on Biodistribution and Preclinical Therapeutic Efficacy of Affibody-Based Drug Conjugates

Torbjörn Gräslund, PhD, Professor, Protein Science, KTH – Royal Institute of Technology, Sweden

Affibody molecules are small engineered alternative scaffold affinity proteins that can be site-specifically loaded with cytotoxic drugs to create homogenous conjugates with a desired drug-to-carrier ratio. The presentation will explore targeting of EGFR, HER2, and HER3 with affibody-based drug conjugates. It will also describe the impact on biodistribution and *in vivo* cytotoxic efficacy of HER2-targeting drug conjugates loaded with auristatin and maytansine-derived payloads.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Networking Coffee Break

NOVEL ADC ENGINEERING & CONJUGATION

11:00 Dual Precision Conjugates Reduce Resistance and Promote Anti-Tumor Immunity

Trevor J. Hallam, PhD, CSO, Sutro Biopharma, Inc.

Emerging clinical data show that precisely conjugated homogeneous ADCs more efficiently target tumors with potential benefit to patients with lower target antigen levels. Now, dual conjugation chemistries promise further advances in targeted therapies exemplified by Immunomodulatory ADCs (iADCs) that cause tumor cell disruption together with innate immune cell stimulation and result in anti-tumor immunity, and ADC^2 's dual-conjugated payloads that disrupt DNA while simultaneously impairing resistance to drive synthetic lethality.

11:30 Dual-Function Antibody Conjugates: Combining Multiple Modes of Action to Maximize ADC Efficacy

Nathan L. Tumey, PhD, Associate Professor, Pharmaceutical Sciences, SUNY Binghamton

We will describe the design, optimization, and preparation of dual-mode ADCs which combine an immuno-stimulant payload with a cytotoxic payload. The results of early proof-of-concept studies will be shown to demonstrate that the resulting dual-payload ADCs retain properties affiliated with both classes of payloads. Challenges associated with biophysical properties will also be addressed.

12:00 pm Bispecific Antibody Drug Conjugates for the Treatment of Acute Myeloid Leukemia – A Safer & More Efficacious Option for Patients?

Oliver Schon, PhD, Vice President Development and CMC, BiVictriX Therapeutics PLC

Gemtuzumab ozogamicin (GO) is the only ADC approved for use in CD33+ AML patients, but is associated with dose-limiting toxicities. The use of bispecific antibodies represents a novel approach to the development of ADCs with the potential of a more efficacious and safer treatment option for patients in the future. Here, we describe the twin antigen validation and target cell selectivity of an aCD7/aCD33 bispecific ADC.

12:30 Close of Summit

BISPECIFICS STREAM
CONFERENCES

MAY 15-16

TS: Intro to Bispecifics

AGENDA

MAY 16-17

Advancing Bispecific Antibodies

AGENDA

MAY 18-19

Engineering Bispecific Antibodies

AGENDA

BISPECIFICS STREAM

Creating First-in-Class Multi-Specific Antibody Modalities

The bispecific antibodies stream at the PEGS Summit will take you through a review of constructs, to the engineering and platform development, all the way to preclinical and clinical data. Newer platforms, innovative approaches, and constructs are combining to yield unprecedented efficacy. Don't miss the most significant forum of the year to hear about new advances in the industry and meet face-to-face with leaders changing the future of biologics.

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DAY 1: MONDAY, MAY 15, 2023 8:30 - 3:20 PM | DAY 2: TUESDAY, MAY 16, 2023 8:30 - 1:10 PM

INTRODUCTION TO BISPECIFIC ANTIBODIES: HISTORY, ENGINEERING, AND APPLICATION

Introduction to Bispecific Antibodies will be organized as an informative and practical guide to get up to speed on critical aspects of bispecific antibody therapeutics. Topics will include historical successes, failures, and lessons learned. Specific practical instruction will span mechanisms of action, engineering, developability, regulatory considerations, and translational guidelines. Perspectives on ideal implementation of bispecifics as targeted and immunomodulatory approaches will be discussed.

Instructor:
G. Jonah Rainey, PhD,
Senior Director, Protein Engineering,
Eli Lilly & Co.

Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, and extensive coverage of the basic science underlying each topic. Experienced Training Seminar instructors offer a mix of formal lectures, interactive discussions, and activities to help attendees maximize their learning experiences. These immersive trainings will be of value to scientists from industry and academic research groups who are entering new fields – and to those working in supporting roles that will benefit from an in-depth briefing on a specific aspect of the industry.

“For me, the PEGS conferences are an important and continuous source to develop new ideas for research and product development. Every visit is a deep dive into a world full of science, insights, and ideas I can discuss with so many scientists establishing new collaborations and networks. Based on these interactions and ideas, PEGS has been the beginning for a significant number of new R&D projects in my career.”

Dennis K., Sartorius Xell GmbH

ADVANCING BISPECIFIC ANTIBODIES AND COMBINATION THERAPY TO THE CLINIC Creating the Killer Combo

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC1: Antibody Drug Discovery: From Target to Lead

**style="font-size: 15px;">Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing

NON-T CELL ENGAGERS AND OTHER BISPECIFIC MECHANISMS

2:15 Chairperson's Remarks

Nathan D. Trinklein, PhD, Co-Founder and President, Rondo Therapeutics

2:20 Antibody-Lectin Bispecifics for Glyco-Immune Checkpoint Blockade

Jessica Carol Stark, PhD, American Cancer Society Postdoctoral Fellow, Stanford University

Tumors use sugars, or glycans, to evade the immune system. I will describe development of antibody-lectin bispecifics as a modular and programmable approach to target glycans for cancer immunotherapy.

2:50 PROTABs for Targeted Degradation of Transmembrane Proteins

Nicholas Agard, PhD, Principal Scientist, Antibody Engineering, Genentech, Inc.

PROteolysis TArgeteing Bispecifcs (PROTABs) are antibodies that colocalize transmembrane E3 ubiquitin ligases with target receptors to induce their ubiquitination and degradation. We will describe the discovery of PROTABs targeting ligases overexpressed in colorectal cancer and their activities *in vitro* and *in vivo*. We further demonstrate applicability of PROTABs for multiple ligases and receptors and describe protein engineering rules for maximizing the efficiency of degradation.

3:20 Talk Title to be Announced

Speaker to be Announced

BERKELEY LIGHTS

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

4:30 Surrogate Cytokine Agonists (SCAs): Unlocking Natural and Novel Cytokine Signals with Nanobody-Based Therapeutics

Sandro Vivona, PhD, Director Biochemistry & Biophysics, Biochemistry & Biophysics, Synthekine, Inc.

At Synthekine we have generated a series of functional synthetic cytokine agonists (SCAs) that mimic and modulate natural signals or create new ones. These molecules are expected to provide therapeutic immunomodulation while exhibiting antibody-like druggability.

5:00 PD1-IL2v: PD-1-Cis IL-2Rbg Agonism Yields Better T Cell Effectors from Stem-Like CD8+ T Cells

Pablo Umaña, PhD, Head Oncology Discovery, Roche

This talk will describe a new generation of PD1-cis-targeted IL-2R agonists resulting from the fusion of a high-affinity PD-1 antibody to an IL-2Rbg agonist. Such agonists maintain the advantages of IL-2Rbg-biased agonists for systemic immunotherapy, but in addition allow the expansion of a unique subset of less exhausted and more cytotoxic effector T cells with enhanced therapeutic potential for the treatment of cancer and chronic infections.

5:30 PANEL DISCUSSION: Surface Proteomics for Target Discovery: Finding Target Combinations That Improve Tissue Specificity and Therapeutic Index

Moderator: Jan E. Schnitzer, MD, Institute Director, Proteogenomics Research Institute for Systems Medicine

This panel will discuss why and how multi-targeting can help, how best to find cell surface targets, how to combine and prioritize targets based on therapeutic goals, and we will give examples of multi-targeting advances.

Panelists:

Rakesh Dixit, PhD, President & CEO, Bionavigen

6:00 Close of Day

6:00 Dinner Short Course Registration

6:30 Recommended Dinner Short Course

SC6: Developability of Bispecific Antibodies

**Separate registration required. See short courses page for details.*

WEDNESDAY, MAY 17

7:30 am Registration and Morning Coffee

TRIGGERED BISPECIFICS

8:25 Chairperson's Remarks

Frank Comer, PhD, Director, Tumor Targeted Delivery, Early Oncology R&D, AstraZeneca

8:30 KEYNOTE PRESENTATION: Triggered Bispecifics

JoAnn A. Suzich, PhD, Head, Research, Immunocore LLC

Bispecifics consisting of a high affinity targeting domain fused to a PD-1 agonist are being developed to treat autoimmune diseases. These molecules activate the PD-1 pathway potently inhibiting inflammatory cytokine production and cytotoxic activity only when bound to target cells. In the absence of target cell binding, they are unable to inhibit T cells. These bispecifics have the potential to deliver tissue-restricted T cell inhibition while avoiding systemic immunosuppression.

9:00 Next-Generation Immune Engagers

Yariv Mazor, PhD, Senior Director, R&D, Biologics Engineering, AstraZeneca

9:30 PANEL DISCUSSION: Overcoming Obstacles with Triggered Bispecifics

Moderator: Frank Comer, PhD, Director, Tumor Targeted Delivery, Early Oncology R&D, AstraZeneca

Panelists:

Yariv Mazor, PhD, Senior Director, R&D, Biologics Engineering, AstraZeneca

JoAnn A. Suzich, PhD, Head, Research, Immunocore LLC

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

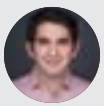
Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

11:30 KEYNOTE PRESENTATION: Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

Rebecca A. Sendak, PhD, Head, Global Large Molecules Research Platform, Sanofi

Addressing disease biology in the clinic with protein therapeutics has become increasingly complex. Turning to innovative and novel scaffolds offers opportunities to tailor therapeutics not previously possible due to advances in host cell engineering and protein design approaches. Designing and developing these modalities requires a next-generation approach as we exploit increased potential design space and also growing data sources to leverage as we invent the next wave of therapeutics.

YOUNG SCIENTIST KEYNOTE



12:15 pm KEYNOTE PRESENTATION: Engineering Prime Editor Proteins for Therapeutic Applications

Andrew V. Anzalone, PhD, Director & Head, Prime Editing Platform, Scientific Co-Founder, Prime Medicine, Inc.

Precision gene editing technologies have the potential to address a wide range of genetic diseases. Prime Editing is a recently developed "search-and-replace" gene editing approach that can precisely perform a wide variety of DNA sequence edits at programmed target sites in human genomes without requiring double-strand DNA breaks or donor DNA templates. I will describe advances to prime editing technology that improve its efficiency, specificity, and capabilities for therapeutic applications.

1:00 Session Break

1:10 Luncheon Presentation to be Announced OmniAb

Speaker to be Announced

1:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

2:10 Find Your Table and Meet Your Moderator

2:15 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

CO-STIMULATION AND COMBINATIONS

3:00 Chairperson's Remarks

Eric Smith, PhD, Senior Director, Bispecifics, Regeneron Pharmaceuticals, Inc.

3:05 Combining Signals 1, 2, and 3 for Optimal T Cell Activation against Tumors

John R. Desjarlais, PhD, CSO, Xencor, Inc.

Xencor is developing a growing pipeline of CD3 and CD28 T cell engagers, together with several potency-optimized cytokine-Fc fusions, including IL15, IL12, and IL18. We will discuss preclinical data exploring combination of these various agents with themselves and PD1 inhibition to promote optimal T cell activation in the tumor microenvironment.

3:35 Targeted Therapies for the Enhancement of Anti-Tumor T Cell Responses

Eric Smith, PhD, Senior Director, Bispecifics, Regeneron Pharmaceuticals, Inc.

This presentation will describe key pre-clinical data from Regeneron's new clinical approaches to enhancing anti-tumor efficacy of T cells, focusing on the combination of costimulatory bispecific antibodies with checkpoint blockade and T cell redirecting bispecifics. In addition, data from new classes of T cell targeted enhancement strategies in pre-clinical development will be discussed.

4:05 Sponsored Presentation *(Opportunity Available)*

4:35 Ice Cream Break in the Exhibit Hall with Poster Viewing

5:10 T Cell Activation via Co-Stimulatory CD28 Bispecific Antibodies

Nicolas Fischer, PhD, CEO, Light Chain Bioscience

Antibodies CD28 bispecific antibodies (bsAbs) were generated to co-stimulate T cells in the presence expressing a selected tumor-associated antigen (TAA) or by co-engaging PD-L1 on cancer cells or antigen-presenting cells. Using our κλ antibody platform, CD28 bsAbs targeting multiple TAAs were designed for tumor-specific activation of the immune system. CD28-engaging κλ enhance the antitumor response via stimulation of T cell proliferation/activation, increased cytokine secretion, and directed cytotoxicity.

5:40 Partners-in-Crime: Co-Stimulation via 4-1BB or CD28 to Boost the Efficacy of T Cell Bispecifics

Christian Klein, PhD, Head of Oncology Programs and Department Head, Cancer Immunotherapy Discovery, Roche Innovation Center Zurich, Roche Pharma Research & Early Development, pRED

The presentation will cover an overview and update on preclinical properties of solid and heme tumor co-stimulators including FAP-4-1BBL, CD19-4-1BBL, and CD19-CD28 in active clinical development in combination with cibisatamab and glofitamab, respectively.

6:10 Strength in Partnerships: Duobody CD40x41BB (GEN1042) Therapeutic for Advanced Solid Tumor Treatment

Homer Adams III, PhD, Associate Director, Genmab US, Inc.

Duobody GEN1042 is a conditional activator of co-stimulatory molecules 4-1BB and CD40 which has shown early promise in the treatment of advanced solid tumors. Preclinical data shows enhanced priming and anti-tumor activity inclusive of T cell proliferation and effector functions. Furthermore, monotherapy and combination data from our FIH, open-label, phase I/II trial (NCT04083599) reveal a manageable safety profile, clinical activity, and pharmacodynamics consistent with the mechanism of action.

6:40 Networking Reception in the Exhibit Hall with Poster Viewing

7:40 Close of Advancing Bispecific Antibodies and Combination Therapy to the Clinic Conference

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

6:00 Recommended Pre-Conference Short Course

SC3: *In silico* **and Machine Learning Tools for Antibody Design and Developability Predictions**

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

6:30 pm Recommended Dinner Short Course

SC6: Developability of Bispecific Antibodies

**Separate registration required. See short courses page for details.*

THURSDAY, MAY 18

7:30 am Registration and Morning Coffee

NOVEL APPROACHES FOR BISPECIFIC ANTIBODIES

8:25 Chairperson's Remarks

Christian Klein, PhD, Head of Oncology Programs and Department Head, Cancer Immunotherapy Discovery, Roche Innovation Center Zurich, Roche Pharma Research & Early Development, pRED

8:30 Trispecific Antibody Platform Triclonics ENGAGE for the Discovery of Next-Generation T Cell Engagers

Pieter Fokko van Loo, PhD, Senior Director, Oncology – Immunology, Merus NV

Avidity driven dual-targeting to achieve tumor selectivity will be explored. Functional screening of antibody panels for lead identification and trispecific T cell engagers for solid and liquid tumors will be discussed.

9:00 Expanding Immunotherapy by Targeting an Intracellular Oncoprotein in MHC 1

Charles S. Craik, PhD, Professor, Departments of Pharmaceutical Chemistry, Pharmacology, and Biochemistry/Biophysics, University of California, San Francisco

Immunotherapies directed at MHC-I complexes have expanded the scope of antigens and enabled direct targeting of intracellular oncoproteins at the cell surface. We have shown that covalent drugs such as sotorasib that alkylate mutated residues on KRas G12C can act as haptens to generate unique MHC-I-restricted neoantigens. Using hapten-specific antibodies our results present a strategy to enhance the efficacy of these covalent drugs and overcome their rapidly arising tumor resistance.

9:30 Talk Title to be Announced

Speaker to be Announced

Alloy Therapeutics

9:45 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

ENGINEERING T CELL ENGAGERS FOR SOLID TUMORS

10:39 Chairperson's Remarks

G. Jonah Rainey, PhD, Senior Director, Protein Engineering, Eli Lilly and Company

10:40 KEYNOTE PRESENTATION: Antibody-Cytokine Fusions for the Treatment of Difficult-to-Cure Cancer Types: Emerging Clinical Results

Dario Neri, PhD, CEO and CSO, Philogen

Results from clinical trials with L19-TNF in second-line glioblastoma multiforme, including numerous durable major objective responses, will be presented. In addition, results from clinical trials with Nidlegy in high-risk basal cell carcinoma patients, candidates for disfiguring surgery who experienced durable complete responses, will be shared. Other clinical trial results in "difficult-to-treat tumors" will be discussed.

11:10 Next-Generation Tetravalent Bispecific Antibodies for Cancer Immunotherapy

Michelle Morrow, PhD, Senior Vice President, Biology & Translational Science, F-Star Therapeutics, Inc.

F-star generates tetravalent bispecific antibodies by introducing an antigen-binding site into the Fc region of human IgG1 (Fc region with antigen binding, or Fcab region). This antibody format has four antigen-binding sites and provides a focused immune activation upon concurrent binding to both receptors. Our proprietary clinical pipeline of bispecific antibodies aims to overcome resistance to current checkpoint inhibitor therapies and improve on the benefit of checkpoint inhibitors.

11:40 Fully Human Multi-Specific Tentacles to Achieve Exquisite Cell and Tissue-Specific Disease Intervention

Stephen J. Demarest, PhD, CSO, Tentarix Biotherapeutics

Designing efficacious therapeutics with conditional activity towards specific cells or tissues is the next frontier in precision medicine. To achieve this goal, we developed a platform for the design and identification of ultra-rare, fully human, multi-specific biologics, called Tentacles, with exquisite cell/tissue-specific activity from libraries of >1 million molecules. Data for our first Tentacle drug candidate combining LAG3 inhibition with LAG3-dependent IL2R activation will be described.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing

1:15 PANEL DISCUSSION: Setting the Right Strategy to Drive Engineering Parameters for Solid Tumor-Targeting T Cell-Engagers

Moderator: G. Jonah Rainey, PhD, Senior Director, Protein Engineering, Eli Lilly and Company

Panelists:

Stephen J. Demarest, PhD, CSO, Tentarix Biotherapeutics

Michelle Morrow, PhD, Senior Vice President, Biology & Translational Science, F-Star Therapeutics, Inc.

Dario Neri, PhD, CEO and CSO, Philogen

2:20 Talk Title to be Announced

Genedata

Speaker to be Announced

2:50 Networking Refreshment Break

IMMUNE CELL ENGAGERS – WHICH ONES TO USE?

3:19 Chairperson's Remarks

Eugene A. Zhukovsky, PhD, CSO, Ichnos Sciences Biotherapeutics SA

3:20 Progress on REV403 TwoGATE, a Sophisticated T Cell Engager Approach for Solid Tumors

Werner Meier, PhD, CSO, Revitope Oncology

Harnessing the immune system has revolutionized cancer treatment. However, on-target off-tumor toxicities limit therapeutic potential. At the heart of REV403 TwoGATE is the split anti-CD3 paratope enabling a true dual Ag "AND" gate by targeting the inactive components to EGFR and PDL1, respectively on the same tumor cell before CD3 binding complex reassembly. REV403 has pM potency *in vitro*, potently regresses tumors *in vivo*, and is well-tolerated in non-human primates.

3:50 Engineering Immune Cell Engagers Based on the BEAT Technology

Eugene A. Zhukovsky, PhD, CSO, Ichnos Sciences Biotherapeutics SA

Ichnos' BEAT platform (Bispecific Engagement by Antibodies based on the TCR) facilitates design of multi-specific antibodies using efficient heavy-chain heterodimerization and a common light chain. Employing this platform, we have generated multi-specific (tri-, tetra-specific, 2+1 biparatopic bispecific) antibodies engaging major types

of immune effector cells. We illustrate the advantages of BEAT-based multi-specific antibodies, which permit leveraging avidity, increased specificity, and potency of experimental therapeutics built by employing Ichnos' antibody platform.

