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2022 CONFERENCE PROGRAMS

- ENGINEERING
- ONCOLOGY
- BISPECIFICS
- IMMUNOTHERAPY
- EXPRESSION
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- SC SHORT COURSES
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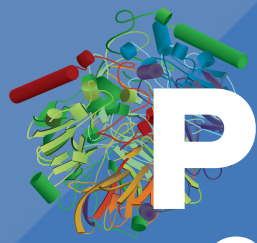

18th ANNUAL

PEGS BOSTON CONFERENCE & EXPO

The Essential Protein Engineering and Cell Therapy Summit

MAY 2-6, 2022 | BOSTON, MA HYNES CONVENTION CENTER & ONLINE

RETURNING IN-PERSON
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Flexible Registration

PLENARY KEYNOTES

Jennifer Cochran, PhD
Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

Roger M. Perlmutter, MD, PhD, Chief Executive Officer, and Chairman, Eikon Therapeutics

YOUNG SCIENTIST KEYNOTE

Xin Zhou, PhD
Assistant Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Principal Investigator, Cancer Biology, Dana-Farber Cancer Institute

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VIEW Driving Clinical Success in Antibody Drug Conjugates

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VIEW Engineering Bispecific Antibodies

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VIEW Optimizing Protein Expression

VIEW Maximizing Protein Production Workflows

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IMMUNOGENICITY

VIEW TRAINING SEMINAR: Introduction to Immunogenicity

VIEW Immunogenicity Assessment and Management

VIEW TRAINING SEMINAR: Introduction to Bioassay Design, Development, Analysis, Validation, and Monitoring

SC SHORT COURSES

Training SEMINARS

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

PEGS Boston: The Essential Protein Engineering and Cell Therapy Summit will be returning to Boston, Massachusetts as an in-person event on May 2-6, 2022, at the Hynes Convention Center with a live virtual feed as well. PEGS Boston is the leading biologics event with comprehensive programming covering all aspects of protein and antibody engineering and cell therapy. PEGS brings together international participants to discuss research and development opportunities, and to make vital connections for their work.

2 Ways to Attend, 1 Shared Experience

Your safety and comfort are our priority.

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.

Our new hybrid event model gives you the option to experience the summit in-person or online, and our flexible registration policy allows you to register with confidence.

VIEW CONFERENCE AT-A-GLANCE

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CONFERENCE AT-A-GLANCE

All Short Courses and Training Seminars are being offered in-person only.*

2022 STREAMS

- ENGINEERING
- ONCOLOGY
- BISPECIFICS
- IMMUNOTHERAPY
- EXPRESSION
- ANALYTICAL
- IMMUNOGENICITY

SUNDAY PM ONLY	MONDAY - TUESDAY AM (MAY 2-3)	TUESDAY AM ONLY	TUESDAY PM - WEDNESDAY (MAY 3-4)	THURSDAY ALL DAY/ FRIDAY MORNING (MAY 5-6)
SC SHORT COURSES *in-person only*	Display of Biologics	SC SHORT COURSES *in-person only*	Engineering Antibodies	Machine Learning Approaches for Protein Engineering
SC1: Antibody Drug Discovery: From Target to Lead	Antibodies for Cancer Therapy	SC6: Introduction to Gene Therapy Product Manufacturing and Analytics	Emerging Targets & Novel Approaches	Driving Clinical Success in Antibody Drug Conjugates
SC2: Introduction to Lipid Nanoparticle Characterization and Formulation	TS: Introduction to Bispecific Antibodies	SC7: Developability of Bispecific Antibodies: Formats and Applications	Advancing Bispecific Antibodies	Engineering Bispecific Antibodies
SC3: Analytical Technologies and Comparability Study of Biotechnology Products	Improving Immunotherapy Efficacy and Safety	SC8: CAR T Cell Therapy from A-Z	Cell-Based Immunotherapies	Next Generation Immunotherapies
SC4: Stromal Biology: from Basic Science to the Clinic	Difficult-to-Express Proteins	SC9: Development of Neutralizing Antibody Assays: Technical Considerations and Case Studies	Optimizing Protein Expression	Maximizing Protein Production Workflows
SC5: Selection Against Post-Translationally Modified Neoepitopes	Characterization for Novel Biotherapeutics	SC10: Use and Troubleshooting of Eukaryotic Expression Systems	Biophysical Methods	Gene Therapy R&D Analytics
*Separate registration required.	TS: Introduction to Immunogenicity	*Separate registration required.	Immunogenicity Assessment	TS: Introduction to Bioassay Design

Training SEMINARS

- Introduction to Bispecific Antibodies
- Introduction to Immunogenicity
- Introduction to Protein Engineering
- Introduction to Structure-Based Drug Design and Development
- Introduction to Immunology for Drug Discovery Scientists

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

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

2022 **PLENARY KEYNOTE SPEAKERS**

MONDAY, MAY 2 AT 4:00 PM

Challenges and Opportunities in Developing Non-Antibody Protein Therapeutics

JENNIFER R. COCHRAN, PhD

Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

Protein therapeutics are dominating the pharmaceutical market, a steadily increasing trend that started with human insulin in 1982. Monoclonal antibodies used to treat cancer, rheumatoid arthritis and other diseases now account for a large share of these efforts, yet the notion that an antibody could be manufactured at scale and delivered to a patient as an effective therapeutic regimen was initially met with much skepticism. My presentation will discuss challenges and opportunities for developing non-antibody engineered protein therapeutics as next-generation medicines.

WEDNESDAY, MAY 4 AT 11:20 AM

Future Directions in Drug Discovery & Development

ROGER M. PERLMUTTER, MD, PhD

Chief Executive Officer, and Chairman of Eikon Therapeutics

The intrinsic complexity of human physiology has generally defeated attempts to model normal cellular functions, meaning that until recently we have had few tools to disentangle the molecular pathology associated with common illnesses. Now, dramatic improvements in instrumentation, automation, and computing provide ways to measure dynamic responses in living cells, and to use these measurements to identify both new disease targets, and new chemical starting points for future medicines. These fundamental advances, coupled with improvements in clinical trial design and execution, together offer hope that the new therapeutics landscape will include compounds with superior therapeutic indices, developed at lower cost. I will illustrate how these opportunities might materialize, drawing examples from current research that integrates image analysis, computation, engineering, molecular biology, and medicinal chemistry.

YOUNG SCIENTIST KEYNOTE | **MONDAY, MAY 2 | 4:55 PM**

Designing Signaling Antibodies to Enact Anti-tumor Responses

XIN ZHOU, PhD

Assistant Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Principal Investigator, Cancer Biology, Dana-Farber Cancer Institute

The world of protein engineering is fascinating, full of possibilities to create molecules with new and desirable structures and functions. My presentation will introduce how we work at the interface of disease biology and protein engineering, designing, constructing, and evolving versatile proteins for the development of next-generation molecular technologies, diagnostics, and therapeutics.

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SHORT **COURSES***

*Separate registration required.

SUNDAY, MAY 1 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 trend 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 actors influencing transfection efficiency and tissue/cell targeting, stability of the nucleic acid load and the effects of lipid nanoparticle composition thereon, characterization of lipid nanoparticles and recent developments in patent landscape.

TUESDAY, MAY 3 6:30-9:00 PM

SC6: Introduction to Gene Therapy Product Manufacturing and Analytics (Dinner Short Course)

Instructors: *Claire Davies, PhD, Associate Vice President, Bioanalytics, Sanofi*

Scott Dooley, 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.

SC7: Developability of Bispecific Antibodies: Formats and Applications (Dinner Short Course)

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 benefit and potentially uncover novel biological mechanisms. However, multiple formats and a tedious candidate selection process to select functional and developable bispecific antibodies makes such programs cumbersome. This short course highlights the rapid growth in the field, therapeutic applications and 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.

Separate registration required. All short courses are offered in-person only.

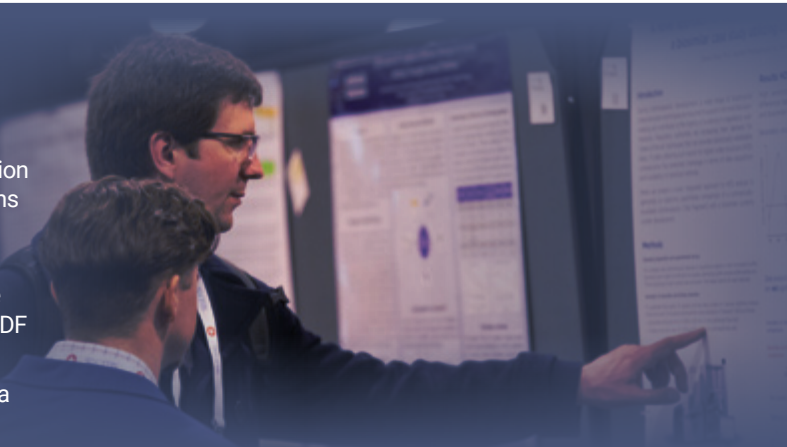
PRESENT A **POSTER** SAVE $50*

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To ensure your poster presentation is included in the conference materials, your full submission must be received, and your registration paid in full by March 25, 2022.

Register and indicate that you would like to present a poster. Once your registration has been fully processed, we will send an email with a unique link and instructions for submitting your abstract and other materials.

Scientific poster presentation materials will include:

- Poster Title
- Text-only Abstract. It can be an in-depth, one-page abstract, or just a short description.
- 3-5 minute voice-over PowerPoint presentation. You may substitute the PowerPoint with a one-page, static PDF of your poster.
- In-Person Attendees will also bring a one-page, static PRINTED poster to the event.



*this discount does not apply to product or service providers

*All Training Seminars are offered in-person only.

MONDAY, MAY 2 8:30 AM-4:00 PM, TUESDAY, MAY 3 8:30 AM-12:30 PM

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

Instructor: *G. Jonah Rainey, PhD, Vice President, Antibody Engineering, AlivaMab Discovery Services*

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: *Bonnie Rup, PhD, Biotechnology Consultant, Bonnie Rup Consulting*

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

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

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.

TS8A: Introduction to Protein Engineering

Instructor: *David Bramhill, PhD, Founder, Bramhill Biological Consulting LLC*

The seminar presents a comprehensive tutorial in the concepts, strategies and latest tools of protein engineering applied to biotherapeutic research and development, particularly antibody-related products. The class is for scientists new to industry or working in support roles, academics, and protein scientists wanting a detailed update on the current state of the field.

TS9A: Introduction to Structure-Based Drug Design and Development

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

Traian Sulea, PhD, Principal Research Officer, Human Health Therapeutics Research Centre, National Research Council Canada

This course offers an introduction to the concepts, strategies and tools of structure-based biologics design. It consists of presentations and demonstrations of the tools used in the field, covering techniques to triage sequences, modulate affinity, create novel constructs along with increasing manufacturability. The course is directed at scientists new to the field and protein engineers wanting an introduction into how structure can aid in guiding experimental design.

TS10A: Introduction to Immunology for Drug Discovery Scientists

Instructor: *Masha Fridkis-Hareli, PhD, Founder & President, ATR LLC*

This seminar covers the fundamentals of human immunology for an audience of scientists working in pharmaceutical and biotech organizations in programs related to immunotherapy. The course covers a historical perspective, basic mechanisms, fundamental concepts and practical approaches to developing therapeutics and their combinations to modulate the immune system. Additionally, the class will offer perspectives on how immune responses can be monitored by assessment of biomarkers and modulated through biopharmaceutical intervention.

TUESDAY, MAY 3 2:15-6:00 PM, WEDNESDAY, MAY 4 8:30 AM-6:00 PM

TS8B: 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 MGH, MIT, 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.

THURSDAY, MAY 5 8:30 AM-4:20 PM, FRIDAY, MAY 6 8:30 AM-12:30 PM

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 design of experiments (DOE) to bioassay development, validation, and monitoring. Examples (mostly from cell-based bioassays; some using robotics) will illustrate strategic ways to design bioassays to make it (relatively) easy to use DOE differently in early bioassay development, when measuring the capability of a bioassay, when improving an existing bioassay, and when doing validation. We will cover ways that these strategic assay design considerations, when combined with good assay analysis methods, also support good assay monitoring with graphical and quantitative tools as part of a lifecycle approach.

ENGINEERING STREAM
CONFERENCES

MAY 2-3

Display of Biologics

AGENDA

MAY 3-4

Engineering Antibodies

AGENDA

MAY 5-6

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, new technologies to accelerate and optimize antibody engineering and the increasing role of machine learning in discovery and engineering. The Stream also explores developments in therapeutic antibodies for neurodegeneration, autoimmunity, cardiovascular disease and infectious diseases. Plan to join these essential tracks and see why PEGS has become the industry's must-attend event in biotherapeutics R&D.

CONFERENCE STREAMS

- ENGINEERING
- ONCOLOGY
- BISPECIFICS
- IMMUNOTHERAPY
- EXPRESSION
- ANALYTICAL
- IMMUNOGENICITY

PEGSBOSTON

SUNDAY, MAY 1

1:00 pm Registration for Pre-Conference Short Courses (Hynes Main Lobby)

2:00 Recommended Pre-Conference Short Course*

SC1: Antibody Drug Discovery: From Target to Lead

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

2:00 Main Conference Registration Open (Hynes Main Lobby)

MONDAY, MAY 2

7:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom B

CONDITIONAL ACTIVATION

8:20 Chairperson's Opening Remarks

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

8:30 Probody Technology to Improve Efficacy and Reduce Toxicity of Cancer Treatment

Madan Paidhungat, PhD, Director, Protein Engineering, CytomX Therapeutics, Inc.

Probody therapeutics (PbTx) are engineered with peptide masks that limit their activity and toxicity in healthy tissue. Protease activity in the tumor microenvironment (TME) removes the mask and activates the PbTx in the TME. Kinetic and mutagenesis studies of peptide masks and PbTx are providing insights into how a mask engages a PbTx and blocks its activity in healthy tissue while permitting rapid activation after protease cleavage in the TME.

9:00 Focused Library Approach to Generate Environment-Responsive Antibodies

Shun Shimizu, PhD, Researcher, Discovery Research, Chugai Pharmaceutical Co. Ltd.

One of the remaining issues of anti-tumor antibody therapeutics is on-target off-tumor toxicity induced by binding to target antigens expressed in normal tissues. To overcome this issue, we have established a novel antibody technology, called Switch-Ig, which binds to antigens in response to extracellular ATP accumulated higher in tumor microenvironment. We will describe the generation of such environment-responsive antibodies with focused library approach.

9:30 An Update on Customized Microfluidics Solutions for Antibody Discovery with Challenging TPPs

Volker Lang, PhD, Managing Director, AbCheck s.r.o.

Novel technology solutions are needed to overcome the challenges of today's drug discovery and development. In particular, tailored solutions beyond antibody-antigen binding affinity criteria are required for the discovery of therapeutic antibodies with challenging Target Product Profiles (TPPs). AbCheck's customized microfluidics solutions address these challenges by meeting the key requirements for potent, function-specific antibodies and enabling functional screening of millions of single cells/day.

10:00 Networking Coffee Break (Pre-function Hall A & Ballroom Pre-Function)

SINGLE-DOMAIN ANTIBODY ENGINEERING PLATFORMS

10:25 Chairperson's Remarks

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

10:30 Sharks as an Alternative Source of Nanobodies

Helen Dooley, PhD, Assistant Professor, Microbiology & Immunology, University of Maryland, Baltimore

Cartilaginous fishes (sharks, skates, rays, and chimera) diverged from the common ancestor with other vertebrates over 450 million years ago and are the oldest lineage to possess immunoglobulins. Among their immunoglobulin repertoire sharks, like camelids, have a heavy chain only isotype (IgNAR) with small, soluble, single-domain variable regions (VNARs). We will discuss the generation, selection, and downstream engineering of VNARs for development as diagnostic and therapeutic agents.

11:00 Discovery and Engineering of Heavy Chain-Only Antibodies Using a Yeast-Based Camelid Immune Library Platform

Noel T. Pauli, PhD, Senior Scientist, Antibody Discovery, Adimab LLC

The unique characteristics of heavy chain-only antibodies (HCAbs) endow these molecules with the potential to target novel epitopes and reduce the complexity of downstream engineering. We have adapted our yeast-based platform to allow for the selection of high-affinity, target-specific HCAbs from immunized camelids. Using this methodology, we have discovered and optimized HCAbs against a diverse range of antigens, including multi-spanning membrane proteins and other difficult targets.

11:30 LUNCHEON PRESENTATION: The Pioneer Library – A New Player in the Therapeutic Antibody Discovery Space

Francisco Ylera, PhD, R&D Team Leader, New Technologies, Bio-Rad Laboratories Inc.

Pioneer is a new phage display Fab antibody library for the selection of therapeutic antibodies. The design incorporates Bio-Rad's extensive experience of phage display to create a superior library. Pioneer is the largest functional Fab antibody library available, and incorporates a novel selection principle. The design, features, and data will be presented for the first time, including SpyDisplay, the new selection system based on SpyTag protein ligation technology.

12:00 LUNCHEON PRESENTATION: LoopSeq—Long-Read Sequencing for Antibody and Protein Engineering

Tuval Ben-Yehezkel, PhD, CEO, Loop Genomics

Loop Genomics has developed a synthetic long read sequencing technology that leverages existing short read sequencers to enable highly accurate single-molecule long-read sequencing on any short-read sequencer. In this talk we will explore LoopSeq and how it is applied to provide additional, previously inaccessible layers of information from short-read sequencers for a wide variety of applications such as phage display, single B-cell discovery and more.

12:30 pm Find Your Table and Meet Your Discussion Moderator

12:45 Interactive Discussions (Ballroom Pre-Function)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

DISPLAY OF BIOLOGICS | CONTINUED

TABLE 1: Breaking Away from Nature: Using *de novo* Designed Proteins as Therapeutics

Chris Bahl, PhD, CSO and Co-Founder, AI Proteins

- Problems that can only be solved using ***de novo*** designed proteins
- Computational ***de novo*** design methods: past, present and future. How and when will machine learning replace the current way that we design proteins ***de novo***
- ***De novo*** designed proteins are an unprecedented modality. What are the challenges of implementing them and how will the unique properties of these proteins help us to we solve them? (e.g. immunogenicity, manufacturing, administration)

CUSTOM-BUILT BIOTHERAPEUTICS

1:45 Chairperson's Remarks

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

1:50 *De novo* Designed Synthetic Mini-Protein Therapeutics

Chris Bahl, PhD, CSO and Co-Founder, AI Proteins

Miniproteins are a powerful yet underutilized therapeutic modality. They are only 30-90 amino acids in length, yet they adopt a folded tertiary structure like a much larger protein; this structure enables miniproteins to bind with high affinity and specificity to their targets. Miniproteins found in nature are very challenging to engineer to bind new targets. We solved this problem using computational ***de novo*** design, finally unlocking miniproteins for therapeutic development.

2:20 Protein-Small Molecule Hybrids for Selective Enzymatic Inhibition

Benjamin J. Hackel, PhD, Associate Professor, Chemical Engineering & Materials Science, University of Minnesota

We have developed a chemical biology platform to engineer protein-small molecule hybrids. Combinatorial libraries of protein variants are displayed on yeast, chemically conjugated with pharmacophore, and sorted for strong, selective binders. We engineered hybrids that exhibit superior enzymatic inhibitory potency and selectivity relative to either protein or pharmacophore alone. Hybrids were engineered with different conjugation sites, linkers, protein sequences, and targets, which demonstrates the breadth of the approach.

2:50 Twist Biopharma: Writing the Future of Biologics

Aaron K. Sato, PhD, Chief Scientific Officer, Twist Bioscience

Twist Biopharma, a division of Twist Bioscience, combines high-throughput DNA synthesis technology with deep expertise in antibody engineering to provide end-to-end antibody discovery solutions. The result is a make-test cycle that yields better antibodies against more diverse and challenging targets. Twist Biopharma will continue to optimize and expand its library synthesis and screening capabilities in partnership with other discovery technologies to further utilize the Twist make-test cycle.

3:20 Networking Refreshment Break (Pre-function Hall A & Ballroom Pre-Function)

3:50 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

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

4:10 KEYNOTE PRESENTATION: Challenges and Opportunities in Developing Non-Antibody Protein Therapeutics

Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

Protein therapeutics are dominating the pharmaceutical market, a steadily increasing trend that started with human insulin in 1982. My presentation will discuss challenges and opportunities for developing non-antibody engineered protein therapeutics as next-generation medicines.

YOUNG SCIENTIST KEYNOTE

4:55 KEYNOTE PRESENTATION: Engineering new "Signaling" Proteins to Enact Anti-tumor Responses

Xin Zhou, PhD, Assistant Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Principal Investigator, Cancer Biology, Dana-Farber Cancer Institute

The world of protein engineering is fascinating, full of possibilities to create molecules with new and desirable structures and functions. My presentation will introduce how we work at the interface of disease biology and protein engineering, designing, constructing, and evolving versatile proteins for the development of next-generation molecular technologies, diagnostics, and therapeutics.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Day

TUESDAY, MAY 3

8:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom B

NON-ANTIBODY PROTEIN ENGINEERING

8:25 Chairperson's Remarks

Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

8:30 GI Device Development in a Few Movements

Giovanni Traverso, PhD, Assistant Professor, Mechanical Engineering, Massachusetts Institute of Technology

Medication non-adherence (non-compliance) represents a major barrier to effective clinical care. In developed nations, only 50% of patients take their medications as prescribed. In his seminar, Dr. Traverso will present a series of novel technologies being developed with the goal to enhance and facilitate medication administration. Specifically, Dr. Traverso will discuss the development of new technologies for the delivery of macromolecules through the oral route.

9:00 Discovery and Versatile Use of Peptide-Based Agonists of Hetero-Dimeric Gamma$_c$ Cytokine Receptors

Ronald W. Barrett, PhD, CEO, Medikine, Inc.

Novel peptides that mimic IL-2 and IL-7 in a variety of cell-based assays and demonstrate desired activity in animal models will be described. The peptides have been successfully incorporated as components of bispecific constructs to add cellular selectivity through cis-activation or to incorporate multiple cytokine activities in a single molecule. Being unrelated in sequence to the natural cytokine, a major advantage is the avoidance of ADAs that neutralize endogenous cytokine.

9:30 Decrypting Cytokine Functional Pleiotropy with Protein Engineering

Ignacio Moraga Gonzalez, PhD, Principal Investigator, Cell Signalling & Immunology, University of Dundee

Cytokines control all immune cell activities. Cytokines dimerize/oligomerize surface receptors to activate signalling. Given the strong crosstalk and shared usage of key components of their signalling pathways, a long-standing question in the field pertains to how functional diversity is achieved by cytokines. I will present recent work from my laboratory addressing how cytokine-receptor binding parameters modify cytokine responses and how this helped to design less toxic cytokine-based therapies.

DISPLAY OF BIOLOGICS | CONTINUED

10:00 Eliciting Anti-Tumor Immunity via Targeted Immunostimulant Therapy

Caitlyn Lee Miller, PhD, Bioengineering, Stanford University

To promote immune activation within tumors, we chemically conjugated a TLR9 agonist to a unique engineered integrin-binding peptide that localizes to various types of solid tumors. Intravenous dosing of this tumor-targeted immunostimulant transforms the immunosuppressive tumor microenvironment into one abundant with activated lymphocytes and results in robust T cell-mediated tumor regression, and in some cases cures, in murine breast and pancreatic cancer models.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

GENERATING SUPERIOR ANTIBODIES

11:05 Chairperson's Remarks

Andrew R.M. Bradbury, PhD, CSO, Specifica, Inc.

11:10 Rapid Mutation and Evolution of Proteins and Antibodies *in vivo*

Chang C. Liu, PhD, Associate Professor, Biomedical Engineering, University of California, Irvine

I will discuss our work on OrthoRep, a highly error-prone orthogonal DNA replication system that drives the rapid continuous mutation and evolution of user-selected genes. I will focus on OrthoRep's application to yeast-display antibody evolution and comment on the value of depth and scale in evolutionary search.

11:40 An Introduction to Biopharmaceutical Informatics

Sandeep Kumar, PhD, Senior Research Fellow, Computational Biochemistry and Bioinformatics, Boehringer Ingelheim Pharmaceuticals

I will provide an introduction to my strategic vision, Biopharmaceutical Informatics, and describe how it can be used to improve the efficiency of biologic drug discovery and development cycles.

12:10 Attobody Platform for Novel Therapeutic Antibody Discovery

Christopher Bunker, PhD, Vice President, Biopharma Business Development, Alamar Biosciences

Higher affinity antibodies may expand the druggable target space and be more efficacious, particularly as agonists or antagonists. Attobodies are bi-epitopic nanobodies using proprietary engineering for superior potency and specificity. We routinely deliver Attobodies with low picomolar affinity without affinity maturation, reducing development time by 3 – 6 months and avoiding off-target risk. Attobodies are small and stable, easily humanized, and easily modified, e.g., Fc fusion, bispecific configuration.

12:40 Drug-Like Antibodies and Other Binders Directly from Semi-Synthetic Naive Libraries

Andrew Bradbury, CSO, Specifica

The Specifica Generation3 Library Platform is based on highly developable clinical scaffolds, into which natural CDRs purged of sequence liabilities have been embedded. The platform directly yields highly diverse, high affinity (20% subnanomolar), developable (>80% lack biophysical liabilities), drug-like antibodies as potent as those from immune sources. This talk will discuss the Generation3 concept and its application to antibodies and VHH scaffolds of clinical interest.