4:20 Close of Day

FRIDAY, MAY 19

7:00 am Registration Open

INTERACTIVE DISCUSSIONS

7:30 Interactive Discussions with Continental Breakfast

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

INNOVATIVE PLATFORMS AND STRATEGIES

8:25 Chairperson's Remarks

Mahiuddin Ahmed, PhD, President and CSO, VITRUVIAE

8:30 Cystine-Dense-Peptide (CDP)-Based PD-L1:CD3 Bispecific T Cell Engager: *Ex silico* Engineering and Nonclinical Activity Studies

James M. Olson, PhD, Professor, Clinical Research, Fred Hutchinson Cancer Research Center

Using a combination of I-TASSER and Rosetta protein modeling software, we predicted the structure of >4000 CDP mini-proteins. From a diversity library generated around those that showed *in silico* binding to PD-L1, we used mammalian display-based screening and affinity maturation to identify a high-affinity (KD=202 pM) binder.

9:00 PROTABs: A Tool for Leveraging E3 Ubiquitin Ligases as Cell Surface Protein Degraders

Hadir Marei, PhD, Scientist III, Genentech

E3 ubiquitin ligases with exposed extracellular domains represent attractive tools for targeted protein degradation approaches. Indeed, through developing Proteolysis Targeting Antibodies (PROTABs) we enable the repurposing of ZNFR3, a Wnt-responsive E3 ubiquitin ligase, as a tumor-specific cell-surface protein degrader. Importantly, PROTABs are also amendable to additional cell-surface targets and ligases. Altogether, this strategy expands on current degrader technologies allowing the development of effective, bioavailable, and tissue-selective cell-surface protein degraders.

9:30 A Tetravalent TREM2 Agonistic Antibody Fused with a TfR Binding scFv for Enhanced Brain Delivery and Improved Efficacy in 5XFAD Mice

Ningyan Zhang, PhD, Professor & Co-Director, Texas Therapeutics Institute, University of Texas Health Science Center

Triggering receptor expressed on myeloid cells 2 (TREM2) plays a crucial role in regulating microglial functions and removal of amyloid plaques in Alzheimer's disease. We recently reported a novel TREM2 targeting bispecific antibody (TVD-Ig/αTfR) with tetra-variable domains targeting TREM2 (TVD-Ig), and a single chain variable fragment (scFv) binding to transferrin receptor (TfR). The TVD-Ig/αTfR bispecific antibody improved antibody brain entry by more than 10-fold in comparison with the anti-TREM2 counterpart.

10:00 Talk Title to be Announced

Speaker to be Announced

10:30 Networking Coffee Break

ENGINEERING BISPECIFICS: STRUCTURE, FORMAT, AND FUNCTION

10:59 Chairperson's Remarks

Shelley Force Aldred, PhD, Co-Founder & CEO, Rondo Therapeutics

11:00 Presentation to be Announced

Simone Oostindie, PhD, Senior Scientist, Translational Research, Genmab BV

11:30 Engineering and Preclinical Development of ZW171: A 2+1 Format Anti-MSLN T Cell Engager

Chayne Piscitelli, PhD, Senior Scientist, Protein Engineering, Zymeworks, Inc.

ZW171 is a mesothelin (MSLN)-targeting T cell engager with bivalent binding to MSLN and a novel CD3 binding domain. By tuning affinity and format, we achieved a molecule with potent MSLN-specific activity both *in vitro* and *in vivo*, with minimal MSLN-independent T cell binding and activation. Development data suggest that ZW171 has the potential to be an efficacious and safe therapeutic for the treatment of MSLN-expressing cancers.

12:00 pm Reduction of Antigenicity and Immunogenicity for Clinical Success of Multi-Specific Antibodies

Stefan Warmuth, PhD, Vice President, Head CMC, Numab Therapeutics AG

Treatment-emergent (TE) ADAs and pre-existing (PE) ADAs became a major hurdle in the successful development of multi-specific antibodies. A limited set of point mutations can prevent binding of PE ADAs to the framework and generation of TE ADAs to CDR regions. *In silico* design, immunogenicity prediction and an exhaustive array of characterization assays led to the design of optimized sequences that facilitate better development of bi- and multi-specific antibodies.

12:30 Close of Engineering Bispecific Antibodies Conference

IMMUNOTHERAPY STREAM
CONFERENCES

MAY 15-16

Improving Immunotherapy Efficacy and Safety

AGENDA

MAY 16-17

Cell-Based Immunotherapies

AGENDA

MAY 18-19

Next-Generation Immunotherapies

AGENDA

IMMUNOTHERAPY STREAM

Supercharging Immunotherapies for Cancer and Immune Disorders

The Immunotherapy Stream at PEGS BOSTON highlights the most exciting technologies, modalities, and engineering strategies driving cellular and non-cellular immunotherapies for cancer and immune disorders. Part One examines recent breakthroughs in immunotherapy efficacy and safety, across a range of modalities; Part Two focuses on supercharging CAR T therapies and other cell immunotherapies against liquid and solid tumors; with Part Three focusing on the next generation of smarter, more targeted immunotherapies for reprogramming the immune system. All tracks feature brand new data, exciting, inspiring science, and unrivaled networking opportunities with both industry and academic leaders.

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IMPROVING IMMUNOTHERAPY EFFICACY AND SAFETY

Creating More Potent, Targeted Immunotherapies

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC1: Antibody Drug Discovery: From Target to Lead

**Separate registration required.* See short courses page for details.

MONDAY, MAY 15

7:00 am Registration and Morning Coffee

NEW FRONTIERS IN IMMUNOTHERAPY

8:20 Chairperson's Remarks

Laszlo G. Radvanyi, PhD, President & Scientific Director, Ontario Institute for Cancer Research

8:30 Engineering Human Neuraminidase as a Novel Cancer Immunotherapy to Enhance T Cell Immunity by Degrading Immunosuppressive Sialoglycans

Li Peng, PhD, CSO, Palleon Pharmaceuticals

Sialoglycans have emerged as an important immune checkpoint orthogonal to the PD-1/PD-L1 axis. We engineered a novel first-in-class drug candidate (Bi-Sialidase), consisting of an engineered human sialidase (Neu2) Fc fusion, to degrade immunosuppressive sialoglycans. Bi-Sialidase potentiates T cell immune response and demonstrates single-agent antitumor activity and a wide safety margin in preclinical animal models, offering a novel immunomodulatory approach to treat cancer.

9:00 Boosting the Efficacy of Bispecific T Cell Engagers via Removal of Cell-Surface Sialoglycans

Peng Wu, Professor, Chemical Physiology, Scripps Research Institute

Bispecific T cell engager (BiTE)-based cancer therapies that activate T cells of a patient's own immune system have had success in treating blood cancers, but with limited efficacy in targeting solid tumors. Here, I will discuss the development of BiTE-sialidase fusion proteins that enhance tumor cell susceptibility to BiTE-mediated cytolysis by T cells via targeted desialylation at the T cell-tumor cell interface.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Networking Coffee Break

10:30 Current Trends and Future Opportunities in Immunotherapy

Nageatte Ibrahim, MD, Vice President, Oncology & Global Clinical Development, MSD

11:00 KEYNOTE PRESENTATION: Immunomodulation by Genomic "Dark Matter" and Extracellular Vesicles in Cancer

Laszlo G. Radvanyi, PhD, President & Scientific Director, Ontario Institute for Cancer Research

Non-coding regions or the 'dark matter' of the genome have been largely ignored in cancer immunotherapy. This presentation will describe how otherwise silent, non-coding regions of the human genome containing retroelements (REs) and human endogenous retroviruses (HERVs) are activated in human cancer and their implications on immunoregulation. REs and HERVs can induce anti-tumor immune responses, but we have also found that they can induce chronic inflammation and a profound immunosuppression.

11:30 Luncheon Presentation to be Announced

Speaker to be Announced

charles river

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

INTERACTIVE DISCUSSIONS

12:30 Find Your Table and Meet Your Moderator

12:45 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

1:30 Session Break

ENHANCING IMMUNOTHERAPY AND LONG-TERM FUNCTION

1:45 Chairperson's Remarks

Julia Carnevale, MD, Assistant Professor, School of Medicine, University of California, San Francisco

1:50 Engineering Next-Generation Proteins to Enhance Adoptive Cell Therapy

Shannon K. Oda, PhD, Principal Investigator & Associate Professor, Center for Childhood Cancer Research, Seattle Children's Research Institute

Adoptive cell therapy (ACT) with genetically modified T cells is a promising approach, however, the tumor microenvironment can establish several obstacles. We develop engineered fusion proteins (FPs) that combine a receptor ectodomain with a different costimulatory endodomain. Intentionally engineered FPs can "armor" T cells by multiple mechanisms and new generations also promote endogenous antitumor immunity, resulting in significantly improved therapeutic efficacy against hematological and solid tumors.

2:20 RASA2 Ablation in T Cells Boosts Antigen Sensitivity and Long-Term Function

Julia Carnevale, MD, Assistant Professor, School of Medicine, University of California, San Francisco

Multiple genome-wide CRISPR screens under different immunosuppressive conditions converged on RASA2, a RasGAP that we identify as a signaling checkpoint in human T cells. RASA2 ablation in T cells enhanced antigen-dependent signaling and cytolytic activity, as well as persistent effector function with repeated tumor antigen stimulations. Ablation of RASA2 in multiple preclinical models of TCR and CAR T cell therapies prolonged survival in mice xenografted with either liquid or solid tumors.

2:50 Talk Title to be Announced

Speaker to be Announced

BERKELEY LIGHTS

3:20 Networking Refreshment Break

3:50 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

4:10 KEYNOTE PRESENTATION: Advances in CAR T Therapy

Carl H. June, MD, Richard W. Vague Professor in Immunotherapy; Professor of Medicine; Director, Center for Cellular Immunotherapies; Director, Parker Institute for Cancer Immunotherapy, University of Pennsylvania Perelman School of Medicine

Advances in the understanding of basic immunology have ushered in two major approaches for cancer therapy over the past 10 years. The first is checkpoint therapy to augment the function of the natural immune system. The second uses the emerging discipline of synthetic biology and the tools of molecular biology and genome engineering to create new forms of engineered cells with enhanced functionalities.

4:55 KEYNOTE PRESENTATION: The Next Frontier in Machine Learning and Biologics: "Lab in a Loop" Large Molecule Drug Discovery, From Optimization to *de novo* Discovery

John Marioni, PhD, Senior Vice President and Head of Computation, Research and Early Development, Genentech

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

TUESDAY, MAY 16

8:00 am Registration and Morning Coffee

IMPROVING RESPONSE AND CURE RATES

8:25 Chairperson's Remarks

Andrew Sewell, PhD, Distinguished Research Professor and Wellcome Trust Senior Investigator, Division of Infection and Immunity, Cardiff University School of Medicine

8:30 Uncovering the Mode of Action of Engineered T Cells in Patient Cancer Organoids

Anne Rios, PhD, Principal Investigator, Princess Maxima Center Pediatric Oncology

Here we describe a system, called BEHAV3D, developed to study the dynamic interactions of immune cells and patient cancer organoids by means of imaging and transcriptomics. We apply BEHAV3D to live-track >150,000 engineered T cells cultured with patient-derived, solid-tumor organoids, identifying a 'super engager' behavioral cluster comprising T cells with potent serial killing capacity.

9:00 New Modes of T Cell Recognition and Novel Broadly-Expressed T Cell Epitopes by Dissection of Cancer Immunotherapy Success

Andrew Sewell, PhD, Distinguished Research Professor and Wellcome Trust Senior Investigator, Division of Infection and Immunity, Cardiff University School of Medicine

We have employed three different successful pipelines for discovering what so-called "orphan T cells" recognize and applied these to dissect what dominant persistent anti-cancer T cells recognize during successful immunotherapy for solid cancer. This work has uncovered a new, unanticipated, mode of T cell recognition. I will discuss these results and how they point to potentially exploitable correlates of success.

9:30 A Genome-Scale Screen for Synthetic Drivers of T Cell Proliferation

Mateusz Legut, PhD, Postdoc Fellow, Biology & Genomics, New York University

The engineering of autologous patient T cells has revolutionized the treatment of cancer. However, further improvements are needed to increase response and cure rates. CRISPR-based loss-of-function screens have been limited to negative regulators of T cell functions and raise safety concerns owing to the permanent modification of the genome. Here we identify positive regulators of T cell functions through overexpression of around 12,000 barcoded human open reading frames (ORFs).

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Scalable Discovery Systems for Human Cell Therapies

Theodore Roth, MD, PhD, Resident, Clinical Pathology, Stanford University; Co-Founder, Arsenal Bio

Effective cellular therapies for solid tumors remain elusive. We present a highly scalable platform to rapidly associate large pools of T cell genetic modifications with high-dimensional single-cell phenotypes across diverse disease contexts. The resulting genotype x phenotype maps have nominated unique novel cell therapy targets with improved *in vitro* and *in vivo* performance for further clinical development.

11:40 Engineering T Cell Antigen Density Sensors for Cancer Immunotherapy

Rogelio A. Hernandez-Lopez, PhD, Associate Professor, Cellular Molecular Pharmacology, Stanford University

Current CAR T cells fail to discriminate between cells expressing high and low levels of antigens which limits its use against solid tumors. We are engineering T cell circuits that can sense antigen density with an ultrasensitive tunable response. We have designed a two-step recognition-activation circuit where an initial recognition event, via a Synthetic Notch receptor, alters the potency of a subsequent response, CAR expression, and activation.

12:10 pm Engineering Bacteria Cancer Therapy

Tal Danino, PhD, Associate Professor, Biomedical Engineering, Columbia University

Synthetic biology is driving a new era of medicine through the genetic programming of living cells. One focus has been on engineering bacteria for cancer therapy, where several studies have demonstrated selective bacterial colonization of solid tumors due to reduced immune surveillance at the tumor core. In this talk, I will discuss efforts in programming bacterial safety systems and delivery of therapeutic payloads ranging from cytotoxic to immunomodulatory agents.

12:40 LUNCHEON PRESENTATION: Specificity Testing of Antibodies, Bispecifics, and CAR T Therapeutics for IND Using the Membrane Proteome Array

Rachel Fong, Director of Sales and Alliances, Integral Molecular

1:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:40 Close of Improving Immunotherapy Efficacy and Safety Conference

6:30 Recommended Dinner Short Course

SC8: CAR T Cells: Improving Safety While Retaining Therapeutic Activity

**Separate registration required. See short courses page for details.*

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC3: In silico and Machine Learning Tools for Antibody Design and Developability Predictions

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing

ENGINEERING SMARTER CAR T THERAPIES

2:15 Chairperson's Remarks

Yan Chen, PhD, Founder & CEO, Elpis Biopharmaceuticals

2:20 KEYNOTE PRESENTATION: Towards *In Vivo* Engineering of the Immune System

Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

Ex vivo CAR-engineered T cells showed remarkable clinical efficacy, especially in a subset of patients with B cell malignancies. Nevertheless, hurdles related to access, manufacturing, and performance across broader disease categories warrant development of novel therapeutic platforms. *In vivo* precision engineering of the immune system utilizing synthetic nano-formulations may overcome both logistical and mechanistic limitations thereby potentially expanding the footprint of immunotherapy.

2:50 Synthetic Immune Receptors and Signalling

Kole T. Roybal, PhD, Associate Professor, Microbiology & Immunology, University of California, San Francisco

Programmed and highly targeted activity of cell therapies has the potential to both reduce toxicity and concentrate the therapeutic effect where it is most needed, improving safety and efficacy. Our mission is to engineer and distribute a comprehensive toolkit of clinically optimized technologies for cell-based therapeutics, so we can make an impact across diseases with high unmet needs.

3:20 Talk Title to be Announced

Speaker to be Announced

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

4:30 Synthetic Immune Receptor (SIR), a Next-Generation CAR Platform

Preet M. Chaudhary, MD, PhD, Professor & Chief Hematology & Director, Blood & Marrow Transplant, University of Southern California

Despite the success with CAR T cells in hematologic malignancies, there are several limitations to this approach including toxicities, CAR T cell exhaustion, and lack of persistence. To overcome the above design limitations of the current generation CAR T constructs, we have generated a next-generation CAR T platform designated Synthetic Immune Receptor (SIR) that provides physiological TCR-like signaling and overcomes most of the limitations of current generation CAR constructs.

5:00 CAR T Cells Targeting Tumor Glycosylation and TME

Avery D. Posey, Jr., PhD, Assistant Professor, Systems Pharmacology & Translational Therapeutics, University of Pennsylvania

Chimeric antigen receptor T cells are genetically modified lymphocytes conventionally re-targeted towards specific macromolecules defined by the variable domains of monoclonal antibodies. Most CAR T cell therapies have been developed to target cell-surface protein antigens; however, antibody-based re-targeting expands the repertoire of macromolecules T cells can target, including carbohydrate-based antigens. Here, we demonstrate that truncated O-glycoforms of tumor-associated antigens are a class of actionable immune targets for CAR T cells.

5:30 Disinhibition of Early CAR T Cell Activation via CD5 Knockout Enhances the Anti-Tumor Activity of Adoptive T Cell Therapies against Cancer

Marco Ruella, MD, Assistant Professor of Medicine, Scientific Director, Lymphoma Program, Division of Hematology and Oncology and Center for Cellular Immunotherapies, University of Pennsylvania

One of the main barriers to the effective activity of adoptively transferred T cells is their inhibition when they reach the tumor bed. In this study, we discovered that CD5 inhibits CAR T activation and that the knockout (KO) of CD5 using CRISPR-Cas9 enhances the anti-tumor effect of CAR and TCR T cells in multiple hematological and solid cancer models.

6:00 Close of Day

6:00 Dinner Short Course Registration

6:30 Recommended Dinner Short Course

SC8: CAR T Cells: Improving Safety While Retaining Therapeutic Activity

**Separate registration required. See short courses page for details.*

WEDNESDAY, MAY 17

7:30 am Registration and Morning Coffee

TARGETING SOLID TUMORS

8:25 Chairperson's Remarks

Rizwan Romee, PhD, Associate Professor Medicine & Director, Haploidentical Donor Transplant Program, Dana-Farber Cancer Institute

8:30 Overcoming Suppression of NK Cells in the Tumor Microenvironment

Michal Sheffer, PhD, Instructor, Medical Oncology, Dana-Farber Cancer Institute

NK cell immunotherapy is a promising approach for cancer treatment, with low risk of graft versus host disease and adverse effects. One of the major hurdles of this approach is the immune suppressive tumor-microenvironment. In our work, we applied unbiased large-scale CRISPR screens on both the tumors and the NKs, to identify mechanisms of tumor cell resistance to NKs, for improved NK cell immunotherapies.

9:00 Engineering NK Cells for Improved Immunotherapy

Jianzhu Chen, PhD, Professor, Biology, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

One challenge of CAR T cell therapy is tumor relapse due to loss of target antigen on tumor cells or poor persistence of CAR T cells in patients. To overcome this challenge, we have developed CARs that recognize peptide-MHC where the peptides are derived from oncogenic mutations. Arming cytokine-induced memory-like NK cells, which can persist in patients for months, with tumor-specific CARs may lead to better long-term efficacy of CAR-NK cell therapies.

9:30 NK Cell Engineering for Enhanced Targeting of Advanced Solid Tumors

Rizwan Romee, PhD, Associate Professor Medicine & Director, Haploidentical Donor Transplant Program, Dana-Farber Cancer Institute

We have recently demonstrated the safety and promising activity of using memory-like NK cells in AML and MDS. In my talk, I will describe key properties of the memory-like NK cells; summarize the

preclinical development of the CAR-armed memory-like NK cells in ovarian and pancreatic cancer, and describe early clinical results and correlative labs from our ongoing clinical trial of cytokine-engineered allogeneic NK cells in combination with CTL4 blockade.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

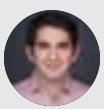
Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

11:30 KEYNOTE PRESENTATION: Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

Rebecca A. Sendak, PhD, Head, Global Large Molecules Research Platform, Sanofi

Addressing disease biology in the clinic with protein therapeutics has become increasingly complex. Turning to innovative and novel scaffolds offers opportunities to tailor therapeutics not previously possible due to advances in host cell engineering and protein design approaches. Designing and developing these modalities requires a next-generation approach as we exploit increased potential design space and also growing data sources to leverage as we invent the next wave of therapeutics.

YOUNG SCIENTIST KEYNOTE



12:15 pm KEYNOTE PRESENTATION: Engineering Prime Editor Proteins for Therapeutic Applications

Andrew V. Anzalone, PhD, Director & Head, Prime Editing Platform, Scientific Co-Founder, Prime Medicine, Inc.

Precision gene editing technologies have the potential to address a wide range of genetic diseases. Prime Editing is a recently developed "search-and-replace" gene editing approach that can precisely perform a wide variety of DNA sequence edits at programmed target sites in human genomes without requiring double-strand DNA breaks or donor DNA templates. I will describe advances to prime editing technology that improve its efficiency, specificity, and capabilities for therapeutic applications.

1:00 Session Break

1:10 Luncheon Presentation to be Announced

Speaker to be Announced

1:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

2:10 Find Your Table and Meet Your Moderator

2:15 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

SOLID TUMORS AND IMPROVING TARGETING

3:00 Chairperson's Remarks

Michael Hudecek, MD, Professor, Cellular Immunotherapy of Malignant Diseases, University of Wuerzburg

3:05 Advances in CAR-M Cellular Immunotherapy

Michael Klichinsky, PharmD, PhD, Co-Founder & Vice President, Discovery, Carisma Therapeutics

Adoptive cell therapies have demonstrated remarkable outcomes in hematologic malignancies, but efficacy in solid tumors is still lacking. We have established a novel, proprietary monocyte and macrophage-based cell therapy platform based on chimeric antigen receptor macrophages (CAR-M).

3:35 Novel Solid Tumor Targets and Technologies to Increase Potency in the Pipeline

Michael Hudecek, MD, Professor, Cellular Immunotherapy of Malignant Diseases, University of Wuerzburg

This talk will feature novel mechanisms of resistance to CAR T therapy, novel target antigens and CAR T cell products for treating multiple myeloma, virus-free transposon-based gene-transfer for CAR T manufacturing, and a novel application for CAR T in fungal infections.

4:05 Sponsored Presentation *(Opportunity Available)*

4:35 Ice Cream Break in the Exhibit Hall with Poster Viewing

5:10 Off-the-Shelf Allogeneic EBV CAR T Cells

Jakob Dupont, MD, Global Head, R&D, Atara Biotherapeutics

Allogeneic T cells have qualities that make them an ideal platform for treating disease. Evolution of CAR T designs and next-generation armoring technologies to overcome the hostile tumor microenvironment will be explored, including the promise of a platform that doesn't require HLA or TCR gene editing and safety, expansion, and persistence implications.

5:40 dAb vs scFv in CAR

Mathieu Ferrari, PhD, Director, Binder Discovery, Autolus Therapeutics plc

Despite the recent approval of CARVYKTI, historically scFv has been the preferred binding format in CAR T cell therapies. Single domain antibodies (dAb), however, display several favorable biophysical characteristics such as smaller size, increased paratope diversity, and improved stability. Here we compare a set of 20 affinity and domain-matched dAb and scFv-based CARs, evaluate their biophysical properties, and compare their functionality head-to-head to assess which format may prevail.

6:10 Novel Protein Engineering Concepts to Improve the Safety and Specificity of CAR T Cells

Michael Traxlmayr, PhD, Head, Laboratory for Next-Generation CAR T Cells, University of Natural Resources & Life Sciences

Major limitations in the CAR field include the poor controllability of CAR T cells after administration *in vivo* and their limited tumor specificity. To address these important challenges, we have engineered protein-based switches for CAR T cell regulation with an orally available and non-toxic small molecule drug. In addition, we have generated avidity-controlled CARs (AvidCARs) for combinatorial antigen recognition and small molecule-mediated CAR T cell control *in vivo*.

6:40 Networking Reception in the Exhibit Hall with Poster Viewing

7:40 Close of Cell-Based Immunotherapy Conference

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

6:00 Recommended Pre-Conference Short Course

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

6:30 pm Recommended Dinner Short Course

SC8: CAR T Cells: Improving Safety While Retaining Therapeutic Activity

**Separate registration required. See short courses page for details.*

THURSDAY, MAY 18

7:30 am Registration and Morning Coffee

THE ERA OF *IN VIVO* CELL ENGINEERING AND DELIVERY

8:25 Chairperson's Remarks

Christian J. Buchholz, PhD, Professor & Head, Molecular Biotechnology & Gene Therapy, Paul Ehrlich Institut

8:30 KEYNOTE PRESENTATION: *In vivo* Engineering Considering Probability of Technical, Regulatory, and Commercial Success

Nicholas A. Boyle, PhD, CEO, Abintus Bio

In vivo genetic medicines are poised to disrupt a range of therapeutic areas. The ideal product profile for these agents include: 1) Safety and tolerability with intravenous administration and flexibility for repeat dosing; 2) Gene delivery to target cells using an off-the-shelf, standardized vehicle; and 3) Scalable manufacturing of purified product with low immunogenicity. Building on lessons learned, this presentation will address approaches to mitigate technical, regulatory, and commercial risks.

9:00 Engineering Retargeted Fusogens for *in vivo* Gene Delivery to T Cells

Jagesh V. Shah, Vice President, Gene Therapy Technologies, Sana Biotechnology

We have developed a novel platform for engineering fusogens to target cellular molecules of choice, thereby enabling *in vivo* cell-specific delivery across many cell types with a fusogen-directed gene therapy vector. *In vivo* generation of CAR T cells, using gene therapy vectors with T cell targeting fusogens for *in vivo* CAR delivery, show promise in preclinical models and may provide broader access to CAR therapies.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

10:40 Surface Engineered Gene Vectors for *in vivo* CAR T Cell Generation

Christian J. Buchholz, PhD, Professor & Head, Molecular Biotechnology & Gene Therapy, Paul Ehrlich Institut

Highly effective, yet complex to manufacture, simplifying CAR T cell generation is at the forefront of current research. The vision of generating CAR T cells directly in the patient will heavily rely on vector technology, particularly high selectivity for T lymphocytes. This presentation will discuss different vector platforms, especially focusing on engineered lentiviral and AAV vectors using T cell markers as entry receptors achieved through display of DARPins or scFv.

11:10 Enabling *in situ* Re-Engineering of Cellular Functions

Philip R. Johnson, MD, CEO, Interius Biotherapeutics

The Interius bioplatform is based on an innovative, proprietary lentiviral vector that can be engineered to target, transduce, and reprogram specific cells in the body. This bioplatform has direct applicability for oncologic indications and as an *in vivo* delivery vehicle for gene replacement, nucleic acid editing, and therapeutic protein biosynthesis. Our lead programs are focused on treating hematologic malignancies through *in vivo* generation of tumor-specific CAR T cells.

11:40 *In vivo* Production of Functional CAR T Cells by mRNA Targeted Lipid Nanoparticle

Haig Aghajanian, PhD, Co-Founder and Vice President of Research, Capstan Therapeutics

Using targeted lipid nanoparticles (tLNP), we were able to transiently reprogram T cells *in vivo* by delivering modified mRNA encoding a CAR against fibroblast activation protein (FAP). This treatment resulted in the reduction of cardiac fibrosis and the restoration of cardiac function. The ability to produce transient, functional CAR T cells *in vivo* with mRNA addresses some of the biggest hurdles in cell therapy including manufacturing, scalability, and safety concerns.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing

CELLULAR REPROGRAMMING USING RNA AND LNPs

1:15 Chairperson's Remarks

Nicholas A. Boyle, PhD, CEO, Abintus Bio

1:20 *In situ* CAR Therapy Using oRNA

Robert Mabry, PhD, CSO, Orna Therapeutics

We have developed a novel, synthetic, circular coding RNA platform (oRNA technology) which exhibits significant improvements in production, expression, and formulation compared to mRNAs. Given the successes as well as remaining challenges with CAR T cell therapies, we combined our oRNA technology with novel immunotropic LNPs to create an off-the-shelf "autologous" *in situ* CAR (isCAR) therapy that effectively delivers anti-CD19 CAR to immune cells and regresses tumors *in vivo*.

1:50 *In situ* CAR Therapy Using oRNA CAR T Cells Manufactured Rapidly *in situ* Using Virally Activated Endogenous APC

Larry R. Pease, PhD, Professor, Biochemistry & Molecular Biology & Immunology, Mayo Clinic & Foundation

In situ CAR T cells are generated directly in immune reactive lymph nodes in just 3 days from T cells responding to virus-encoded major histocompatibility alloantigens presented by endogenous APC. Following *in vivo* retargeting with viruses encoding chimeric antigen receptors, the resulting *in situ* CAR T cells are capable of targeting antigen-positive cells systemically in the blood and in a solid tumor setting.

2:20 Talk Title to be Announced

Speaker to be Announced

Alloy Therapeutics

2:50 Networking Refreshment Break

3:20 *In vivo* Reprogramming of CAR T Cells Using Targeted LNPs

Viktor Lemgart, Research Fellow, Tidal Therapeutics, a Sanofi Company

Ex vivo CAR T cell therapies have proven successful in the clinic but still face significant challenges due to the elaborate and expensive

engineering and manufacturing of T cells. Tidal Therapeutics has developed a new technology that allows the generation of CAR T cells directly *in vivo*. The technology uses mRNA, formulated in lipid nanoparticles that are specifically targeted to circulating T cells to transiently express CARs on the surface.

COMMERCIALIZING *IN VIVO* ENGINEERED CELL THERAPIES

3:50 PANEL DISCUSSION: Promise or Reality? – Delivery Platforms Shaping the Future of *in vivo* Engineering

Moderator: Nicholas A. Boyle, PhD, CEO, Abintus Bio

This panel will ask, what are the major strengths and weaknesses of a chosen gene delivery system and how well that matches the original reasons for choosing it? How are you mitigating technical, regulatory, and commercial risks? What product profiles will best serve patient need? How are key stakeholders such as FDA, payers, investors, and clinicians viewing the promise of *in vivo* genetic medicines? And more!

Panelists:

Haig Aghajanian, PhD, Co-Founder and Vice President of Research, Capstan Therapeutics

Viktor Lemgart, Research Fellow, Tidal Therapeutics, a Sanofi Company

4:20 Close of Day

FRIDAY, MAY 19

7:00 am Registration Open

INTERACTIVE DISCUSSIONS

7:30 Interactive Discussions with Continental Breakfast

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

ADVANCES IN CELLULAR ENGINEERING AND DELIVERY

8:25 Chairperson's Remarks

Bakul Gup, PhD, CEO, Immtune Therapies

8:30 Tuning the T Cell Synapse for Logic-Gated CAR Behavior

Timothy Riley, PhD, Senior Scientist, A2 Biotherapeutics

Logic-gated, two receptor systems amplify many of the challenges associated with CAR design. Here, we leverage concepts from the kinetic segregation model to design a tuneable CAR platform (Tmod) for optimal T cell activation and inhibition. Furthermore, by rationally integrating structural differences between activator and blocker targets, the Tmod platform is broadly applicable to a wide variety of therapeutic indications.

9:00 Generation of CAR T Cells *in vivo* Using Nanoparticles

Bakul Gup, PhD, CEO, Immtune Therapies

ImmTune is developing a delivery technology, which allows us to safely, and effectively deliver genetic cargoes to targeted cells directly inside patients. This in-body generation of therapeutically active cells is cheaper and produces more effective and longer-lasting curative products.

9:30 *In vivo* Programming with MT-302

Thomas E. Prod'homme, PhD, Vice President, Translational Research, Myeloid Therapeutics

Myeloid's novel *in vivo* engineering platform specifically targets and activates myeloid cells to elicit broader anti-tumor adaptive immunity. Through this approach, Myeloid demonstrates that delivery of lipid-nanoparticles (LNPs) encapsulating mRNA results in selective uptake and expression by myeloid cells *in vivo*, leading to potent tumor killing in multiple cold tumor models. These data demonstrate the potential for Myeloid's technology to program cells directly *in vivo*.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Networking Coffee Break

11:00 Bispecific RNA Nanoparticles Carrying Ligands to Bridge Cancer Cells and T Cells in Therapy

Peixuan Guo, PhD, Sylvan G. Frank Professor & Endowed Chair, Pharmaceutics, Ohio State University

We have constructed many bispecific-RNA nanoparticles harboring ligands, aptamers, cell-binging chemical drugs, or immune-checkpoint-targeting molecules to bind receptors of T cells or cancer cells. RNA's ability to form various 3D configurations allows the creation of bispecific RNA nanoparticles carrying various ligands to bridge cancer cells and T cells in therapy.

11:30 Viral Vectors for *in vivo* Engineering of B and T Cells

Samuel Lai, PhD, Professor, Pharmacoengineering & Molecular Pharmaceutics, University of North Carolina at Chapel Hill

A platform that can selectively transduce specific immune cells *in vivo* can enable a range of personalized cellular and biologics immunotherapy. Towards this goal, our group has employed various principles from molecular biology and pharmaceutics to engineer different viral vector systems that can selectively transduce B and T cells *in vivo* with exceptional fidelity and potency. We will present both published and unpublished data.

12:00 pm Engineering Viral Vectors for Gene Delivery to Antigen-Specific T Cells

Ellen Xu, Graduate Student, Birnbaum Lab, MIT

Selective transduction of cell populations has the potential to unlock a new generation of therapies. We recently developed a novel pseudotyping strategy in which VSVGmut, an affinity-ablated version of the VSVG, is coexpressed with a targeting protein to enable cell-type specific infection. Incorporating a peptide-MHC targeting protein enables antigen-specific infection of T cells, allowing us to pair pMHCs with cognate TCRs and to set the stage for cell-specific gene therapy.

12:30 Close of Next-Generation Immunotherapies Conference

EXPRESSION STREAM
CONFERENCES

MAY 15-16

Difficult-to-Express Proteins

AGENDA

MAY 16-17

Optimizing Protein Expression

AGENDA

MAY 18-19

Protein Production Workflows

AGENDA

EXPRESSION STREAM

Maximizing Quantity and Quality while Minimizing Time and Cost

Meeting industry's growing demands for recombinant protein expression and production requires next-gen strategies and breakthrough research while developing and applying cutting-edge tools and technologies. The Expression Stream 1) explores expression, production, and purification of difficult-to-express proteins 2) examines expression hosts what is the best expression system for expressing your protein of choice? and 3) concludes management strategies of an efficient protein production laboratory. These strategic back-to-back meetings investigate the newest data, innovations, and strategies to make the expression of therapeutic proteins more efficient, effective, and trouble-free.

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MONDAY, MAY 15

7:00 am Registration and Morning Coffee

PRODUCTION OF MEMBRANE PROTEINS

8:20 Chairperson's Opening Remarks

Matthew Coleman, PhD, Senior Scientist & Group Leader, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory

8:30 Production of Human A2AAR in Lipid Nanodiscs for 19F-NMR and Single Molecule Fluorescence Spectroscopy

Matthew T. Eddy, PhD, Assistant Professor, Chemistry, University of Florida, Gainesville

We describe production of human A2A adenosine receptor (A2AAR), a G protein-coupled receptor (GPCR), samples in lipid nanodiscs for both NMR spectroscopy and single molecule fluorescence (SMF) spectroscopy. We explain steps shared between the two sample preparation strategies, including expression and isolation of A2AAR and assembly of A2AAR in lipid nanodiscs and procedures for incorporation of either 19F-NMR or fluorescence probes.

9:00 Applying Nanodisc Technologies for *de novo* Cell-Free Synthesis of Membrane Proteins

Matthew Coleman, PhD, Senior Scientist & Group Leader, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory

We are developing approaches to produce full-length functional forms of recombinant membrane-bound proteins using nanodisc technologies coupled with cell-free co-translation. This approach focuses on utilizing high-density apolipoproteins or styrene-maleic anhydride polymers (SMALPs) or branched polyethylene glycol-based telodendrimers, which can all form nanodisc scaffolds in the presence of phospholipids. Discs range in size from 10-40 nm in diameter and overcome problems associated with poor solubility regarding membrane proteins.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Networking Coffee Break

10:30 FEATURED PRESENTATION: Molecular Engineering of Water-Soluble Integral Membrane Proteins and Their Application

Matthew DeLisa, PhD, Director, Cornell Institute of Biotechnology, Cornell University; Co-Founder, UbiquiTx, Inc.

Integral membrane proteins (IMPs) play crucial roles in all cells and represent attractive pharmacological targets. However, access to these membrane-embedded proteins for basic and applied research is limited by technical difficulties associated with their recombinant expression. In this talk, I will describe a universal strategy called SIMPLEx (solubilization of IMPs with high levels of expression) for topologically converting IMPs into water-soluble proteins, which are expressed solubly with retention of activity.

11:00 The Simplicity and Complexity of T Cell Receptor Signal Spanning Transmembrane Domains

Kristine N. Brazin, PhD, Principal Scientist, Medical Oncology, Dana-Farber Cancer Institute

The aßT cell receptor recognition of peptide presented by major histocompatibility complex molecules leads to intracellular signaling events that activate the T lymphocyte to generate an immune system response against virally-infected or cancerous cells. It is critical to understand these TCR processes to uncover T cell-specific therapeutics. Thus, innovative methodologies have been developed to produce the TCR transmembrane proteins to gain insight into their role in TCR signal regulation.

11:30 LUNCHEON PRESENTATION I: The Pelican Expression Technology Platform: Robust Biotherapeutic Manufacturing Using *Pseudomonas fluorescens*

Russell Coleman, Director, Strain Engineering, Ligand Pharmacueticals

The Pelican Expression Technology is a robust, validated, cost-effective and scalable platform for recombinant protein production, and is especially well-suited for complex, large-scale protein production where traditional systems are not suitable. An overview of how this Pseudomonas-based expression platform was developed specifically for recombinant protein production will be presented.

12:00 pm LUNCHEON PRESENTATION II: Overcoming Challenges in the Production and Biophysical Characterization of Difficult Protein Reagents

Deborah Moore-Lai, Senior Director of Protein Development, R&D Leadership, abcam

More than ever, speed and quality are of utmost importance in reagent generation for early stage research and drug discovery. Generating high-quality reagents requires time, resources and an array of protein production methods. Scientists at Abcam have developed a large toolbox of techniques, including multiple expression systems and a complimentary suite of bioanalytical characterization methods. The talk will highlight the robustness of the platforms generating commercial reagents meeting stringent release criteria.

INTERACTIVE DISCUSSIONS

12:30 Find Your Table and Meet Your Moderator

12:45 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

1:30 Session Break

MEMBRANE PROTEIN TARGETS

1:45 Chairperson's Remarks

Matthew DeLisa, PhD, Director, Cornell Institute of Biotechnology, Cornell University; Co-Founder, UbiquiTx, Inc.

1:50 Expression, Purification, and Characterization of Human Membrane Proteins for Structure-Based Drug Discovery by cryoEM

Scott Jackson, PhD, Senior Research Associate, Molecular Sciences, Astex Pharmaceuticals Ltd.

Astex has a state-of-the-art cryo-EM facility that has opened the door to challenging human membrane protein targets. The reliable production of high-quality functionally relevant protein is essential for the determination of reproducible and meaningful high-resolution liganded structures by single particle cryoEM. I will share our experience in expressing, purifying, and characterizing these challenging membrane protein targets and how this is enabling structure-based drug discovery.

2:20 A Semi-Automated DoE-Based Approach to Accelerate Discovery and Engineering

Eric R Sterner, PhD, Sr Scientist, Biologics Discovery, Merck Research Labs

Large molecule R&D efforts are increasingly shifting to molecules of greater complexity in design, structure, and engineering. To keep pace with the rapid iterative design of these complex molecules, increased throughput and automation-based technologies to deliver

high-quality protein reagents are critical to identifying the best therapeutic candidates in early discovery pipelines. This presentation will focus on efforts to build semi-automated, design-of-experiment based platforms to meet the demands of complex purifications.

2:50 Sponsored Presentation *(Opportunity Available)*

3:20 Networking Refreshment Break

3:50 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

4:10 KEYNOTE PRESENTATION: Advances in CAR T Therapy

Carl H. June, MD, Richard W. Vague Professor in Immunotherapy; Professor of Medicine; Director, Center for Cellular Immunotherapies; Director, Parker Institute for Cancer Immunotherapy, University of Pennsylvania Perelman School of Medicine

Advances in the understanding of basic immunology have ushered in two major approaches for cancer therapy over the past 10 years. The first is checkpoint therapy to augment the function of the natural immune system. The second uses the emerging discipline of synthetic biology and the tools of molecular biology and genome engineering to create new forms of engineered cells with enhanced functionalities.