1:10 pm Enjoy Lunch on Your Own

1:40 Close of Display of Biologics

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*

SC7: Developability of Bispecific Antibodies: Formats and Applications

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*
SC1: Antibody Drug Discovery: From Target to Lead
**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

ROOM LOCATION: Ballroom B

ENGINEERING EXTRACELLULAR PROTEIN DEGRADATION

2:15 Chairperson's Opening Remarks
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

2:20 Engineering Antibody-PROTAC Conjugates
Yaxian (Sherry) Zhou, Researcher, Pharmaceutical Sciences, School of Pharmacy, University of Wisconsin, Madison

LYsosome TArgeting Chimera (LYTAC) recently emerged as a promising technology to deliver extracellular protein targets to the lysosome for degradation. Here, we describe the potential of different lysosomal targeting receptors such as asialoglycoprotein receptor (ASGPR), which is specifically expressed on liver cells, for the degradation of extracellular proteins including membrane proteins by a new class of antibody conjugates.

2:50 Inducing Extracellular Protein Degradation
James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco

The cell surface proteome (surfaceome) is the major biohub for cells to engage their extracellular world and represents the primary target for small molecules and virtually all biologics. We have developed a new technology called AbTAC, that is fashioned after intracellular PROTACs, but utilize genetically encoded bi-specific antibodies that recruit transmembrane E3 ligases to membrane targets of interest inducing their degradation. We will discuss their properties and structure activity relationships.

3:20 Featured Poster Presentation: Discovery and Characterization of Intracellularly Functional hnRNPA2/B1 Specific Nanobodies for Live-cell Imaging and Targeted Protein Degradation
Azady Pirhanov, PhD Candidate, Bioengineering & Biomedical Engineering, University of Connecticut

Nanobodies (sdAbs) are antibody fragments derived from heavy-chain-only antibodies. Owing to their small size (~15 kDa) and unique biochemical properties, nanobodies emerged as promising protein based reagents. In this presentation, a high-throughput nanobody discovery platform using yeast surface display libraries will be introduced. Approaches to characterize nanobody stability and specificity along with the live cell imaging and targeted protein degradation applications will be discussed.

3:50 pm Refreshment Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

ENGINEERING FOR EMERGING MODALITIES

4:30 Mechanism-Driven Selection of Multi-Specific Antibody Architecture
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

One of the most advantageous features of antibody-based therapeutics is their diverse and multi-layered mechanisms of action, including activities such as neutralization, signal modulation, and immune recruitment. For each of these various mechanisms, the format of the employed antibody plays a critical role in determining its efficacy. This talk will highlight the effects of antibody geometry on functional performance for several representative multi-specific antibodies that act through distinct therapeutic mechanisms.

5:00 Understanding TCR-pMHC Binding to Guide TCR Mimetic Antibody Design
Matthew Raybould, PhD, Postdoctoral Researcher, Immunoinformatics, University of Oxford, United Kingdom

TCR mimetic (TCRm) antibodies represent a powerful new therapeutic/diagnostic modality in immuno-oncology. By recognizing specific peptide:major histocompatibility complexes (pMHCs), they offer a vector to target cancerous cells with pinpoint accuracy through intracellular biomarkers and an ability to sidestep immunosuppressive microenvironments that downregulate T cell signaling. In this talk, I will share a computational analysis of immunoglobulin:general antigen and immunoglobulin:pMHC complexes which yields guiding principles for future pMHC-specific TCRm design.

5:30 Case Study: Activation of an Antibody by a Single Amino Acid Change in the Framework
Wei-Ching Liang, Senior Principal Scientific Researcher, Antibody Engineering, Genentech, Inc.

Antibody function is typically dictated by the CDRs, while the framework acts as a scaffold for the CDRs to maintain overall structure of the variable domain. Here I will present a dramatic and unexpected discovery during antibody humanization where two variants with identical CDRs exhibited distinct differences in activity. Further structural characterization revealed that single amino acid variation on the heavy chain framework interconverts antibody property in function.

6:00 Close of Day

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*
SC7: Developability of Bispecific Antibodies: Formats and Applications
**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

WEDNESDAY, MAY 4

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom B

TARGETING CHALLENGES

8:25 Chairperson's Remarks
Shohei Koide, PhD, Professor, Biochemistry & Molecular Pharmacology, New York University School of Medicine; Perlmutter Cancer Center, NYU Langone Health

8:30 Targeting Intracellular Oncoproteins with Biologics
Shohei Koide, PhD, Professor, Biochemistry & Molecular Pharmacology, New York University School of Medicine; Perlmutter Cancer Center, NYU Langone Health

Advances in biologics discovery have rendered essentially all cell surface and extracellular proteins druggable. In contrast, there remain many intracellular targets that are undruggable using conventional therapeutic modalities. Intracellular biologics, such as genetically encoded monobodies and monobody-VHL fusions ("bio-degraders"), are invaluable tools to advance mechanistic understanding of target biology and inform drug discovery strategies. This talk will illustrate opportunities and challenges of such approaches with focus on RAS oncoproteins.

9:00 Antibody Discovery Solutions to Complex Membrane Protein Multi-Spanner Targets

Agnieszka Kielczewska, PhD, Director, Research, Antibody Discovery and Screening, Biologics Discovery, Amgen, Canada

Multi-spanner receptors, including GPCRs, constitute a therapeutically interesting yet technically challenging target class for therapeutic antibodies. Factors contributing to the difficulty of targeting these receptors include high homology across species resulting in immune silencing during immunization, relatively low or transient cell-surface expression levels, and difficulty in formulation as a soluble protein applicable to immunogen and screening reagent applications. This talk will cover some examples of approaches to overcome these challenges.

9:30 KEYNOTE PRESENTATION: From Alpha to Epsilon: A Global Consortium Study to Define Variant Resistant Epitopes on SARS-CoV-2 Spike

Kathryn M. Hastie, PhD, Instructor, La Jolla Institute for Immunology

The Coronavirus Immunotherapeutic Consortium (CoVIC) was formed to develop prevention and therapeutic strategies against SARS-CoV-2 that could be mobilized in low- and middle-income countries. By mapping the epitope landscape on the spike protein, CoVIC has identified key communities of receptor-binding domain (RBD)-targeted antibodies that are resistant to major emerging variants. These results provide a framework for selecting antibody treatment cocktails and understanding how viral variants might affect antibody therapeutic efficacy.

10:00 Biophysical Characterization and Developability Workflows in Biotherapeutics Discovery

Teresa Barata, Head of Protein Science Division, Protein Science Division, FlowEighteen38

Discovery and selection of biotherapeutics, as antibodies, is traditionally driven by affinity, PK profiles and potency. Optimization of such properties does not necessarily translate in candidates with favourable biophysical properties. This can lead to longer timelines in CMC and downstream process development. It is, therefore, imperative to include biophysical characterization early in discovery workflows and insure a fit for purpose design of screening cascades for every stage of the discovery process.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

11:10 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

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

11:30 KEYNOTE PRESENTATION: Future Directions in Drug Discovery & Development

Roger M. Perlmutter, MD, PhD, Chairman and CEO, Eikon Therapeutics, Inc.

The intrinsic complexity of human physiology has generally defeated attempts to model normal cellular functions, meaning that until recently we have had few tools to disentangle the molecular pathology associated with common illnesses. Now, dramatic improvements in instrumentation, automation, and computing provide ways to measure dynamic responses in living cells, and to use these measurements to identify both new disease targets, and new chemical starting points for future medicines.

12:15 pm Session Break

ROOM LOCATION: Ballroom B

12:30 LUNCHEON PRESENTATION: Rapid, Function-Forward mAb Discovery against a Cell Surface Target via Concurrent Use of Humanized and Hyperimmune Mice

Tracey Mullen, SVP, Operations, Abveris, A Division of Twist Bioscience

In this presentation, Tracey Mullen, VP/GM of Abveris, a division of Twist Bioscience will discuss:

- Challenges in the therapeutic mAb discovery against cell surface receptors and transmembrane proteins such as GPCR & ion channels
- Overview of key technologies to access development-ready lead candidates for conventionally challenging targets
- A case study of a discovery campaign against a cell surface receptor using both humanized & hyperimmune mice for risk-mitigation & expanded diversity

1:00 LUNCHEON PRESENTATION: The Leap-in Transposase Platform: Past, Present and Future

Oren Beske, Amalgamator of Business and Biology, 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.

1:30 Find Your Table and Meet Your Discussion Moderator

1:35 Interactive Discussions (Exhibit Hall A & B)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 1: Emerging Immunizations in Antibody Discovery

Wei-Ching Liang, Senior Principal Scientific Researcher, Antibody Engineering, Genentech, Inc.

TABLE 2: Developing an Antibody Discovery Pipeline from the Ground Up

Kathryn M. Hastie, PhD, Instructor, La Jolla Institute for Immunology

ENGINEERING FOR NEXT-GENERATION DRUG DELIVERY

2:20 Chairperson's Remarks

Agnieszka Kielczewska, PhD, Director, Research, Antibody Discovery and Screening, Biologics Discovery, Amgen, Canada

2:25 Replicating RNA for the Delivery of Gene-Encoded Antibodies

Jesse H. Erasmus, PhD, Director, Virology, HDT Bio; Assistant Professor, University of Washington School of Medicine

Monoclonal antibody (mAb) products have broad applications in infectious and autoimmune diseases as well as oncology. Alternative approaches to mAb delivery could expand both the applications and use of this impactful technology. We are developing replicating RNA for the delivery of gene-encoded mAbs in order to enable 1) enhanced antibody expression following peripheral administration, including intramuscular injection routes, 2) rapid response to pandemics, and 3) sequence-independent manufacturing processes.

ENGINEERING ANTIBODIES | CONTINUED

2:55 Delivery of IL-15 to PD1+ Lymphocytes for Cancer Immunotherapy

Patrick Holder, PhD, Scientist, Protein Chemistry, Genentech, Inc.

Therapeutic administration of IL-15 to enhance the number and effector status of tumor-reactive lymphocytes is desired for cancer immunotherapy. To accomplish this goal, we designed a recombinant IL-15 that selectively agonizes lymphocytes that express PD1, a marker of T cell activation. In this talk, we will demonstrate how protein engineering enables long half-life, PD1+ selectivity ***in vitro***, and efficacy in a range of tumor models ***in vivo***.

3:25 Development and Novel Administration Approaches of SARS-CoV-2 Neutralizing Antibodies

Mart Ustav, Jr., PhD, CSO, Icosagen Cell Factory OÜ

During this talk I will highlight the potential of Icosagen's proprietary technology platforms in developing highly potent SARS-CoV-2 neutralizing antibodies. Although neutralizing antibodies against SARS-CoV-2 demonstrate efficacy in reducing the development of severe COVID-19, the cumbersome intravenous administration of antibodies limits the effective use of such therapies. Here we demonstrate the potential use of inhalation based delivery of SARS-CoV-2 neutralizing antibodies for generating rapid passive immunity.

3:55 Ice Cream Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

THERAPEUTIC ANTIBODIES FOR NON-CANCER INDICATIONS

4:30 How COVID Learnings Will Impact the Future Course of Drug Development for Infectious Diseases

Gregory C. Ippolito, PhD, Research Associate Professor, Molecular Biosciences, University of Texas at Austin

A compilation of COVID-19 lessons and their application to human immunology, future vaccines, and how we might continue to address the enduring threat of emerging infectious diseases and novel pandemic pathogens shall be discussed.

5:00 Brain Uptake of Brain Shuttle Gantenerumab (RG6102)

Jens Niewoehner, PhD, Matrix Lead, Roche Pharmaceuticals, Germany

Brain uptake of therapeutic antibodies has been reported using different experimental systems and diverse methodologies, but the precise measurement of drug levels in all relevant brain compartments is often hampered by technical difficulties. We present the comprehensive characterization of a Brain Shuttle anti-amyloid antibody in Cynomolgus monkeys, including modeling-supported plasma and brain pharmacokinetics, and provide first evidence for brain uptake in humans.

5:30 Deep Biology Approach for Development of Biotherapeutics for Autoimmunity and Inflammation

Ali Zarrin, PhD, Executive Director, Discovery, TRex Bio

Regulatory T cells (Tregs) control inflammation in a tissue-specific manner, but the unique biology of human tissue Tregs was poorly understood. We developed a high-resolution map of human immune-regulatory pathways in healthy, inflammatory, or cancer tissues. Computational tools paired with rapid functional validation in disease-relevant human Tregs allow us to prioritize pathways for modulation in disease and forms the foundation of our growing pipeline of tissue-Treg-focused therapeutics.

6:00 Networking Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Engineering Antibodies

THURSDAY, MAY 5

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom B

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

8:25 Chairperson's Opening Remarks
Maria Wendt, PhD, Head, Biologics Research US, Sanofi

8:30 KEYNOTE PRESENTATION: Protein Structure Prediction in a Post-AlphaFold2 World
Mohammed AlQuraishi, PhD, Assistant Professor, Systems Biology, Columbia University

In this talk, I will argue that with AlphaFold2, the core problem of static protein structure prediction is in some sense finished, but that further maturation is necessary before structure prediction informs questions beyond those of structure determination itself. I will outline some of these developments highlighting one in particular: the prediction of structure from individual protein sequences, presenting new results on predicting structures of orphan and designed proteins.

9:00 Learned Surface Fingerprints for Protein Function Prediction and Design
Bruno Correia, PhD, Assistant Professor, Laboratory of Protein Design & Immunoengineering, University of Lausanne

A high-level representation of protein structure, the molecular surface, displays patterns of chemical and geometric features that fingerprint a protein's modes of interactions with other biomolecules. We present MaSIF (molecular surface interaction fingerprinting), a conceptual framework based on a geometric deep learning method to capture fingerprints that are important for specific biomolecular interactions. Learned surface fingerprints hold exquisite information that enables us to understand functional features and for *de novo* design.

9:30 Protein Engineering Guided by Accurate *in silico* Modeling of Disulfide Formation and Its Effect on Thermostability
Dmitry Lupyan, PhD, Senior Principal Scientist, Schrödinger

Introducing disulfide bonds into protein has shown to improve protein thermostability and enhance function. Here we use a combination of bioinformatics and structure-based descriptors to predict putative disulfide crosslinking, and use rigorous physics-based methods (FEP+) to interrogate the effect of disulfides on protein thermostability or affinity. We show the approach can predict the effect of disulfide bonds on physical properties and is a valuable tool for *in silico* protein engineering.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

10:40 Computational Design of a Synthetic PD-1 Agonist
Cassie Bryan, PhD, Senior Scientist, Synthetic Biology, Charles Stark Draper Laboratory, Inc.

Using a combination of computation and experiment, we designed a hyperstable 40-residue miniprotein, PD-MP1, with an all-beta interface that specifically binds the T cell receptor PD-1 at the PD-L1 interface. The apo crystal structure shows that the binder folds as designed and trimerization of PD-MP1 resulted in a PD-1 agonist that strongly inhibits T cell activation. Trimeric PD-MP1 has potential for the treatment of autoimmune and inflammatory diseases.

11:10 Learning a Language Spoken by Nature: Protein Language Model, a Useful Tool for Protein Engineering
Yu Qiu, PhD, Senior Principal Scientist, Sanofi Genzyme R&D Center

Natural antibodies are optimized for general "fitness" by evolution and *in vivo* selections. Taking natural protein sequences as a language spoken by nature, learning the underlying "grammars" and "semantics" can help various engineering tasks. We have built protein language models (PLMs) trained on >2 billion natural human antibody sequences. The model showed promising results in predicting affinity, expression, and functional readout when trained and evaluated on retrospective data.

11:40 CO-PRESENTATION: Deep Dive into Machine Learning Models for Protein Engineering
Deeptak Verma, PhD, Senior Scientist, Merck & Co.
Yuting Xu, PhD, Associate Principal Scientist, Biostatistics, Merck Sharp & Dohme Corp.

Recently, there has been an increased interest in using machine learning to assist protein redesign, since prediction models help to virtually screen large amount of novel sequences. However, many state-of-the-art ML models and protein sequence descriptors have not been extensively explored. Our benchmark study suggests that Convolution Neural Networks built with amino acid property descriptors are the most widely applicable to the types of protein redesign problems in the pharmaceutical industry.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing (Exhibit Hall A & B)

RULES FOR DEVELOPABILITY

1:15 Chairperson's Remarks
M. Frank Erasmus, PhD, Head, Bioinformatics, Specifica, Inc.

1:20 Predicting Antibody Developability Profiles through Experimental and *in silico* Approaches
Laurence Fayadat-Dilman, PhD, Executive Director, Protein Sciences, Merck Research Laboratories

Selection of multi-parameter optimized antibody molecules, taking into consideration biological function, safety, and developability, allows for streamlined and successful development. We developed an efficient and practical high-throughput developability workflow, which identified novel patterns and correlations between biophysical assays. These patterns and correlations represent the basis for training deep neural networks and establishing machine learning algorithms for *in silico* interrogation and prediction of developability profiles.

1:50 Protein Language Models for Improved Prediction of Immunogenicity and Biophysical Properties
Paolo Marcatili, PhD, Associate Professor, Bio & Health Informatics, Danish Technical University

Transformer-based language models are powerful machine learning algorithms that can digest and extract information from huge text-based datasets. By applying language models to proteins, we can generate meaningful representations of their structural and sequence landscape, which in turn can be exploited to improve downstream prediction tasks, such as immunogenicity prediction, mutagenesis, and biophysical characterization.

2:20 Novel Deep Learning Models Enable Lead Antibody Optimization by Predicting Affinity and Naturalness of Sequence Variants
Roberto Spreafico, PhD, Principal AI Scientist, AbSci

Therapeutic antibodies require optimization of binding affinity and other properties. Traditional engineering approaches are time-consuming and explore only a subset of the solution sequence space. To address these challenges, we assist antibody development with AI. Models trained with affinity measurements of sequence variants of trastuzumab could quantitatively predict the binding strength of unseen variants. Models can also score antibody sequences for naturalness by comparison with human antibody repertoires, mitigating downstream developability issues.

MACHINE LEARNING APPROACHES FOR PROTEIN ENGINEERING | CONTINUED

2:50 Networking Refreshment Break (Hynes Main Lobby)

3:20 *De novo* Design of Epitope Specific Antibodies with Machine Learning Methods

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

I will present a set of machine learning technologies for the ***de novo*** design of antibodies as high-affinity binders to given epitopes. Our methods encompass structure-based design of CDRs for optimal epitope recognition and sequence-based generative models ensuring favorable developability properties. We show that we obtain nanomolar Fab binders to a specified novel epitope.

3:50 A Cloud-Based Platform that Uses Unsupervised Machine Learning to Identify Hundreds of SARS-CoV-2 Antibodies with Optimal Properties

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

Efficient exploration of sequence outputs from discovery campaigns is often hindered by inefficient sampling of the CDR diversity and technical hurdles involved with the handling of big data, particularly from multiplexed experiments. To overcome these limitations, we developed a cloud-based bioinformatics platform, AbXtract™, which utilizes population-based statistics and unsupervised clustering of next-generation sequencing (NGS) data to rapidly identify leads from distinct and/or overlapping populations.

4:20 *In Silico* High Throughput Screening and Mutagenesis of Signal Peptides to Mitigate N-Terminal Miscleavage of Monoclonal Antibodies

Xin Yu, PhD, Senior Scientist, Global Biologics Discovery, Abbvie Bioresearch Center

We developed a novel high-throughput computational pipeline capable of generating millions of signal peptide mutants and utilizes a deep learning model to predict which of these mutants can alleviate the N-terminal miscleavage in antibodies. The pipeline was optimized to screen a library of 296077 unique mutants for each input antibody.

4:50 Close of Day

FRIDAY, MAY 6

7:00 Registration and Morning Coffee (Hynes Main Lobby)

7:30 Interactive Discussions with Continental Breakfast (Ballroom Pre-Function)

Grab your breakfast and Coffee and join a Discussion Group. 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 Discussion page on the conference website for a complete listing of topics and descriptions.

CO-PRESENTATION: TABLE 1: Best Practices for Using Machine Learning in NGS-Guided Antibody Discovery

Andrew R.M. Bradbury, PhD, CSO, Specifica, Inc.

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

- How does unsupervised or supervised machine learning aid your discovery efforts (e.g., clustering, classification, inference)?
- What experimental and/or bioinformatics processing steps do you employ to ensure you have established an accurate ground truth for select population (e.g., binders / non-binders from FACS) and classification strategies do you employ as it pertains to antibody discovery?

ROOM LOCATION: Ballroom B

MACHINE LEARNING FOR ANTIBODY DISCOVERY

8:25 Chairperson's Remarks

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

8:30 How Structure-Based Machine Learning Can Drive the Development of Biotherapeutics

Matthew Raybould, PhD, Postdoctoral Researcher, Immunoinformatics, University of Oxford, United Kingdom

Machine learning has shown its power across all of biology and in this talk, I will describe some of the novel machine learning tools we are pioneering in the area of biotherapeutics from computational humanization to accurate rapid structure prediction and virtual high-throughput screening.

9:00 Antibody CDR Design for Specific Binding Using High-Capacity Machine Learning

David K. Gifford, PhD, Professor, Electrical Engineering & Computer Science, Massachusetts Institute of Technology

We improve the binding of antibodies to a desired target and eliminate non-specific binders using machine learning (ML) models that are trained on CDR H3 sequences from high-throughput phage display assays. We tested 77,599 novel ML designed sequences from 6 ML methods and found that ML could provide superior binders. We next used single-target ML models to eliminate non-specific antibodies and observed that ML methods outperformed conventional affinity competition assays.

9:30 Identifying Prospective Variants of SARS-CoV-2 by Deep Mutational Learning

Sai Reddy, PhD, Associate Professor, Systems and Synthetic Immunology, ETH Zurich, Switzerland

The continual evolution of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and the emergence of variants that show resistance to vaccines and neutralizing antibodies threatens to prolong the coronavirus disease 2019 (COVID-19) pandemic. Selection and emergence of SARS-CoV-2 variants are driven in part by mutations within the viral spike protein is a primary target site for neutralizing antibodies.

10:00 Clonal Hit Expansion to Discover Diverse Llama Vhhs Using Alicanto Abterra bio

Natalie Castellana, CEO, Abterra Biosciences, Inc.

Next-generation sequencing of antibody repertoires has provided new insights into the single domain antibody repertoire. The correlation between the B-cell receptor repertoire and the serological antibody repertoire has only been analyzed in a small number of studies. In this talk, we will discuss the use of serum antibodies to guide antibody discovery in an immunized llama. Further, we use an autoencoder to deeply mine the clonal lineage of serum-identified antibodies.

10:30 Networking Coffee Break (Hynes Main Lobby)

11:00 A Compact Vocabulary of Paratope-Epitope Interactions Enables Predictability of Antibody-Antigen Binding

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

The prediction of antibody-antigen binding is a central question in biotechnology. A fundamental premise for the predictability of antibody-antigen binding is the existence of paratope-epitope interaction motifs universally shared among antibody-antigen structures. In a dataset of non-redundant antibody-antigen structures, we discovered a motif vocabulary of paratope-epitope interactions that govern antibody specificity providing the proof-of-principle that antibody-antigen binding is predictable with implications for ***de novo*** antibody and (neo-)epitope design.

11:30 *De novo* Design of Nanobodies Targeting Specific Epitopes

Pietro Sormanni, PhD, Group Leader, Royal Society University Research Fellow, Chemistry of Health, Yusuf Hamied Department of Chemistry, University of Cambridge

De novo design methods promise a cheaper and faster route to antibody discovery, while enabling the targeting of predetermined epitopes and the screening of multiple biophysical properties. I will present recent advances to design antibodies targeting structured epitopes and to predict solubility and formulation condition.

12:00 pm Close of PEGS Summit

ONCOLOGY STREAM
CONFERENCES

MAY 2-3
Antibodies for Cancer Therapy
AGENDA

MAY 3-4
Emerging Targets and Novel Approaches for Oncology & Beyond
AGENDA

MAY 5-6
Driving Clinical Success in Antibody Drug Conjugates
AGENDA

ONCOLOGY STREAM

Advancing Antibody Therapeutics to the Clinic

The Oncology Stream at PEGS is back to share what is new and exciting in the fight against cancer, and the antibody developments that are leading the charge. Drug discovery in oncology has long relied on antibodies and antibody-based products as a tool to achieve therapeutic success. Bispecific antibodies, cell engagers, ADCs, nanobodies and combinatorial therapies are being explored to improve targeted therapy and drug delivery. This year, we are adding a new conference on *Emerging Targets and Novel Targets for Oncology & Beyond*, which will look at hot targets, re-emergence of old targets, as well as unconventional or alternative approaches for cancer therapy. Together, the 3 conferences in this stream will present a comprehensive look at strategies driving toward clinical success.

CONFERENCE STREAMS

ENGINEERING | ONCOLOGY | BISPECIFICS | IMMUNOTHERAPY | EXPRESSION | ANALYTICAL | IMMUNOGENICITY

PEGSBOSTON

SUNDAY, MAY 1

1:00 pm Registration for Pre-Conference Short Courses (Hynes Main Lobby)

2:00 Recommended Pre-Conference Short Course*

SC1: Antibody Drug Discovery: From Target to Lead

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

2:00 Main Conference Registration Open (Hynes Main Lobby)

MONDAY, MAY 2

7:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom A

BISPECIFIC AND MULTI-SPECIFIC ANTIBODIES

8:20 Chairperson's Opening Remarks

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

8:30 Identifying Synergistic Target Pairs to Increase Cell Specificity in Cancer Therapeutic Design

Jonathan H. Davis, PhD, Vice President of Innovation and Strategy, Invenra, Inc.

Bispecific antibodies targeting two receptors expressed on a cell of interest can have much higher specificity than mAbs targeting either receptor alone. Avidity drives this specificity, and multiple factors contribute to the observed synergy. Success requires finding the right epitopes, then tuning affinities to optimize selectivity. We discuss some of the physical parameters and strategies involved, then share real-world data on bispecific antibodies targeting cancer cells and tumor-localized Tregs.