4:55 KEYNOTE PRESENTATION: The Next Frontier in Machine Learning and Biologics: "Lab in a Loop" Large Molecule Drug Discovery, From Optimization to *de novo* Discovery

John Marioni, PhD, Senior Vice President and Head of Computation, Research and Early Development, Genentech

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

TUESDAY, MAY 16

8:00 am Registration and Morning Coffee

EXPRESSION AND PRODUCTION OF CHALLENGING PROTEINS

8:25 Chairperson's Remarks

Inna Zilberleyb, Scientist 4, Biomolecular Resources, Genentech, Inc.

8:30 Development of mRNA Vaccines and Therapeutics Requires Small- to Mid-Scale Production of Difficult-to-Produce Recombinant Proteins

Ethan Dunn, Manager, Protein Sciences, Moderna, Inc.

Moderna is developing over 40 mRNA vaccines and therapeutics, all of which require recombinant proteins. mRNA drug-products can deliver proteins to patients that are otherwise not easily produced on a large-scale (multi-subunit complexes, multi-pass membrane proteins, novel fusions). This mRNA advantage presents unique challenges for laboratory-scale recombinant protein production due to the diversity and complexity of targets. We overcome these challenges by continually building and utilizing a robust expression/purification toolbox.

9:00 End-to-End Multi-Host Screening Platform for Difficult-to-Express Proteins and Protein Complexes

Inna Zilberleyb, Scientist 4, Biomolecular Resources, Genentech, Inc.

Recombinant protein production is an integral part of drug discovery. As therapeutic targets become more challenging, we are constantly looking for ways to triage protein variants more efficiently, while reducing cost and shortening timelines. To reduce the burden on large-scale protein production and to allow for faster triaging of multiple variants, we have developed a mid-scale platform that enables delivery of small quantities of proteins for biochemical and structural screening.

9:30 Presentation to be Announced

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

EXPRESSION AND PRODUCTION OF ENZYMES AND TOXIC PROTEINS

12:40 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:40 Close of Difficult-to-Express Proteins Conference

6:30 Recommended Dinner Short Course

SC7: Use and Troubleshooting of Eukaryotic Expression Systems

**Separate registration required. See short courses page for details.*

> **"I had a brilliant time attending #pegs22. The conference gave me a unique opportunity to network with pharma companies from across the globe as well as hosting a wide range of speakers who are experts in their fields. I found it particularly interesting to see how the renaissance of machine learning in biology is being used to solve many problems including predicting affinity and immunogenicity of antibodies as well as protein structures using RoseTTAFold and Alphafold2."**
>
> **Conor M.,** University of Leeds in collaboration with AstraZeneca

TUESDAY, MAY 16

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing

TOOLS FOR ENHANCING PRODUCTION

2:15 Chairperson's Remarks

Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

2:20 Whole System Engineering: Enhancing Cell Factory Capacities and Vector-Encoded Capacity Utilization

Adam J. Brown, PhD, Associate Professor, Chemical & Biological Engineering, University of Sheffield

This talk will focus on coordinated whole system engineering solutions to enhance both i) critical cellular capacities that underpin CHO cell bioproduction phenotypes (e.g. lipid biosynthesis and mitochondrial capacities) and ii) vector-encoded utilisation of the cell factory's product biosynthesis capacity (i.e. product transcription, translation, translocation, and folding capacities). An engineering toolkit comprising programmable genetic control nodes and synthetic component assemblies of promoters, signal peptides, UTRs, and CDSs will be presented.

2:50 Myth Busted: Flexibility and Robustness of Modern Mammalian Expression Platforms under Various Conditions

Iman Farasat, PhD, Director, Biologics Discovery, Janssen R&D LLC

As newer therapeutic proteins tend to have much greater complexity than traditional mAbs, an expression host toolbox to target production of ~1-10mg of purified material for 100s of molecules is highly desired to accelerate the drug discovery process. Here, we selected three cell lines and collected multidimensional data for over 2000 samples at medium expression scale (~40ml) to evaluate their robustness on our newly designed end-to-end robotic platform.

3:20 Talk Title to be Announced

Speaker to be Announced

FUJIFILM Irvine Scientific

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

4:30 Novel Poly(Beta-Amino-Ester) Compounds to Enhance Transient Transfection Efficiency for Recombinant Protein Expression

Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

Transient transfection is a critical tool for recombinant protein production, as it allows rapid screening for expression without stable integration of genetic material into the target cell genome. Current gold-standard reagents for transient gene transfer are limited by toxicity of the polymer. We developed a panel of cationic polymers, poly(beta-amino ester)s (PBAEs), as reagents for transient transfection and observed enhanced expression of both cytosolic and secreted proteins.

5:00 Transient Transfection and Purification of SARS-CoV-2 Spike Protein from Mammalian Cells

Priyamvada Acharya, PhD, Associate Professor & Director Structural Biology, Surgery & Biochemistry, Duke University

SARS-CoV-2 spike (S) protein purification can be challenging, with engineered and natural variations often resulting in lower yields. Here, we present methods for producing SARS-CoV-2 S ectodomain, its Receptor Binding Domain (RBD), and N terminal Domain (NTD) by transient transfection in mammalian cells. These methods reproducibly yield high-quality preparations of these S protein domains for use in structural, biochemical, and biophysical studies.

5:30 Optimization of Automated Transient HEK and CHO Production Workflows on Our Rapid Antibody and Protein Therapeutic Omni Robot (RAPTOR) to Reduce Costs, Expedite Production, and Improve Yields

Ayla O. Sessions, PhD, Associate Principal Scientist, Biologics Discovery & Engineering, Merck Research Labs

An integral component in early drug discovery efforts is the rapid expression and purification of recombinant proteins. We have optimized automated HEK and CHO transient expression workflows with non-proprietary reagents to reduce costs, enabling the screening of thousands of biological candidates. We also leverage automated magnetic bead-based technologies for higher-throughput, clog-free purifications which further accelerates fit-for-purpose biologics production on our custom platform: Rapid Antibody and Protein Therapeutic Omni Robot (RAPTOR).

6:00 Close of Day

6:00 Dinner Short Course Registration

6:30 Recommended Dinner Short Course

SC7: Use and Troubleshooting of Eukaryotic Expression Systems

**Separate registration required. See short courses page for details.*

WEDNESDAY, MAY 17

7:30 am Registration and Morning Coffee

CHO CELL LINE ENGINEERING & DEVELOPMENT

8:25 Chairperson's Remarks

Bjørn Voldborg, MSc, Head, National Biologics Facility, DTU Bioengineering, Technical University of Denmark

8:30 KEYNOTE PRESENTATION: Evaluation of Site-Specific Methylation of the CMV Promoter and Its Role in CHO Cell Productivity of a Recombinant Monoclonal Antibody

Susan Sharfstein, PhD, Professor, Nanobioscience, Nanoscale Science and Engineering, SUNY Polytechnic Institute

In this presentation, I will discuss the differences in methylation patterns in various positions along the cytomegalovirus (CMV) promoter driving the expression of monoclonal antibody heavy and light chains in different Chinese hamster ovary clones. Interaction between the methylated regions of transcription-factor binding sites and nuclear proteins influences transcript levels, leading to higher productivity phenotypes.

9:00 Cell Line Development Technologies for Antibody Discovery

Pragya Shah, PhD, Senior Scientist I, Biologics, AbbVie

In this talk, I will be sharing the use of cell lines for antibody drug discovery process across all stages from early exploratory to candidate nomination and selection. I will describe some of the technologies we use at AbbVie to generate stable cell lines for difficult to express proteins and the uses thereof in the antibody screening process.

9:30 Repressing Difficult-to-Express Recombinant Proteins Expression during Stable CHO Pools Selection Increases Their Productivity

Jean-Sebastien Maltais, PhD, Research Officer, Human Health Therapeutics, National Research Council Canada

Many next-generation therapeutics remain intrinsically challenging to produce in CHO cells. We exploited a cumate-inducible CHO platform allowing reduced expression of various classes of r-proteins during selection of stable pools. Fed-batch productions showed that pools generated without cumate (OFF-pools) were significantly more productive. Using an inducible system to minimize r-protein expression during pool selection can contribute to reduce cellular

stresses, including ER stress and metabolic burden, leading to improved productivity.

10:00 A Standardized Affinity Method for Recombinant Protein Purification

Emma Lind, Global Product Manager, Cytiva

An affinity chromatography technology for the purification of any recombinant protein in research and process development workflows. This method allows the resulting pure protein to be in its native and natural state. This will improve workflows for researchers and process developers who purify recombinant proteins.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

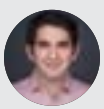
Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

11:30 KEYNOTE PRESENTATION: Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

Rebecca A. Sendak, PhD, Head, Global Large Molecules Research Platform, Sanofi

Addressing disease biology in the clinic with protein therapeutics has become increasingly complex. Turning to innovative and novel scaffolds offers opportunities to tailor therapeutics not previously possible due to advances in host cell engineering and protein design approaches. Designing and developing these modalities requires a next-generation approach as we exploit increased potential design space and also growing data sources to leverage as we invent the next wave of therapeutics.

YOUNG SCIENTIST KEYNOTE



12:15 pm KEYNOTE PRESENTATION: Engineering Prime Editor Proteins for Therapeutic Applications

Andrew V. Anzalone, PhD, Director & Head, Prime Editing Platform, Scientific Co-Founder, Prime Medicine, Inc.

Precision gene editing technologies have the potential to address a wide range of genetic diseases. Prime Editing is a recently developed "search-and-replace" gene editing approach that can precisely perform a wide variety of DNA sequence edits at programmed target sites in human genomes without requiring double-strand DNA breaks or donor DNA templates. I will describe advances to prime editing technology that improve its efficiency, specificity, and capabilities for therapeutic applications.

1:00 Session Break

1:10 Luncheon Presentation I Luncheon Presentation to be Announced

Speaker to be Announced

1:40 Luncheon Presentation II Luncheon Presentation to be Announced

Speaker to be Announced

INTERACTIVE DISCUSSIONS

2:10 Find Your Table and Meet Your Moderator

2:15 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

ALTERNATIVE EXPRESSION AND PRODUCTION HOSTS

3:00 Chairperson's Remarks

J. Christopher Love, PhD, Professor, Chemical Engineering, Massachusetts Institute of Technology

3:05 FEATURED PRESENTATION: AltHost Consortium: Engineering Yeast to Optimize Protein Production and Post-Translational Modifications

J. Christopher Love, PhD, Professor, Chemical Engineering, Massachusetts Institute of Technology

Eukaryotic microorganisms, and specifically yeast, can enable protein production in a fast, efficient, and cost-effective manner. The production of a heterologous protein is shaped by the host's genome, its cultivation conditions, and the target of interest. This talk will present advances in systematic approaches to enhance the protein expression by Komagataella phaffii (aka Pichia) with examples from the Alternative Host Consortium – an MIT/Industry precompetitive research consortium.

3:35 Biotinylated Protein Production in the Baculovirus Expression System

William Romanow, Senior Associate Scientist, Discovery Protein Sciences, Amgen, Inc.

The use of biotin to immobilize a recombinant protein to a surface is useful in the study of binding kinetics (SPR) as well as synthesis and screening of organic molecules (DEL screen). Here we discuss the use of the baculovirus expression system to produce avi-tagged recombinant proteins, *in vitro* and *in vivo* methods of biotinylation, N- and C- tag placement, and the use of orthogonal tags to optimize screening.

4:05 Sponsored Presentation *(Opportunity Available)*

4:35 Ice Cream Break in the Exhibit Hall with Poster Viewing

5:10 Customizing *Escherichia coli* for Recombinant Protein Production

Alexandros Karyolaimos, PhD, Researcher, Department of Biochemistry & Biophysics, Stockholm University

To maximize *E. coli's* capacity for producing recombinant proteins, production strains have to be customized. Therefore, we have developed a platform enabling to rapidly -i- identify the optimal production rate for a protein and -ii- identify and combine genomic modifications promoting protein's stability. Compared to mainstream ***E. coli*** protein production setups, up to 10-fold increases in production yields were achieved for a variety of targets using customized protein production strains.

5:40 Tips and Tricks for Adding *Vibrio natriegens* to Your Lab

William Gillette, PhD, Principal Scientist / Deputy Director, Protein Expression Laboratory, Frederick National Laboratory for Cancer Research

Vibrio natriegens has attracted much attention as an additional expression host for recombinant protein expression, largely due to the allure of shorter fermentations as a result of faster growth rate. While this is a unique and useful feature, there are important considerations in adopting the system that are not well described in the literature. Complications (and our solutions) will be discussed along with examples of proteins that are preferentially produced.

6:10 PANEL DISCUSSION: Employing Cell Factories

Moderator: J. Christopher Love, PhD, Professor, Chemical Engineering, Massachusetts Institute of Technology

Recombinant expression of a protein or a protein complex can be an overwhelming challenge. Countless options for choosing

TUESDAY, MAY 16

6:30 pm Recommended Dinner Short Course

SC7: Use and Troubleshooting of Eukaryotic Expression Systems
**Separate registration required. See short courses page for details.*

THURSDAY, MAY 18

7:30 am Registration and Morning Coffee

WORKFLOW MANAGEMENT: MEETING YOUR CUSTOMERS' NEEDS BY INCREASING PRODUCTION EFFICIENCY

8:25 Chairperson's Remarks
Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

8:30 FEATURED PANEL DISCUSSION: Protein Production Lab Challenges: Methodologies, Strategies, and the Art of Managing Multiple Projects
Moderator: Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific
Protein production laboratories provide crucial support to drug discovery efforts. There are numerous challenges in the effective operation of these critically needed facilities. This panel discussion focuses on the concepts, technologies, and strategies necessary to meet the ever-increasing need for recombinant proteins.
- How to build an effective expression facility
- Prioritizing projects
- Total workflow efficiency
- Engaging and developing team members
- The importance of tech development to long-term success

Panelists:
David Blum, PhD, Director, Bioexpression & Fermentation Facility, Biochemistry & Molecular Biology, University of Georgia
Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory
Bjørn Voldborg, MSc, Head, National Biologics Facility, DTU Bioengineering, Technical University of Denmark
Jessica Williamson, PhD, US Protein Sciences Lead, UCB

9:30 Talk Title to be Announced
Fabian Mohr, PhD, Vice President Research & Development, IBA Lifesciences

9:45 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

WORKFLOW MANAGEMENT: ENHANCING QUALITY CONTROL PROCESSES

10:40 Standardizing Methodologies for High-Quality Recombinant Protein Production
Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory
Generating high-quality, reproducible recombinant proteins is a significant challenge facing the protein production field. The FNL STAR TREC initiative aims to assist in standardization of protein production SOPs and quality control, with the goal of helping to improve reproducibility and minimize financial costs and time wasted in support of early-stage drug discovery efforts. We will explore ways STAR TREC can guide researchers to improve protein quality and ensure consistency across laboratories.

11:10 Industrial Quality and Academic Creativity: How to Get the Best of Both Worlds
Bjørn Voldborg, MSc, Head, National Biologics Facility, DTU Bioengineering, Technical University of Denmark
The National Biologics Facility at the Technical University of Denmark is based on a decade of cutting edge research into the generation of the next generation of CHO cells for industrial production of therapeutics. Throughout the program a strict focus has been on adhering to high quality and documentation levels, while maintaining the flexibility and creativity from the academic setting.

11:40 What Are the Key Considerations for Setting Up and Maintaining an Efficient Protein Production Laboratory?
Richard Altman, MS, Field Application Scientist, Life Science Solutions, Thermo Fisher Scientific

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing

OPTIMIZING WORKFLOWS WITH AUTOMATION

1:15 Chairperson's Remarks
Jessica Williamson, PhD, US Protein Sciences Lead, UCB

1:20 Optimization of Our Rapid Antibody and Protein Therapeutic Omni Robot (RAPTOR) to Improve Throughput
Ayla O. Sessions, PhD, Associate Principal Scientist, Biologics Discovery & Engineering, Merck Research Labs
While advances in lab automation have improved transfection efficiencies and throughput, the purification step is a bottleneck while the cumulative costs of producing thousands of samples can be prohibitive. We have optimized our RAPTOR platform to use cheap, non-proprietary reagents in our methods and leveraged a custom magnetic workflow that captures magnetic affinity beads directly from cell cultures. Optimized elution methods allow for higher protein recovery from these affinity purifications.

1:40 Semi-Automated Multi-Host Mid-Scale Expression and Purification Platform
Inna Zilberleyb, Scientist 4, Biomolecular Resources, Genentech, Inc.
We have built a multi-host mid-scale recombinant protein expression platform to accelerate drug discovery research at Genentech. This platform enables quick triage of challenging proteins and complexes for biochemical and structural screening. Our semi-automated workflow leverages in tip affinity chromatography, integrated with robotic liquid handlers, and SEC to purify multiple samples in parallel. It provides sufficient quantities of proteins for biochemical characterization, assay development, and negative stain EM screens.

2:00 Establishing a Workflow for Modern Mammalian Expression Platforms
Iman Farasat, PhD, Director, Biologics Discovery, Janssen R&D LLC
Transfection and purification are typically the first identified targets as rate-limiting steps for building mammalian-based HT protein expression workflow. However, with increase in number of samples or expression scale, other factors become visible as rate-limiting steps such as safety, inputs/outputs, task scheduling, and data handling. Here, we introduce our end-to-end data and hardware automation platform for expressing 100s of proteins at medium scale (~40ml cell culture) in three cell lines.

2:20 Talk Title to be Announced
Speaker to be Announced

2:50 Networking Refreshment Break

THINK TANKS – IN-PERSON ONLY

3:20 Expression Think Tanks: Reducing Costs for Protein Expression, Challenges, and Opportunities; Collaborate and Communicate

• What challenges have we faced?

• What types of improvements in expression hosts we have discussed here today?

• What might address the future and what is needed?

Join a group (topic of your choice) to share and experience and hear what others have learned:

1) Issues and challenges with current expression systems
2) New expression systems and process improvements
3) Parallel simultaneous testing of expression systems
4) Issues and challenges with end-to-end protein production

3:50 Think Tank Report-Outs: Listen and Learn

During the Think Tank Table discussions, we shared our experiences and working solutions for end-to-end protein production workflows. Now as a collective community, let's hear from the table facilitators as they share key discussion points and strategies, and provide a wrap-up of their table's discussion. What can we take away and apply?

4:20 Close of Day

FRIDAY, MAY 19

7:00 am Registration Open

INTERACTIVE DISCUSSIONS

7:30 Interactive Discussions with Continental Breakfast

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

MEETING PRODUCTION CHALLENGES: DOING MORE WITH LESS

8:25 Chairperson's Remarks

Dominic Esposito, PhD, Director, Protein Sciences, Frederick National Laboratory

8:30 Unique Challenges and Robust Solutions for Protein Production at an mRNA Company

Ethan Dunn, Manager, Protein Sciences, Moderna, Inc.

The Protein Sciences group at Moderna is responsible for delivering recombinant proteins to support the over 40 mRNA development programs and research projects, from infectious and rare diseases to oncology and autoimmunity, from early platform research to mRNA manufacturing. Close collaboration, attention to detail, and a productive protein production team utilizing a robust toolbox is required to deliver. Some of our challenges, learnings, and future directions will be presented here.

8:50 The Daft Punk Approach to Maximizing Protein Production – Faster, Better, Stronger via Leveraging Open Source Robotics, Optimal Scaling, and High Throughput Analytics

Lauren P. Carter, Principal Research Scientist & Engineer, Biochemistry, University of Washington

The Institute for Protein Design has developed powerful processes for computational protein design, most recently the Diffusion model, which combines structural prediction networks with generative diffusion with the ability to generate highly accurate designs optimized for soluble expression. This results in a high numbers of proteins requiring experimental validation. The IPD has developed methods to express, purify, and characterize these designed proteins that can keep pace with design velocity.

9:10 Managing People, Priorities, and Proteins: Challenges and Solutions in Protein Science when Facing Headwinds

Jessica Williamson, PhD, US Protein Sciences Lead, UCB

Protein Sciences at UCB makes non-antibody proteins to support drug discovery research across our global organization. Like many, we have navigated retention challenges with the Great Resignation and work/life balance during the global pandemic. Managing a protein science team not only means balancing resources and producing the highest quality proteins, it also means creating growth opportunities for scientists and innovating new methods and technologies to do more with less.