9:00 Development of Next-Generation Antibody Therapeutics against Refractory Cancer Utilizing DDS and Molecular Imaging

Masahiro Yasunaga, MD, PhD, Chief, Division of Developmental Therapeutics, National Cancer Center, Japan

Tumor stroma and immunosuppressive microenvironment are major obstacles for the clinical application of antibody-drug conjugates (ADCs) and bispecific antibodies (BsAbs) in refractory cancer. To overcome these drawbacks, we are developing analytical methods of pharmacokinetics/pharmacodynamics /mechanism of action. Moreover, we are also exploiting new technologies to improve antibody delivery and T cell migration. Here I will present our recent work of ADCs and BdAbs using DDS and molecular imaging.

9:30 Generation of Fully Human Antibodies for HLA-Peptide Complexes Using HLA Transgenic RenMice

Qingcong Lin, CEO, Business and Operation, Biocytogen Boston Corporation

The *in vivo* complexity of B cell differentiation, selection, and affinity maturation cannot be recapitulated *in vitro*. To facilitate therapeutic antibody discovery, several strains of humanized immunoglobulin mice were engineered, including a common human light chain model for bispecific/multispecific antibody discovery, drug target knockout mice to induce hyperimmunity, and an HLA-transgenic model for discovery of TCR-mimic antibodies. Together, these platforms serve to uncover best-in-class or first-in-class antibodies for novel targets

10:00 Networking Coffee Break (Pre-function Hall A & Ballroom Pre-Function)

10:30 Bispecific Antibodies Can Drive Synergistic Immune Activation through Simultaneous Engagement of Multiple Immune Targets

Joel Goldstein, PhD, Executive Director R&D, Celldex Therapeutics

Multi-specific therapeutics have the potential to overcome PD-(L)1 checkpoint resistance in cancer treatment. CDX-527 is a clinical-stage bsAb targeting PD-L1 and CD27. CDX-585 is a preclinical bsAb candidate that binds PD-1 and ILT4. Both bsAbs have demonstrated synergistic activity relative to the combination of individual parental mAbs in cultured immune assays and exhibited anti-tumor activity in animal models. The design, development, and preclinical characterization of these bispecifics will be presented.

11:00 The Synergistic Anti-Tumor Activities of CD47-Based Bispecific Molecules in Experimental Solid Tumors Are Dependent on Interaction of Tumor Targets

Frank Zhang, PhD, Director, Business Development, Immuneonco

Our company has designed six CD47-based bispecific mAb-Trap molecules and tested them in various mouse tumor models. Surprisingly, while four (IMM0306: CD47/CD20, IMM2902: CD47/Her2, IMM2520: CD47/PD-L1, IMM5601: CD47/CD38) revealed potent synergistic anti-tumor activities, two (IMM0404: CD47/EGFR, IMM3202: CD47/VEGFR2) did not generate such effect. Thus the synergistic anti-tumor activities of CD47-based bi-specific molecules in solid tumors are dependent on interaction of tumor targets; structural design and target selection deserve careful consideration.

11:30 LUNCHEON PRESENTATION: Hitting the Right Epitope on Multipass Membrane Proteins to Obtain Functional mAbs

Ross Chambers, Vice President of Antibody Discovery, Integral Molecular

Multipass membrane proteins remain valuable yet elusive targets for therapeutic antibodies. The MPS antibody discovery platform has a >95% success rate to reliably target these proteins. We describe recent advances including antigen engineering, mRNA immunization, use of divergent species, chicken antibody humanization, and bispecific screening to show how these approaches have yielded rare and functional antibodies against complex targets such as SARS-CoV-2, GPRC5d, Claudin 6, Claudin 18.2, P2X7 and SLC2A4.

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

12:30 Find Your Table and Meet Your Discussion Moderator

12:45 Interactive Discussions (Ballroom Pre-Function)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 2: Engineering Better CARs for Solid Tumors

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

- Targets in the tumor microenvironment: tumor cells vs myeloid cells
- CAR design for better efficacy and safety: bispecific, hinge, costimulatory
- CAR T vs CAR NK

TABLE 3: Beyond Cell Engagers: What More Can Bispecific Antibodies Contribute to the Fight Against Cancer?

Jonathan H. Davis, PhD, Vice President of Innovation and Strategy, Invenra, Inc.

Bispecific antibodies targeting two receptors expressed on a cell of interest can have much higher specificity than mAbs targeting either receptor alone. Avidity drives this specificity, and multiple factors contribute to the observed synergy. Success requires finding the right epitopes, then tuning affinities to optimize selectivity. We discuss some of the physical parameters and strategies involved, then share real-world data on bispecific antibodies targeting cancer cells and tumor-localized Tregs.

TABLE 4: Targeting Intracellular Antigens – Challenges and Opportunities

Cheng Liu, PhD, Founder & CEO, Eureka Therapeutics, Inc.

- Intracellular antigens as new pool of tumor-specific targets
- TCR mimic antibody vs TCR: affinity and specificity
- Can ADCC and ADC be viable MOA in addition to anti-CD3 bispecific approach?
- HLA-restriction of targeting Intracellular antigens

1:30 Session Break

COMBINATION THERAPY WITH RADIATION

1:45 Chairperson's Remarks

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

1:50 Optimal Integration of Radiation and Immunotherapy

Silvia C. Formenti, MD, Chairman & Professor, Radiation Oncology, Cornell University

It is becoming clear that rules applied to standard use of RT need to be modified to best exploit the immunogenic effects of ionizing radiation. Evidence of radiation immunogenicity at low dose of RT is also available, encouraging clinical trials to further test this approach. The need to define the optimal sequencing of radiation with immunogenic systemic therapy is emerging, particularly when RT is combined with anti-PD1 immunotherapy.

2:20 Radiation and Immune Checkpoint Inhibitors, a Simple Combination with a Complex Interaction

Sandra Demaria, MD, Professor of Radiation Oncology, Professor of Pathology and Laboratory Medicine, Weill Cornell Medicine

T cell-devoid "cold" tumors evade the immune response at one or more of three steps: 1) failure to express or present immunogenic antigens; 2) exclusion of effector T cells; and 3) production of immune-suppressive signals and/or recruitment of immune suppressive cells. Radiation therapy affects each of these three steps, and its ability to enhance responses to immunotherapy can be improved by countering radiation-enhanced immunosuppressive signals.

2:50 SMab, a Novel Single B-cell Based Platform for mAb Discovery

Daniel Chupp, Business Development Scientist, Yurogen Biosystems LLC

3:05 International leading innovative antibody drug integrated R&D platform

Yan Run, Ph.D., Sanyou Biopharmaceuticals Co., Ltd.

3:20 Networking Refreshment Break (Pre-function Hall A & Ballroom Pre-Function)

3:50 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

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

4:10 KEYNOTE PRESENTATION: Challenges and Opportunities in Developing Non-Antibody Protein Therapeutics

Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

Protein therapeutics are dominating the pharmaceutical market, a steadily increasing trend that started with human insulin in 1982. My presentation will discuss challenges and opportunities for developing non-antibody engineered protein therapeutics as next-generation medicines.

YOUNG SCIENTIST KEYNOTE

4:55 KEYNOTE PRESENTATION: Engineering new "Signaling" Proteins to Enact Anti-tumor Responses

Xin Zhou, PhD, Assistant Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Principal Investigator, Cancer Biology, Dana-Farber Cancer Institute

The world of protein engineering is fascinating, full of possibilities to create molecules with new and desirable structures and functions. My presentation will introduce how we work at the interface of disease biology and protein engineering, designing, constructing, and evolving versatile proteins for the development of next-generation molecular technologies, diagnostics, and therapeutics.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Day

TUESDAY, MAY 3

8:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom A

MODULATING THE TUMOR MICROENVIRONMENT

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 KEYNOTE PRESENTATION: Targeting Myeloma Cells with Nanobody-Based Heavy Chain Antibodies, Bispecific Killer Cell Engagers, CAR-NK Cells, and AAV Vectors

Friedrich Koch-Nolte, PhD, Professor, Immunology & Molecular Biology, Institute of Immunology, University Medical Center Hamburg-Eppendorf

CD38 is an established target for immunotherapy of multiple myeloma. Because of their high solubility as single immunoglobulin domains, nanobodies are particularly suited for constructing bi- and multispecific therapeutics. We demonstrate the utility of nanobodies to target CD38 overexpressing multiple myeloma cells using nanobody-based CD38-specific heavy chain antibodies, bispecific killer cell engagers (BiKEs), CAR-NK cells, and nanobody-retargeted AAV vectors.

ANTIBODIES FOR CANCER THERAPY | CONTINUED

9:00 Targeting Intracellular Tumor Antigens with TCR Mimics

Cheng Liu, PhD, Founder & CEO, Eureka Therapeutics, Inc.

- Designing ARTEMIS Antibody TCR (AbTCR) T cells to address the major hurdles in treating solid tumor
- Infiltrating into solid tumor under immunosuppressive microenvironment
- Targeting Alpha-fetoprotein (AFP) and Glypican 3 (GPC3) in advanced hepatocellular carcinoma (HCC)
- Demonstrating superior safety and efficacy profile of ARTEMIS T cells

9:30 CB307: A Novel T Cell Costimulatory Humabody VH Therapeutic for PSMA-Positive Tumours

Colette Johnston, PhD, VP, Discovery, Crescendo Biologics Ltd

10:00 Fit-for-Purpose Strategies for Therapeutic Antibody Discovery

Jane Seagal, PhD, Vice President of Antibody Discovery, AlivaMab Discovery Services

AlivaMab Discovery Services' (ADS) antibody discovery workflows are optimized for fast and efficient drug discovery and development for both standard and next generation antibody formats. To ensure success of every antibody discovery campaign, we implement custom immunization and screening strategies tailored to each set of antibody design goals. In this talk, examples of fit-for-purpose strategies will be presented.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

STRATEGIES TO ADVANCE CELLULAR IMMUNOTHERAPIES

11:05 Chairperson's Remarks

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

11:10 From Antibodies to Next-Generation CAR Therapy

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

Antibody and gene engineering technologies have been successfully translated to a first wave autologous CAR T cell products directed at B cell malignancies, with curative potential in a subset of patients. We discuss strengths and limitations of the current CAR T cell platform, major learnings to date, and next-generation immunotherapy applicable to a broader category of disease indications.

11:40 CAR T for Pediatric Cancer, Moving from Leukemias to Solid Tumors

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

The first approved CAR T cell product was for a pediatric indication, pre-B ALL. The rapid responses seen reflect the biology of the disease, with non-transformed B cells and leukemia cells driving response. In pediatric solid tumors, the physiological context suppresses CAR T activity as in other solid tumor indications. By optimizing the CAR T cell product and subverting myeloid cell-induced immunosuppression, we may develop new therapeutic advances.

12:10 Antibody-Based Quantitative Control of Universal CAR T Cells via Image-Guided Delivery

Daniel J. Powell Jr., PhD, Associate Professor, Pathology & Laboratory Medicine, University of Pennsylvania

To allow for quantitative control of CAR T cell activity, we first developed universal immune receptors (UnivIRs), a highly versatile platform that decouples the CAR antigen specificity domain from the intracellular signaling domains to permit on-demand, personalized redirection of UnivIRs-expressing T cells against a wide array of antigens using repurposed, tagged antigen-specific antibodies, with an advanced theranostic UnivIR platform that utilizes clinically actionable agents that permit imaging for tumor monitoring.

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

1:40 Close of Antibodies for Cancer Therapy

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:00 Close of Day

6:30 Dinner Short Courses

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

EMERGING TARGETS AND NOVEL APPROACHES FOR ONCOLOGY & BEYOND

Unconventional and Alternative Approaches

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*

SC1: Antibody Drug Discovery: From Target to Lead

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

ROOM LOCATION: Ballroom A
NOVEL TARGETS

2:15 Chairperson's Opening Remarks

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

2:20 A New Immunotherapy Target: Co-Development of a Therapeutic Antibody and a Radioimmune Diagnostic Targeting Oxidized Macrophage Migration Inhibitory Factor (oxMIF)

Michael Thiele, PhD, Founder & CSO, Biology Research, OncoOne R&D GmbH

OxMIF, the disease-related isoform of macrophage migration inhibitory factor (MIF), was discovered as an attractive target for the development of novel treatments for patients with solid tumors due to its exclusive presence in diseased tissue. OncoOne is combining their lead therapeutic candidate targeting oxMIF with a corresponding radiolabeled anti-oxMIF antibody as companion diagnostic. This combination will guide future combination trials and enable the targeted treatment of patients with oxMIF-positive tumors.

2:50 BT7480, a Novel Bicycle Nectin-4-Targeted Agonist of the Immune Cell Costimulatory Receptor CD137

Kristen Hurov, PhD, Director, Oncology/Immuno-Oncology, Bicycle Therapeutics

CD137 has been recognized for its potential as a drug target but this promise has not been realized due to toxicity and limited efficacy. Bicycles are small, structurally constrained peptides discovered via phage display and optimized using medicinal chemistry. We have developed BT7480, a multifunctional molecule that induces tumor antigen-dependent agonism of CD137 that leads to complete tumor regressions and subsequent resistance to tumor re-challenge in syngeneic mouse models.

3:20 Platform Technology for Developing Fully Human Nanobodies and Multi-Specific Antibodies LEVERAGEN

Weisheng Chen, Founder and CEO, Leveragen, Inc.

Using cutting-edge gene editing and targeted replacement technologies, we have engineered the Singularity Sapiens Mouse that produces heavy chain only antibodies from the entire human VH repertoire, but none of the conventional antibodies (IgM/IgD/IgG/IgE/IgA). A rapid sequence-driven pipeline has been established to profile, select, clone, and express nanobodies for large scale high-throughput screens to identify target-specific binders for developing nanobody based next generation biologics, including multispecific antibodies, intrabodies, and CAR-T therapies.

3:50 Refreshment Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

MESOTHELIN AS A THERAPEUTIC TARGET FOR SOLID TUMORS

4:30 Highly Active CAR T Cells Containing an Fv that Binds to a Juxta-Membrane Non-Shed Region of Mesothelin

Ira H. Pastan, PhD, Co-Chief, Head & Distinguished Investigator, Molecular Biology, NIH NCI

Mesothelin is shed from cells by the action of proteases that cut close to the membrane. MAb15B6 binds to the protease-sensitive region of mesothelin proximal to the membrane, inhibits mesothelin shedding, and makes a very active CAR T cell that is superior in activity in mouse tumor models to CAR T cells made with mab SS1 that binds to a distal epitope.

5:00 Mesothelin-Targeted CAR T Cell Therapy for Solid Tumors

Prasad Adusumilli, MD, FACS, FCCP, Deputy Chief and Associate Attending, Thoracic Surgery; Director, Mesothelioma Program; Head, Solid Tumors Cell Therapy, Cellular Therapeutics Center (CTC), Memorial Sloan-Kettering Cancer Center; Associate Professor, Cardiothoracic Surgery, Weill Cornell Medical Center

Our laboratory developed, optimized, and translated mesothelin-targeted CAR T cell therapy. We have treated 41 thoracic cancer patients with remarkable safety and evidence of anti-tumor efficacy. Following existing demonstration of safety and efficacy of combination immunotherapy with CAR T cells and checkpoint blockade (CPB) agents in pleural mesothelioma patients, we translated PD1 dominant-negative receptor within the CAR T cell, patients are being treated in an ongoing clinical trial. Preclinical supportive rationales and clinical trial results will be presented.

5:30 Gavo-Cel: A TRuC-T Cell Therapy Targeting Treatment Refractory Mesothelin-Expressing Solid Tumors

Alfonso Quintas-Cardama, MD, PhD, CMO, TCR2 Therapeutics, Inc.

This presentation will give an introduction to the TRuC T cell platform, and outline the advantages of TRuC T cells over CAR T cells in solid tumors. Details around the ongoing clinical trials with TRuC T cells will also be shared.

6:00 Close of Day

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*

SC9: Development of Neutralizing Antibody Assays: Technical Considerations and Case Studies

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

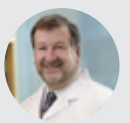
WEDNESDAY, MAY 4

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom A
TARGETING MHC PEPTIDES

8:25 Chairperson's Remarks

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



8:30 KEYNOTE PRESENTATION: On-Targets and Off-Targets of Peptide-MHC Reactive Agents

David A. Scheinberg, MD, PhD, Vincent Astor Chair & Director, Molecular Pharmacology Program and Center for Experimental Therapeutics, Deputy Director, Sloan Kettering Institute for Therapeutic Discovery, Memorial Sloan Kettering Cancer Center

TCR-based therapeutic cells and agents are a new class of effective cancer therapies that can access intracellular cancer-associated proteins by targeting peptides displayed on major histocompatibility complex receptors. Cross-reactivities of these agents to off-target cells and tissues have resulted in serious adverse events. Using a high-throughput genetic platform (termed "PresentER") that encodes MHC-I peptide minigene libraries for functional immunological assays, we seek to understand the reactivities of TCR-based agents.

TABLE OF CONTENTS

EMERGING TARGETS AND NOVEL APPROACHES FOR ONCOLOGY & BEYOND | CONTINUED

9:00 Development of Therapeutic Assets against Known and Novel pHLA Targets for Solid Tumors

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

We describe a target identification and cross-reactivity screening platform (3T-TRACE) and its utility to identify novel, intracellular targets, and their corresponding T cell receptors (TCRs) for the treatment of solid tumors. We focus on patient tumor profiling to identify key TCR populations for our immune-response guided approach for target identification and the development of TCR-based therapeutics against broadly expressed novel targets.

9:30 MHC Class I and MHC Class II Immunopeptidomics in Drug Discovery

Domenick Kennedy, PhD, Senior Scientist, Drug Discovery Science and Technology, Discovery Platform Technologies, Chemical Biology and Emerging Therapeutics, AbbVie, Inc.

Protective immune responses and immunotherapies rely on T cell recognition of peptides presented in MHC class I and MHC Class II. Identifying MHC-presented peptides through immunopeptidomics provides opportunities to understand and modulate immune responses. We will highlight this powerful approach and how it can be used in drug discovery research for oncology and beyond.

10:00 From T cell epitope discovery to MHC/epitope targeted therapeutics

IMMUNITRACK

Sune Justesen, PhD, CSO, Immunitrack ApS

The Major Histocompatibility Complex (MHC) is critical to the immune response. Immunitrack has world-leading expertise in manufacturing and studying MHC I and II molecules and their interactions with peptide epitopes. In this presentation we will present our capabilities within the MHC area and how they can be applied as the best starting point for generating MHC/epitope targeted therapeutics

10:15 Sponsored Presentation *(Opportunity Available)*

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

11:10 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B

PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

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

11:30 KEYNOTE PRESENTATION: Future Directions in Drug Discovery & Development

Roger M. Perlmutter, MD, PhD, Chairman and CEO, Eikon Therapeutics, Inc.

The intrinsic complexity of human physiology has generally defeated attempts to model normal cellular functions, meaning that until recently we have had few tools to disentangle the molecular pathology associated with common illnesses. Now, dramatic improvements in instrumentation, automation, and computing provide ways to measure dynamic responses in living cells, and to use these measurements to identify both new disease targets, and new chemical starting points for future medicines.

12:15 pm Session Break

12:30 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Find Your Table and Meet Your Discussion Moderator

1:35 Interactive Discussions (Exhibit Hall A & B)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 3: Emerging Strategies to Discover Therapeutic Antibodies and Novel Targets

Jorge Dias, PhD, Principal Scientist, Alchemab Therapeutics Ltd

- Identifying antibodies with therapeutic potential from polyclonal pools / libraries / immune repertoires
- Strategies to identify, express and characterise novel targets
- Engineering and formats for non-antibody protein therapeutics

TABLE 4: Challenges and Opportunities in Precision Medicine for CNS Diseases

Miroslaw Janowski, MD, Associate Professor, Diagnostic Radiology, University of Maryland Baltimore

- Precision medicine enables the ability to see how much drug gets into the brain and if the amount is sufficient - a more expensive way but enables scientists to finally understand where the problem lies
- Closing the gap in drug delivery by capturing biodistribution dynamics of biologics for 3D pharmacokinetics
- Obstacles - slow disease progression; animal data not relevant to clinical settings

ROOM LOCATION: Ballroom A

NOVEL AND ALTERNATIVE APPROACHES

2:20 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

2:25 Novel Therapies to Remodel the Tumor Microenvironment

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

eBAT (EGF bispecific angiotoxin) consists of full-length epidermal growth factor (EGF) linked to the amino-terminal fragment (ATF) of urokinase-type plasminogen activator (uPA) and to a genetically modified Pseudomonas exotoxin (PE). In addition to targeting malignant tumor cells that express EGFR and/or uPAR, we have shown that eBAT also remodels the tumor microenvironment by depleting immunosuppressive macrophages, promoting phagocytosis by myeloid dendritic cells, and allowing infiltration of T cells.

2:55 LIGHT (TNFSF14) Co-Simulation Enhances Myeloid Cell Activation and Anti-Tumor Immunity in the Setting of PD-(L)1 and TIGIT Checkpoint Blockade

George J. Fromm Jr., PhD, Vice President, R&D, Shattuck Labs, Inc.

TIGIT-Fc-LIGHT was designed to block all TIGIT-ligand interactions and provide broad immune co-stimulation to CD8+ T and NK cells via HVEM, and myeloid cells by LTBR. TIGIT-Fc-LIGHT does not depend upon DNAM-1 co-stimulation for activity, like TIGIT antibodies, and unlike DNAM-1, HVEM is not down-regulated on TIL in advanced tumors, nor directly inhibited by PD-1. We demonstrate this translates to TIGIT-Fc-LIGHT anti-tumor activity in PD-L1-low and CPI acquired resistant tumors.

3:25 Parallel Discovery of Therapeutic Antibodies and Novel Targets Using the Antibody Repertoires of Resilient Individuals

Jorge Dias, PhD, Principal Scientist, Alchemab Therapeutics Ltd

At Alchemab, we are harnessing the power of the immune system to counter complex diseases. By mining the antibody repertoires of individuals who demonstrate exceptional resilience to disease we are able to pinpoint antibodies which are linked to improved outcomes or delayed disease onsets. Selected antibodies are characterised by function and target specificity before entering preclinical disease models.

EMERGING TARGETS AND NOVEL APPROACHES FOR ONCOLOGY & BEYOND | CONTINUED

3:55 Ice Cream Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 A Novel CXCR4 Protein Complex Identified by Salipro DirectMX Reveals New Possibilities in Drug Discovery

Robin Loeving, PhD, CSO, Salipro Biotech AB

Membrane proteins are important drug targets yet are notoriously difficult to work with. Our proprietary approach, Salipro DirectMX, incorporates membrane proteins directly from cells into lipid Salipro nanoparticles. Salipro DirectMX presents new opportunities for *de novo* development and characterization of biologics and small molecule drugs. We will present our latest developments and showcase how CXCR4 oligomers can be reconstituted into Salipro-CXCR4 nanoparticles, enabling new possibilities for development of oncology therapeutics.

5:00 Image Guidance for Precision Medicine of the Central Nervous Diseases

Miroslaw Janowski, MD, Associate Professor, Diagnostic Radiology, University of Maryland Baltimore

The field of molecular imaging and image guided neurointerventions are rapidly unfolding and they provide an outstanding opportunity especially for early phase clinical trials to get report on how much of the drug got to the brain and where it is exactly located and if it overlaps with pathological changes. I will talk about how radiolabeled biological drugs and image guidance enables improved delivery to the brain using advanced methods.

5:30 Enhanced Function via Novel Fc Engineering of Antibodies

Nathan Robertson, PhD, Head, Protein Engineering, MiroBio

We describe the generation of artificial signaling through immune receptors by engineered antibodies designed to enforce a very narrow immune synapse. We have adopted this strategy to develop ligand blocking antibodies targeting checkpoint receptors for immunotherapy, a mucin linker modification increasing its size forces the immune checkpoint receptor out of cell contacts due to steric hindrance upon receptor engagement, suppressing both tonic and ligand-dependent signaling, further improving immune checkpoint blockade.

6:00 Networking Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Emerging Targets and Novel Approaches for Oncology & Beyond

DRIVING CLINICAL SUCCESS IN ANTIBODY-DRUG CONJUGATES

Creating the Magic Bullet

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*

SC1: Antibody Drug Discovery: From Target to Lead

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

6:30 pm Recommended Dinner Short Course*

SC9: Development of Neutralizing Antibody Assays: Technical Considerations and Case Studies

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

THURSDAY, MAY 5

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom A

OLD TARGETS, NEW APPROACHES

8:25 Chairperson's Opening Remarks

Gail D. Lewis, Principal Scientist, Discovery Oncology, Genentech, Inc.

8:30 Advanced ADC Designs for Improved Therapeutic Margins – Making Old Targets New Again

Robert J. Lutz, PhD, Principal Consultant, Crescendo Biopharma Consulting

Incorporation of new approaches in ADC design yield compounds with improved efficacy and tolerability. These new approaches include advanced antibody engineering, novel bioconjugation technologies, and tumor-selective payload release and activation chemistries that provide differentiated outcomes when compared to clinical benchmarks against known targets. Evaluation of these differentiated ADCs to "old" targets provides validation of the new designs for use in developing ADCs to "old" and "new" targets alike.

9:00 Expanding the Success of ADCs: Quantitative Pharmacology Lessons from Currently Approved Agents

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

The past several years have seen dramatic growth in the number of approved ADCs, particularly for solid tumors. These approved agents have unique properties tailoring them to their specific target. However, there are several notable features shared among these agents, particularly related to the dosing and payload properties. Here, we'll present the common features from current agents and how we can apply these lessons to develop even more effective therapeutics.

9:30 Evaluation of an ADC with a Novel Microtubule Inhibitor Payload

Priyaranjan Pattanaik, PhD, Head - NBE Services, NBE Services, Aurigene Pharmaceutical Services

10:00 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

LEARNINGS FROM RECENT APPROVALS AND CURRENT ADCs IN THE CLINIC

10:40 KEYNOTE PRESENTATION: Zynlonta – In 5 Years from FIH to Regulatory Approval: Lessons Learnt from the Preclinic, Phase 1 and Phase 2 Studies

David Ungar, MD, Head of US Oncology Clinical Development, ADC Therapeutics

Zynlonta (loncastuximab tesirine) is a CD19 targeted ADC linked to a pyrrolobenzodiazepine-dimer toxin. Preclinical data showed exquisite potency and tolerability and are compared to clinical data. Discussion of the Phase 1 study design, which enabled testing of multiple doses and dose regimens for early signal detection, follows. Design and results of LOTIS-2, the pivotal Phase 2 study leading to regulatory approval, is the focus of the remaining presentation.

11:10 Clinical Update of a Novel Anti-EGFR ADC MRG003

Mary Hu, PhD, Chairman and CEO, Shanghai Miracogen

MRG003 is a novel antibody drug conjugate comprised of a humanized anti-EGFR antibody to the monomethyl auristatin E (MMAE) via a valine-citrulline linker. In Phase I clinical study evaluating the safety, tolerability, preliminary anti-tumor activity, and pharmacokinetics, MRG003 showed a manageable safety profile in patients with advanced solid tumors and demonstrated promising antitumor activity in patients with EGFR-positive nasopharyngeal cancers and squamous cell carcinomas of head and neck.

11:40 Sacituzumab Govitecan, a Novel ADC for Solid Tumors

Bilal Piperdi, PhD, VP, Clinical Research Oncology, Gilead

Sacituzumab govitecan (SG) was developed as a novel antibody drug conjugate for Trop-2 overexpressing tumors. SG utilizes a novel linker (CL2A) which afforded several key attributes, including increased payload to antibody ratio and release of payload extracellularly. SG has demonstrated activty clinically and is now approved for treatment of metastatic triple negative breast cancer and metastatic urothelial cancer, with additional tumors under study.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing (Exhibit Hall A & B)

NOVEL APPROACHES FOR NEXT-GENERATION ADC DESIGN

1:15 Chairperson's Remarks

John M. Lambert, PhD, Consultant

1:20 KEYNOTE PRESENTATION: The Renaissance of Antibody-Drug Conjugates – Progress, Challenges and the Future

Puja Sapra, PhD, Senior Vice President, Biologics Engineering & Oncology Targeted Delivery, AstraZeneca Pharmaceuticals, Inc.

1:50 Drug Conjugates Based on Affibody Molecules

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 creating homogenous conjugates with a desired drug-to-carrier ratio. The presentation will explore the targeting of different cancer-relevant receptors, as well as the impact of affibody-carrier architecture, drug load, and peptide-linker composition on the biodistribution and *in vitro* and *in vivo* cytotoxic efficacy.

2:20 Multi-Functional, Multi-Targeting Anti-Glycan

DRIVING CLINICAL SUCCESS IN ANTIBODY-DRUG CONJUGATES | CONTINUED

Monoclonal Antibodies

Mireille Vankemmelbeke, PhD, Principal Scientist, Biodiscovery, Scancell Ltd

Glycans are excellent tumor targets. Notably, the same glycan expressed on a range of glycoproteins/lipids allows mAbs to target multiple antigens some of which can internalize whilst others are retained on the cell surface. Our mAbs can be potent ADCs but also retain ADCC/CDC activity and can cause membrane perturbation resulting in direct cell lysis. Additionally, Avidimab increases the avidity of any mAb and results in improved tumor killing.

2:50 Networking Refreshment Break (Hynes Main Lobby)

3:20 A METxMET Antibody-Drug Conjugate with Cleavable Linker Is Processed in Recycling and Late Endosomes

Andres Perez Bay, PhD, Senior Staff Scientist, Oncology & Angiogenesis, Regeneron Pharmaceuticals, Inc.

Most antibody-drug conjugates (ADCs) approved for the treatment of cancer contain protease-cleavable linkers. Although it has been proposed that endosomes can process cleavable ADCs, the relative contributions of various endosomal compartments to ADC processing remain undefined. Our studies provide insight into the relationship between trans-endosomal trafficking and ADC processing and suggest that receptors that preferentially recycle to the plasma membrane via recycling endosomes might be suitable targets for cleavable ADCs.

3:50 A CD79b Targeting ADC with Superior Anti-Tumor Activity and Tolerability

Philipp Spycher, PhD, CEO, Araris Biotech AG

The Araris' site-specific and 1-step linker conjugation technology aims at generating safe and highly potent ADCs without the need for antibody engineering prior to linker-payload conjugation. We developed a very stable anti-CD79b-MMAE ADC with this technology showing a 4-6-fold higher therapeutic index compared to polatuzumab-vedotin in preclinical models. Our ADC may represent a safe and efficacious alternative for the treatment of patients with diffuse-large B-cell lymphoma (DLBCL).

4:20 Close of Day

FRIDAY, MAY 6

7:00 Registration and Morning Coffee (Hynes Main Lobby)

7:30 Interactive Discussions with Continental Breakfast (Ballroom Pre-Function)

Grab your breakfast and coffee and join a Discussion Group. 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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 2: The Linker in ADCs: Small but Important

Philipp Spycher, PhD, CEO, Araris Biotech AG

- Role of linker in ADC design and its key properties
- Review of current and novel linker technologies
- Cleavable and non-cleavable linkers

TABLE 3: Improving the Efficiency of the ADC Development Pipeline

John M. Lambert, PhD, Consultant

ROOM LOCATION: Ballroom A
ADCs WITH NEW PAYLOADS

8:25 Chairperson's Remarks

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

8:30 Challenges in Developing PBD-Based ADCs: Early Development Results of a HER2 ADC Containing a Reduced Potency PBD Dimer Conjugated to a Novel HER2 Antibody

Gail D. Lewis, Principal Scientist, Discovery Oncology, Genentech, Inc.

Antibody-drug conjugates with PBD dimer payloads are dose-limited due to high potency and toxicities of PBDs. DHES0815A is a HER2-directed ADC with a reduced potency PBD to achieve dosing in the linear PK range for improved efficacy and tolerability. DHES0815A was efficacious in HER2+ and HER2-low tumor models. The HNSTD in cynomolgus monkey was 12 mg/kg. Preclinical efficacy and safety data and Phase 1 results for DHES0815A will be presented.

9:00 Antibody Targeted Amanitin Conjugates (ATACs) Provide New Options to Fight Cancer

George Badescu, PhD, Vice President, Business Development, Heidelberg Pharma AG

9:30 ADCs with KSP Inhibitor Payloads: Linker Impact on Efficacy and Safety

Hans-Georg Lerchen, PhD, CSO, Vincerx Pharma, Inc.

To achieve a preferential activation of ADCs in tumor versus healthy tissues we developed ADCs with novel linkers which are efficiently and selectively cleaved by the tumor-associated protease legumain. Additional tuning of the physicochemical profile of the active metabolite resulted in highly potent ADCs against different targets. A favorable safety profile with regard to neutropenia, thrombocytopenia, and liver toxicity could be shown in preclinical studies.

10:00 Development of Novel, Homogeneous Antibody Drug Conjugates Using Cell Free Protein Synthesis and Site-Specific Conjugation Technologies: The Sutro Biopharma Experience

Arturo Molina, MD, MS, CMO, Sutro Biopharma, Inc.

10:30 Networking Coffee Break (Hynes Main Lobby)

11:00 Antibody-Mediated Delivery of Chimeric Protein Degraders

Peter S. Dragovich, PhD, Senior Fellow, Discovery Chemistry, Genentech, Inc.

Heterobifunctional chimeric molecules that effect the intracellular degradation of specific proteins offer several potential advantages over conventional small-molecule inhibitors. However, they are also relatively large compounds that often possess molecular characteristics which may compromise oral bioavailability and/or ***in vivo*** pharmacokinetic properties. The conjugation of these chimeric entities to monoclonal antibodies to enable alternate delivery options will be discussed.

11:30 FORCE Platform Delivers Multiple Payload Types, Tailored to Treat Serious Muscle Diseases

Timothy Weeden, Senior Director & Head, Platform Development, Dyne Therapeutics, Inc.

- The FORCE platform was developed for the targeted delivery of oligonucleotide-based therapeutics to treat neuromuscular disorders.
- Highlighting the design and modularity of the platform
- Presenting the delivery and potency across various disease models

12:00 pm Close of PEGS Summit

BISPECIFICS STREAM
CONFERENCES

MAY 2-3

Introduction to Bispecific Antibodies

AGENDA Training SEMINAR

MAY 3-4

Advancing Bispecific Antibodies and Combination Therapy to the Clinic

AGENDA

MAY 5-6

Engineering Bispecific Antibodies

AGENDA

BISPECIFICS STREAM

Achieving Unprecedented Efficacy in Biologics

The bispecific antibodies stream at the PEGS Summit will take you from a comprehensive review of these constructs, through the engineering and platform development all the way to preclinical and clinical data. The improved functionality along with newly developed, innovative solutions for reducing toxicity and limiting side effects is resulting in unprecedented efficacy of bispecific antibodies. Don't miss this exciting agenda and meet face to face with leaders in the industry.

CONFERENCE STREAMS

ENGINEERING | ONCOLOGY | BISPECIFICS | IMMUNOTHERAPY | EXPRESSION | ANALYTICAL | IMMUNOGENICITY

PEGS BOSTON

DAY 1: MONDAY MAY 2 – 8:30AM-4:00PM | DAY 2: TUESDAY, MAY 3 – 8:30AM-12:30PM

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, Vice President, Antibody Engineering, AlivaMab Discovery Services

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.

ADVANCING BISPECIFIC ANTIBODIES AND COMBINATION THERAPY TO THE CLINIC

Creating the Killer Combo

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*

SC1: Antibody Drug Discovery: From Target to Lead

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

ROOM LOCATION: 306

CO-STIMULATORY BISPECIFIC ANTIBODIES

2:15 Chairperson's Opening Remarks

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

2:20 Beyond Signal 1: Using Bispecific Antibodies and Potency-Tuned Cytokines to Optimize T Cell Activity

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

Xencor has used its bispecific antibody platform to create a second type of T cell engager, TAA x CD28 bispecific antibodies, which safely promote the activation of signal 2 in T cells via tumor-selective agonism of CD28. This new modality synergizes with classic TCEs to promote greater T cell activation and expansion. In parallel, potency-reduced cytokines (signal 3) bring additional opportunities to activate T cells to maximize therapeutic benefit.

2:50 KEYNOTE PRESENTATION: Bispecific Antibodies – Fit for Purpose

Roland Kontermann, PhD, Professor & Deputy Head, Biomedical Engineering, University of Stuttgart

Bispecific antibodies are molecules with a multitude of talents. A short overview of current developments will be presented and examples from our own work are used to highlight the influence of format, geometry, affinity, and valency on the efficacy of bispecific T cell engagers.

3:20 CMC Strategy to take Bispecifics from DNA to IND in 13 Months

Lonza

Andrew Brown, EngD, Support Manager, Global Process Development, Lonza

Lonza has applied it's 35 years of CMC experience in Biologics to develop an end-to-end comprehensive DS/DP DNA to IND strategy in 13 months. This presentation will highlight key approaches and technologies that enable this timeline. Case study examples will be shared for application in vector, process, analytic and formulation development of bispecific molecules during pre-clinical development.

3:50 pm Refreshment Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 Combinatorial Approaches to Enhance Bispecific Anti-Tumor Efficacy

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

This presentation will describe key preclinical data from Regeneron's new clinical approaches to enhancing anti-tumor efficacy, 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 bispecifics in pre-clinical development will be discussed.

5:00 Trispecific T Cell Engagers: Optimal and Tumor Specific T Cell Mediated Eradication of Solid Tumors

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

The therapeutic window of T cell engagers for solid tumors is limited by expression of tumor-associated antigens (TAA) on both solid tumors as well as on healthy tissue. Triclonics, Merus trispecific antibody platform, provides the technology for solid tumor-specific T cell engagers. The solution is a trispecific TAA1×TAA2×CD3 T cell engager co-targeting two tumor targets that are only co-expressed on solid tumors and not on healthy tissue.

5:30 Developing Combination Therapies Based on Bispecific Antibodies and Fusion Proteins

Christian Klein, PhD, Cancer Immunotherapy Discovery, Roche Innovation Center Zurich, Roche Pharma Research & Early Development, pRED

Developing bispecific antibodies and fusion proteins for combination therapy of solid and hematological tumors. Co-stimulatory fusion proteins including FAP-4-1BBL, CEA-4-1BBL, and CD19-4-1BBL for combination with T cell bispecific antibodies. Novel approaches for co-stimulatory pathways.

6:00 Close of Day

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*

SC7: Developability of Bispecific Antibodies: Formats and Applications

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

WEDNESDAY, MAY 4

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 306
NK CELL ENGAGERS AND OTHER BISPECIFICS

8:25 Chairperson's Remarks

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

8:30 Development of Novel Wnt Signal Modulators

Wen-Chen Yeh, PhD, CSO, Surrozen, Inc.

We focus on engineering antibodies that replicate the function of Wnt pathway proteins to repair tissue damages. We have developed technologies to modulate the Wnt pathway, Wnt mimetics, and R-spondin mimetics, that provide robust and flexible platforms. Our strategy is to harness the full breadth of potential by identifying disease states responsive to Wnt pathway modulation, design specific antibodies, and advance candidates into development in indications with unmet needs.

9:00 A Bispecific Antibody Agonist of the IL-2ßγ Receptor Promotes *in vivo* Expansion of CD8+ and NK Cells

Katherine Harris, PhD, Vice President, Discovery, Amgen

The use of recombinant IL-2 as a therapeutic has been limited by significant toxicities despite its ability to induce durable tumor-regression in patients. We have developed a novel bispecific heavy-chain only antibody which binds to and activates signaling through the IL-2ßγ receptor complex, expanding T and NK effector cells while avoiding IL-2Ra and the toxicities associated with the trimeric IL-2 receptor.

ADVANCING BISPECIFIC ANTIBODIES AND COMBINATION THERAPY TO THE CLINIC | CONTINUED

9:30 Harnessing NK Cell in Cancer Therapies by Antibody-Based NK Cell Engager Therapeutics (ANKET)

Éric Vivier, DVM, PhD, CSO, Innate Pharma

Tetra-specific ANKET molecule is the first NK cell engager technology to engage two NK cell activating receptors, NKp46 and CD16, a tumor antigen and the interleukin-2 receptor via a single molecule. We will present an update on our ANKET platform as a new generation of therapeutic molecules against cancer.

10:00 Leave No Hit Behind: Accelerating Lead Molecule Discovery against Difficult Targets

Renee Tobias, Senior Director, Marketing Antibody Theraputics, Marketing, Berkeley Lights, Inc.

This presentation will introduce Berkeley Lights' Opto™ Plasma B Discovery 4.0 workflow that enables recovery of 1000s of hits by screening up to 100,000 plasma cells, down-selection of lead candidates by functional screening, and sequencing and re-expression of >1000 functionally-characterized antibodies all in 1 week. By maximizing the diversity of antibodies through direct functional profiling of plasma cells, the OPBD 4.0 workflow allows users to tackle even the most challenging targets.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

11:10 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

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

11:30 KEYNOTE PRESENTATION: Future Directions in Drug Discovery & Development

Roger M. Perlmutter, MD, PhD, Chairman and CEO, Eikon Therapeutics, Inc.

The intrinsic complexity of human physiology has generally defeated attempts to model normal cellular functions, meaning that until recently we have had few tools to disentangle the molecular pathology associated with common illnesses. Now, dramatic improvements in instrumentation, automation, and computing provide ways to measure dynamic responses in living cells, and to use these measurements to identify both new disease targets, and new chemical starting points for future medicines.

12:15 pm Session Break

ROOM LOCATION: 306

12:30 LUNCHEON PRESENTATION: Antibody Discovery Powered by OmniAb

Bill Harriman, PhD., Senior Vice President, Antibody Discovery, OmniAb

The OmniAb platform couples cutting edge screening and data mining technologies with highly validated antibody generation systems. This session will provide an overview of OmniAb and offer a few examples of how the platform can be implemented for a variety of antibody discovery campaigns.

1:00 Luncheon Presentation to be Announced

Daniel Buckley, Lead Scientist, non-GMP DSP, Samsung Biologics

1:30 Find Your Table and Meet Your Discussion Moderator

1:35 Interactive Discussions (Exhibit Hall A & B)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 5: Challenges and Solutions to Engineering Multi-Specific Antibodies

Carole Estoppey, PhD, Head of Structure-Guided Antibody Engineering, Ichnos Sciences Biotherapeutics SA

- What are the most useful assays in predicting developability of bispecific and trispecific antibodies? Is this different than for mAbs?
- In your experience, what are some of the most effective ***in silico*** tools to guide the engineering of multispecific antibodies? How can they be improved?

NK CELL ENGAGERS AND OTHER BISPECIFICS *(CONT.)*

2:20 Chairperson's Remarks

Frank Comer, PhD, Associate Principal Scientist, AstraZeneca

2:25 Synthekines: A Novel Platform for Combinatorial Engineering of Cytokine Receptor Agonists

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

Cytokines are immunomodulatory proteins that activate key signaling pathways by receptor dimerization. While many cytokines are approved as therapeutics, native structure restricts their potential to pathways activated by their cognate receptors. We implemented a platform to dimerize native and non-native pairs of cytokine receptors using VHH antibodies, allowing us to design synthetic cytokines that generate targeted and modulated signals on key cell types to improve on first-generation cytokine therapeutics.

2:55 Highly Targeted Therapies Based on an Advanced Anticalin Platform

Hitto Kaufmann, PhD, CSO & Senior Vice President, Pieris Pharmaceuticals GmbH

Successfully developing novel highly-targeted protein therapies for injection and inhalation requires comprehensive platform understanding. Our Anticalin platform has translated to clinical successes and we will present the key features of our advanced platform including accelerated discovery, a comprehensive developability framework, and sophisticated data science capabilities.

3:25 Engineering Human Antibodies Discovered with AlivaMab Mouse into a Dual-Antagonist Bispecific Antibody Therapeutic

Jonah Rainey, PhD, Vice President of Antibody Engineering and Protein Science, AlivaMab Discovery Services

The best way to generate advanced biologics with requisite activity and drug-like properties is to generate large panels of leads with diversity along several axes: sequence, epitope, affinity and geometry. A case study details generation of diverse panels of lead antibodies against two targets and characterization for binding, function, kinetics and developability. A matrix of 200 bispecifics was generated, resulting in multiple lead candidates with favorable expression, potency and stability.

3:55 Ice Cream Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 Zanidatamab: Engineering a HER2-Biparatopic Antibody with Unique Functionality Compared to the Combination of Parental Antibodies

Nina E. Weisser, PhD, Director, Multispecific Antibody Therapeutics, Zymeworks, Inc.

Biparatopic antibodies are designed to simultaneously bind two non-overlapping epitopes on the same target and are promising next-

ADVANCING BISPECIFIC ANTIBODIES AND COMBINATION THERAPY TO THE CLINIC | CONTINUED

generation antibody formats. We review our approach to biparatopic antibody development and characterization, including design tools and high-throughput screening techniques. As a case study, we review the mechanisms of action of zanidatamab, an anti-HER2 biparatopic antibody, with improved activity and unique functionality not observed with the parental or combination of parental antibodies.

5:00 Bispecific Antibodies in Esophagogastric Cancer: Rationale and Early Clinical Data

Geoffrey Ku, MD, Assistant Attending and Head, Esophagogastric Section, Gastrointestinal Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center

This presentation discusses the rationale and initial results of studies that are evaluating bispecific and biparatopic antibodies in esophagogastric cancer, including several novel anti-Her2 therapies.

5:30 Unique Properties and Clinical Progress of Leading FIT-Ig-Based Bispecific Antibodies

Yang Chen, PhD, Senior Director, Clinical Pharmacology, EpimAb Biotherapeutics Inc

Bispecific antibodies represent a major class of molecular modality in current global biopharmaceutical development. Based on FIT-Ig, EpimAb's bispecific antibody technology, a number of therapeutic molecules have been developed and several are in clinical development, including cancer cell targeting cMET/EGFR (EMB-01) and dual check-point PD-1/LAG-3 (EMB-02). Current data reveals more aspects concerning the clinical validation of the FIT-Ig technology, as well as the synergistic mechanism of these dual-targeting bispecific antibodies.

6:00 Networking Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Advancing Bispecific Antibodies and Combination Therapy to the Clinic

TUESDAY, MAY 3

6:30 pm Recommended Dinner Short Course*

SC7: Developability of Bispecific Antibodies: Formats and Applications

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

THURSDAY, MAY 5

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 306 CONDITIONAL BIOLOGICS

8:25 Chairperson's Opening Remarks

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

8:30 Guided Antibody Tumor Engagers (TwoGATE), the Next-Generation T Cell Redirecting Therapeutics for Solid Tumors

Werner Meier, CSO, Revitope Oncology

Harnessing the immune system has revolutionized cancer treatments, but toxicities limit the potential. Revitope develops T cell engagers (TwoGATE) designed to elicit a potent tumor-focused immune response. The split anti-CD3 paratope requires two antigens on the same tumor cell for activity, which may enable greater tumor specificity and drive potent *in vitro* and *in vivo* tumor cell killing. TwoGATE are well-tolerated in non-human primates and have excellent developability properties.

9:00 The PROTECT Platform: A Multi-Specific Multi-Functional Design to Act in the Right Place at the Right Time

Florian Heinkel, PhD, Scientist, Protein Engineering, Zymeworks Inc.

Many novel immune-oncology biologics are limited in clinical utility due to a narrow therapeutic window. The PROTECT (PROgrammed Tumor Engagement & Checkpoint/Costimulation Targeting) platform is designed to employ orthogonal mechanistic features in a multispecific design to increase the therapeutic window. In particular, we bring TME-specific activity and localized immune modulation in a single transferable, conditionally active design. We show that the PROTECT design is more active than treatment with combinations.

9:30 Streamline T Cell Engager Discovery with Diverse CD3 Antibodies and an Integrated Bispecific Engineering Platform

Raffi Tonikian, Head of Target Product Profile Integration, AbCellera

T cell engagers are widely recognized for their tremendous potential for cancer therapies, but with hundreds in development, only two are on the market. Limited pools of parental antibodies and limited access to bispecific engineering technologies have been barriers to bringing T cell engagers to the clinic. We combine a diverse panel of fully human CD3-binding antibodies with our clinically-validated bispecific engineering platform to streamline discovery of T cell engager therapies.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

10:40 Developing Protease-Activated T Cell Engager Prodrugs with Better Spatial and Temporal Controls

S. Jack Lin, PhD, Senior Director, New Technologies, Harpoon Therapeutics

T cell engagers are a potent therapeutic modality but often require careful management of cytokine release syndrome and other on-target toxicities. Here, we discuss our approaches to engineering protease-activated T cell engager prodrugs, present preclinical evidence on how these different approaches help improve the safety of T cell engagers and propose their utility in diseases previously intractable to T cell engagers.

11:10 Improving the Therapeutic Index of T Cell Engagers and Cytokines with Pro-XTEN Protease-Releasable Masking

Volker Schellenberger, PhD, President & CEO, Amunix

XPATs are conditionally active T cell engagers (TCEs) designed to exploit the dysregulated protease activity in tumors. In preclinical studies across multiple tumor targets XPATs 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 TCEs; 3) Masking increases tolerated Cmax in NHP by greater than 400-fold for HER2-XPAT.

11:40 Cytokine Engineering and Split Assembly

Matthew J Bick, PhD, Director, Protein Science, Neoleukin Therapeutics Inc

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing (Exhibit Hall A & B)

BISPECIFIC ANTIBODIES TARGETING NEOANTIGENS VIA pHLA RECOGNITION

1:15 Chairperson's Remarks

G. Jonah Rainey, PhD, Vice President, Antibody Engineering, AlivaMab Discovery Services

1:20 Oncodriver Mutation-Targeted T Cell Engagers

Sandra B. Gabelli, PhD, Assistant Professor, Biophysics & Biophysics Chemistry, Johns Hopkins University

We have selected antibody fragments by phage display that target mutant peptides derived from the tumour suppressor gene, p53R175H, and from oncogenes KRASG12V and IDH2R140Q. While it remains to be determined which class of therapeutics will prove more efficacious in humans, we present here two avenues, off-the-shelf bispecifics, and CAR T cell, to treat cancer harboring intracellular targets.

1:50 Targeting Intracellular WT1 in AML with a Novel RMF-Peptide-MHC Specific T Cell Bispecific Antibody

Alejandro Carpy, PhD, Principal Scientist, Biologics Core Technologies, Roche Innovation Center Munich, Roche Pharma Research & Early Development, pRED

Antibody-based immunotherapy is a promising strategy for targeting tumor cells. However, classical antibody-based approaches are restricted to targeting cell-surface antigens. We engineered a novel T cell bispecific (TCB) antibody, containing a bivalent T cell receptor-like binding domain that recognizes the intracellular tumor antigen Wilms' tumor 1 (WT1) via pHLA. WT1-TCB facilitates potent *in vitro*, *ex vivo* and *in vivo* killing of AML cell lines and primary AML cells.

2:20 Measurement of PROTAC Ternary Complex Formation Using the switchSENSE Y-Structure and FRET Signals

Jonathon Faherty, Head of Operations, Dynamic Biosensors Inc.

Proteolysis targeting chimeras (PROTACs) are essential bifunctional small molecules that engage the formation of a ternary complex consisting of an E3-ubiquitin-ligase, a target protein of interest and the PROTAC itself. Using switchSENSE technology and the novel DNA Y-structure, an E3-ligase and a target protein can be functionalized on separate ends of two FRET pair color-coded Y-arms, thereby performing high-throughput PROTAC screening to gain information on binary and ternary binding.