9:30 Building Your Own Bioreactor to Increase Throughput for Process Development

David Blum, PhD, Director, Bioexpression & Fermentation Facility, Biochemistry & Molecular Biology, University of Georgia

Bioreactors for process development typically cost between $30,000 to $100,000 making acquisition nearly impossible for startups with low cash flow. We are developing a do-it-yourself (DIY) Bioreactor to address this problem. The system utilizes off-the-shelf software from BlueSens and can incorporate a range of parts that are easily accessible reducing the cost by 5 to 10 fold.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Networking Coffee Break

THINK TANKS – IN-PERSON ONLY

11:00 Workflow Think Tanks: Reducing Costs, Challenges, and Opportunities; Collaborate and Communicate

• What challenges have we faced?

• What types of improvements we have discussed here today?

• What might address the future and what is needed?

Join a group to share and experience and hear what others have learned:

1) Workflow vs technology development?
2) Scale-up: when and how to go from research to manufacturing?
3) Doing more with less: how do you test new methods and workflows without blowing up your annual budget?
4) Keeping staff motivated and engaged?
5) Tearing down silos: how do you foster cross-functional collaborations to innovate and improve?

11:45 Think Tank Report Outs: Listen and Learn

During the Think Tank Table discussions, we shared our experiences and working solutions for end-to-end protein production workflows. Now as a collective community, let's hear from the table facilitators as they share key discussion points and strategies and provide a wrap-up of their table's discussion. What can we take away and apply?

12:30 pm Close of Maximizing Protein Production Workflows Conference

ANALYTICAL STREAM
CONFERENCES

MAY 15-16

Digital Integration in Biotherapeutic Analytics

AGENDA

MAY 16-17

Biophysical Methods

AGENDA

MAY 18-19

Characterization for Novel Biotherapeutics

AGENDA

ANALYTICAL STREAM

Best Practices and Solutions for Characterization of Novel Biologics

The popular PEGS Analytical Stream focuses on the application of characterization tools to help gain a detailed knowledge of proteins from discovery through all the stages of development and production. For 2023, this three-meeting stream offers comprehensive individual programs focused on novel therapeutic modalities, biophysical methods and the implementation and impacts of digital tools and big data in this function. The more than fifty conference speakers in this stream will be augmented by focused short courses and hosted roundtable discussions on themes related to this field.

TABLE OF CONTENTS

DIGITAL INTEGRATION IN BIOTHERAPEUTIC ANALYTICS

Best Practices for Adopting and Optimizing Big Data Impacts in the Analytical Function

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC3: *In silico* **and Machine Learning Tools for Antibody Design and Developability Predictions**

**Separate registration required. See short courses page for details.*

MONDAY, MAY 15

7:00 am Registration and Morning Coffee

DATA HANDLING AND CONSOLIDATION

8:20 Chairperson's Remarks

Sukru Kaymakcalan, Director, R&D Information Research, AbbVie, Inc.

8:30 Case Studies in Data Automation at Pfizer

Chris Burns, Senior Manager, Pfizer Inc.

In this talk, two case studies will demonstrate how Pfizer data scientists use the power of automation to analyze and understand the vast quantities of data that are generated on a daily basis. Discussion topics will include why data automation is so useful, data automation strategy, and the impact of two data automation projects that were completed at Pfizer.

9:00 Executing a Digital Strategy for BioTherapeutics Development – Data Lakes Generating Data Flow: A Journey of Standards, Systems, and Culture

Steven J. Mehrman, PhD, Principal Scientist, Pharmaceutical Development, Johnson & Johnson Pharmaceutical R&D

This presentation will highlight Janssen BioTherapeutics development digital maturity journey. Beginning with defining a holistic program partnering with IT to build a scalable, supportable infrastructure and deliver useful tools/apps/data access to project teams.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Networking Coffee Break

10:30 The Lab of the Future – Instrument and Data Flow via AutoLab

Manuela Machatti, Data and Automation Scientist, Roche, Germany

As a central interface in Roche pRED's vision of the lab-of-the-future, AutoLab enables seamless and automated data flow between instruments and various data sources. AutoLab increases research efficiency by providing easy-to-use digital workflows, guiding the scientists in their daily work and automating several time-consuming tasks. The digital representation of lab and data workflows supports FAIRification of data collected along the entire value chain.

11:00 KEYNOTE PRESENTATION: Best Practices for Successful Digital Transformations

Rachel R. Kroe-Barrett, PhD, Executive Director, Biophysics, Boehringer Ingelheim Pharmaceuticals, Inc.

Digital Transformation of a more than 130-year-old pharmaceutical company is no small feat. Integration of well-established data infrastructure with modern tools is highly complex. An even greater challenge is changing the mindset and culture of data-generating scientists. In this talk, we will share our journey thus far from the perspective of Biotherapeutics Discovery at Boehringer Ingelheim.

11:30 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

12:30 pm Find Your Table and Meet Your Moderator

12:45 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

1:30 Session Break

IMPLEMENTATION AND ORGANIZATION

1:45 Chairperson's Remarks

Ruojia Li, PhD, Associate Director, CMC Statistics & Data Science, Bristol Myers Squibb Co.

1:50 Implementation Challenges: Staffing, IT/Data Landscape, and Change Management

Sukru Kaymakcalan, Director, R&D Information Research, AbbVie, Inc.

The success or failure of projects centered around digital transformation can be determined overall by an organization's vision, alignment, resources, and capabilities. Focusing specifically on digital integration in busy research laboratories, we'll explore how these themes manifest and interact to shape the outcomes and impact of projects.

2:20 Implementation of Data Science and Digital Applications in Analytical Development

Ruojia Li, PhD, Associate Director, CMC Statistics & Data Science, Bristol Myers Squibb Co.

Data science and digital applications are being more widely used nowadays to accelerate analytical development. In this talk, a few case studies will be shared to show how CMC statisticians, data scientists, analytical scientists, and IT partners work together to implement solutions that help gain deeper insights, quantify risks, enable quality-by-design and data-driven decisions, and improve efficiency.

2:50 Sponsored Presentation *(Opportunity Available)*

3:20 Networking Refreshment Break

3:50 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

4:10 KEYNOTE PRESENTATION: Advances in CAR T Therapy

Carl H. June, MD, Richard W. Vague Professor in Immunotherapy; Professor of Medicine; Director, Center for Cellular Immunotherapies; Director, Parker Institute for Cancer Immunotherapy, University of Pennsylvania Perelman School of Medicine

Advances in the understanding of basic immunology have ushered in two major approaches for cancer therapy over the past 10 years. The first is checkpoint therapy to augment the function of the natural immune system. The second uses the emerging discipline of synthetic biology and the tools of molecular biology and genome engineering to create new forms of engineered cells with enhanced functionalities.

4:55 KEYNOTE PRESENTATION: The Next Frontier in Machine Learning and Biologics: "Lab in a Loop" Large Molecule Drug Discovery, From Optimization to *de novo* Discovery

John Marioni, PhD, Senior Vice President and Head of Computation, Research and Early Development, Genentech

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

TUESDAY, MAY 16

8:00 am Registration and Morning Coffee

MODELING APPLICATIONS AND IMPACTS

8:25 Chairperson's Remarks

Kevin Metcalf, PhD, Senior Scientist, Merck & Co.

8:30 Integration with Discovery Stage Computational Models and Machine Learning

Kevin Metcalf, PhD, Senior Scientist, Merck & Co.

Model-based prediction of biologics developability will increase speed to clinic. Previous program data can be used to train models but requires data quality control and compensation for biased sampling of sequence space. In my talk, I will describe how we incorporated historical data using data quality control protocols and used sequence similarity clustering to improve prediction of critical quality attributes of monoclonal antibodies.

9:00 Integration of Process Analytical Technology and Model Predictive Control for Bioprocessing

Tony Wang, Senior Manager, Data Sciences, Amgen

As Process Analytical Technology (PAT) matures and becomes more robust, it offers more incentive for companies to integrate PAT into real-time processing. Additionally, when PAT is implemented, it opens up additional opportunity for companies to explore higher level of control. In this presentation, we will share a case study of how PAT can be integrated with Model Predictive Control to improve bioprocess efficiency.

9:30 Adapting Antibody Developability Assays to Machine Learning

Dennis Åsberg, PhD, Senior Scientist, Biophysics and Injectable Formulation, Novo Nordisk A/S, Denmark

In silico assessment of antibody developability has the potential to speed up antibody development, especially lead optimization. However, advances in computational tools such as machine learning are often limited by the lack of suitable training data sets. Here, I present improvements of common antibody developability assays, e.g., AC-SINS, with the aim of enabling optimal data for modelling. Important parameters like dynamic range, calibration, and data processing are discussed.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

PROBLEMS AND SOLUTIONS

11:10 Introduction to Ontology-Based Standards for Biopharmaceutical Manufacturing

Milos Drobnjakovic, Research Associate, Systems Integration, NIST

This talk will address the benefits of utilizing smart data models (ontologies) in transitioning to Biopharma 4.0. First, a comparison between ontologies and traditional data standards will be given. Next, success stories of utilizing ontologies will be outlined, along with the most prominent ontologies in the field. Finally, the application of ontologies to two critical use cases will be demonstrated: cross-domain data integration and improvements in data-driven and hybrid modeling.

11:40 Empowering Analytical Scientists in the Digital Age

Leonard Blackwell, PhD, Associate Director, Strategic Analytics, Analytical Development, Biogen

Analytical scientists have come to expect access to their information much the same way they do with their personal devices. Scientists want to use information to gain insights and make their work empowered by the very information they generate. To meet this demand pharma will need to overcome challenges in data access, data FAIRification, and developing in people the skills necessary to accelerate their science in the digital age.

12:10 pm Structured Content and Data Management to Enable Digital Pharmaceutical Development and Automated Dossier Authoring

Gang Xue, PhD, Senior Scientific Director, Janssen Pharmaceuticals, Inc.

Throughout years of cross-functional collaboration, research and development of each pharmaceutical candidate accumulates tremendous amounts of data. However, due to the segregation and heterogeneity of these data, knowledge extraction has been tedious and limited while dossier authoring becomes an excruciating exercise. Enterprise data lake and ontology enabled data curation and semantic transformation enables structured content and data management that democratizes scientific data, enabling deep data analytics and automated dossier authoring.

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:40 Close of Digital Integration in Biotherapeutic Analytics Conference

6:30 Recommended Dinner Short Course

SC5: Introduction to Gene Therapy Product Manufacturing and Analytics

**Separate registration required. See short courses page for details.*

BIOPHYSICAL METHODS

New Strategies and Technologies for Next-Generation Analyses of Complex Biologics

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing

INCREASING THE THROUGHPUT OF BIOPHYSICAL METHODS

2:15 Chairperson's Remarks

Alexey Rak, PhD, Head, Biostructure and Biophysics, Sanofi, France

2:20 Contemporary Biophysical Methods for More Efficient, Higher Resolution Analysis of Biopharmaceutical Higher Order Structure

Anne Kim, PhD, Senior Principal Scientist and Group Leader, Analytical R&D, Pfizer Inc.

Protein higher order structure (HOS) is an important product quality attribute that governs the structure-function characteristics, safety, and efficacy of therapeutic proteins. In this presentation, we are going to highlight contemporary biophysical methods for more efficient, higher resolution analysis of biopharmaceutical HOS with automated CD, DSC, microfluidic modulation IR, and NMR for protein characterization and comparability/biosimilarity studies for biopharmaceutical process and product development.

2:50 High-Throughput Bioanalytical Analyses of Bispecific Antibodies Using Intact Protein Mass Spectrometry Combined with Affinity Capture, Sample Stream, and FAIMS

Rachel Liuqing Shi, PhD, Principal Scientist, Genentech, Inc.

Here, we present an intact mass spectrometry (MS)-based assay that combines affinity capture with the SampleStream (SS) platform and FAIMS. The captured samples are directly loaded into the SS platform where each sample is injected within 30 seconds. FAIMS further offers improvements in signal-to-noise by separating ions prior to MS analysis. The established methods enable the high-throughput measurement of drug concentration and biotransformation for bispecific antibodies during preclinical studies.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Talk Title to be Announced

Gael Nicolas, Senior Technical Sales Specialist, Sales, Refeyn Ltd

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

EMERGING METHODS AND INSTRUMENTS

4:30 Cryo-Electron Microscopy Revolutionizing Rational Biologics Drug Discovery

Alexey Rak, PhD, Head, Biostructure and Biophysics, Sanofi, France

Structural biology's utility in drug discovery lies in its ability to rationalize targeting approaches for both large and small molecules projects, facilitate project execution, and to make these projects both more time- and cost-effective. Cryo-EM has revolutionized structural biology providing atomic resolution data to elucidate MOA, to map epitope/paratope, to modulate affinity, etc., in just a day's time. A couple of examples on multi-specific drugs and ADCs will be discussed.

5:00 Epitope Mapping of Biologics Using Carbene Chemical Footprinting and Mass Spectrometry

Jason Hogan, PhD, Senior Principal Scientist, Bristol Myers Squibb Co.

Antibody epitope characterization is an important component of therapeutic drug discovery as the binding site directly affects the biological activity. Chemical footprinting with mass spectrometry using carbenes generated from irradiation of diazirine-containing reagents was used to characterize antibody binding sites at the residue level. The structural resolution obtained allows panels of epitope-binned antibodies to be mapped and enables mechanistic understanding of function to support antibody therapeutic lead selection.

5:30 Automated Westerns for Product and Impurity Characterization

Julyana Acevedo, PhD, Scientist II, Analytical Development, Sangamo Therapeutics, Inc.

Gene therapy drugs using adeno-associated viruses (AAV) have been shown to be safe and effective in multiple clinical trials and two commercial products approved in the US. Understanding the physicochemical properties of these gene therapies is critical to patient safety. Here we used a capillary-electrophoresis Western system (CE-Western) to develop assays for characterizing process-related impurities and product attributes.

6:00 Close of Day

6:00 Dinner Short Course Registration

6:30 Recommended Dinner Short Course

SC5: Introduction to Gene Therapy Product Manufacturing and Analytics

**Separate registration required. See short courses page for details.*

WEDNESDAY, MAY 17

7:30 am Registration and Morning Coffee

MASS SPECTROMETRY APPLICATIONS

8:25 Chairperson's Remarks

Yuetian Yan, PhD, Senior Staff Scientist, Regeneron Pharmaceuticals, Inc.

8:30 High-Throughput MS for Biopharma: Developing a Universal Modality and Target Independent Analytical Method and Its Application for Multi-Specific Antibody Characterization and Quantitation

Iain Campuzano, PhD, Senior Principal Scientist, Molecular Analytics, Amgen, Inc.

Reversed-phase liquid chromatographic-mass spectrometry (rpLC-MS) is a universal, platformed, and essential analytical technique within pharmaceutical and biopharmaceutical research. Typical rpLC method gradient times can range from 5-20 mins. As monoclonal antibody (mAb) therapies continue to evolve and bispecific antibodies (BsAbs) become more established, research-stage engineering panels will clearly evolve in size. Therefore, high-throughput (HT) mass spectrometric (MS) and automated deconvolution methods are key for success.

9:00 A Competitive Binding Mass Spectrometry Strategy for High-Throughput Evaluation of Potential Critical Quality Attributes of Therapeutic Monoclonal Antibodies

Yuetian Yan, PhD, Senior Staff Scientist, Regeneron Pharmaceuticals, Inc.

Identification of potential CQAs (pCQAs) that impact mAb target binding is important during the development of therapeutic mAbs. Here, we developed a novel competitive binding-MS strategy that enables high-throughput and multiplexed assessment of pCQAs directly from unfractionated and unstressed mAb drug samples. Specifically, by leveraging the differences in target binding capability under competitive binding conditions, the criticality of multiple mAb attributes can be simultaneously evaluated by quantitative mass spectrometry analysis.

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9:30 KEYNOTE PRESENTATION: Biophysical Characterization of Difficult-to-Express Proteins

Anne Skaja Robinson, PhD, Trustee Professor & Department Head, Chemical Engineering, Carnegie Mellon University

The A2A receptor (A2AR), one of four adenosine G protein-coupled receptor subfamily members, shows exceptional expression and membrane trafficking. We created chimeric A1 and A3 receptors with A2AR C-termini that show improved localization to the plasma membrane and bind to their selective ligands as well as native G proteins. In this talk, we will discuss the binding studies of purified receptors and cognate Gsa that elucidate key protein-protein interactions.

10:00 Talk Title to be Announced

Speaker to be Announced

halo labs

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

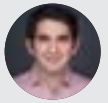
Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

11:30 KEYNOTE PRESENTATION: Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

Rebecca A. Sendak, PhD, Head, Global Large Molecules Research Platform, Sanofi

Addressing disease biology in the clinic with protein therapeutics has become increasingly complex. Turning to innovative and novel scaffolds offers opportunities to tailor therapeutics not previously possible due to advances in host cell engineering and protein design approaches. Designing and developing these modalities requires a next-generation approach as we exploit increased potential design space and also growing data sources to leverage as we invent the next wave of therapeutics.

YOUNG SCIENTIST KEYNOTE



12:15 pm KEYNOTE PRESENTATION: Engineering Prime Editor Proteins for Therapeutic Applications

Andrew V. Anzalone, PhD, Director & Head, Prime Editing Platform, Scientific Co-Founder, Prime Medicine, Inc.

Precision gene editing technologies have the potential to address a wide range of genetic diseases. Prime Editing is a recently developed "search-and-replace" gene editing approach that can precisely perform a wide variety of DNA sequence edits at programmed target sites in human genomes without requiring double-strand DNA breaks or donor DNA templates. I will describe advances to prime editing technology that improve its efficiency, specificity, and capabilities for therapeutic applications.

1:00 Session Break

1:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

2:10 Find Your Table and Meet Your Moderator

2:15 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

ADVANCING HIGHER-ORDER STRUCTURE CHARACTERIZATION

3:00 Chairperson's Remarks

Ivan Budyak, PhD, Director, Analytical Development, Biophysical Characterization, Eli Lilly and Co.

3:05 Applications of NMR and Statistical Methods in Establishing Analytical Comparability and Process Consistency of HOS in mAbs

Igor Dikiy, PhD, Scientist, Protein Biochemistry, Regeneron Pharmaceuticals, Inc.

During development of mAbs, it is essential to establish comparability of key properties, including higher-order structure, following manufacturing process changes. NMR spectroscopy is a non-destructive and data-rich analytical method that can report on these properties. Recent advances in NMR allow reproducible fingerprint spectra of mAbs to be collected. We show phase-appropriate applications of NMR in characterizing mAb comparability and process consistency, using unbiased statistical approaches to work without residue-specific assignments.

3:35 In-Depth Biophysical Characterization of Alpha-Synuclein and Tau Fibrils – Understanding the Critical Properties of Seeding Potent Amyloid Fibrils

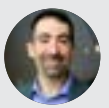
Xue (Snow) Yang, PhD, Senior Scientist, AbbVie, Inc.

Intrinsically disordered proteins aggregation into fibrils is a common pathological feature of neurodegenerative diseases including Alzheimer's Disease and Parkinson's Disease. Recombinant preformed fibrils (PFFs) are a widely used tool to mimic disease initiation and progression. However, little is known about PFFs' polymorphism and their biological behavior. Here, we used a suite of in-depth bioanalytical techniques to understand the critical properties that influence PFFs seeding potency in biological model systems.

4:05 Sponsored Presentation *(Opportunity Available)*

4:35 Ice Cream Break in the Exhibit Hall with Poster Viewing

METHODS AND MODELS FOR PREDICTION OF AGGREGATION AND STABILITY



5:10 KEYNOTE PRESENTATION: Reduction of Therapeutic Antibody Self-Association Using Yeast-Display Selections and Machine Learning

Peter M. Tessier, PhD, Albert M. Mattocks Professor, Pharmaceutical Sciences & Chemical Engineering, University of Michigan

We report a high-throughput protein engineering method for rapidly identifying antibody candidates with both low self-association and high affinity. We conjugate IgGs that strongly self-associate to quantum dots and use these conjugates to enrich yeast-displayed antibody libraries for variants with low levels of immunoconjugate binding. Deep sequencing and machine learning analysis enables identification of extremely rare variants with co-optimized levels of low self-association and high affinity.

5:40 Analytical Ultracentrifugation for Aggregate Quantitation – The Dos (and Some Don'ts)

Ivan Budyak, PhD, Director, Analytical Development, Biophysical Characterization, Eli Lilly and Co.

Analytical ultracentrifugation (AUC) is an important technique that is routinely used for aggregate characterization and quantitation. This presentation will review key considerations for design and execution of a successful AUC experiment as well as discuss potential challenges and pitfalls. Emphasis is placed on the instrumentation and analysis methods used in the pharmaceutical industry for assessing aggregates in monoclonal antibody formulations.

6:10 *In situ* Monitoring of Protein Unfolding and Structural States

Susana Teixeira, PhD, Neutron Scientist, Guest Researcher at NIST, University of Delaware

Biopharma and food proteins are often exposed to high-pressure (HP) and low-temperature conditions during processing and storage. Sub-freezing temperatures, found during lyophilization or freezing, create aggressive environments that pose technical challenges for *in situ* measurements, both in the presence and absence of ice. Pressure-assisted small-angle neutron scattering (SANS) studies on monoclonal antibodies will be presented, and the advantages of SANS for freeze-thaw studies will be highlighted.

6:40 Networking Reception in the Exhibit Hall with Poster Viewing

7:40 Close of Biophysical Methods Conference

> **"I never thought I'd enjoy networking but PEGS is full of welcoming, innovative, accomplished people. It's exciting to learn from them and share ideas."**

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

6:00 Recommended Pre-Conference Short Course

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

6:30 pm Recommended Dinner Short Course

SC5: Introduction to Gene Therapy Product Manufacturing and Analytics

**Separate registration required. See short courses page for details.*

THURSDAY, MAY 18

7:30 am Registration and Morning Coffee

WORKFLOWS AND ASSAYS FOR ASSESSING AND CHARACTERIZING NOVEL MODALITIES

8:25 Chairperson's Remarks

Jianzhong Wen, PhD, Principal Science & Group Leader, Merck & Co., Inc.

8:30 Characterizing the *in vivo* Stability of Atypical Large Molecule Modalities Using Complementary Bioanalytical Tools

Cong Wu, PhD, Senior Scientist, Biochemical & Cellular Pharmacology, Genentech, Inc.

Novel protein modalities are emerging to deliver sophisticated mechanisms of action canonical antibodies cannot. However, little is known about the *in vivo* stability liabilities (i.e.; biotransformation) with these new modalities. A multi-pronged approach was established using LC-MS and capillary electrophoresis-based methods to characterize and quantify biotransformation liabilities and the *in vitro/ex vivo* vs. *in vivo* translatability including but not limited to chemical linker deconjugation, clipping, and amino acid level modifications.

9:00 KEYNOTE PRESENTATION: What's in Your Toolbox? Analytical Strategies for Agile Viral Vector PD

Brenna Kelley-Clarke, Senior Director, Gene Delivery Process & Analytical Development, Bristol Myers Squibb Co.

Viral vectors are used in both gene and cell therapy applications. However, analytical methods for viral vectors are far from plug-and-play. What do you do when you want to launch a new vector program, but you lack basic tools to measure quantity or quality? We'll discuss a virologist's approach to deciding where to save, spend, and splurge when it comes to building analytical tools to enable early vector development.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

NOVEL CONJUGATES

10:40 Characterization of Antibody-Drug Conjugates Created by New Site-Specific Conjugation Methods

Dobeen Hwang, PhD, Research Associate, Rader Lab, University of Florida Scripps Biomedical Research

Antibody-drug conjugates (ADCs) have become clinically and commercially successful cancer treatments that maximize therapeutic potency and limit systemic toxicity through the selective delivery of highly potent drugs. Further broadening the therapeutic index of ADCs, current efforts including our dual variable domain (DVD)-based technology use site-specific and orthogonal bioconjugation methods for single and dual payloads. Their analytical characterization and functional evaluation will be discussed.

11:10 Bioanalytical Strategy and Streamlined Methods to Characterize Novel Drug Conjugates to Understand Efficacy/Toxicity

Jianzhong Wen, PhD, Principal Science & Group Leader, Merck & Co., Inc.

ADCs are amongst the fastest-growing drug classes in oncology evidenced by the boom of recent new approvals. *In vivo* PK, biotransformation, and payload tumor delivery are key information to guide linker drug design and selection. This presentation will share our bioanalytical strategy and methods to characterize novel drug conjugates from *in vivo* samples, and how the data is used to understand efficacy/toxicity to select molecules with optimized therapeutic index.

11:40 Investigation of a Novel Site-Specific Antibody-Drug Conjugate

Young-ok You, PhD, Scientist, Analytical Sciences, Macrogenics

Antibody-drug conjugates (ADCs) have become a promising class of antitumor agents for treating cancer patients. For the ADC conjugations, traditional and site-specific approaches are being considered. To overcome the heterogeneity observed by traditional conjugations, site-specific conjugations are becoming more and more prevalent. They have been shown to eliminate heterogeneity and improve conjugate stability. This presentation will focus on the various analytical techniques used for analyzing a site-specific ADC molecule.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing

RNA THERAPEUTICS, LNPS, AND VIRAL VECTORS

1:15 Chairperson's Remarks

Sharon Polleck, Senior Research Scientist, Analytical R&D, Pfizer Inc.

1:20 Characterization of mRNA Fragments to Evaluate Risk of Truncated or Off-Target Antigen Expression

Thomas F. Lerch, PhD, Senior Director, Analytical R&D, Pfizer Inc.

mRNA vaccines are a newly established class of safe and effective biotherapeutics. The mRNA is manufactured using an *in vitro* transcription process followed by purification, and the drug product process involves formation of mRNA-containing lipid nanoparticles. A comprehensive control strategy ensures consistent quality, and characterization studies strengthen process and product knowledge. This presentation introduces novel approaches to mRNA fragment characterization to evaluate the risk of off-target or truncated antigen translation.

1:50 Analytical Characterization of Therapeutic siRNAs

Daniel Dayeh, PhD, Scientist, Protein Biochemistry, Regeneron Pharmaceuticals, Inc.

RNA interference (RNAi) offers a promising therapeutic approach for the treatment of genetic diseases. Triggered by small interfering RNAs (siRNAs), RNAi silences genes by inhibiting translation of problematic transcripts. Fundamentally distinct from antibodies and small molecules, siRNAs require different strategies to evaluate purity and stability as well as support developmental and regulatory processes. Here, we show a series of analytical methods characterizing the purity and biophysical properties of therapeutic siRNAs.

2:20 Sponsored Presentation *(Opportunity Available)*

2:50 Networking Refreshment Break

3:20 Sedimentation Velocity Analytical Ultracentrifugation (SV-AUC) is a Must-Have, First-Principles Tool in Gene Therapy Characterization

Ronald T. Toth, PhD, Senior Scientist, Characterization, Sanofi

While SV-AUC is revered as a gold-standard technique, it is also maligned as an outdated and cumbersome technique. This talk seeks to introduce the audience to the modern AUC platform and to highlight the unique insights offered by SV-AUC with case studies covering the characterization of AAVs, LNPs, and nucleic acid. Along the way, several myths regarding SV-AUC will be dispelled showing SV-AUC can be a medium-throughput, must-have technique!

3:50 Automated, High-Throughput Analysis of Multiple RNA Physicochemical Attributes

Sharon Polleck, Senior Research Scientist, Analytical R&D, Pfizer Inc.

mRNA-containing lipid nanoparticle (LNP) vaccines allow for a rapid response to seasonal and emerging viral threats given the shortened process/product development timelines. Assay development to measure CQAs like mRNA concentration and average size are rate-limiting steps. We introduce a novel automated analytical technology (commercialized) that assesses mRNA concentration in LNPs and LNP size for 96 samples in ~1 hour, using 2 µL/well and without dyes, which outperforms current methods.

4:20 Close of Day

FRIDAY, MAY 19

7:00 am Registration Open

INTERACTIVE DISCUSSIONS

7:30 Interactive Discussions with Continental Breakfast

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

CHARACTERIZATION FOR EMERGING MODALITIES AND FORMATS

8:25 Chairperson's Remarks

Hilda Hernández-Barry, Scientist, Genentech, Inc.

8:30 Middle-Down and Bottom-Up Analysis of a Tri-Specific Protein Using Electron Activated Dissociation

Jenifer Kaplan, PhD, Principal Scientist I, Novartis Institutes for Biomedical Research

Mass spectrometry is part of the traditional toolbox for biotherapeutic characterization. For multi-specific proteins, challenges arise when new domains contain complex PTMs or necessary linkers lead to clipping events. Using electron activated dissociation, we are able to characterize clipping events for species annotation and get unambiguous assignment of glycan species using middle-down and bottom-up analysis, respectively, for a more in-depth understanding of our therapeutic candidates.

9:00 Genetically-Encoded Degraders: Beyond Small Molecules for Precision Proteome Editing

Matthew DeLisa, PhD, Director, Cornell Institute of Biotechnology, Cornell University; Co-Founder, UbiquiTx, Inc.

Ubiquibodies are engineered proteins that direct otherwise stable proteins to the proteasome for degradation. Here, I will discuss the design and engineering of novel ubiquibodies based on AI/ML-derived "guide" peptides and "stand-alone" E3 ligases that together enable selective and customizable target degradation. Overall, our results suggest that engineered ubiquibodies are a modular proteome editing technology with the potential to expand the degradable target space for pharmacological modulation of disease-causing proteins.

9:30 Impact of Oxidation, Glycation, and Thermal Stress on the Structure and Function of the Efanesoctocog Alfa (BIVV001) Fusion Protein

Fatemeh Tousi, PhD, Senior Scientist, Bioanalytics, Sanofi

BIVV001, Efanesoctocog alfa, is a novel fusion protein consisting of functional domains of recombinant human FVIII, von Willebrand factor (vWF), half-life extending XTEN, and Fc domain for treatment of hemophilia A. Degradation pathways studies of BIVV001 evaluating oxidation, thermal, and glycation stresses were conducted, followed by characterization using an array of analytical techniques. The study results provided insight into BIVV001 chemical and physical routes of degradation and their functional impact.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Networking Coffee Break

NOVEL METHODS AND INSTRUMENTS

11:00 Utility of SPR Technology in Biotherapeutic Development: Qualification for Intended Use

Wei Wang, PhD, Principal Scientist, Therapeutic Discovery, Amgen, Inc.

Surface plasmon resonance (SPR) has been widely used in biotherapeutic development for decades. However, no systematic study has been performed on how to qualify SPR assays for the various SPR result types need for regulatory documents. This talk will discuss methods and guidelines for SPR assay qualification in various scenarios. We hope our studies can help align SPR applications among the scientific communities involved in drug development.

11:30 Leveraging Biotransformation Information to Engineer the Next-Generation of Novel Therapeutic Modalities

Hilda Hernández-Barry, Scientist, Genentech, Inc.

In recent years, a great percentage of biotechnology and biopharma companies' portfolios have comprised novel protein and antibody-based therapeutics. Developing and optimizing these molecules requires detailed analytical characterization. In our current work, we utilize liquid chromatography coupled with intact or top-down mass spectrometry in order to understand the biotransformation of novel modalities (trimeric Fab, antibody-drug conjugates, VHH), which facilitates the interpretation of *in vivo* findings and (re-)engineering of more stable molecules.

12:00 pm Microfluidic Electrophoresis-Based Detection of dsRNA Contaminants in mRNA Vaccines

Adriana Coll De Pena, Graduate Student, Biomedical Engineering, Tripathi Lab, Brown University

mRNA vaccines are currently at the forefront of the vaccine industry due to their safety, efficacy, and fast turnaround times between pathogen detection and vaccine development. However, proper analytical methods to assess the purity of these samples are still lagging. Here, we propose a tool that can streamline the characterization of mRNA vaccine purity, with a focus on dsRNA contaminants, through the use of microfluidic electrophoresis and differential labeling.

12:30 Close of Summit

IMMUNOGENICITY STREAM
CONFERENCE

MAY 15-16

TS: Intro to Immunogenicity

AGENDA

MAY 16-17

Immunogenicity Assessment and Management

AGENDA

MAY 18-19

TS: Intro to Bioassays

AGENDA

IMMUNOGENICITY STREAM

Strategies and Technologies for Safe and Efficacious Therapeutics

This stream begins with an in-depth introductory training seminar providing a practical and comprehensive overview of immunogenicity. Leading into our Immunogenicity Assessment and Management conference delivering practical case studies on assay development and validation, clinical relevance, drug and target interference, regulatory perspectives, risk factors and management. New challenges posed by novel modalities including cell and gene therapies will be addressed. The conference is followed by an introduction to bioassay design and analysis training seminar including statistical concepts needed for bioassays.

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DAY 1: MONDAY, MAY 15, 2023 8:30 - 3:20 PM | DAY 2: TUESDAY, MAY 16, 2023 8:30 - 1:10 PM

INTRODUCTION TO IMMUNOGENICITY

This 1.5-day training seminar provides a practical, comprehensive overview of immunogenicity – the causes, how to assess, predict and prevent, and what to do if you observe immunogenicity during preclinical, clinical and post-market approval. The seminar begins by detailing the science behind immunogenicity, the latest international Guidance, followed by assay and bioanalytical assessment strategies for traditional and emerging biologics. Other topics include predictive models and reporting immunogenicity.

Instructors:

Chloé Ackaert, PhD, Senior Scientist, Immunogenicity, ImmunXperts, a Q2 Solutions Company

Sofie Pattijn, Founder & CTO, ImmunXperts, a Q2 Solutions Company

Bonnie Rup, PhD, Biotechnology Consultant, Bonnie Rup Consulting

Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, and extensive coverage of the basic science underlying each topic. Experienced Training Seminar instructors offer a mix of formal lectures, interactive discussions, and activities to help attendees maximize their learning experiences. These immersive trainings will be of value to scientists from industry and academic research groups who are entering new fields – and to those working in supporting roles that will benefit from an in-depth briefing on a specific aspect of the industry.

"It was a great experience to be back in-person at PEGS Boston 2022, the presentations were excellent, presenting a lot of novel research and highlighting the fantastic progress being made in biologics/cellular therapies. Highly recommend PEGS for future attendance."

Nathan R., MiroBio

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC3: *In silico* and Machine Learning Tools for Antibody Design and Developability Predictions

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing

RISK ASSESSMENT, MITIGATION, AND TRANSLATION

2:15 Chairperson's Opening Remarks

Timothy Hickling, PhD, Head of Immunosafety, Roche

2:20 Computational and *in vitro* Immunogenicity Strategies for Biotherapeutics and Novel Therapeutic Modalities

Jochem Gokemeijer, PhD, Senior Director, Molecular Discovery Technologies, Bristol-Myers Squibb

Increased complexity and protein engineering of biotherapeutics have increased the potential for human immunogenicity in patients. Comprehensive immunogenicity risk assessment strategies in combination with protein engineering can mitigate these risks resulting in safer and more efficacious therapeutics for patients. Machine learning tools can be used to mine *in vitro* data sets to develop high throughput computational tools to push comprehensive immunogenicity risk assessment earlier into the discovery process.

2:50 De-Risking Strategies and Tools: Simultaneous Humanization, De-Immunization, and Elimination of Chemical Liabilities for Antibody-Based Biologics

Jad Maamary, PhD, Director, immunai

Lead sequence optimization consists of sequential steps addressing efficacy, safety, and developability. However, sequence optimization of one parameter leads to unwanted consequences on the other two resulting in suboptimal drug substances. We present a framework to simultaneously de-risk immunogenic and physico-chemical sequence liabilities while maintaining parental efficacy parameters. This framework employs open source *in silico* tools and is achieved by simultaneous humanization, de-immunization, and sequence optimization of antibody-based biotherapeutics.

3:20 Talk Title to be Announced

Speaker to be Announced

3:35 Sponsored Presentation *(Opportunity Available)*

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

4:30 TO BE CONFIRMED: KEYNOTE PRESENTATION: Innate Immune Response Modulating Impurities Testing for Generics and Biosimilars: Where We Are and What We Are Missing

Daniela Verthelyi, MD, PhD, Chief, Laboratory of Immunology, CDER, FDA

Comparative *in vitro* analytical methods to characterize innate immune response modulating impurities could potentially provide a more robust understanding of immunogenicity risk for generic peptides and biosimilars and help streamline their development. This talk will discuss the risks posed by innate immune response modulating impurities, available assays, and data interpretation, as well as common pitfalls and remaining knowledge gaps.

5:00 Immunogenicity Risk Assessment and Mitigation

Timothy Hickling, PhD, Head of Immunosafety, Roche

THE IMMUNOPEPTIDOME LANDSCAPE

5:30 The Landscape of the MHC II Ligandome

Laura Santambrogio, PhD, Professor, Associate Director, Precision Immunology, Weill Cornell Medicine

I will discuss all the variables which contribute qualitatively and quantitatively, to the composition of the MHC II ligandome. Altogether, ensuring that the immunopeptidome landscape is highly sensitive to any changes in the composition of the intra- and extracellular proteome for a comprehensive survey of the microenvironment for MHC II presentation to CD4 T cells.

6:00 Close of Day

6:00 Dinner Short Course Registration

6:30 Recommended Dinner Short Course

SC8: CAR T Cells: Improving Safety While Retaining Therapeutic Activity

**Separate registration required. See short courses page for details.*

WEDNESDAY, MAY 17

7:30 am Registration and Morning Coffee

CLINICAL RELEVANCE OF ADA

8:25 Chairperson's Remarks

Susan Richards, PhD, FAAPS, Vice President, Translational Medicine and Early Development, Sanofi

8:30 Developing an Integrated Summary of Immunogenicity to Assess Clinical Relevance of ADA/NAb

Susan Richards, PhD, FAAPS, Vice President, Translational Medicine and Early Development, Sanofi

An Integrated Summary of Immunogenicity (ISI) is a component of regulatory dossiers for biopharmaceutical product submissions, facilitating product review, approval, and labeling. A multifactorial approach is required, incorporating immunogenicity risk assessment, bioanalytical strategy, and evaluation of clinical impact of anti-drug antibodies and neutralizing antibodies on pharmacokinetics, clinically relevant biomarkers, efficacy, and safety parameters. This presentation will discuss our experience developing ISIs, including overall strategy and case examples.

9:00 Immune Tolerance and the Dynamics of ADA Responses of Therapeutic Proteins

Theo Rispens, PhD, Head of Lab/PI, Sanquin

ADA responses vary widely not only between different drugs, but also between recipients. Interestingly, it is frequently observed that an ADA response may be transient. Here we discuss examples of such variable responses, the factors contributing to dampening the ADA response, and the clinical significance thereof.

9:30 ADA Results Reporting – A Harmonized Approach

Michele Gunsior, PhD, Senior Director, Astria Therapeutics

The presence of anti-drug antibodies (ADA) is an important factor in contextualizing clinical study data. A cross-industry group established harmonized recommendations and a report template for summarizing the essential aspects of clinical study ADA testing and reporting. The results of the harmonization effects will be presented.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

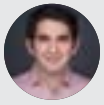
Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

11:30 KEYNOTE PRESENTATION: Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

Rebecca A. Sendak, PhD, Head, Global Large Molecules Research Platform, Sanofi

Addressing disease biology in the clinic with protein therapeutics has become increasingly complex. Turning to innovative and novel scaffolds offers opportunities to tailor therapeutics not previously possible due to advances in host cell engineering and protein design approaches. Designing and developing these modalities requires a next-generation approach as we exploit increased potential design space and also growing data sources to leverage as we invent the next wave of therapeutics.

YOUNG SCIENTIST KEYNOTE



12:15 pm KEYNOTE PRESENTATION: Engineering Prime Editor Proteins for Therapeutic Applications

Andrew V. Anzalone, PhD, Director & Head, Prime Editing Platform, Scientific Co-Founder, Prime Medicine, Inc.

Precision gene editing technologies have the potential to address a wide range of genetic diseases. Prime Editing is a recently developed "search-and-replace" gene editing approach that can precisely perform a wide variety of DNA sequence edits at programmed target sites in human genomes without requiring double-strand DNA breaks or donor DNA templates. I will describe advances to prime editing technology that improve its efficiency, specificity, and capabilities for therapeutic applications.