2:35 Enabling Bispecifics Discovery Through Ongoing Access to Innovation

Casey Matthews, Senior Director, Business Development and Sales, Alloy Therapeutics

2:50 Networking Refreshment Break (Hynes Main Lobby)

ENGINEERING BISPECIFIC ANTIBODIES | CONTINUED

CD3 TUNING

3:15 Chairperson's Remarks

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

3:20 KEYNOTE PRESENTATION: Targeting the Target: Aligning Target and Biologics' Format Biology to Achieve Desired Outcomes

Tariq Ghayur, PhD, Tariq Ghayur Consulting, LLC

Receptor-ligand interactions have co-evolved to maintain specificity of downstream signaling. However, different biologics to the same receptor can have distinct outcomes. Epitope and valency, in addition to other properties, influence biologic-target interaction outcomes. In this presentation, I will discuss the impact of epitope and valency on downstream signaling and how this information could be used to select "better" lead candidates to potentially achieve "better" desired outcomes.

3:50 Can Non-Conventional T Cells Solve the Problems of Classical T Cell Engagers?

Simon Plyte, PhD, CSO, Biomunex

This talk will describe the BiXAb platform for the generation of bivalent, bispecific antibodies. The advantages of targeting non-conventional T cells and redirecting non-conventional T cells with BiXAb therapeutics will be outlined.

4:20 Close of Day

FRIDAY, MAY 6

7:00 Registration and Morning Coffee (Hynes Main Lobby)

7:30 Interactive Discussions with Continental Breakfast (Ballroom Pre-Function)

Grab your breakfast and Coffee and join a Discussion Group. 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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 4: Making Bispecific Antibodies

G. Jonah Rainey, PhD, Vice President, Antibody Engineering, AlivaMab Discovery Services

• Right lead candidate inputs. Can I just use an off-patent sequence?• Platform selection: geometry, valency, and intellectual property• How many candidates need to be made and tested to find a good lead?

TABLE 5: Engineering Off-the-Shelf Bispecifics and CAR T Cells to Treat Cancer Harboring Intracellular Targets

Sandra B. Gabelli, PhD, Assistant Professor, Biophysics & Biophysics Chemistry, Johns Hopkins University

- Selection and engineering of the scfv partner for the bispecific antibodies
- Expression of bispecifics (type of cells, stability, shelf life)
- Structure-based affinity maturation for bispecifics vs CART cell (tighter vs weaker binding vs specific)
- Recognition of neoantigen-MHC with buried mutations

ROOM LOCATION: 306
ENGINEERING BISPECIFIC MOLECULES FOR INFECTIOUS DISEASES

8:25 Chairperson's Remarks

Mahiuddin Ahmed, PhD, President and CSO, VITRUVIAE

8:30 Bispecific Antibody Therapeutics Targeting Entry by Emerging Viruses

Kartik Chandran, PhD, Professor, Microbiology & Immunology, Albert Einstein College of Medicine

Human monoclonal antibody (mAb) therapeutics have demonstrated utility against emerging viruses but are often deployed as cocktails to enhance efficacy and reduce the risks of viral mutational escape. Here, I discuss our recent work to identify combinations of mAbs that recognize distinct epitopes and drive synergistic viral neutralization through multiple mechanisms. I show that combining such mAbs into bispecific antibodies affords enhanced antiviral potency ***in vitro*** and ***in vivo***.

9:00 Human Bispecific Antibodies against Infectious Diseases

Luca Varani, PhD, Group Leader, Institute for Research in Biomedicine

We developed a human, IgG-like bispecific simultaneously targeting two sites on SARS-CoV-2 (Nature, 2021). It potently neutralizes all variants of concern; protects and prevents formation of viral escape mutants ***in vivo***. Bispecifics against Zika (Cell 2017) and Prion also had synergistic properties beyond those of the parental monoclonals.

9:30 Bispecific HIV-1 Envelope (Env) x CD3 DART Molecules for Clearance of HIV-1-Infected Cells

Jeffrey L. Nordstrom, PhD, Director, Preclinical Product Development, MacroGenics, Inc.

HIV-1 Env x CD3 DART molecules, which induce redirected T cell killing of HIV-1 Env-expressing cells, are being developed as clearance agents for use in strategies to reduce or eliminate persistent viral reservoirs in persons with HIV-1 (PWH) maintained on anti-retroviral therapy (ART). ***In vitro*** and ***in vivo*** properties of DART molecules with different anti-Env specificities and results from a first-in-human safety study in PWH on ART will be shared.

10:00 De-Risking Bispecifics Early-On: How Tight is Too Tight? How Weak is Too Weak?

John Burke, PhD, Co-Founder, President, and CEO, Applied BioMath

Bispecifics are exciting due to their improved specificity, additional MOA, and/or improved therapeutic index. They may be more risky due to increased development complexity, experiment combinatorics, cost and time. Here a T-Cell engager case study is used to highlight Applied BioMath Assess, a web enabled model informed drug development and discovery analysis application, that helps quickly generate actionable hypotheses, impacting critical thinking and portfolio decisions, thus derisking projects.

10:30 Networking Coffee Break (Hynes Main Lobby)

11:00 Natural and Engineered Bispecific Antibodies: Lessons from Malaria and COVID-19

Joshua Tan, PhD, Chief, Antibody Biology Unit, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Bispecific antibodies offer potential advantages as therapeutics against infectious pathogens, including resistance to antigen mutations and the possibility of novel interactions due to the covalent linkage between component antibodies. Here, we discuss two studies: 1) the discovery of naturally occurring bispecific antibodies targeting malaria antigens, and 2) the engineering of bispecific antibodies that potently neutralize SARS-CoV-2 variants of concern.

11:30 Engineering *in vivo* Nucleic Acid Launched DMAbs as a Tool for Rapid Intervention in Emerging Infectious Disease (EID) and Immunotherapy

David B. Weiner, PhD, Executive Vice President, The Wistar Institute; Director, Vaccine & Immunotherapy Center; Professor & WW Smith Chair in Cancer Research; Professor Emeritus, University of Pennsylvania - SOM The Wistar Institute

Synthetic Nucleic Acid (DNA) is a novel approach for developing immunotherapies in both the area of infectious disease as well as cancer. Next-generation ***in vivo*** self-assembling designs support biologic generation of designer mAbs as well as more complex bispecific molecules. We will provide examples of this approach for infectious diseases, such as AMR, and for the treatment of pathogenic cells.

12:00 pm Close of PEGS Summit

IMMUNOTHERAPY STREAM
CONFERENCES

MAY 2-3
Improving Immunotherapy Efficacy and Safety

AGENDA

MAY 3-4
Cell-Based Immunotherapies

AGENDA

MAY 5-6
Next Generation Immunotherapies

AGENDA

IMMUNOTHERAPY STREAM

Developing Novel, Supercharged Immunotherapies for Cancer and Immune Disorders

The Immunotherapy stream highlights the most exciting technologies, tools and engineering strategies driving the development of 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 the latest innovations and efforts to improve cell-based immunotherapies such as CAR T and NK cell therapies; with Part Three focusing on developing the next generation of immunotherapies, including reprogramming the immune system, immune cell engineering, *in vivo*, gene and vector editing and delivery, all supported by in-depth case studies, novel engineering approaches and clinical data.

CONFERENCE STREAMS

ENGINEERING | ONCOLOGY | BISPECIFICS | IMMUNOTHERAPY | EXPRESSION | ANALYTICAL | IMMUNOGENICITY

PEGSBOSTON

SUNDAY, MAY 1

1:00 pm Registration for Pre-Conference Short Courses (Hynes Main Lobby)

2:00 Recommended Pre-Conference Short Course*

SC1: Antibody Drug Discovery: From Target to Lead

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

2:00 Main Conference Registration Open (Hynes Main Lobby)

MONDAY, MAY 2

7:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom C

CURRENT CHALLENGES IN IMMUNOTHERAPY

8:25 Chairperson's Opening Remarks

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

8:30 KEYNOTE PRESENTATION: Current Challenges in Immunotherapy

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

Immunotherapy has become front and center in our armamentarium against cancer, but, where do we go from here, especially given the need for combination therapies to really push the needle in terms of long-term patient survival? In this talk we will try to separate the hype from the reality summarizing the current landscape of cancer immunotherapy, new trends emerging, and some of the key challenges still ahead.

9:00 Enhancing Anti-Tumor Immune Response and Overcoming Resistance

Yan Chen, PhD, Founder & CEO, Elpis Biopharmaceuticals

We utilize proprietary mRNADis and mSCAFold platforms to precisely engineer biologics and modulate immune activation. We will report the preclinical studies of EPIM-001, a bispecific IL2/PD-L1 biologics that has demonstrated multiple mechanisms of action and potent anti-tumor activity; EPB-001, a human anti-Siglec15 antibody that reversed immune suppression and inhibited tumor growth. EPIM-001 and EPB-001 could be promising therapeutics for tumors that are non-responding or resistant to immune checkpoint inhibitor treatment.

9:30 Biophysical Characterization of Protein Reagents for Batch-to-Batch Reproducibility abcam

Deborah Moore-Lai, Senior Director of Protein Development, Protein Development, Abcam, PLC

Abcam is committed to quality and supporting efforts to address the reagent reproducibility crisis. In this talk, Deborah Moore-Lai will discuss biophysical characterization of protein reagents for batch-to-batch reproducibility, providing an overview of Abcam's Premium Bioactive Proteins and analytical tools for assessing physical and functional characteristics of the product line.

10:00 Networking Coffee Break (Pre-function Hall A & Ballroom Pre-Function)

10:30 T Cell Intrinsic Mechanisms of Resistance to Immune Checkpoint Blockade

Michelle Krogsgaard, PhD, Associate Professor, Pathology, New York School of Medicine

Blockade of PD-1 can be an effective immunotherapy for cancers, but many patients do not respond, and the mechanisms that drive resistance are not well understood. We investigate how the intrinsic properties of tumor-specific T cells and the overarching influence of T cell receptor affinity in determining T cell responsiveness to PD-1 blockade to overcome therapeutic resistance.

11:00 Bispecific IgM T Cell Engagers Against CD20 or CD38 with Enhanced Potency and Safety

Bruce Keyt, PhD, CSO, R&D, IGM Biosciences, Inc.

11:30 LUNCHEON PRESENTATION: Discovery and Optimization of CD22 VHH Antibodies for CAR T Cell Therapy charles river

John Wheeler, Director of Protein Technology Discovery, Century Therapeutics

CD22 CAR T cell therapies have shown efficacy in relapsed or refractory B-lineage acute lymphoblastic leukemia (B-ALL) alone and in combination with CD19 CAR T cell therapies. We identified novel single domain antibodies (VHH) to CD22 for CAR-iNK immunotherapy in B-ALL and formatted as CARs, both in monovalent and tandem, bivalent formats. The combination of two VHHs in tandem, binding to both N- and C-terminal epitopes is most effective at eliminating CD22-positive tumor cells.

12:00 LUNCHEON PRESENTATION: Implementing MOA-Reflective ADCC assays Using Ready-to-Use KILR Target & Effector Cells from Screening to Lot Release eurofins | DiscoverX

Gaurav Agrawal, Scientific Development Manager, Eurofins DiscoverX

Evaluation of Fc effector mechanisms of the therapeutic antibodies is an important regulatory requirement. Eurofins DiscoverX's MOA-reflective KILR cytotoxicity assays specifically measure direct killing of antigen-expressing target cells in co-culture with effector cells mediated via ADCC using an easy-to-use, dye-free, and radioactivity-free protocol. Here we share phase-appropriate qualification data for the KILR Raji bioassay model demonstrating that these assays are fit-for-purpose for screening and relative potency applications in lot-release testing.

12:30 pm Find Your Table and Meet Your Discussion Moderator

12:45 Interactive Discussions (Ballroom Pre-Function)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 5: Understand and Overcoming Resistance for Immunotherapies

Michelle Krogsgaard, PhD, Associate Professor, Pathology, New York School of Medicine

TABLE 6: Immunotherapy Safety and Managing Toxicity

Saad Kenderian, PhD, Assistant Professor, Medicine and Oncology, Mayo Clinic College of Medicine

Despite CAR T cell therapy's success in hematological malignancies, toxicities following CAR T cell therapy remain the main limitation to the wider application of the therapy for the treatment of diseases. Here we will discuss lessons learned with regard to mechanisms of toxicities after CAR T cell therapy and review new directions to mitigate such toxicities.

1:30 Session Break

NEW MODES OF T CELL RECOGNITION, GAMMA DELTAS

1:45 Chairperson's Remarks

Yan Chen, PhD, Founder & CEO, Elpis Biopharmaceuticals

1:50 Therapeutic Antibodies to Modulate the Activity of Cytotoxic Gamma Delta T Cells *in Situ*

Mihriban Tuna, PhD, MBA, CSO, Adaptate Biotherapeutics Ltd.

Gamma delta T cells are a unique class of lymphocytes that bridge innate and adaptive immunity. Adaptate has developed monoclonal and bispecific antibodies which target gamma delta T cells. These antibodies selectively modulate gamma delta T cell activity with a potential for superior efficacy and safety compared to conventional immunomodulatory therapies such as pan T cell activators and are being developed primarily for solid tumour indications.

2:20 FEATURED PRESENTATION: 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 developed a successful pipeline for discovering what so-called "orphan T cells" recognize and applied this to dissect what dominant persistent anti-cancer T cells recognize during successful immunotherapy. This work has uncovered a new, unanticipated, mode of T cell recognition. I will describe this new mode of recognition in atomic-level detail and describe why and how it might be linked to successful clearance of solid cancers.

2:50 Screening Biotherapeutics for On- and Off-Target Binding: Aiding Lead Selection and De-Risking Programs Early

Nick Brown, Group Leader, Charles River

The Retrogenix Cell Microarray technology identifies on- and off-target binding for a range of therapeutic modalities by profiling against >6,300 human cell surface and secreted proteins - now including human prenatal targets - each expressed in human cells. Data generated can inform lead selection decisions and provide IND-enabling data for regulatory submissions, accepted by global regulators either in complement with, or as an alternative for, IHC-based tissue cross reactivity data.

3:20 Networking Refreshment Break (Pre-function Hall A & Ballroom Pre-Function)

3:50 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B

PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

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

4:10 KEYNOTE PRESENTATION: Challenges and Opportunities in Developing Non-Antibody Protein Therapeutics

Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

Protein therapeutics are dominating the pharmaceutical market, a steadily increasing trend that started with human insulin in 1982. My presentation will discuss challenges and opportunities for developing non-antibody engineered protein therapeutics as next-generation medicines.

YOUNG SCIENTIST KEYNOTE

4:55 KEYNOTE PRESENTATION: Engineering new "Signaling" Proteins to Enact Anti-tumor Responses

Xin Zhou, PhD, Assistant Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Principal Investigator, Cancer Biology, Dana-Farber Cancer Institute

The world of protein engineering is fascinating, full of possibilities to create molecules with new and desirable structures and functions. My presentation will introduce how we work at the interface of disease biology and protein engineering, designing, constructing, and evolving versatile proteins for the development of next-generation molecular technologies, diagnostics, and therapeutics.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Day

TUESDAY, MAY 3

8:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom C

INTRATUMORAL IMMUNOTHERAPY TO IMPROVE OUTCOMES

8:25 Chairperson's Opening Remarks

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

8:30 Intratumoral Immunotherapy Principles and Practice

Noor Momin, PhD, Postdoc Fellow, Center for Systems Biology, Harvard Medical School

The job of an immunotherapy drug is to instruct the adaptive immune system – in other words, to act as a vaccine. We will present our recent work developing new molecules and recently published design principles for such intra-tumoral immune therapeutics, as well as unpublished data from our ongoing clinical trial treating companion dogs with naturally occurring melanoma and soft tissue sarcoma.

9:00 FEATURED PRESENTATION: Targeting Intratumoral T Cell Retention to Boost Immunotherapy

Amanda Lund, PhD, Associate Professor, Ronald O. Perelman Department of Dermatology Associate Professor, Department of Pathology, NYU Langone Health

The tumor microenvironment regulates the infiltration, retention, function, and exit of tumor-infiltrating lymphocytes. We find that tumor-associated lymphatic vessels facilitate T cell exit out of melanoma. We explored the interstitial trafficking of CD8+ T cells and identified molecular "stay and go" signals that direct CD8+ T cell retention or exit and will discuss the implications for tumor immune surveillance and response to therapy.

9:30 Intratumoral Immunotherapy with Aluminum Hydroxide-Tethered Cytokines Induces Potent Local and Systemic Immunity with Minimal Toxicity

Michael Schmidt, PhD, CSO, R&D, Ankyra Therapeutics

Ankyra's platform enables stable tethering of cytokines and other immune agonists to the common vaccine adjuvant aluminum hydroxide through a novel phosphopeptide linkage. When administered intratumorally (IT), these complexes form an extended

depot in the tumor leading to prolonged immune activation and potent local and systemic anti-tumor efficacy after a single injection with minimal toxicity.

10:00 High-Throughput Visualization of Cell-Cell Interactions for Therapeutic Development Using the Berkeley Lights platform.

Dawson Ray, Business Development Manager, Services Center, Berkeley Lights, Inc.

Berkeley Lights' Optofluidic platforms enable deterministic isolation and culturing of single or multiple cells in nanoliter-sized chambers, allowing for sequential functional assays on the same cell sample, thereby linking cytotoxicity and cytokine secretion. We recently demonstrated organoid structure formation on chip and are looking to use this capability in tumor microenvironment research.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

11:10 FEATURED PRESENTATION: Cross-HLA Targeting of Intracellular Oncoproteins with Peptide-Centric CARs

Mark Yarmarkovich, PhD, Senior Scientist, Children's Hospital of Philadelphia

We developed peptide-centric chimeric antigen receptors (CARs) using a counter-panning strategy with predicted potentially cross-reactive peptides. Our data suggest that peptide-centric CARs have the potential to vastly expand the pool of immunotherapeutic targets to include non-immunogenic intracellular oncoproteins and widen the population of patients who would benefit from such therapy by breaking conventional HLA restriction.

REDUCING TOXICITIES, INCREASING SAFETY

11:40 New Insights into CAR T Cell Toxicities

Saad Kenderian, PhD, Assistant Professor, Medicine and Oncology, Mayo Clinic College of Medicine

Despite CAR T cell therapy success in hematological malignancies, toxicities following CAR T cell therapy remain a main limitation to the wider application of the therapy for the treatment of diseases. Here we will discuss lessons learned with regard to mechanisms of toxicities after CAR T cell therapy and review new directions to mitigate such toxicities.

12:10 Managing Cytokine Release Syndrome

Caroline Diorio, MD, Fellow, Cancer Center, Children's Hospital of Philadelphia

The most common severe toxicity associated with chimeric antigen receptor T cells targeting CD19 (CART19) is cytokine release syndrome (CRS). To obtain a more robust understanding of CRS biology, we performed comprehensive secretome profiling to measure more than 1400 serum analytes on serial serum samples collected from patients treated with the 41BB-containing CTL019 on two clinical trials. We identify pre-infusion biomarkers for CRS and potentially targetable pathways.

12:40 pm Enjoy Lunch on Your Own

1:40 Close of Improving Immunotherapy Efficacy and Safety

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*

SC7: Developability of Bispecific Antibodies: Formats and Applications (Dinner Short Course)

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*
SC1: Antibody Drug Discovery: From Target to Lead
**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

ROOM LOCATION: Ballroom C
THE NEW ERA OF CAR T THERAPIES

2:15 Chairperson's Opening Remarks
Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

2:20 KEYNOTE PRESENTATION: Engineering the Next-Generation of CAR T Therapies
Michel Sadelain, PhD, Stephen & Barbara Friedman Chair & Director, Centre for Cell Engineering, Memorial Sloan Kettering Cancer Centre

Chimeric antigen receptors (CARs) are synthetic receptors that target and reprogram T cells. CARs specific for CD19 have demonstrable efficacy in a range of hematological malignancies. Despite remarkable complete remission rates, relapses do occur in a significant fraction of patients. Insufficient functional persistence and antigen sensitivity have emerged mechanisms of tumor escape or relapse. Engineering the epigenetic profile of T cells and novel receptors designs may overcome these limitations.

2:50 FEATURED PRESENTATION: Translating Lessons Learned from Approved CAR T Cell Products to Next-Generation Treatments
Adrian Bot, MD, PhD, CSO, Executive Vice President, R&D, Capstan Therapeutics

Development and evaluation of first wave autologous CAR T cell products directed at B cell malignancies, showed that this treatment modality can be curative in a subset of patients. We discuss major mechanisms of treatment response, resistance and toxicities, and impact of this learning on next-generation treatments in a broader category of disease indications.

3:20 The *in vitro* Measure of Avidity Between Tumor & Effector Cells Predicts Optimal *in vivo* Response LUMICKS
Will Singleterry, Commercial Director - Immuno-Oncology, Cell Avidity, LUMICKS

- We present data discussing how increased specific avidity, those TCR's with strongest antigen binding with the lowest background, correlate with improved TCR function *in vitro* and *in vivo*.
- How CAR T and TCR T avidity is significantly more correlative to *in vivo* outcome than either cytotoxicity assays or IFN-g release.
- Methods for using cell avidity to screen constructs and more reliably select lead candidates

3:50 pm Refreshment Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

LATEST DEVELOPMENTS IN TARGETING HEMATOLOGIC MALIGNANCIES

4:30 Developing CAR T Cell Therapies against Deadly Hematologic Malignancies
Maksim Mamonkin, PhD, Assistant Professor, Center for Cell and Gene Therapy, Baylor College of Medicine

CAR T cells have shown remarkable efficacy in patients with B-cell malignancies but extending this therapy to other hematologic cancers remains challenging. I will summarize results of our latest efforts in developing engineered T cell therapies against non-B cell leukemia and lymphoma and evaluating these approaches in Phase I clinical trials.

5:00 New Targets and Technologies for CAR T Cells
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- 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.

5:30 Advances in CAR T Therapies: Understanding Resistance to CAR T immunotherapy to Develop Next-Generation Therapies
Marco Ruella, MD, Assistant Professor of Medicine, Scientific Director, Lymphoma Program, Division of Hematology and Oncology and Center for Cellular Immunotherapies, University of Pennsylvania

CAR T therapy is changing the treatment paradigm for lymphoid malignancies. However, there are still significant challenges to be overcome as the majority of patients will eventually fail this therapy. Moreover, CAR T therapy is still not working satisfactorily in most cancer types. Dr. Ruella will provide an overview of the latest findings of his group on resistance mechanisms to CAR T immunotherapy and strategies to overcome them.

6:00 Close of Day

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*
SC7: Developability of Bispecific Antibodies: Formats and Applications (Dinner Short Course)
**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

WEDNESDAY, MAY 4

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom C
ADVANCING ALLOGENEIC CELL THERAPIES

8:25 Chairperson's Opening Remarks
Bob Valamehr, PhD, Chief Research and Development Officer, Fate Therapeutics

8:30 Developing Tumor Microenvironment CARs
Paul Neeson, PhD, Associate Professor, Cancer Immunoloy Research, Peter MacCallum Cancer Centre

To date, clinical trials with CAR T cells have had limited efficacy in patients with solid tumors. To improve patient outcomes, we have specifically explored human cancer immune context and revealed immune suppression pathways. We have then engineered human CAR T cells to address these immuno-suppressive pathways to maintain CAR T cell effector function and persistence in the tumor microenvironment.

9:00 Advancements in the Development of Off-the-Shelf CAR T Cell Therapies
Laurent Poirot, PhD, Senior Vice President, Immunology, Cellectis
This presentation will discuss advancing the CAR T field from autologous to allogeneic approaches; TALEN: gene-editing platform to optimize persistence, potency, and safety of CAR T; and broadening success of allogeneic CAR T therapies from hematologic malignancies to solid tumors.

CELL-BASED IMMUNOTHERAPIES | CONTINUED

9:30 Employing NK and T Cell CARs and Off-the-Shelf iPSC Platform for Solid Tumor Therapy

Bob Valamehr, PhD, Chief Research and Development Officer, Fate Therapeutics

Clonal master iPSC lines can be used as a renewable source for repeatedly and cost-effectively manufacturing cell therapy products that can be delivered off-the-shelf to treat many patients. Our cells of interest are the cells of the immune system. And our cell therapy product candidate pipeline is comprised of immuno-oncology programs, including off-the-shelf NK- and T cell product candidates, that target a broad range of liquid and solid tumors.

10:00 Synthetic Gene Circuits for Cancer Immunotherapy – Turning Cancer Cells Against Themselves

Ming-Ru Wu, MD/PhD, Assistant Professor, Department of Cancer Immunology and Virology, Dana-Farber Cancer Institute. Harvard Medical School

We have developed synthetic cancer-targeting gene circuits that specifically target cancer cells. Once the circuits enter cells, they will sense the activity of several cancer-associated transcription factors and get activated in tumor cells, to trigger tumor-localized combinatorial immunotherapy. Circuits mediate robust therapeutic efficacy in ovarian cancer mouse models. This platform can be adjusted to treat multiple cancer types and can potentially trigger any genetically-encodable immunomodulators as therapeutic outputs.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

11:10 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

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

11:30 KEYNOTE PRESENTATION: Future Directions in Drug Discovery & Development

Roger M. Perlmutter, MD, PhD, Chairman and CEO, Eikon Therapeutics, Inc.

The intrinsic complexity of human physiology has generally defeated attempts to model normal cellular functions, meaning that until recently we have had few tools to disentangle the molecular pathology associated with common illnesses. Now, dramatic improvements in instrumentation, automation, and computing provide ways to measure dynamic responses in living cells, and to use these measurements to identify both new disease targets, and new chemical starting points for future medicines.