1:00 Session Break

1:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

2:10 Find Your Table and Meet Your Moderator

2:15 Interactive Discussions

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NEUTRALIZING ANTIBODY CHARACTERIZATION

3:00 Chairperson's Remarks

Michael Partridge, PhD, Director, Bioanalytical Sciences, Regeneron

3:05 NAB Assay Strategies and Mitigation of Matrix Interference

Jason DelCarpini, Associate Director, Quantitative Bioanalytics, Moderna

Determining the neutralizing activity of an anti-drug antibody response is critical to understanding the safety and efficacy profile of a therapeutic. In order to achieve a sensitive assay, the concentrations of reagents in the assay system need to be carefully balanced; excess amounts of target or therapeutic can lead to inaccurate results. We will discuss considerations for mitigating the influence of these interferents during assay development.

3:35 Novel Approach to Overcome Drug Interference in Neutralizing Antibody Assays

Dilki Wickramarachchi, PhD, Associate Principal Scientist, PPDM, Merck & Co.

Interference from free drug in patient serum is a key challenge in assessment of neutralizing antibodies (NAb). PABAD (Precipitation, acid Dissociation and Biotin-drug as Assay Drug), our new approach for assaying NAbs improve the drug tolerance of NAb assay while being compatible with both acid-sensitive and stable NAbs. Minimal requirement of Biotin-drug, unnecessity for magnetic beads, are additional advantages of PABAD that reduce cost and time of NAb assessment.

4:05 Sponsored Presentation *(Opportunity Available)*

4:35 Ice Cream Break in the Exhibit Hall with Poster Viewing

RECENT ADVANCES WITH NOVEL MODALITIES

5:10 Risk Mitigation of Next-Generation CAR T Modalities through Reverse Translation

Vibha Jawa, PhD, Executive Director, Nonclinical Disposition and Bioanalysis, Bristol Myers Squibb Co.

5:40 Assessment of Transgene Immunogenicity in Gene Therapies

Michael Partridge, PhD, Director, Bioanalytical Sciences, Regeneron

Discussion of gene therapy immunogenicity has focused mainly on anti-AAV antibodies, particularly pre-existing responses. However, the transgene protein may also induce a humoral or cellular immune response. This presentation will discuss the approaches to assessing immunogenicity against the expressed transgene product.

6:10 Immunogenicity Characterization for a Bispecific and ADA

Weiping Shao, PhD, Senior Group Director and Head of US GxP Testing Lab, AstraZeneca

Bispecific antibodies are a novel class of complex molecules. Despite great interest in these new modalities to increase efficacy for treatment of complex diseases, recent clinical data indicate unique development challenges with high immunogenic potential which could potentially cause the failure of clinical program. Here, we present the evaluation of preexisting reactivity, anti-drug antibodies, and domain specificity to understand the immunogenicity response to multiple domain biotherapeutics.

6:40 Networking Reception in the Exhibit Hall with Poster Viewing

7:40 Close of Immunogenicity Assessment and Management Conference

DAY 1: THURSDAY, MAY 18, 2023 8:30 - 11:00 AM | DAY 2: FRIDAY, MAY 19, 2023 8:30 - 12:30 PM

INTRODUCTION TO BIOASSAY DESIGN, DEVELOPMENT, ANALYSIS, VALIDATION, AND MONITORING

This course will build from an introduction to the statistical concepts needed for bioassays (all illustrated with useful and relevant examples) and some review of the properties of bioassays. These inform the choices we make in applying DOE to bioassay development, validation, and monitoring. We will cover ways that strategic assay design considerations support good assay monitoring with graphical and quantitative tools as part of a lifecycle approach.

Instructor:
David Lansky, PhD,
President, Precision Bioassay, Inc.

Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, and extensive coverage of the basic science underlying each topic. Experienced Training Seminar instructors offer a mix of formal lectures, interactive discussions, and activities to help attendees maximize their learning experiences. These immersive trainings will be of value to scientists from industry and academic research groups who are entering new fields – and to those working in supporting roles that will benefit from an in-depth briefing on a specific aspect of the industry.

THERAPEUTICS STREAM
CONFERENCES

MAY 15-16

Emerging Indications for Therapeutic Antibodies

AGENDA

MAY 16-17

mRNA Therapeutics

AGENDA

MAY 18-19

Next-Generation Immunotherapies

AGENDA

THERAPEUTICS STREAM

Dawn of the Age of mRNA and Biotherapeutics for Non-Cancer Indications, and *in vivo* Cell and Gene Therapies

A convergence of factors, including pipeline pressures, technology advances and the imperatives of the COVID-19 pandemic, have combined to make this an exciting time for biotherapeutics. Therapeutic Antibodies are no longer only for cancer, and the pandemic crash-tested and soundly proved the concept of mRNA as a scaffold – validating a flexible platform with applications in both vaccines and therapeutics. The PEGS Therapeutics stream showcases exciting new antibody strategies for therapeutic areas including autoimmunity, cardiovascular and metabolic diseases, infectious diseases and neurodegeneration, and showcases exciting progress in groundbreaking applications of mRNA. The stream concludes with a track on novel immunotherapies and reprogramming the immune system via *in vivo* engineering and delivery.

TABLE OF CONTENTS

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC1: Antibody Drug Discovery: From Target to Lead

**Separate registration required. See short courses page for details.*

MONDAY, MAY 15

7:00 am Registration and Morning Coffee

AUTOIMMUNITY AND INFLAMMATION

8:20 Chairperson's Remarks

Ruud M. De Wildt, PhD, Senior Director & Head of Antibody Lead Discovery, GlaxoSmithKline

8:30 Optimizing C7 Antibodies for High Affinity, Developability, and Functionality for Treatment of Myasthenia Gravis

Ruud M. De Wildt, PhD, Senior Director & Head of Antibody Lead Discovery, GlaxoSmithKline

In this presentation, we will describe complementary methods to improve affinity and developability whilst maintaining function in a panel of C7 antibodies. We identified antibodies that had desired cross-reactive profiles and each had a distinct, novel mechanism of C7 inhibition. The lead antibody was effective in preventing experimental Myasthenia Gravis in rats in both prophylactic and therapeutic dosing regimens.

9:00 Antibody-Based Inhibition of Proteases to Target Inflammatory Diseases

James T. Koerber, PhD, Distinguished Scientist and Group Leader, Antibody Engineering, Genentech, Inc.

Proteases play an essential role in maintaining tissue homeostasis and aberrant activation leads to cancer or inflammatory diseases. The development of selective and potent protease inhibitory antibodies offers tremendous therapeutic potential. I will outline two case studies where we develop inhibitory antibodies with picomolar affinities and new modes of action. We leverage these antibodies to reveal the role of proteases as primary drivers of inflammatory disease in several mouse models.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Networking Coffee Break

10:30 Presentation to be Announced

Benjamin J. Hackel, PhD, Associate Professor, Chemical Engineering & Materials Science, University of Minnesota

Aberrant signaling of the tumor necrosis factor receptor family has significant detrimental effects in multiple disease states. Ligand competition impacts multiple pathways, causing an array of side effects, and is challenged by native potency and high local concentrations. Synthetic scaffolds were engineered to bind receptors (separately TNFR1 and DR5) and inhibit signaling and downstream processes without competing for native ligand binding. Mechanistic impacts of receptor conformation were evaluated.

11:00 KEYNOTE PRESENTATION: The State of the Science in Disease Modeling across Diverse Indications

Alex Zhavoronkov, PhD, Founder & CEO, Insilico Medicine

In this talk, we will present the combinations of several AI approaches for target discovery, protein structure prediction using AlphaFold, and generative chemistry for rapid design of novel drugs. We will present the case of hit identification for CDK20 with no experimentally-derived crystal structure.

11:30 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

12:30 pm Find Your Table and Meet Your Moderator

12:45 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

1:30 Session Break

NEUROLOGY INDICATIONS

1:45 Chairperson's Remarks

Karen Silence, PhD, Head, Preclinical Product Development, ArGEN-X

1:50 Development of ARGX-119, an Agonistic Antibody Targeting MuSK

Karen Silence, PhD, Head, Preclinical Product Development, ArGEN-X

ARGX-119 is an agonistic anti- muscle-specific kinase (MuSK) antibody, derived from the SIMPLE antibody platform, with broad potential in neuromuscular diseases. Congenital myasthenia (CM) is a devastating neuromuscular disease and mutations in DOK7 are a major cause of CM. We developed agonist antibodies against MUSK and show that these antibodies restored neuromuscular synapse formation and prevented neonatal lethality and late-onset disease in mouse model for DOK7 CM.

2:20 Strategies for Selective Targeting of Metalloproteinases Responsible in Neurodegenerative Diseases

Maryam Raeeszadeh-Sarmazdeh, PhD, Assistant Professor, Graduate Program Director, Chemical and Materials Engineering, University of Nevada

Metalloproteinases (MPs) play key physiological and pathological roles in the central nervous system by regulating signaling pathways during neuroinflammation, blood-brain barrier disruption, or synaptic dysfunction which makes them great targets for developing therapeutics for neurodegenerative diseases. Due to multifaceted role of MPs in cellular function, it is desired to use protein engineering approaches to generate inhibitors that inhibit specific MPs upregulated in the brain tissue of AD patients.

2:50 Sponsored Presentation *(Opportunity Available)*

3:20 Networking Refreshment Break

3:50 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

4:10 KEYNOTE PRESENTATION: Advances in CAR T Therapy

Carl H. June, MD, Richard W. Vague Professor in Immunotherapy; Professor of Medicine; Director, Center for Cellular Immunotherapies; Director, Parker Institute for Cancer Immunotherapy, University of Pennsylvania Perelman School of Medicine

Advances in the understanding of basic immunology have ushered in two major approaches for cancer therapy over the past 10 years. The first is checkpoint therapy to augment the function of the natural immune system. The second uses the emerging discipline of synthetic biology and the tools of molecular biology and genome engineering to create new forms of engineered cells with enhanced functionalities.

4:55 KEYNOTE PRESENTATION: The Next Frontier in Machine Learning and Biologics: "Lab in a Loop" Large Molecule Drug Discovery, From Optimization to *de novo* Discovery

John Marioni, PhD, Senior Vice President and Head of Computation, Research and Early Development, Genentech

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing

7:00 Close of Day

TUESDAY, MAY 16

8:00 am Registration and Morning Coffee

OTHER EMERGING INDICATIONS

8:25 Chairperson's Remarks

Ahuva Nissim, PhD, Professor, Antibody and Therapeutic Engineering, William Harvey Research Institute, Queen Mary University of London

8:30 Discovery and Characterization of a Ligand-Selective Anti-Notch2 Antibody for Muco-Obstructive Pulmonary Disorders

Adel ElSohly, PhD, Group Leader, Protein Chemistry, Genentech, Inc.

The Notch pathway is conserved in all metazoans, but safely drugging this target has remained an elusive challenge. Herein we describe the discovery and characterization of a Jag-ligand selective anti-Notch2 antibody that binds a unique epitope on Notch2. We demonstrate this selectivity via systemic administration of this antibody, which causes selective transdifferentiation of the mouse airway without causing DLL-dependent systemic phenotypes.

9:00 Autoantibody and T Cell Responses to Oxidative Post-Translationally Modified Insulin Neoantigenic Peptides in Type 1 Diabetes

Ahuva Nissim, PhD, Professor, Antibody and Therapeutic Engineering, William Harvey Research Institute, Queen Mary University of London

Antibodies specific to oxidative post-translationally modified insulin (oxPTM-INS) are present in most individuals with type 1 diabetes (T1D), even before the clinical onset. We investigated the antibody response to oxPTM-INS neoepitope peptides (oxPTM-INSPs) and evaluated their ability to stimulate humoral and T cell responses in T1D. We combined size-exclusion chromatography, LC-MS/MS, ELISA, and T cells proliferation assays to identify the oxPTM-INSPs that are involved in the immunopathogenesis of T1D.

9:30 Novel Yeast Display Platform Optimizes for Multiple Characteristics in Parallel

Eric Furfine, PhD, Co-CEO & CSO, Mosaic Biosciences, Inc.

A poorly-expressed p95-binding mAb was optimized for nearly an order of magnitude improvement in potency and nearly two orders of magnitude increased expression. Potency of a humanized tyrosine kinase receptor (TKR) mAb with modest cross-reactivity to the murine TKR was improved by nearly two orders of magnitude against both species. A mouse mAb against a soluble extracellular protein was humanized and optimized for potency by approximately two orders of magnitude.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Monoclonal Antibodies, Small Interfering RNAs, and Anti-Sense Oligonucleotides to Treat Hyperlipidemia

Nicholas Marston, MD, Assistant Professor, Medicine, Brigham and Women's Hospital

PCSK9 and ANGPTL3 are two targets that have FDA-approved monoclonal antibodies against them, both causing significant reductions in LDL cholesterol and triglycerides. RNA therapies, including small interfering RNAs (siRNAs) and antisense oligonucleotides (ASOs), work intracellularly to inhibit protein translation. This prevents key proteins of interest, such as PCSK9, ANGPTL3, APOC3, or Lp(a), from being produced in the cell, reducing serum levels by as much as 95%.

11:40 A Novel GIPR Antagonist Antibody and GLP-1 Peptide Conjugate (AMG 133) for Treatment of Obesity

Yuan Cheng, PhD, Senior Principal Scientist, Therapeutic Discovery, Amgen, Inc.

AMG 133 is a novel gastric inhibitory polypeptide receptor (GIPR) antagonistic antibody and GLP-1 peptide conjugate that exhibited remarkable body weight loss and significant improvement of metabolic parameters in preclinical models. In human Phase 1 trial AMG 133 demonstrated weight loss and tolerability. The design, conjugation process, and preclinical activity will be discussed.

12:10 pm *In silico* Design of a Highly Protective Anti-Malarial Antibody

Reda Rawi, PhD, Staff Scientist & Co-Head, Structural Bioinformatics Core, NIH NIAID

We developed a novel *in silico* pipeline to improve antibody functionality by optimizing the binding energy to its target antigen. In a test case, we improved antibody CIS43 which protects against malaria infection for up to 9 months. The best-designed variant, antibody P3-43, showed ~10-fold improvement in protection relative to CIS43. This novel *in silico* pipeline provides a powerful and generally applicable tool to improve antibody functionality.

12:40 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:40 Close of Emerging Indications for Therapeutic Antibodies Conference

6:30 Recommended Dinner Short Course

SC6: Developability of Bispecific Antibodies

**Separate registration required. See short courses page for details.*

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

2:00 Recommended Pre-Conference Short Course

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing

INNOVATING RNA THERAPEUTICS

2:15 Chairperson's Remarks

Nelson Chau, PhD, Senior Vice President, Platform, Orna Therapeutics

2:20 Presentation to be Announced

Nelson Chau, PhD, Senior Vice President, Platform, Orna Therapeutics

2:50 Talk Title to be Announced

Grace Chen, PhD, Assistant Professor, Immunobiology, Yale University

3:20 Sponsored Presentation *(Opportunity Available)*

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

4:30 Circular RNAs: Unexpected Outputs of Many Protein-Coding Genes

Jeremy E. Wilusz, PhD, Associate Professor, Biochemistry & Molecular Biology, Baylor College of Medicine

Circular RNAs are widely generated across eukaryotic genomes. In fact, for some genes, the abundance of the circular RNA exceeds that of the associated linear mRNA by >10-fold. We are developing methods to identify/characterize circular RNAs as well as understand how the spliceosome selects exons for backsplicing. By characterizing these mechanisms in detail and identifying the functions of mature circular RNAs, we aim to reveal novel therapeutic targets and modalities.

5:00 Presentation To Be Announced

5:30 GlycoRNAs: Building a Bridge between RNA Biology and the Cell Surface

Ryan A Flynn, PhD, Assistant Professor, Stem Cell and Regenerative Biology, Boston Children's Hospital

Glycans modify lipids and proteins across all domains of life. RNA is not traditionally thought to be a major target of glycosylation. RNA-glycan conjugates, or glycoRNAs, are present across many tissues. Analysis of living cells revealed that the majority of glycoRNAs were present on the cell surface and can interact with Siglec receptors. New tools and insights into the molecular nature of glycoRNAs will be presented.

6:00 Close of Day

6:00 Dinner Short Course Registration

6:30 Recommended Dinner Short Course

SC5: Introduction to Gene Therapy Product Manufacturing and Analytics

**Separate registration required. See short courses page for details.*

WEDNESDAY, MAY 17

7:30 am Registration and Morning Coffee

BIOANALYTICS AND BIOMARKERS

8:25 Chairperson's Remarks

Darshana Jani, PhD, Head, Global Bioanalytical Sciences, Moderna

8:30 Isotyping Anti-PEG Antibody Responses to mRNA Therapeutics

Jason DelCarpini, Associate Director, Quantitative Bioanalytics, Moderna

Lipid nanoparticles for mRNA vaccines and therapeutics are coated with polyethylene glycol (PEG) to aid in delivery of the mRNA. However, it is widely reported that a high percentage of humans have pre-existing antibodies to PEG. To better understand how pre-existing or treatment boosted anti-PEG antibodies impact delivery of the mRNA, a suite of assays were developed to isotype the anti-PEG antibody response.

9:00 Characterization of Immune Response to mRNA-1230 (Influenza, RSV, and SARS-CoV-2) Vaccine Candidate: A Case Study

Liang Zhu, PhD, Director, Moderna, Inc.

Moderna has launched a respiratory combination vaccine program, mRNA-1230, to target three of the most significant viruses causing respiratory disease in older adults: the SARS-CoV-2 virus, influenza virus, and respiratory syncytial virus (RSV). This case study describes clinical assays developed to characterize the immune responses to various strains of the three viruses with a focus on the qualification strategy and results.

9:30 Model-Informed Development of RNA Medicines

Husain Attarwala, PhD, Vice President, DMPK and Clinical Pharmacology, Stealth NewCo.

The role of pharmacometrics or modeling and simulation in the development of siRNA therapeutics and mRNA vaccines will be presented. The session will include the following topics:

- ?Translational modeling approaches for siRNA and mRNA therapeutics
- Modeling and simulation approaches for Phase III dose selection of siRNA therapeutics and mRNA vaccines
- Dose selection for special cases-- dose modeling for mRNA cancer vaccine and pediatric vaccine dose selection

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing

11:10 Transition to Plenary Keynote Session

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

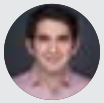
Maria Wendt, PhD, Head, Biologics Research US & Global Head, Digital Biologics Platform (ML/AI), Large Molecule Research, Sanofi

11:30 KEYNOTE PRESENTATION: Advancing Innovative Biologics Modalities from Research to Clinical Application – Novel Platforms, Automation, and Computation

Rebecca A. Sendak, PhD, Head, Global Large Molecules Research Platform, Sanofi

Addressing disease biology in the clinic with protein therapeutics has become increasingly complex. Turning to innovative and novel scaffolds offers opportunities to tailor therapeutics not previously possible due to advances in host cell engineering and protein design approaches. Designing and developing these modalities requires a next-generation approach as we exploit increased potential design space and also growing data sources to leverage as we invent the next wave of therapeutics.

YOUNG SCIENTIST KEYNOTE



12:15 pm KEYNOTE PRESENTATION: Engineering Prime Editor Proteins for Therapeutic Applications

Andrew V. Anzalone, PhD, Director & Head, Prime Editing Platform, Scientific Co-Founder, Prime Medicine, Inc.

Precision gene editing technologies have the potential to address a wide range of genetic diseases. Prime Editing is a recently developed "search-and-replace" gene editing approach that can precisely perform a wide variety of DNA sequence edits at programmed target sites in human genomes without requiring double-strand DNA breaks or donor DNA templates. I will describe advances to prime editing technology that improve its efficiency, specificity, and capabilities for therapeutic applications.