12:15 pm Session Break

ROOM LOCATION: Ballroom C

12:30 LUNCHEON PRESENTATION: Evaluation of Safety and Efficacy of Bispecific Antibodies and CAR T Therapies in Humanized Mice

James Keck, PhD, Senior Director, Innovation and Product Development, The Jackson Laboratory

Data will be presented that demonstrates a PBMC humanized mouse platform can be used to de-risk therapeutic antibody and cell-based preclinical drug development. The assay is fast, sensitive, reliable, reproducible and allows a holistic approach to drug discovery where, in one platform, you can simultaneously evaluate efficacy, cytokine induction, immunophenotyping, mouse clinical evaluation and downstream organ toxicity.

1:00 LUNCHEON PRESENTATION: CRISPR-Cas9 Materials for Human Cell Therapy Research

Jason Potter, R&D Director, Cell Biology, Thermo Fisher Scientific

We have established new manufacturing and quality control processes to produce a recombinant CRISPR/Cas9 protein that is suitable as an ancillary material for cell and gene therapy applications. Here we demonstrate the use of this newly manufactured Cas9 protein under our Cell Therapy Systems "CTS" brand – CTS TrueCut Cas9 Protein – as benchmarked against our catalog Cas9 product in primary T cells with both the bench scale Neon and newly released large scale CTS Xenon electroporation system.

1:30 Find Your Table and Meet Your Discussion Moderator

1:35 Interactive Discussions (Exhibit Hall A & B)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 6: Beyond First-Generation CAR T Therapies

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

CO-PRESENTATION: Table 12: Understanding Resistance to CAR T Immunotherapy

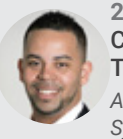
Marco Ruella, MD, Assistant Professor of Medicine, Scientific Director, Lymphoma Program, Division of Hematology and Oncology and Center for Cellular Immunotherapies, University of Pennsylvania

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

ENGINEERING AGAINST SOLID TUMORS

2:20 Chairperson's Remarks

Paul Neeson, PhD, Associate Professor, Cancer Immunoloy Research, Peter MacCallum Cancer Centre



2:25 FEATURED PRESENTATION: CAR T Cells Targeting Carbohydrate-Based Cancer Targets in Solid Tumors

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.

CELL-BASED IMMUNOTHERAPIES | CONTINUED

2:55 Development of Dual-Targeted Fine-Tuned Immune Restoring (DFIR) CAR T Cell Therapy for Achieve CURES of Clear Cell Renal Cell Carcinoma (ccRCC)

Wayne Marasco, MD, PhD, Professor of Medicine, Cancer Immunology & Virology, Dana-Farber Cancer Institute

Dual-targeted Fine-tuned Immune Restoring (DFIR) CAR T cells have been designed for CURE of ccRCC. Elevated safety is addressed through fine-tuned CARs which have affinities of the scFv targeting moieties tailored to only recognize high-density tumor-associated antigens (TAAs). Immune restoration is attained through delivery of checkpoint blockade inhibitor antibody payloads that act locally on the tumor microenvironment.

3:25 Toward Commercializing Tumor Infiltrating Lymphocyte Cell Therapy for Treatment of Solid Tumors

Madan H. Jagasia, Senior Vice President, Medical Affairs, Iovance Biotherapeutics

3:55 Ice Cream Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 First-in-Human Trial of CAR T Targets MUC1 Transmembrane Cleavage Product

Cynthia C. Bamdad, PhD, CEO, Minerva Biotechnologies Corp.

Minerva Biotechnologies is focused on cancer and stem cell therapeutics. We are developing cancer immunotherapies targeting 80% of solid tumors and to prevent cancer metastasis.

5:00 Optimizing CAR T Cells for Solid Tumors through Affinity Tuning and Tracking

Eric von Hofe, PhD, Senior Advisor, AffyImmune Therapeutics, Inc.

The paucity of tumor-specific antigens is a challenge for all targeted therapies, most are simply overexpressed tumor-associated antigens. Affinity tuning CAR T cells provides both selectivity to tumor cells overexpressing a tumor-associated antigen to reduce on-target/off-tumor toxicity and enhances CAR T cell activity in animal models. We have initiated a Phase I trial of an affinity tuned CAR T cell that also can be tracked in real time in patients.

5:30 Targeting Solid Tumors

Travis S. Young, PhD, Vice President, Biologics, California Institute for Biomedical Research

6:00 Networking Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Cell-Based Therapies

TUESDAY, MAY 3

6:30 pm Recommended Dinner Short Course*

SC7: Developability of Bispecific Antibodies: Formats and Applications (Dinner Short Course)

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

THURSDAY, MAY 5

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: Ballroom C

SCREENING FOR THE NEXT-GENERATION OF T CELLS

8:25 Chairperson's Opening Remarks

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

8:30 High-Throughput Screening of Chimeric Antigen Receptor T Cells

Stuart A. Sievers, PhD, Senior Scientist, Research & Cell Biology, Kite a Gilead Co.

Chimeric antigen receptor (CAR) T cells have been shown to be an effective treatment option against B cell malignancies. Early ***in vitro*** characterization efforts have been largely manual and low-throughput. Using automated liquid handling and data analysis, we can now screen hundreds of unique CAR T cells; thereby allowing for the discovery of functionally relevant, lead binders and the assessment of structure-activity relationships among CAR components.

9:00 Next-Generation Screening Technologies for T Cell Therapies

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

Effective cellular therapies for solid tumors have proved elusive. We present new platforms to rapidly assess the functional effects of large pools of T cell genetic modifications in parallel non-virally. Pooled knock-ins combined with single-cell sequencing also revealed high-dimensional cellular phenotypes associated with improved clearance of solid tumor xenografts. Scalable discovery and engineering of T cell therapies will enable more rapid clinical development of curative cell therapies for solid tumors.

9:30 Discovery of Next-Generation Biotherapeutic TCR Mimic Antibodies in Cancer Immunotherapy Alloy Therapeutics

Dongxing Zha, CTO, TCR Discovery and Engineering, Alloy Therapeutics

Despite the success of high-potency oncology biologics in treating liquid tumors, they are limited as solid tumor therapeutics. Keyway TCR Discovery at Alloy Therapeutics discovers antibodies mimicking T cell receptors (TCRm) and TCRs engineered in high affinity and specificity to pHLA tumor antigens, so these new modalities can successfully treat solid tumors. Keyway embraces Alloy's business strategy integrating related platforms, services, and venture studio new company creation focused on this modality.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

REPROGRAMMING THE IMMUNE SYSTEM VIA *IN VIVO* ENGINEERING

10:40 Next-generation Delivery of CARs to Cells

Michael E. Birnbaum, PhD, Assistant Professor, Biological Engineering, Massachusetts Institute of Technology

Cell and gene immunotherapies are revolutionizing how we treat disease, with multiple FDA-approved therapies that have transformed cancer treatments. However, advances in gene delivery, manufacturing, and therapeutic cargoes are still required to increase the impact and scope of these promising approaches. Our laboratory is working to develop approaches that improve the specificity of cellular engineering, and the potency of cells once engineered.

11:10 Engineering Retargeted Fusogens for *in vivo* Gene Delivery to T Cells

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

11:40 CAR T Cell Therapy for the Treatment of Fibrotic Conditions

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

Fibrosis is seen in nearly every form of heart disease and is a significant factor in disease progression. Current treatments for fibrosis remain limited, necessitating new approaches. In a mouse model of heart disease, we were able to target and ablate activated cardiac fibroblasts in hearts will established fibrosis using Fibroblast Activation Protein (FAP) CAR T cells. This treatment significantly reduced cardiac fibrosis and rescued cardiac function.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing (Exhibit Hall A & B)

ENGINEERING SMARTER CELL THERAPIES

1:15 Chairperson's Remarks

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

1:20 FEATURED PRESENTATION: Engineered B Cells as a Novel Off-the-Shelf Therapy in Oncology

Richard A. Morgan, PhD, CSO, Be Biopharma

The ability to engineer primary human B cells to differentiate into long-lived plasma cells and secrete ***de novo*** proteins permits the creation of novel plasma cell therapies for the next generation of immunotherapies. Efficient engineering is achieved by CRISPR/Cas9 editing in combination with AAV DNA templates and results in site-specific gene insertion. Our results demonstrate a novel strategy for modifying human plasma cells to secrete therapeutic proteins.

1:50 Chimeric Antigen Receptor Macrophages for Cancer 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). In this talk we will review the CAR-M platform, present novel preclinical data, and discuss the ongoing Phase I, first-in-human CAR-M trial for HER2+ metastatic solid tumors.

2:20 Our Commitment to Provide Excellence to Cell & Gene Therapy Acro

Teng Peng, PhD, Senior Technique Application Manager, Technique Application, ACROBiosystems

This presentation will briefly introduce the trends in cancer cell therapy based on the published data. It will mainly focus on Acro's solutions to support cell gene therapy (CGT) at different stages from early drug discovery, manufacture /quality control to preclinical and clinical research. It will introduce Acro's key products, new

technology platform and new product pipeline including Star staining fluorescent conjugation and GMP grade products, etc.

2:50 Networking Refreshment Break (Hynes Main Lobby)

3:20 Overcoming Solid Tumor CAR-T Toxicity with Next-Generation T Cell Reprogramming

Vijay Reddy Peddareddigari, MD, Executive Vice President, Chief Research and Development Officer, Tmunity

Our first-in-human armored CAR targeting PSMA coupled with a dominant-negative TGFBR2, showed anti-tumor effects but also severe immune toxicity. We designed a CAR with additional armor (a PD1-CD28 switch) and compared the 41BB endodomain with a novel CD2 domain. Preliminary data indicated the CD2 based endodomain tricistronic CAR against PSMA maintained cytotoxicity, memory profile, and activation while having a significantly reduced risk of inducing macrophage activation.

3:50 Gene Editing Platform to Enhance CAR T and NK Cell Functions in Hematological and Solid Tumors

Justin Eyquem, PhD, Parker Senior Fellow, Microbiology & Immunology, University of California San Francisco

Although CAR T cells have shown remarkable results against hematological malignancies, many aspects of this technology remain to be improved. Despite remarkable initial responses, relapses occur in a large proportion of patients with poor CAR T cell persistence or tumors expressing very low levels of target antigen. We are using pooled CRISPR KI to screen for novel CAR architectures with improved proliferation, persistence, or sensitivity against low antigen densities.

4:20 Close of Day

FRIDAY, MAY 6

7:00 Registration and Morning Coffee (Hynes Main Lobby)

7:30 Interactive Discussions with Continental Breakfast (Ballroom Pre-Function)

Grab your breakfast and Coffee and join a Discussion Group. 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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 6: Next-Generation Immunotherapies

Jonathan Gilbert, PhD, Vice President, Exploratory Research, SQZ Biotech

ROOM LOCATION: Ballroom C
EMERGING IMMUNOTHERAPIES

8:25 Chairperson's Remarks

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

8:30 BEAT, a Plug-and-Play Platform for Engineering Novel Multi-Specific Antibodies Against Cancer

Ankita Srivastava, PhD, Vice President, Protein Sciences and Rational Design, Ichnos Sciences Biotherapeutics SA

Ichnos' BEAT® platform (Bispecific Engagement by Antibodies based on the TCR) facilitates design of multispecific antibodies using efficient heavy chain heterodimerization and a common light chain. ISB 1442, a first-in-class 2+1 biparatopic BEAT® 2.0 bispecific (CD38xCD47) antibody, demonstrates higher potency and tumor growth inhibition preclinically relative to daratumumab. A Phase 1 study in hematologic malignancies is planned for mid-2022.

9:00 FEATURED PRESENTATION: First-in-Human Clinical Study Evaluating GD2-CAR NKTs Co-Expressing IL15 in Patients with Neuroblastoma

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

CAR-NKT cells expanded ***in vivo***, localized to tumors and, in one patient, induced an objective response with regression of bone metastatic lesions. These initial results suggest that CAR-NKT cells can be expanded to clinical scale and safely applied to treat patients with cancer.

9:30 Targeting NK Cells to Treat Cancer: Individual to Off-the-Shelf Products

Jeffrey Miller, MD, Professor of Medicine, Deputy Director, Masonic Cancer Center, 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. Trispecific killer engagers (TriKE) that target endogenous NK cells or enhance cell products are in clinical development. Off-the-shelf NK cells from induced pluripotent stem cells containing multiple gene edits will promote specificity, persistence, and enhanced activity ***in vivo*** to enhance cancer therapy.

10:00 Clinical Translation of Novel Cell Therapies for Diverse Applications Using Microfluidic Cell Squeezing

Jonathan Gilbert, PhD, Vice President, Exploratory Research, SQZ Biotech

Cell Squeeze technology enables precise cell engineering while preserving cell health and function. Our lead program, engineered APCs, has demonstrated safety and stimulation of immune responses in certain patients with HPV16+ tumors. Other platforms include activating antigen carriers (AACs), and tolerizing antigen carriers (TACs) manufactured from RBCs for antigen-specific activation or suppression respectively. Currently, billions of cells can be processed per minute and personalized therapies are manufactured in <24hrs.

10:30 Networking Coffee Break (Hynes Main Lobby)

11:00 Polyfunctional Engineering of Immune Cells to Advance Allogeneic Cellular Therapies

Beau R Webber, PhD, Assistant Professor, Pediatrics, University of Minnesota

11:30 Maximizing the Therapeutic Potential of Allogeneic Natural Killer Cells

Sasha Lazetic, Director R&D, Platform & Antibody Development, Nkarta Inc

Natural Killer (NK) cells are innate immune cells that can eliminate target cells in an antigen-independent fashion. NK cells can be engineered to express chimeric antigen receptors (CARs), expanded under different conditions, and gene edited to further enhance cytotoxicity, selectivity, and persistence. Nkarta is developing off-the-shelf CAR NK cells to maximize the therapeutic potential of allogeneic NK cells alone or in combination with other agents.

12:00 pm Close of PEGS Summit

EXPRESSION STREAM
CONFERENCES

MAY 2-3
Difficult-to-Express Proteins

AGENDA

MAY 3-4
Optimizing Protein Expression

AGENDA

MAY 5-6
Maximizing Protein Production Workflows

AGENDA

EXPRESSION STREAM

Maximizing Quantity and Quality while Minimizing Time and Cost

The growing demand for recombinant proteins requires simultaneous strategic development, application, and adoption of technologies for the efficient expression and production of these valuable biomolecules. The Expression Stream begins with "Difficult-to-Express Proteins" What makes a protein difficult to produce? is followed by "Optimizing Protein Expression" What is the best expression system for producing your protein of choice? and concludes with "Maximizing Protein Production Workflows" What are your throughput goals? 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.

CONFERENCE STREAMS

ENGINEERING | ONCOLOGY | BISPECIFICS | IMMUNOTHERAPY | EXPRESSION | ANALYTICAL | IMMUNOGENICITY

PEGSBOSTON

SUNDAY, MAY 1

1:00 pm Registration for Pre-Conference Short Courses (Hynes Main Lobby)

2:00 Recommended Pre-Conference Short Course*
SC2: Introduction to Lipid Nanoparticle Characterization and Formulation
**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

2:00 Main Conference Registration Open (Hynes Main Lobby)

MONDAY, MAY 2

7:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 304

EXPEDITIOUS EXPRESSION AND PRODUCTION

8:25 Chairperson's Opening Remarks
Yves Durocher, PhD, Research Officer & Head, Mammalian Cell Expression, National Research Council Canada

8:30 Rapid, High-Yield Production of Full-Length SARS-CoV-2 Trimeric Spike Ectodomains Using Stable CHO Pools
Yves Durocher, PhD, Research Officer & Head, Mammalian Cell Expression, National Research Council Canada

Stably transfected CHO clonal cell line is the standard platform for manufacturing recombinant glycoprotein therapeutics. The current pandemic, concurrently with improvements in the performance of stable CHO pool platforms, have contributed to their wider acceptance by the regulatory authorities to accelerate clinical evaluation of potentially life-saving drugs. I will present our recent efforts using stable CHO pools to manufacture the SARS-CoV-2 trimeric spike protein as a vaccine subunit antigen.

9:00 Production of an RBD-Based Recombinant Protein Vaccine against SARS-CoV-2 in *Pichia pastoris*
Zhuyun Liu, Research Director, Upstream Process Development, Baylor College of Medicine

The wild-type RBD protein expressed in yeast has low yield and tendency to aggregate. By introducing two genetic modifications, we greatly improved the protein expression and stability without changing its biological function. Fermentation process was developed with an average yield of 428 ± 36 mg/L. This production process has been transferred to an industrial manufacturer, who has successfully advanced this vaccine candidate into Phase 3 clinical trials.

9:30 Precision Execution of Bispecifics at Scale from Design to Delivery Lonza
Lisa Prendergast, PhD, Associate Director of Expression System Sciences, Licensing, Lonza

Generating a bispecific antibody, which is correctly and stably paired, is challenging. Various platforms have developed Heavy-Light chain (HC-LC) mispairing fixes, but there are many rate limiting steps for efficiently expressing these molecules in a CHO system including adaptation of downstream processes. bYlok technology is a design engineering approach that stabilises the interaction between the HC and LC, essentially removing the mispairing problem whilst retaining a more natural antibody structure.

10:00 Networking Coffee Break (Pre-function Hall A & Ballroom Pre-Function)

10:30 Scalable, High-Resolution Purification of SARS-CoV-2 Spike Protein
Raja Ghosh, PhD, Professor, Chemical Engineering, McMaster University

Recombinant SARS-CoV-2 Spike protein has been proposed as a vaccine candidate for immunization against COVID-19. It is a very large, fragile, and difficult to purify protein. Its large size restricts its access to binding sites present in typical resin media used for chromatographic purification and thereby limits its binding capacity. A membrane chromatography-based rapid and scalable method for purification of recombinant SARS-CoV-2 Spike protein will be discussed.

11:00 Strategies to Accelerate Process Development from Preclinical to Manufacturing for Gene Therapy
Hassan Sakhtah, PhD, Associate Director, Bioprocess Development, CuriRx Inc

11:30 LUNCHEON PRESENTATION: Overcoming the Challenges for High-Throughput Production of Diverse Custom Proteins Used in Discovery Applications WuXi Biologics Global Solution Provider
Sam Zhang, Senior Director of CMC Management, CMC, WuXi Biologics

We will discuss the challenges in high-throughput protein production for small and large molecule drug discovery. We demonstrate the parameters and design space required to generate high-quality proteins for HTS, antibody discovery, ***in vivo*** and developability studies. Supported by our industry-leading platforms, the Protein Sciences department at WuXi Biologics provides production services utilizing various expression systems for the generation of monoclonal, bispecific and multispecific antibodies, and other recombinant proteins.

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

12:30 Find Your Table and Meet Your Discussion Moderator

12:45 Interactive Discussions (Ballroom Pre-Function)
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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 7: Challenges in Finding/Training/Retaining Technical Staff Post-pandemic
Anne Skaja Robinson, PhD, Trustee Professor & Department Head, Chemical Engineering, Carnegie Mellon University

- Best practices in remote recruiting and onboarding?
- Job flexibility as a retention incentive?
- How do we train or retrain entry-level scientists with limited hands-on experience?
- What skills are missing in entry-level or more experienced scientific staff?

TABLE 8: Challenges in Working with Protein Complexes
Oleg Brodsky, Senior Principal Scientist, Structural Biology & Protein Sciences, Pfizer Inc.

- Protein expression and purification strategies
- Biochemical/biophysical/structural characterization
- Opportunities and pitfalls – what works and what doesn't

1:30 Session Break

STRUCTURALLY COMPLEX TARGETS

1:45 Chairperson's Remarks
Anne Skaja Robinson, PhD, Trustee Professor & Department Head, Chemical Engineering, Carnegie Mellon University

1:50 Insights into the Role of N-Linked Glycosylation in Directing Subcellular Localization of Membrane Proteins Expressed in Yeast and Its Impact on Function

Monica D. Rieth, PhD, Assistant Professor of Biochemistry, Southern Illinois University

Glycosylation is the process of the attachment of sugar moieties to proteins during co-translational or post-translational modification and occurs during expression in organisms like ***Saccharomyces cerevisiae***. For membrane proteins, which are difficult to produce due to their physiochemical properties, high-level production is especially challenging. This work aims to uncover factors affecting protein subcellular localization during expression. We postulate a critical link between subcellular localization and production of functional proteins.

2:20 FEATURED PRESENTATION: Functional Expression of Adenosine A3 and A1 Receptors in Yeast Utilizing a Chimera with the A2AR C-Terminus

Anne Skaja Robinson, PhD, Trustee Professor & Department Head, Chemical Engineering, Carnegie Mellon University

The adenosine A_{2A} receptor ($A_{2A}R$) shows exceptional yields in all expression hosts, unlike the closely related G protein-coupled receptors A_1R and A_3R. By creating chimeric A_3R and A_1R proteins with $A_{2A}R$ we examined the G-protein coupling specificity. In this talk, I will describe these results as well as binding of G-protein to different purified chimeras.

2:50 Optimizing a Bispecific Format for Antigen Design

Richard Buick, PhD, Chief Scientific Officer, Fusion Antibodies

Multiple antigen formats are often needed for antibody discovery to overcome issues associated with avidity and stability. If molecules cannot be standardized, optimization may be needed for each new antigen. Fusion Antibodies has developed a process for the routine production of multiple antigen formats using a unique application of knob-in-hole technology. The molecules generated give greater diversity compared with approaches that use a small number of standard antigens.

3:05 Sponsored Presentation *(Opportunity Available)*

3:20 Networking Refreshment Break (Pre-function Hall A & Ballroom Pre-Function)

3:50 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

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

4:10 KEYNOTE PRESENTATION: Challenges and Opportunities in Developing Non-Antibody Protein Therapeutics

Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

Protein therapeutics are dominating the pharmaceutical market, a steadily increasing trend that started with human insulin in 1982. My presentation will discuss challenges and opportunities for developing non-antibody engineered protein therapeutics as next-generation medicines.

YOUNG SCIENTIST KEYNOTE

4:55 KEYNOTE PRESENTATION: Engineering new "Signaling" Proteins to Enact Anti-tumor Responses

Xin Zhou, PhD, Assistant Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Principal Investigator, Cancer Biology, Dana-Farber Cancer Institute

The world of protein engineering is fascinating, full of possibilities to create molecules with new and desirable structures and functions. My presentation will introduce how we work at the interface of disease biology and protein engineering, designing, constructing, and evolving versatile proteins for the development of next-generation molecular technologies, diagnostics, and therapeutics.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Day

TUESDAY, MAY 3

8:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 304
PRODUCTION OF MEMBRANE PROTEINS

8:25 Chairperson's Remarks

Oleg Brodsky, Senior Principal Scientist, Structural Biology & Protein Sciences, Pfizer Inc.

8:30 Production of a Human Histamine Receptor for NMR Spectroscopy in Aqueous Solutions

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

A major bottleneck in human GPCR structural biology is the production of sufficient quantities of folded and functional receptors. Expressing GPCRs for nuclear magnetic resonance experiments is made even more challenging by the requirement to incorporate stable-isotope probes. We present an optimized workflow for recombinant production of human GPCRs in ***Pichia pastoris*** for biophysical experiments, illustrated by the production of a human histamine receptor.

9:00 Deorphanizing Tough Membrane Targets Using Recombinant Extracellular Vesicles

Shengya Cao, PhD, Senior Scientist, Genentech

Membrane proteins are major drug targets because of their central roles in regulating cellular communication. Despite this, membrane receptors remain underrepresented in interaction databases because of technical limitations. To overcome these challenges, we developed an extracellular vesicle-based method for membrane protein display that enables purification-free and high-throughput detection of receptor-ligand interactions in membranes. We demonstrate that this platform is broadly applicable and can be used to profile endogenous vesicles.

9:30 Self-Assembling Peptides for Membrane Protein Purification and Stabilization

Sotirios Koutsopoulos, PhD, Researcher, Center for Biomedical Engineering, Massachusetts Institute of Technology

Membrane proteins are integral proteins of the cell membrane and are directly involved in the regulation of many biological functions and in drug targeting. However, our knowledge of such proteins is limited due to difficulties in producing sufficient quantities in a soluble, functional, stable state. Designed, surfactant-like peptides may be used to extract membrane proteins from the cell membrane and stabilize the protein for further studies.

DIFFICULT TO EXPRESS PROTEINS | CONTINUED

10:00 Finding 100+ Functional GPCR Antibodies in 8 Months with an Integrated Antibody Discovery Technology Stack

Katherine Lam, Research Scientist, AbCellera

GPCRs are highly sought-after drug targets, but challenges in producing proteins, driving immune responses, and finding hits have limited the development of antibody therapies against these high-value targets. To address these challenges, we leveraged our fully integrated technology stack to rapidly discover functional antibodies against a GPCR target and identify lead candidates with species cross-reactivity and potencies that rival small molecule clinical-stage benchmarks.

10:15 Shortening Clinical Developments Timeline Using Novel Gpex Lightning Technology

Greg Bleck, PhD, Vice President, Research and Development, Catalent Biologics

During this talk, Catalent will share the latest data leveraging GPEx Lightning to generate highly stable, highly productive cell pools and discuss how the GPEx suite of technologies can be tailored to the specific needs of each individual program on its path to clinical trials.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

PRODUCTION OF FINICKY PROTEINS

11:10 Production of Human Mitochondrial ABC Transporters in *E. coli*

Maria E. Zoghbi, PhD, Assistant Professor, Molecular Cell Biology Department, University of California, Merced

Many biochemical and structural studies require extensive mutational analysis of the protein of interest. This task can be slow and expensive when using eukaryotic expression systems. Therefore, the use of bacteria as expression system can be very advantageous. Thus, we decided to express a mitochondrial human ABC transporter, which does not require post-translation modifications, in bacteria. The human transporter can be successfully purified from bacteria and is fully functional.

11:40 Production of Human MOZ Acetyl Transferase Quaternary Complex in Insect Cells

Oleg Brodsky, Senior Principal Scientist, Structural Biology & Protein Sciences, Pfizer Inc.

This talk will cover protein expression, purification, and biochemical/biophysical characterization of the human full-length MOZ 4-protein complex in insect cells. The talk will highlight the challenges of overexpressing a multimeric complex recombinantly, as well as the enablement of various biochemical and biophysical assays that resulted from it.

12:10 Tags and Buffers for SPR: Perfecting Proteins to Probe Biophysical Behavior

Maya Rao, PhD, Senior Scientist, UCB, Inc.

Binary and ternary complex formation assays are crucial for biotherapeutic research and producing pure, high-quality proteins for SPR analysis may be considered an art. How do we engineer tags and linkers, optimize buffers, and develop workflows for protein complexes, specifically to conserve native folding, promote access to binding pockets, and reduce SPR artifacts? Through thoughtful design and effective strategy, one can accomplish the binding-competence of their SPR dreams.

12:40 LUNCHEON PRESENTATION: High Level Expression of Novel Antibodies Using the Pelican Expression Technology Platform

Russell Coleman, Director, Strain Engineering, Platform Technology & Innovation, Pelican

The Pelican Expression Technology platform (formerly the Pfenex Expression Technology) is a robust, cost-effective, commercially validated platform based on Pseudomonas fluorescens for recombinant protein production with four approved products utilizing the technology. Example expression studies are presented demonstrating the extensive Pelican toolbox of genetic elements, host strains, and automated strain screening that enabled rapid the expression for two complex and challenging antibody formats: a Fab fragment and picobodies.

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

1:40 Close of Difficult-to-Express Proteins

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Dinner Short Courses*

Separate registration required. See short course page for details.

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

8:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 304

WHY CHOOSE CHO?

2:15 Chairperson's Opening Remarks

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

2:20 High ER/Golgi Content Renders a Unique CHO Host with High Antibody Productivity and Product Quality

David Busch, PhD, Associate Principal Scientist, Preclinical Development, Merck Research Labs

We have developed a CHO host with specific productivity similar to the levels observed in professional secretory cells. This CHO host cell also produces complex molecules such as multi-specific antibodies with higher quality compared to other CHO host cells. The superior performance of this host cell may be explained by its significantly higher ER / Golgi content.

2:50 Optimizing Protein Expression: Tailored Glycosylation, Improved Quality and Faster Cell Line Development

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

Based on the outcome of our CHO cell line engineering research, we have developed CHO cell based platforms, enabling rapid production of tailored glycoforms of therapeutic proteins, with improved protein quality and predictable cell line development. Through the glycoengineered CHO platform (geCHO), the effect of N-glycans on therapeutic proteins can be screened, and the optimal glycoform can then be manufactured using the geCHO cell lines.

3:20 Development of an Antibody Targeting Confirmational Epitope

evitria

Kristin Connelly, Research Associate, Protein Sciences Team, Pyxis Oncology

Glycoprotein nonmetastatic melanoma protein B (GPNMB) is a surface protein co-inhibitory receptor expressed on tumor-associated macrophages (TAMs) and myeloid-derived suppressor cells (MDSCs). GPNMB may interact directly with T-cells, impairing T cell activation to down-modulate anti-tumor immune response. Human GPNMB has soluble and membrane-bound forms, and soluble GPNMB may act as a decoy receptor, resulting in an antibody sink. Here we report an approach for developing antibodies binding specifically to membrane-bound GPNMB.

3:50 pm Refreshment Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 Optimization of a Transient Antibody Expression Platform Towards High Titer and Efficiency

Elizabeth A. Greene, Scientist IV, Biotherapeutics Molecule Discovery, Boehringer Ingelheim Pharmaceuticals, Inc.

Chinese Hamster Ovary (CHO) cells are one of the major workhorses for Transient Gene Expression (TGE) of recombinant antibodies. Through a matrix evaluation of multiple factors including inoculum, transfection conditions, amount and type of DNA used (including Filler DNA), and post-transfection culture conditions, we arrived at an uniquely optimized TGE process with higher titer and reduced costs and time, thus increasing the overall efficiency of early antibody material supply.

5:00 Understanding Novel Inhibitory Metabolites on Growth and Protein Synthesis in Mammalian Cells

Seongkyu Yoon, PhD, Professor, Chemical Engineering, University of Massachusetts, Lowell

Mammalian metabolic inefficiencies lead to accumulation of waste by-products. Untargeted and targeted metabolomics for identification of novel metabolites identified six CHO metabolic inhibitors. They negatively impact growth and titer production. Inhibitors were shown to accumulate across different mammalian cell lines. A holistic methodology incorporates metabolomics analysis into cell culture studies.

5:30 Investigating the Influence of Physiologically Relevant Hydrostatic Pressure on CHO Cell Batch Culture

Jongyoon Han, PhD, Professor, Electrical Engineering & Computer Science, Massachusetts Institute of Technology

In this study, hydrostatic pressures similar to ***in vivo*** interstitial pressure values (0~90 mmHg) were applied to batch CHO cell culture, and their cell growth/metabolism and IgG_1 production were examined. Our results indicate that hydrostatic pressure can increase the maximum cell concentration by up to 50%. These findings are important for the optimization of fed-batch or perfusion culture for directing cell growth and improving antibody production.

6:00 Close of Day

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Dinner Short Courses*

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

WEDNESDAY, MAY 4

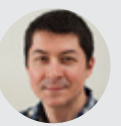
7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 304

CELL-FREE SYSTEMS

8:25 Chairperson's Remarks

Vincent Noireaux, PhD, Professor, Synthetic Biology and Biological Physics, University of Minnesota Twin Cities



8:30 FEATURED PRESENTATION: An All-*E. coli* Cell-free Toolbox: *In vitro* Synthesis of Proteins and Phages

Vincent Noireaux, PhD, Professor, Synthetic Biology and Biological Physics, University of Minnesota Twin Cities

Cell-free transcription-translation (TXTL) has become a highly versatile multidisciplinary technology for bioengineering and synthetic biology. By enabling the rapid expression of genes and gene circuits, TXTL integrates an ever-growing variety of applications. In this talk, I will present an all-***E. coli*** TXTL system and discuss the capabilities of this system to rapidly-produce milligrams amounts of proteins and bacteriophages at high titers.

9:00 Rapid Genetic Sequence Characterization and Expression Optimization with Cell-Free Systems

Matthew W. Lux, Research Biologist, BioSciences, Edgewood Chemical Biological Center

Cell-free expression systems allow evaluation of gene expression from DNA constructs without cloning, accelerating characterization timelines. Low reaction volumes and experimental assembly using acoustic liquid handling further increase the throughput possible. We have shown rapid screening of a library of genetic regulatory sequences by varying PCR primers. We further report use of a similar approach to modify the composition of the cell-free reaction to optimize expression of a target gene.

9:30 From Cells to Cell-Free Protein Synthesis within 24 Hours Using Cell-Free Autoinduction Workflow

Javin Oza, PhD, Assistant Professor, Chemistry & Biochemistry, California Polytechnic State University

Numerous developments have made the cell-free expression platform more accessible to new users and have expanded its range of applications. However, the workflow for ***E. coli*** cell extract preparation has remained a bottleneck. We have developed the Cell-Free AutoInduction (CFAI) workflow that allows users to grow cells, produce extracts, and conduct cell-free protein expression within 24 hrs. Additionally, the CFAI workflow reduces the time and cost of generating cell extracts.

10:00 Rebuilding the Cell-Free System and Their Applications for R&D of Biologics

GeneFrontier

Takashi Ebihara, PhD, COO, GeneFrontier Corporation

Our unique platform technology, PURExfrex, is a fully reconstituted (or rebuilt) cell-free protein expression system. It's easy to customize the system for various applications, and useful for high throughput screening of various kinds of biologics as well. Plus, we established robust ribosome display with customized PURExfrex and named PURExfrexRD, which has great advantage in screening of highly diversified library to generate new biologics such as antibodies or cyclic peptides.

10:15 Fast and Efficient Recombinant Protein Expression Optimization

Polyplus

Cassie-Marie Peigne, PhD, Scientific Support Specialist, Polyplus-transfection

Production of biotherapeutic protein and antibodies relies on successful selection of high performing clone for manufacturing. To accelerate this process, the right transfection reagent is key to produce milligram to gram quantities of proteins and to overcome productivity challenges of diverse proteins from therapeutic antibodies to difficult-to-express proteins. We demonstrate how FectoPRO transfection reagent is the go-to transfection reagent that combines productivity and flexibility in suspension CHO and HEK-293 cell lines.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

11:10 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

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

11:30 KEYNOTE PRESENTATION: Future Directions in Drug Discovery & Development

Roger M. Perlmutter, MD, PhD, Chairman and CEO, Eikon Therapeutics, Inc.

The intrinsic complexity of human physiology has generally defeated attempts to model normal cellular functions, meaning that until recently we have had few tools to disentangle the molecular pathology associated with common illnesses. Now, dramatic improvements in instrumentation, automation, and computing provide ways to measure dynamic responses in living cells, and to use these measurements to identify both new disease targets, and new chemical starting points for future medicines.

12:15 pm Session Break

ROOM LOCATION: 304

12:30 LUNCHEON PRESENTATION: Comprehensive Cell-Line Characterization and Genotypic Stability

SELEXIS

Emanuel Schmid-Siegert, PhD, Computational scientist, NGSAI (JSL) - Head of discovery and products, BIOINFORMATICS, NGSAI - JLS - Selexis

Sequencing of genomes has become an essential tool to study human/viral/microbial and cell-line diversity. CHO cell-line development benefits from these multi-modal sequencing advancements. We will present our solutions that assess comprehensively the genotypic stability of clones, the location and architecture of transgene integration and additionally the quality and risk associated with a clone selection.

1:00 LUNCHEON PRESENTATION: DirectedLuck for Bispecifics - A Transposase System Streamlines Cell Line Development.

ProBioGen

Ellen Hilgenberg, PhD, Business Development Manager, ProBioGen AG

An elegant highly active transposase equipped with epigenetic readers carries expression units to most active spots in the host genome providing desired expression levels and stability. With this foundation the focus for screening producer clones is entirely on correct pairing and PTMs. We will discuss how this system is adapted to various formats and removing a critical bottleneck for bi-specifics during clinical development.

1:30 Find Your Table and Meet Your Discussion Moderator

1:35 Interactive Discussions (Exhibit Hall A & B)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 7: Operating in the Inter-Space Between Academia and Industry

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

- What are the advantages/pitfalls?
- What is needed?
- When to do what? Collaboration, Partnering or Fee-for-Service?
- Which infrastructures, technologies, competences are relevant?
- Funding, Pricing, Priorities & Quality
- Staff: Students? PostDocs? Staff Scientists?

TABLE 8: Cell-Free Gene Expression

Vincent Noireaux, PhD, Professor, Synthetic Biology and Biological Physics, University of Minnesota Twin Cities

- Is poor reproducibility from lab-to-lab or systems-to-systems a big issue?
- Can the preparation and utilization of CFE systems be standardized?
- What are the current major CFE limitations?
- What should the next major improvements to CFE systems be?

ALTERNATIVE EXPRESSION SYSTEMS

2:20 Chairperson's Remarks

Pravin Mahajan, PhD, Associate Director, Molecular Sciences, Astex Pharmaceuticals Ltd.

2:25 Production of TCRαβ for Single Molecule Mechanotransduction Studies: Opportunities and Challenges

Robert J. Mallis, PhD, Instructor, Dermatology, Harvard Medical School

The aßT cell receptor (aßTCR) recognizes peptides bound to surface major histocompatibility complex molecules (pMHC) on virally infected or cancerous cells by aßT cells, recognition which was found to be force-dependent. To probe the origins of mechanosensing, a eukaryotic transient expression toolbox was developed for single-molecule (SM) study of the TCR-pMHC interaction. Production of the heterodimeric aßTCR for SM proved to be robust, allowing systematic deconstruction of TCR mechanosensing.

2:55 Generation and Characterization of a Vaccine Antigen Against SARS-CoV-2 Based on the Nucleocapsid Protein of the Virus Fused to Human CD40L

Thailin Gonzalez, MsC, Agriculture Research Division, Center for Genetic Engineering and Biotechnology, Cuba

The N protein of the SARS-CoV-2 virus constitutes an attractive target to be used in a subunit vaccine. The N protein was fused to the extracellular domain of human CD154 (CD40L) (N-CD protein). Lentiviral particles bearing the N-CD gene were used to transduce HEK-293 cells. Polyclonal populations were obtained and characterized. Next, cell clones were obtained by limiting dilution cloning and adapted to growth in serum-free medium and suspension culture.

3:25 Overcoming Timeline Challenges in Antibody Drug Discovery

Ishita Barman, Field Application Scientist, Life Science, GenScript USA, Inc.

This presentation will focus on key platform technologies to address and overcome timeline challenges in therapeutic drug development. Starting with a high through-put antibody discovery platform (MonoRab) and optimized mammalian expression system (TurboCHO) developed in-house, our goal is to provide key reagents (like anti-ID antibodies and kits to enable PK studies) in an effort to meet faster timelines without compromising quality.

3:40 Finding the Needle in the Haystack – A New Method for Selecting High-Producing Stable Cells

Dennis Karthaus, PhD, Director Protein Products & Assays, IBA Lifesciences

High producing stable mammalian cells are often required for producing recombinant proteins. Traditional methods like antibiotic selection cause high levels of cell stress during the selection or require high initial costs for instruments. Here, we present a new bead based method for generating high producing stable cell pools that avoids substantial negative effects on viability or cell growth after selection and that does not have high acquisition costs for instruments.

3:55 Ice Cream Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 Protein Expression, Purification, and Characterization for Fragment-Based Drug Discovery

Pravin Mahajan, PhD, Associate Director, Molecular Sciences, Astex Pharmaceuticals Ltd.

Astex has successfully applied its proprietary FBDD platform to generate multiple new drug candidates that are progressing in clinical development. The platform employs X-ray crystallography and a range of biophysical methods for FBDD. Moreover, Astex has established a state-of-the-art cryo-EM facility. Production of suitable quality proteins is a prerequisite for supporting these platforms. I will share our experience and case studies on expression, purification, and characterisation of challenging drug targets.

5:00 Characterizing and Advancing Baculovirus Driven Production of Closed-Ended DNA in Sf9 Cells for Gene Therapy

Daniel J. Blackstock, PhD, Principal Scientist, Process Development, Generation Bio

Baculovirus expression systems composed of Cap-, Rep-, and trans-gene baculoviruses are routinely employed for the scalable expression of adeno-associated virus (AAV) gene therapy vectors. Here, we describe the characterization and development of a baculovirus system devoid of the Cap-gene for expression of capsid-free closed-ended DNA (ceDNA) for non-viral gene therapy. The expression challenges faced and methods for controlling and maximizing ceDNA expression yields will be discussed.

5:30 PANEL DISCUSSION: Alternative Expression Systems

Moderator: Pravin Mahajan, PhD, Associate Director, Molecular Sciences, Astex Pharmaceuticals Ltd.

What is your host of choice? Maximizing your productivity may necessitate an alternative host expression system. This panel of experts share their host/platform selections – which may or may not have been their primary host of choice.

Panelists:

Daniel J. Blackstock, PhD, Principal Scientist, Process Development, Generation Bio

Thailin Gonzalez, MsC, Agriculture Research Division, Center for Genetic Engineering and Biotechnology, Cuba

Robert J. Mallis, PhD, Instructor, Dermatology, Harvard Medical School

6:00 Networking Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Optimizing Protein Expression

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

6:30 pm Dinner Short Courses*

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

THURSDAY, MAY 5

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 304

WORKFLOW MANAGEMENT: MEETING YOUR CUSTOMERS NEEDS BY INCREASING PRODUCTION EFFICIENCY

8:25 Welcome by Conference Organizer

Mary Ann Brown, Executive Director, Conferences, Cambridge Healthtech Institute

8:30 PANEL DISCUSSION: Protein Production Lab Challenges: Methodologies, Strategies, and the Art of Managing Multiple Projects

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

Protein production laboratories provide crucial support to drug discovery efforts. As we would expect, there are numerous challenges in the effective operation of these critically needed facilities. This panel discussion will focus on the concepts, technologies, and strategies necessary to meet the ever-increasing need for recombinant proteins.

- Prioritizing projects or asking the right questions
- Total workflow efficiency
- Engaging/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

Oleg Brodsky, Senior Principal Scientist, Structural Biology & Protein Sciences, Pfizer Inc.

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

Ruth L. Saxl, PhD, Protein Chemistry Scientist, Scientific Services, Jackson Laboratory

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

Jessica A. Williamson, PhD, Protein Production Lead, UCB

9:30 Accelerating Clone Selection and Upstream Process Development through Data-Driven Decisions

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Lindsay Morrison, PhD, Principal Scientist, Waters Corporation

Real-time product attribute and spent media information is important to upstream bioprocess optimization, analysis results are often lagging by weeks. Engineers can now take decisions faster by producing their own at-line quality data, accessible workflows coupling small bioreactors like Sartorius Ambr systems to Waters' BioAccord LC-MS system. Drug quality and yield can be maximized, and downstream impurities minimized. Development is accelerated from weeks to days, saving resources from multiple optimization cycles.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

10:40 Operating in the Interspace between Industry and Academia: Development and Management of the Cell Line and Protein Production Facility at the National Biologics Facility

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

The National Biologics Facility at the Technical University of Denmark offers cell line development and protein production services to both academics and industrial customers. This is done in an academic setting and meets all the requirements of an industrial facility. The advantages of a dynamic academic research environment are combined with the documentation and regulatory requirements necessary for the production of biologics that can be used in industrial settings.

11:00 Making Proteins for Geneticists: Life in a Small Protein Facility

Ruth L. Saxl, PhD, Protein Chemistry Scientist, Scientific Services, Jackson Laboratory

The Jackson Laboratory pioneered the use of mice as models for human disease. Today, it discovers precise genomic solutions for human diseases. JAX Protein Production and Purification Service enables the faculty to advance newly identified genes to the proteins they encode. While producing proteins, the service focuses on educating the geneticists about proteins. It strives to provide high-quality services while understanding the limits determined by being a small service.

11:20 Challenges in Moving from Research to GLP/GMP

David Blum, PhD, Director, Bioexpression & Fermentation Facility, Biochemistry & Molecular Biology, University of Georgia

Moving from research-based operations to projects that have GxP requirements can be challenging in a university or start-up. Structural as well as cultural issues can hamper progress. This talk will describe experience in moving from research-based operations to projects that require increasing amounts of documentation. Topics will include how to implement a documentation system, how to manage equipment qualifications, as well as staff training and culture.

11:40 Accelerating Drug Discovery: Getting to the Right Molecule Smarter & Faster

Lucy Holt, PhD, Manager, Biopharm Discovery, GlaxoSmithKline

This presentation discusses the need for identification of exquisite specificities in mAb discovery. It demonstrates GSK's use of automation to keep the discovery funnel wider for longer. This includes the ability to express and purify panels of antibodies in a high-throughput, automated manner, enabling parallel biological and developability screening, and accelerating the drug discovery process.

12:00 pm Session Break

12:10 Luncheon in the Exhibit Hall and Last Chance for Poster Viewing (Exhibit Hall A & B)

WORKFLOW MANAGEMENT: ENHANCING QUALITY CONTROL PROCESSES

1:15 Chairperson's Remarks

Jessica A. Williamson, PhD, Protein Production Lead, UCB

1:20 Solving Challenges to the Production of High-Quality Protein Reagents for Early-Stage Drug Discovery

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

Early-stage drug discovery demands the highest quality protein reagents in support of assay development and deployment, biochemical and biophysical measurement, and structural biology. Failures to control protein quality can lead to lost time and money and adversely impact downstream colleagues and collaborators. We discuss the standard processes used to control protein quality at the Frederick National Laboratory's RAS Initiative and lessons learned from the many proteins we have produced.

1:40 Protein Production QC – A Protein Chemist's Toolbox

Oleg Brodsky, Senior Principal Scientist, Structural Biology & Protein Sciences, Pfizer Inc.

This presentation covers the protein production setup at Pfizer in San Diego from small-scale triage to multi-liter scale-up capabilities. Various techniques employed to characterize the proteins produced in a fit-for-purpose manner, including some specific examples (eg: SEC-MALS, DLS, DSF, ITC, Mass Photometry, Microscale Thermophoresis, etc.) will be discussed.

2:00 Utilizing a Streamlined Automated Workflow to QC Baculovirus Expression

Noel Byrne, Assoc Principal Scientist, Structural Protein Sciences, Merck & Co Inc

Challenges exist with the baculovirus expression system including time and effort to generate, screen, and store large numbers of viruses. We have developed a streamlined process to QC new viral constructs by incorporating; 1) Off-the-shelf automation platforms 2) Screening miniaturization techniques and 3) Data management platforms. This workflow accelerates viral generation through an improved screening funnel and reduces the total number of viral samples that need to be managed.

2:20 Early Production of Therapeutic Candidates from Stable CHO Pools Accelerates Drug Development ABZENA

Simon Keen, Vice President, Cell Line Development, Abzena

Stable CHO pools, generated during cell line development (CLD), can be used to purify material for multiple lead candidates. While CLD continues, in depth characterization of candidates can be combined with knowledge gained on their performance in platform USP and DSP conditions, adding manufacturability data to lead selection. The material produced can also be used to drive key development activities, moving these off the critical path and reducing timelines to IND.

2:35 A Simple, Scalable and Cost-Effective Solution for Automated Medium to High-Throughput Antibody and Protein Purification GenScript Make Research Easy

Sean Taylor, Field Application Scientist Manager, North America, GenScript

The sample pre-purification processes of centrifugation, filtration and concentration of cell culture supernatants and/or lysates coupled with the post-purification concentration of purified protein eluates represent the most costly and labor-intensive components of a typical protein purification workflow. We describe a novel technology to eliminate these steps through target capture directly in live cell culture or lysates using magnetic beads.

2:50 Networking Refreshment Break (Hynes Main Lobby)

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 have shared our experiences and working solutions for end-to-end protein production workflows. Now as a as a collective community, let's hear from the table facilitators as they share key the discussion points, 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 6

7:00 Registration and Morning Coffee (Hynes Main Lobby)

7:30 Interactive Discussions with Continental Breakfast (Ballroom Pre-Function)

Grab your breakfast and Coffee and join a Discussion Group. 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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 7: Future Platforms for Future Modalities

David Wood, PhD, Co-Founder, CSO, Protein Capture Science; Professor, Chemical & Biomolecular Engineering, The Ohio State University

- Are columns here to stay, or is it time to reconsider other approaches?
- What about cleavable tags?
- What kinds of products will be driving this innovation?
- What do those platforms need to look like in terms of scale, performance and cost?
- How open are companies to trying disruptive technologies?
- Are the innovations in the products enough for now, so we should play it safe on the methods?

CO-PRESENTATION: TABLE 8: Common Issues with Transient Protein Production

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

Henry C. Chiou, PhD, Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific

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

- What are the current challenges to transient protein production?
- How has the COVID-19 pandemic affected your workflow and productivity?
- How do we optimize the whole protein expression workflow process?
- How can we maintain volumetric yields while scaling transient expression up or down?
- What cell line(s) should we use and when?
- What parameters can impact the quality or physical attributes of transiently produced proteins?

ROOM LOCATION: 304

WORKFLOW MANAGEMENT: OPTIMIZING PURIFICATION AND PRODUCTION

8:25 Chairperson's Remarks

David Wood, PhD, Co-Founder, CSO, Protein Capture Science; Professor, Chemical & Biomolecular Engineering, The Ohio State University

MAXIMIZING PROTEIN PRODUCTION WORKFLOWS | CONTINUED

8:30 Purification Development and Optimization for Scale-Up Production of SARS-CoV-2 Receptor Binding Domain-Based Vaccines

Jungsoon Lee, PhD, Research Director, Downstream Process Development, Baylor College of Medicine

The COVID-19 pandemic put many scientific communities in the race to develop an effective vaccine. We generated recombinant protein antigens derived from the receptor binding domain (RBD) of SARS-CoV-2 spike protein and developed a vaccine. Here we present the purification method developed to produce highly pure RBD protein from the fermentation culture of *P. pastoris*. Furthermore, we optimized the purification process to support fully scalable production at a low cost.

8:50 Accelerating Protein Research to the Clinic through Self-Removing Affinity Tags

David Wood, PhD, Co-Founder, CSO, Protein Capture Science; Professor, Chemical & Biomolecular Engineering, The Ohio State University

Although tags can enable the rapid purification of proteins for research, their potential immunogenicity precludes their use for clinical material. Consequently, research and clinical production groups have been separated by the different approaches needed to fulfill their customer needs. Here we report our commercially available self-removing affinity tag technology, with the potential to bridge high-throughput research with large-scale clinical production under a single, uniquely optimized purification platform.

9:10 What Are the Key Considerations for Setting Up and Maintaining an Effective Protein Production Laboratory

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

Protein production is more complex than just the act of expressing the protein. This presentation reviews end-to-end protein production workflow process including establishing roadmap for short-and-long-range planning and outfitting, determining what expression systems will be critical components of your expression toolbox, complexity of the total protein production workflow (Cloning, Expression, Purification, and Analytics) and how to identify opportunities to increase its efficiency and productivity in a recombinant protein expression facility.

9:30 Advancements in Workflows to Support the Ever Increasing Demand & Complexity of Protein Production in Drug Discovery

Kanika Bajaj Pahuja, PhD, Scientific Manager, Protein Sciences, Genentech Inc.

This presentation will focus on the evolution of our end-to-end automated high-throughput protein expression and purification workflows. It will emphasize the importance of automation and bioinformatics tools that are integrated to provide efficient solutions. This customizable "one for all" approach significantly alleviates some of the bottlenecks in protein production and accelerates the provision of key protein reagents to ambitious projects.