1:00 Session Break

1:10 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

INTERACTIVE DISCUSSIONS

2:10 Find Your Table and Meet Your Moderator

2:15 Interactive Discussions

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

APPLICATIONS OF RNA MODIFICATION

3:05 Presentation to be Announced

4:20 Sponsored Presentation *(Opportunity Available)*

4:35 Ice Cream Break in the Exhibit Hall with Poster Viewing

5:10 The SMRTs Way to Fix the Heart (Specific Modified mRNA Translational System)

Lior Zangi, PhD, Associate Professor, Department of Medicine, Cardiology and Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai

Chemotherapy leads to loss of cardiomyocytes and leads to heart failure. Therefore, there is a need for therapeutics that can protect cardiomyocytes from cardiotoxic agents. Recently, modified mRNA (modRNA) has emerged as a promising technology for cardiac therapeutics. Using modRNA design, CRISPR technology, and positively charged lipid nanoparticles, we created a cardiomyocytes-specific modRNA translational system that translates exclusively in cardiomyocytes and protects them within minutes after intravenous (IV) injection.

RNA DELIVERY

5:40 Targeted siRNA Nanomedicine for Hepatic and Renal Fibrosis

Hayat Onyuksel, PhD, Professor Emerita, Pharmaceutical Sciences, University of Illinois at Chicago

A novel siRNA nanomedicine specific to connective tissue growth factor (CTGF), a regulator of fibrosis in hepatic and renal cells, is developed. Nanomedicine is targeted to asialoglycoprotein receptors on hepatocytes and renal tubular epithelial cells by surface modification with galactosamine ligand, enhancing the cell uptake. On animals this innovative construct showed long circulation time and high accumulation in hepatic and renal tissues, making it a promising mRNA therapeutic for fibrosis.

6:10 Combinatorial Design of Lipid Nanoparticles for mRNA-Mediated Pulmonary Genome Editing

Bowen Li, PhD, Assistant Professor, Pharmaceutical Sciences, University of Toronto

We describe a high-throughput chemical approach for the synthesis and screening of lipid nanoparticles (LNPs) composed of 720 unique ionizable lipids, which identified key structural features for biodegradable ionizable lipids. The intratracheal administration of lead mRNA-LNP formulations efficiently delivers genes to cells in pulmonary epithelial tissues. The gene editing capabilities were validated using a Cre and CRISPR-Cas9 model, providing a new gateway to treat pulmonary genetic disorders.

6:40 Networking Reception in the Exhibit Hall with Poster Viewing

7:40 Close of mRNA Therapeutics Conference

SUNDAY, MAY 14

1:00 pm - 5:00 pm Main Conference Registration

6:00 Recommended Pre-Conference Short Course

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Separate registration required. See short courses page for details.*

TUESDAY, MAY 16

6:30 pm Recommended Dinner Short Course

SC8: CAR T Cells: Improving Safety While Retaining Therapeutic Activity

**Separate registration required. See short courses page for details.*

THURSDAY, MAY 18

7:30 am Registration and Morning Coffee

THE ERA OF *IN VIVO* CELL ENGINEERING AND DELIVERY

8:25 Chairperson's Remarks

Christian J. Buchholz, PhD, Professor & Head, Molecular Biotechnology & Gene Therapy, Paul Ehrlich Institut

8:30 KEYNOTE PRESENTATION: *In vivo* Engineering Considering Probability of Technical, Regulatory, and Commercial Success

Nicholas A. Boyle, PhD, CEO, Abintus Bio

In vivo genetic medicines are poised to disrupt a range of therapeutic areas. The ideal product profile for these agents include: 1) Safety and tolerability with intravenous administration and flexibility for repeat dosing; 2) Gene delivery to target cells using an off-the-shelf, standardized vehicle; and 3) Scalable manufacturing of purified product with low immunogenicity. Building on lessons learned, this presentation will address approaches to mitigate technical, regulatory, and commercial risks.

9:00 Engineering Retargeted Fusogens for *in vivo* Gene Delivery to T Cells

Jagesh V. Shah, Vice President, Gene Therapy Technologies, Sana Biotechnology

We have developed a novel platform for engineering fusogens to target cellular molecules of choice, thereby enabling *in vivo* cell-specific delivery across many cell types with a fusogen-directed gene therapy vector. *In vivo* generation of CAR T cells, using gene therapy vectors with T cell targeting fusogens for *in vivo* CAR delivery, show promise in preclinical models and may provide broader access to CAR therapies.

9:30 Sponsored Presentation *(Opportunity Available)*

10:00 Coffee Break in the Exhibit Hall with Poster Viewing

10:40 Surface Engineered Gene Vectors for *in vivo* CAR T Cell Generation

Christian J. Buchholz, PhD, Professor & Head, Molecular Biotechnology & Gene Therapy, Paul Ehrlich Institut

Highly effective, yet complex to manufacture, simplifying CAR T cell generation is at the forefront of current research. The vision of generating CAR T cells directly in the patient will heavily rely on vector technology, particularly high selectivity for T lymphocytes. This presentation will discuss different vector platforms, especially focusing on engineered lentiviral and AAV vectors using T cell markers as entry receptors achieved through display of DARPins or scFv.

11:10 Enabling *in situ* Re-Engineering of Cellular Functions

Philip R. Johnson, MD, CEO, Interius Biotherapeutics

The Interius bioplatform is based on an innovative, proprietary lentiviral vector that can be engineered to target, transduce, and reprogram specific cells in the body. This bioplatform has direct applicability for oncologic indications and as an *in vivo* delivery vehicle for gene replacement, nucleic acid editing, and therapeutic protein biosynthesis. Our lead programs are focused on treating hematologic malignancies through *in vivo* generation of tumor-specific CAR T cells.

11:40 *In vivo* Production of Functional CAR T Cells by mRNA Targeted Lipid Nanoparticle

Haig Aghajanian, PhD, Co-Founder and Vice President of Research, Capstan Therapeutics

Using targeted lipid nanoparticles (tLNP), we were able to transiently reprogram T cells *in vivo* by delivering modified mRNA encoding a CAR against fibroblast activation protein (FAP). This treatment resulted in the reduction of cardiac fibrosis and the restoration of cardiac function. The ability to produce transient, functional CAR T cells *in vivo* with mRNA addresses some of the biggest hurdles in cell therapy including manufacturing, scalability, and safety concerns.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing

CELLULAR REPROGRAMMING USING RNA AND LNPs

1:15 Chairperson's Remarks

Nicholas A. Boyle, PhD, CEO, Abintus Bio

1:20 *In situ* CAR Therapy Using oRNA

Robert Mabry, PhD, CSO, Orna Therapeutics

We have developed a novel, synthetic, circular coding RNA platform (oRNA technology) which exhibits significant improvements in production, expression, and formulation compared to mRNAs. Given the successes as well as remaining challenges with CAR T cell therapies, we combined our oRNA technology with novel immunotropic LNPs to create an off-the-shelf "autologous" *in situ* CAR (isCAR) therapy that effectively delivers anti-CD19 CAR to immune cells and regresses tumors *in vivo*.

1:50 *In situ* CAR Therapy Using oRNA CAR T Cells Manufactured Rapidly *in situ* Using Virally Activated Endogenous APC

Larry R. Pease, PhD, Professor, Biochemistry & Molecular Biology & Immunology, Mayo Clinic & Foundation

In situ CAR T cells are generated directly in immune reactive lymph nodes in just 3 days from T cells responding to virus-encoded major histocompatibility alloantigens presented by endogenous APC. Following *in vivo* retargeting with viruses encoding chimeric antigen receptors, the resulting *in situ* CAR T cells are capable of targeting antigen-positive cells systemically in the blood and in a solid tumor setting.

2:20 Talk Title to be Announced

Speaker to be Announced

Alloy Therapeutics

2:50 Networking Refreshment Break

3:20 *In vivo* Reprogramming of CAR T Cells Using Targeted LNPs

Viktor Lemgart, Research Fellow, Tidal Therapeutics, a Sanofi Company

Ex vivo CAR T cell therapies have proven successful in the clinic but still face significant challenges due to the elaborate and expensive

engineering and manufacturing of T cells. Tidal Therapeutics has developed a new technology that allows the generation of CAR T cells directly *in vivo*. The technology uses mRNA, formulated in lipid nanoparticles that are specifically targeted to circulating T cells to transiently express CARs on the surface.

COMMERCIALIZING *IN VIVO* ENGINEERD THERAPIES

3:50 PANEL DISCUSSION: Promise or Reality? – Delivery Platforms Shaping the Future of *in vivo* Engineering

Moderator: Nicholas A. Boyle, PhD, CEO, Abintus Bio

This panel will ask, what are the major strengths and weaknesses of a chosen gene delivery system and how well that matches the original reasons for choosing it? How are you mitigating technical, regulatory, and commercial risks? What product profiles will best serve patient need? How are key stakeholders such as FDA, payers, investors, and clinicians viewing the promise of *in vivo* genetic medicines? And more!

Panelists:

Haig Aghajanian, PhD, Co-Founder and Vice President of Research, Capstan Therapeutics

Viktor Lemgart, Research Fellow, Tidal Therapeutics, a Sanofi Company

4:20 Close of Day

FRIDAY, MAY 19

7:00 am Registration Open

INTERACTIVE DISCUSSIONS

7:30 Interactive Discussions with Continental Breakfast

Interactive Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each discussion will be led by a facilitator who keeps the discussion on track and the group engaged. To get the most out of this format, please come prepared to share examples from your work, be a part of a collective, problem-solving session, and participate in active idea sharing. Please visit the Interactive Discussions page on the conference website for a complete listing of topics and descriptions.

ADVANCES IN CELLULAR ENGINEERING AND DELIVERY

8:25 Chairperson's Remarks

Bakul Gup, PhD, CEO, Immtune Therapies

8:30 Tuning the T Cell Synapse for Logic-Gated CAR Behavior

Timothy Riley, PhD, Senior Scientist, A2 Biotherapeutics

Logic-gated, two receptor systems amplify many of the challenges associated with CAR design. Here, we leverage concepts from the kinetic segregation model to design a tuneable CAR platform (Tmod) for optimal T cell activation and inhibition. Furthermore, by rationally integrating structural differences between activator and blocker targets, the Tmod platform is broadly applicable to a wide variety of therapeutic indications.

9:00 Generation of CAR T Cells *in vivo* Using Nanoparticles

Bakul Gup, PhD, CEO, Immtune Therapies

ImmTune is developing a delivery technology, which allows us to safely, and effectively deliver genetic cargoes to targeted cells directly inside patients. This in-body generation of therapeutically active cells is cheaper and produces more effective and longer-lasting curative products.

9:30 *In vivo* Programming with MT-302

Thomas E Prod'homme, PhD, Senior Director, Immunology, Myeloid Therapeutics

Myeloid's novel *in vivo* engineering platform specifically targets and activates myeloid cells to elicit broader anti-tumor adaptive immunity. Through this approach, Myeloid demonstrates that delivery of lipid-nanoparticles (LNPs) encapsulating mRNA results in selective uptake and expression by myeloid cells *in vivo*, leading to potent tumor killing in multiple cold tumor models. These data demonstrate the potential for Myeloid's technology to program cells directly *in vivo*.

10:00 Sponsored Presentation *(Opportunity Available)*

10:30 Networking Coffee Break

11:00 Bispecific RNA Nanoparticles Carrying Ligands to Bridge Cancer Cells and T Cells in Therapy

Peixuan Guo, PhD, Sylvan G. Frank Professor & Endowed Chair, Pharmaceutics, Ohio State University

We have constructed many bispecific-RNA nanoparticles harboring ligands, aptamers, cell-binging chemical drugs, or immune-checkpoint-targeting molecules to bind receptors of T cells or cancer cells. RNA's ability to form various 3D configurations allows the creation of bispecific RNA nanoparticles carrying various ligands to bridge cancer cells and T cells in therapy.

11:30 Viral Vectors for *in vivo* Engineering of B and T Cells

Samuel Lai, PhD, Professor, Pharmacoengineering & Molecular Pharmaceutics, University of North Carolina at Chapel Hill

A platform that can selectively transduce specific immune cells *in vivo* can enable a range of personalized cellular and biologics immunotherapy. Towards this goal, our group has employed various principles from molecular biology and pharmaceutics to engineer different viral vector systems that can selectively transduce B and T cells *in vivo* with exceptional fidelity and potency. We will present both published and unpublished data.

12:00 pm Engineering Viral Vectors for Gene Delivery to Antigen-Specific T Cells

Ellen Xu, Graduate Student, Birnbaum Lab, MIT

Selective transduction of cell populations has the potential to unlock a new generation of therapies. We recently developed a novel pseudotyping strategy in which VSVGmut, an affinity-ablated version of the VSVG, is coexpressed with a targeting protein to enable cell-type specific infection. Incorporating a peptide-MHC targeting protein enables antigen-specific infection of T cells, allowing us to pair pMHCs with cognate TCRs and to set the stage for cell-specific gene therapy.

12:30 Close of Next-Generation Immunotherapies Conference

SPONSORSHIP & EXHIBIT OPPORTUNITIES

CHI offers comprehensive packages that can be customized to your budget and objectives. Sponsorship allows you to achieve your goals before, during, and long after the event. Packages may include presentations, exhibit space and branding, as well as the use of delegate lists. Signing on early will maximize your exposure to qualified decision-makers and drive traffic to your website in the coming months.

PODIUM PRESENTATIONS

— Available within Main Agenda!

Showcase your solutions to a guaranteed, targeted audience through a 15- or 30-minute presentation during a specific program, lunch, or a pre-conference workshop. Package includes exhibit space, onsite branding, and access to cooperative marketing efforts by CHI. Lunches are delivered to attendees who are already seated in the main session room. Presentations will sell out quickly! Sign on early to secure your talk.

INVITATION-ONLY VIP DINNER/ HOSPITALITY SUITE

Select specific delegates from the pre-registration list to attend a private function at an upscale restaurant or a reception at the hotel. From extending the invitations, to venue suggestions, CHI will deliver your prospects and help you make the most of this invaluable opportunity

ONE-TO-ONE MEETINGS

CHI will set up 6-8 in-person meetings during the conference, based on your selections from the advance registration list. Our staff will handle invites, confirmations and reminders, and walk the guest over to the meeting area. This package also includes a meeting space at the venue, complimentary main-conference registrations, branding, an 8'x10' exhibit space, and more.

EXHIBIT

Exhibitors will enjoy facilitated networking opportunities with qualified delegates, making it the perfect platform to launch a new product, collect feedback, and generate new leads. Exhibit space sells out quickly, so reserve yours today!

ADDITIONAL BRANDING AND PROMOTIONAL OPPORTUNITIES ARE AVAILABLE, INCLUDING:

- Conference Tote Bags
- Literature Distribution (Tote Bag Insert or Chair Drop)
- Badge Lanyards
- Conference Materials Advertisement
- Padfolios and More...

FOR MORE INFORMATION, PLEASE CONTACT:

COMPANIES A-K:

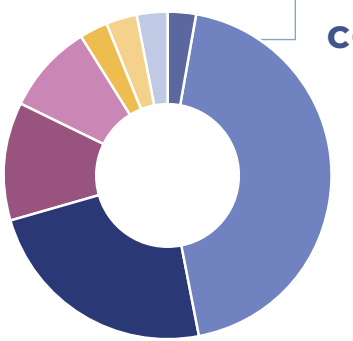
Jason Gerardi | Senior Manager, Business Development
781-972-5452 | jgerardi@healthtech.com

COMPANIES L-Z:

Ashley Parsons | Manager, Business Development
781-972-1340 | ashleyparsons@healthtech.com

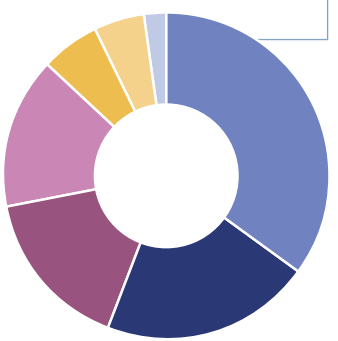
2022 ATTENDEE DEMOGRAPHICS

COMPANY TYPE



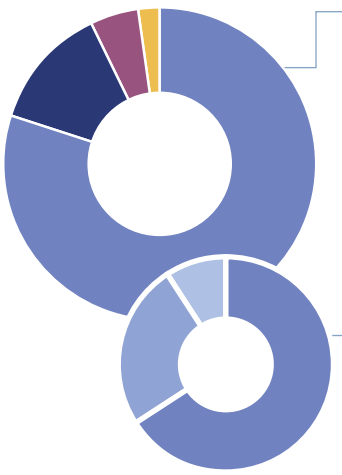
Biotech	67%
Pharma	15%
Academic	8%
Healthcare	4%
Services	3%
Financial	1%
Government	1%
Societies	1%

DELEGATE TITLE



Scientist/Technologist	35%
Sales & Marketing	21%
Executive	16%
Director	15%
Manager	6%
Professor	5%
Assistant	2%

GEOGRAPHIC LOCATION



USA	80%
Europe	13%
Asia	5%
Rest of World	2%

US BREAKDOWN

East Coast	66%
West Coast	25%
Midwest	9%

HOTEL & TRAVEL INFORMATION

Conference Venue:

Hynes Convention Center
900 Boylston St,
Boston, MA 02115

Host Hotel:

Sheraton Boston
39 Dalton Street
Boston, MA 02199

Discounted Room Rate:
$325.00 single/double
Discounted Room Cut-off date: April 17, 2023

Additional Hotel

Marriott Boston Copley Place
110 Huntington Avenue
Boston, MA 02116

Discounted Room Rate:
$329.00 single/double
Discounted Room Cut-off date: April 17, 2023

Visit the Travel page of PEGSummit.com to make your hotel reservations and for additional information.

MEDIA SPONSORS

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DDN

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Web Partners

1stOncology

Big4Bio

CHATS WITH CHAUDHREY

REGISTRATION & PRICING INFORMATION

SHORT COURSE ONLY PRICING

Short Courses will be held in-person only.	Commercial	Academic, Government, Hospital-Affiliated
1 Short Course	$599	$399
2 Short Courses	$999	$599

CONFERENCE PACKAGE PRICING

Training Seminars will be held in-person only.	Commercial	Academic, Government, Hospital-Affiliated
PREMIUM PACKAGE		
Includes access to all conferences & training seminars Monday-Friday. Save 10% off your Short Course registration and receive on-demand access for one year. Excludes short courses.		
Early Registration until February 10	$3,099	$1,549
Advance Registration until March 31	$3,299	$1,699
Registration after March 31 and Onsite	$3,499	$1,799
STANDARD PACKAGE		
Includes access to two conferences and/or training seminars. In addition, you will have on-demand access for one year. Excludes short courses.		
Early Registration until February 10	$2,749	$1,349
Advance Registration until March 31	$2,949	$1,449
Registration after March 31 and Onsite	$3,149	$1,549
BASIC PACKAGE		
Includes access to 1 conference or training seminar. In addition, you will have on-demand access for one year. Excludes short courses.		
Early Registration until February 10	$1,849	$929
Advance Registration until March 31	$1,999	$1,029
Registration after March 31 and Onsite	$2,199	$1,129
POST-EVENT ON-DEMAND ONLY OPTIONS		
Includes post-event recorded access to ALL conference programs. Does not include access to short courses, training seminars, live Q&A, and networking.		
Early Registration until February 10	$2,649	$1,099
Advance Registration until March 31	$2,799	$1,199
Registration after March 31 and Onsite	$2,899	$1,299

GROUP DISCOUNTS ARE AVAILABLE!
Have your colleagues or entire team attend the PEGS Boston.

Purchase a full price registration here and participants from the same organization will receive a 25% discount when registering through the Group Registration page.

For more information on group discounts contact Uma Patel at 781-972-5447 or upatel@healthtech.com.

(Group registration package must be equal to or less than the value of the full price package.)

ALUMNI DISCOUNT - SAVE 20%:
CHI appreciates your participation at its events. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate.

**Alumni, Twitter, LinkedIn, Facebook or any other promotional discounts cannot be combined.*

Each registration includes all conference sessions, posters and exhibits, and access to the on-demand library.

To view our Substitutions/Cancellations Policy, go to healthtech.com/regdetails

Cambridge Healthtech Institute
250 First Avenue, Suite 300, Needham, MA 02494
Phone: 781.972.5400 | Fax: 781-972-5425
Healthtech.com

How to Register: PEGSummit.com

reg@healthtech.com · P: 781.972.5400 or
Toll-free in the U.S. 888.999.6288

PLEASE USE KEYCODE **PEG F** WHEN REGISTERING!

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