10:00 Overcoming Process Bottlenecks Utilizing Automated End-to-End Synthetic Biology Solutions CODEX DNA

Jason Lehmann, PhD, Senior Product Marketing Manager, Marketing and Product Management, Codex DNA

In an industry facing increasingly challenging deliverables, the ability to rapidly build synthetic DNA, mRNA, and protein is critical. Imagine a development pipeline where it was possible to build biology overnight. Join us to learn about how the BioXp™ System, the world's only fully automated benchtop instrument enables numerous synthetic biology workflows by providing a turn-key, end-to-end solution for generating synthetic DNA and mRNA starting from DNA sequence.

10:30 Networking Coffee Break (Hynes Main Lobby)

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 have shared our experiences and working solutions for end-to-end protein production workflows. Now as a as a collective community, let's hear from the table facilitators as they share key the discussion points, strategies and provide a wrap-up of their table's discussion. What can we take away and apply?

12:30 pm Close of PEGS Summit

ANALYTICAL STREAM
CONFERENCES

MAY 2-3
Characterization for Novel Biotherapeutics
AGENDA

MAY 3-4
Biophysical Methods
AGENDA

MAY 5-6
Gene Therapy R&D Analytics
AGENDA

ANALYTICAL STREAM

Best Practices and Solutions for Characterization of Novel Biologics, Emerging Biophysical Methods and Gene Therapy R&D

The 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 2022, this three-meeting stream offers comprehensive individual programs focused on novel therapeutic modalities, biophysical methods and the analytical technologies employed for gene therapies from research through preclinical development. 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.

CONFERENCE STREAMS

ENGINEERING | ONCOLOGY | BISPECIFICS | IMMUNOTHERAPY | EXPRESSION | ANALYTICAL | IMMUNOGENICITY

PEGSBOSTON

SUNDAY, MAY 1

1:00 pm Registration for Pre-Conference Short Courses (Hynes Main Lobby)

MONDAY, MAY 2

7:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 302

NOVEL CONJUGATES

8:20 Chairperson's Opening Remarks
Adam Parks, PhD, Associate Director, Molecular Engineering, NexImmune, Inc.

8:30 Characterization of Heterogeneous PEGylated Proteins and Polymer Excipients in the Formulation
Ross Yang, Scientist, Merck Research Labs

PEGylated proteins and many non-ionic polymeric surfactants and excipients, such as polysorbates and poloxamers that are used in formulation of biopharmaceuticals share the same building block which is polyoxyethylene. Characterization of PEGylated proteins and polymer excipients with a combination of liquid chromatography, charge reduced mass spectrometry and software-assisted composition analysis will be presented. This method offers advantages such as retaining intact polymeric structures, visualization, and fast profiling of polymeric species.

9:00 Novel Strategies for Developing Site-Specific Antibody Conjugates and the Challenges of Characterizing These Conjugates
Andrew Tsourkas, PhD, Co-Director, Center for Targeted Therapeutics and Translational Nanomedicine; Professor, Bioengineering, University of Pennsylvania

Most standard approaches used to prepare antibody conjugates suffer from non-quantitative, indiscriminate labeling. The value of introducing cargo at specific sites has become increasingly apparent. However, current site-specific labeling methods are not amenable to high-throughput screening and pose characterization challenges. I will discuss several bioconjugation techniques that we developed to enable the rapid, highly efficient, and site-specific labeling of full-length antibodies and how we characterize these conjugates.

9:30 Taking Complex Molecule Characterization to the Next Level: Connecting the Dots by Connecting the Columns
Thomas Martens, Business Development & Sales Manager, RIC biologics

As protein therapeutics become more complex, our analytical tools need to rise to the challenge. Unravelling these structural complexities by combining multiple chromatographic dimensions holds great promise. We will share some real-life examples of how this innovative approach dramatically improves our analytical understanding of novel conjugates and other biotherapeutics.

10:00 Networking Coffee Break (Pre-function Hall A & Ballroom Pre-Function)

VACCINES

10:30 Data-Independent Acquisition Mass Spectrometry for Site-Specific Glycoproteomics Characterization of SARS-CoV-2 Spike Protein
Joseph Zaia, PhD, Professor, Biochemistry and Bioinformatics, Boston University

Alteration in spike protein glycosylation is a mechanism whereby viruses evolve to remain fit as they circulate in the human population. Glycosylation is inherently heterogeneous, making rigorous comparison of the complete glycosylated structures of viral proteins a statistical problem. In response, we have used high-definition MSE (HDMSE) on a cyclic ion mobility MS instrument to produce optimal depth and confidence for calculating similarities of viral spike glycoproteins during evolution.

11:00 KEYNOTE PRESENTATION: Improved Analytics to Support Vaccine Development and Manufacturing
Christopher J. Roberts, PhD, Professor, Chemical & Biomolecular Engineering, University of Delaware

There is a need for improved potency assays and biophysical characterization analytics for vaccines across multiple modalities. NIIMBL (the National Institute for Innovation in Manufacturing Biopharmaceuticals) is working with a range of partners from industry, academia, not-for-profit organizations, and federal stakeholders to support programs that will assess and develop key analytical technologies for the industry. This presentation will highlight short- and long-term efforts and facilitate further community engagement.

11:30 LUNCHEON PRESENTATION: Dashboards for Biologics Attributes - A New Tool to Accurately Monitor CQAs and Other Metrics
Michelle English, Dr, Data Science Product Manager, Protein Metrics

Biologics development needs to summarize and explain very complex data - in this workshop we will show how LC-UV-MS experiment outcomes can be represented in shareable, web-based dashboards. Some of the most complex analyses are easily digestible, and become understandable by an entire organization, and reduce the burden on needing expert explanation. Usable for MAM, screening, system suitability, Protein Metrics' Deep Query tools will be useful to any biotherapeutics organization.

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

12:30 Find Your Table and Meet Your Discussion Moderator

12:45 Interactive Discussions (Ballroom Pre-Function)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 9: Characterization Challenges for New Biotherapeutic Modalities
Ming Huang, PhD, Scientist, Regeneron Pharmaceuticals, Inc.

TABLE 10: Analytical Challenges in the Characterization of Biotherapeutics: Sample Preparation, Analysis and Data Processing
Ross Yang, Scientist, Merck Research Labs

1:30 Session Break

CELL THERAPIES

1:45 Chairperson's Remarks
Mary McDonald, Researcher, Analytical Development, Synlogic, Inc.

1:50 Design and Characterization of Novel HLA and Antibody for Presentation of Disease Antigen Peptides for Adoptive Cellular Therapy

Adam Parks, PhD, Associate Director, Molecular Engineering, NexImmune, Inc.

Nanoparticle-based artificial antigen presenting cells (aAPCs) that present peptide-HLA complexes target specific T cell populations for expansion and enrichment. Adapting aAPCs for diverse patient populations requires identification and characterization of HLA-restricted peptides that are distinctly expressed on target cells. We present modular nanoparticle components, combined with a systematic approach for the identification and evaluation of antigen derived peptides, to target a variety of therapeutic indications.

2:20 Identification and Qualification of CQAs for Live Biotherapeutic Products

Mary McDonald, Researcher, Analytical Development, Synlogic, Inc.

The characterization of Live Biotherapeutic Products (LBPs) includes the examination of novel attributes outside of classical protein-based biotherapeutic properties. The FDA has set regulatory guidance for the evaluation of LBPs. Identification of novel attributes and the qualification of the release assays are critical to moving products into regulatory compliance. This presentation will discuss the development and qualification of assays used to dose LBPs.

SELECTED POSTER PRESENTATION

2:50 Selected Poster Presentation: Mapping Structurally Significant Areas of G-CSF During Thermal Degradation with NMR

Mark-Adam Kellerman, PhD Researcher, Biochemical Engineering, University College London, United Kingdom

A protein's structure-function relationship refers to a trade-off between stability and bioactivity, molded by its evolution. Here, characteristics of residues in granulocyte-colony stimulating factor (G-CSF) are probed with 15N-1H HSQC NMR during a denaturing thermal melt. We confirm a previously observed aggregation-prone conformation change in loop AB and uncover a "switch mechanism" significant to bioactivity. Thus, we found residues H43, V48 and S63 to be pivotal to the stability-bioactivity trade-off.

3:20 Networking Refreshment Break (Pre-function Hall A & Ballroom Pre-Function)

3:50 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

4:00 Plenary Keynote Introduction

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

4:10 KEYNOTE PRESENTATION: Challenges and Opportunities in Developing Non-Antibody Protein Therapeutics

Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

Protein therapeutics are dominating the pharmaceutical market, a steadily increasing trend that started with human insulin in 1982. My presentation will discuss challenges and opportunities for developing non-antibody engineered protein therapeutics as next-generation medicines.

YOUNG SCIENTIST KEYNOTE

4:55 KEYNOTE PRESENTATION: Engineering new "Signaling" Proteins to Enact Anti-tumor Responses

Xin Zhou, PhD, Assistant Professor, Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Principal Investigator, Cancer Biology, Dana-Farber Cancer Institute

The world of protein engineering is fascinating, full of possibilities to create molecules with new and desirable structures and functions. My presentation will introduce how we work at the interface of disease biology and protein engineering, designing, constructing, and evolving versatile proteins for the development of next-generation molecular technologies, diagnostics, and therapeutics.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Day

TUESDAY, MAY 3

8:00 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 302
MULTI-SPECIFICS

8:25 Chairperson's Remarks

Gary Hao, PhD, Vice President, Analytical Development, Codiak BioSciences

8:30 Integrated Developability Strategy to Safeguard the Discovery and Optimization of Multi-Specific Biotherapeutics at Sanofi

Melanie Fischer, PhD, Head of Assays and Analytics, Biologics Research, Sanofi

The complexity of multi-specific biotherapeutics requires a comprehensive set of analytical techniques and an appropriate developability strategy to guide lead discovery and optimization. An overview of the integrated developability concept at Sanofi will be presented with a focus on chemical and physical stability of multi-specific drug candidates. The strategic overview will be augmented with case examples highlighting the challenges in characterization and developability of multi-specific molecules.

9:00 Monitoring the Purity and Stability of Multi-Specific Antibodies *in vitro* and *in vivo* with CE and CE-MS Intact Mass Analysis

Morgan Stickney, PhD, Scientist, Amgen, Inc.

Multi-specific antibodies are rapidly becoming attractive modalities as they bind to multiple targets simultaneously, reducing side effects and toxicity build-up. Monitoring the impurity/stability/modification of large complexed molecules is vital during drug discovery and development to ensure the potency of the drug and can be done efficiently through capillary electrophoresis (CE) and intact mass analysis by CE-MS. Immunoaffinity purification-CE-MS can effectively monitor protein stability ***in vivo*** and identify the cleavage sites.

9:30 Design and Characterization of a Tri-Specific Antibody Discovery Platform

John de Kruif, PhD, Senior Vice President & CTO, Merus NV

Triple-targeting formats hold great therapeutic promise but translation of concepts into active molecules is challenging both in obtaining differentiated functional activity, as well as meeting stringent developability criteria. We discuss the discovery and characterization of the components and final candidates of a tri-specific antibody format referred to as Triclonics that permits high-throughput in-format repertoire screening to result in active molecules that harness the developability characteristics of regular human monoclonal antibodies.

CHARACTERIZATION FOR NOVEL BIOTHERAPEUTICS | CONTINUED

10:00 Characterization of Protein Secondary Structure and Aggregation Utilizing Microfluidic Modulation Spectroscopy

David Sloan, PhD, Director of Applications, RedShiftBio

The AQS^{3}pro system, built upon Microfluidic Modulation Spectroscopy, is an automated infrared platform optimized to determine biomolecule structure in a complex buffer and at formulation concentration. The AQS^{3}pro combines a 24 or 96-well plate, a quantum cascade laser, built-in automation, and a microfluidic flow cell to produce highly precise, higher-order structure measurements for determining stability, aggregation, lot-to-lot similarity, and formulation optimization of biomolecules.

10:15 Quantification of Bispecific Antibody Mediated T-Cell Activation with Engineered CD3 Effector and Tailored Target Cells

Michael Schwenkert, Ph.D, CSO, Svar Life Science

Bispecific antibodies efficiently trigger T-cells mediated cytotoxicity and many T-cell engaging biopharmaceuticals are in clinical development. Current analytical methods measuring T-cell activation are not optimal. Here we showcase an improved bioassay platform for reliable assessment of T-cell activation using CD3xCD19. Effector T-cells carry a reporter gen downstream the CD3 signalling cascade and a pair of engineered target cells is used as antigen-positive/-negative control

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

OTHER EMERGING MODALITIES

11:10 Analytical Technology Development for Extracellular Vesicle-Based Therapeutics

Gary Hao, PhD, Vice President, Analytical Development, Codiak BioSciences

Extracellular vesicles (EV) have emerged as an important therapeutic modality for delivering pharmacological payloads via cell-derived lipid nanoparticles. Despite the considerable opportunities in disease intervention, the complex properties of EV impose unique challenges distinct from other classes of Advanced Therapy Medicinal Products. Here an overview of the current status and emerging trends in the analytical technologies for characterization of EV are discussed.

11:40 Analytical Characterization of DNA and RNA Oligonucleotides by Hydrophilic Interaction Liquid Chromatography-Tandem Mass Spectrometry (HILIC)

Ming Huang, PhD, Scientist, Regeneron Pharmaceuticals, Inc.

In this study, we developed and evaluated a generic hydrophilic interaction liquid chromatography (HILIC) hyphenated with tandem mass spectrometry method in the absence of ion-pairing reagents and demonstrated its capability as an attractive and robust alternative for oligonucleotide and siRNA analysis. Coupling to high-resolution mass spectrometric (HRMS) analysis, the established HILIC-MS method could provide in-depth analytical characterization for oligonucleotide and siRNA standards and their impurities.

12:10 Characterization of ONCR-021, a Novel Synthetic Oncolytic Virus

Pam Wang, PhD, Senior Scientist, Oncorus

Oncorus is a clinical-stage biotechnology company focused on developing next-generation viral immunotherapies for the treatment of cancer. While oncolytic viruses are potent tumor killing agents, their therapeutic benefit has largely been limited to intratumoral administration. Oncorus' pioneering synthetic virus approach involves encapsulating viral RNA genomes in lipid nanoparticles to enable intravenous delivery. This talk will provide an overview of analytical methods used to characterize synthetic viral RNA and LNP products.

12:40 CO-PRESENTATION: LUNCHEON PRESENTATION: Antibody Specificity Profiling for IND Using the Membrane Proteome Array

Rachel Fong, Director of Sales and Alliances, Integral Molecular

Michael Phelan, PhD, Application Scientist, Integral Molecular

IND applications for biotherapeutics require cross-reactivity assessment to prevent adverse events, but ~25% of antibodies in development are polyspecific. The Membrane Proteome Array is a comprehensive approach to rapidly identify off-target protein-protein interactions. We will provide an update on the newest additions to this 6,000-protein cell array and the adoption of MPA technology for regulatory filings—including case studies for CAR-T and cell-therapy profiling where conventional approaches did not suffice.

1:10 LUNCHEON PRESENTATION: Two Birds, One Stone: A Single Homogeneous Assay for Bispecific Antibody Binding

Liz Christian, Senior Scientist, AstraZeneca

Characterizing bispecific antibody binding properties is critical during biotherapeutic development, where data is leveraged to predict efficacy and potency, assess critical quality attributes and improve antibody design. Traditional single-target, single-readout approaches have limited usefulness for interpreting complex bispecific binding. To address these deficiencies, we developed and implemented a new dual-target binding assay using AlphaPlex® technology that accurately dissects the affinities of both target binding domains directly and simultaneously.

1:40 pm Close of Characterization for Novel Biotherapeutics

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*

SC6: Introduction to Gene Therapy Product Manufacturing and Analytics

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

ROOM LOCATION: 302
ESSENTIAL BIOPHYSICAL STUDIES

2:15 Chairperson's Opening Remarks

Marilia Barros, PhD, Research Investigator, Drug Product Science & Technology, Bristol Myers Squibb Co.

2:20 Antigen Improves Binding of IgGs to Fc Gamma Receptors in SPR Analysis

Wei Wang, PhD, Principal Scientist, Therapeutic Discovery, Amgen

A novel SPR method testing interaction of Fc gamma receptors with Antibody-Antigen immunocomplex was developed. Although assay orientation had some effect, antigen had even more impact on the binding affinity of IgGs to most activating FcgRs, especially on IgG1-FcgRI interaction, and IgG2-FcgRIIIa (158F) interaction. These data suggest it may be useful to evaluate the IgG-FcgR interaction in the presence of antigen to help design safer and more effective biotherapeutics.

2:50 Ultra-Dilute Solution Measurements of Antibody Self-Association

Charles G. Starr, PhD, Scientist, Developability & Preformulation Sciences, Sanofi Group

Identification of mAbs with low levels of self-association has traditionally required relatively concentrated protein solutions, confounding identification of such molecules during early discovery campaigns. We have developed charge-stabilized self-interaction nanoparticle spectroscopy (CS-SINS), a colormetric assay that measures colloidal self-interaction of antibodies in ultra-dilute solutions (0.01 mg/mL). CS-SINS results are predictive of high concentration properties such as viscosity and opalescence, which only emerge at orders of magnitude higher concentrations (100+ mg/mL).

3:20 Mass Spectrometry Advances for the Characterization of Emerging Protein Therapeutics and Cell Therapies

Guanghui Han, PhD, Senior Director, San Jose Mass Spectrometry Center, BGI Americas Corporation

Advances in mass spectrometry (MS) make this technology uniquely suited for characterizing protein therapeutics and cell therapies as well as fulfilling current unmet needs for such product knowledge. The San Jose Mass Spectrometry Center of BGI Americas is an innovation lab where it offers one of the industry's most comprehensive multi-omics service portfolios. This presentation focuses on the Center's MS techniques and applications for these emerging therapeutics.

3:35 Real-Time Label-Free Protein Analysis: Next-Generation Surface Plasmon Resonance (SPR)

Darius Wilson, PhD, Product Manager, BioAnalytics Workflow, Sartorius

Biolayer interferometry (BLI) and surface plasmon resonance (SPR) are leading technologies in real time label-free protein analysis, each with distinct features and benefits. One major difference, however, are the variety of injections offered by different SPR platforms. This presentation will discuss features of both technologies, the range of novel injections featured on the new Octet® SF3 SPR, and their potential applications across a number of different research areas.

3:50 pm Refreshment Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 Opalescence Measurements: Improvements in Fundamental Knowledge, Identifying Sources of Analytical Biases, and Advanced Applications for the Development of Therapeutic Proteins

Marilia Barros, PhD, Research Investigator, Drug Product Science & Technology, Bristol Myers Squibb Co.

Opalescence of biopharmaceutical solutions can indicate suboptimal colloidal stability which is a generally undesirable attribute that requires investigation and remediation. While there are numerous instrumentation options available for measuring opalescence, cross-instrument comparisons and detailed knowledge of analytical biases are limited. We highlight key findings from a multi-instrument investigation and demonstrate advanced applications of a 90°angle light scattering instrument as a suitable approach for making low volume, temperature-controlled, nephelometric opalescence measurements.

DIGITAL METHODS IN BIOPHYSICAL ANALYSIS

5:00 Design of Biopharmaceutical Formulations Accelerated by Machine Learning

Paolo Arosio, PhD, Assistant Professor, Chemistry & Applied Biosciences, ETH Zurich

Successful biologics must exhibit a series of suitable properties which depend on both protein sequence and buffer composition. In the context of this high-dimensional optimisation problem, we will show how machine learning algorithms can accelerate the design of biopharmaceutical formulations. These methods provide high speed of converging to optimal combinations of excipients, the ability to transfer prior knowledge, and the identification of trade-offs in optimising multiple biophysical properties.

5:30 Machine Learning Analysis of Particles and Cells in Bioprocesses

Theodore Randolph, PhD, Professor, Chemical and Biological Engineering, University of Colorado

We describe techniques combining flow imaging microscopy with machine learning to analyze populations of particles, protein aggregates, and cells. "Particle facial recognition" allows detection particles that may appear during bioprocessing, even in samples that contain a background of pre-existing particles. Applications will be discussed, including root-cause analysis of aggregates in monoclonal antibody formulations, detection of particles formed during fill-finish operations for adjuvanted vaccines, and detection of microbial infections in blood.

6:00 Close of Day

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*

SC6: Introduction to Gene Therapy Product Manufacturing and Analytics

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

WEDNESDAY, MAY 4

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 302

AGGREGATION AND PARTICLE CHARACTERIZATION

8:25 Chairperson's Remarks

Borries Demeler, PhD, Professor, Chemistry & Biochemistry, University of Lethbridge

8:30 Density Matching Multi-Wavelength Analytical Ultracentrifugation to Measure Drug Loading of Lipid Nanoparticle Formulations

Borries Demeler, PhD, Professor, Chemistry & Biochemistry, University of Lethbridge

Like viral vectors, lipid nanoparticle formulations can be characterized by multi-wavelength analytical ultracentrifugation in high resolution to differentiate heterogeneous mixtures based on nucleic acid loading state, morphology, and particle size. In this talk, I will discuss how a D_2O density matching approach can be employed to characterize particles based on their partial specific volume, or loading density. This adds a third characterization dimension to the hydrodynamic and spectral separation.

9:00 Analytical Strategies to Detect Denaturation and Small Oligomers of Therapeutic Monoclonal Antibodies

Claire Smadja, PhD, Professor, Nanobiotechnology, University Paris-Sud, France

Therapeutic monoclonal antibodies (mAbs) treatments represent high immunological risk due to denaturation and aggregation that may occur during manipulations at a hospital. To provide information on mAbs states before administration to patients, native mass spectrometry (MS) is a promising approach using near-physiological conditions. The coupling of separative methods to native-MS has been investigated to study mAbs states. Another approach based on electrophoretic methods coupled to multivariate analysis has been also studied.

9:30 KEYNOTE PRESENTATION: Ultra-Dilute Developability Analysis for Identifying Antibodies with Drug-Like Biophysical Properties

Peter M. Tessier, PhD, Albert M. Mattocks Professor, Pharmaceutical Sciences & Chemical Engineering, University of Michigan

There is intense interest in early-stage screening of antibody candidates to identify those with drug-like biophysical properties, including low self-association in formulation conditions and low non-specific binding in physiological conditions. We have developed two ultra-dilute characterization methods for evaluating antibody colloidal interactions, namely the charge-stabilized self-interaction nanoparticle spectroscopy (CS-SINS) and polyspecificity particle (PSP) assays. We are using these methods in concert to identify antibodies with drug-like colloidal properties.

10:00 Complete Characterization of Protein, Gene and Cell Therapy Subvisible Aggregates and Extrinsic Contaminants

halo labs

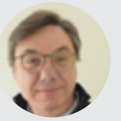
Bernardo Cordovez, PhD, CSO and Founder, Halo Labs

Subvisible particles are critical quality attributes for biologics. Gene and cell therapies present unique stability challenges since they are more complex than protein therapeutics. Here we show how the Aura counts, images, sizes, and identifies subvisible biologic aggregates and extrinsic particles in a rapid and low-volume format. We present case studies overviewing protein therapeutic stability from cell line development through manufacturing, AAV stability, and cell therapy aggregation and particle purity.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

11:10 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION



11:20 Plenary Keynote Introduction

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

11:30 KEYNOTE PRESENTATION: Future Directions in Drug Discovery & Development

Roger M. Perlmutter, MD, PhD, Chairman and CEO, Eikon Therapeutics, Inc.

The intrinsic complexity of human physiology has generally defeated attempts to model normal cellular functions, meaning that until recently we have had few tools to disentangle the molecular pathology associated with common illnesses. Now, dramatic improvements in instrumentation, automation, and computing provide ways to measure dynamic responses in living cells, and to use these measurements to identify both new disease targets, and new chemical starting points for future medicines.

12:15 pm Session Break

ROOM LOCATION: 302

12:30 LUNCHEON PRESENTATION: The Power of Biophysical Tools for Protein Personality Assessment

FUJIFILM Diosynth Biotechnologies

Katherine Bowers, PhD, Senior Principal Scientist and Group Leader for the Formulation Development Group, FUJIFILM Diosynth Biotechnologies

Proteins have personalities, reflected in stability challenges and formulation selections. Investigating >100 diverse proteins, my appreciation continues to increase for the depth of data that can be gleaned from a well-equipped formulation/biophysical assessment lab. This presentation will review some of the informative science behind several key biophysical tools and applications for challenging molecules. Together, we will take a deeper dive into information-rich biophysical data used in successful protein development.

1:00 LUNCHEON PRESENTATION: Viscosity Reducing Excipients for Highly Concentrated Antibody Formulations

Comera Life Sciences

Robert P. Mahoney, PhD, CSO, R&D, Comera Life Sciences, Inc.

Patients would rather have a subcutaneous injection than an IV infusion, so biologics are often formulated at high concentration to enable self-administration in a small volume. Many antibody

drugs have viscosity limitations and there is a need for new ideas to address this. Caffeine can mask protein-protein interactions, leading to reduced viscosity. This presentation will include examples and a discussion of the safety and regulatory aspects of caffeine as an excipient.

1:30 Find Your Table and Meet Your Discussion Moderator

1:35 Interactive Discussions (Exhibit Hall A & B)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 9: Characterization Methods and Technologies for Gene Therapies

Borries Demeler, PhD, Professor, Chemistry & Biochemistry, University of Lethbridge

MASS SPECTROMETRY APPLICATIONS

2:20 Chairperson's Remarks

Jeffrey R. Fishpaugh, PhD, Senior Principal Research Scientist, Analytical Chemistry R&D, Abbott Laboratories

2:25 Mass Spectrometry in Characterization of Highly Heterogeneous Biopharmaceuticals and Non-Biological Complex Drugs

Igor A. Kaltashov, PhD, Professor, Chemistry, University of Massachusetts, Amherst

Structural heterogeneity remains a formidable problem limiting the utility of intact-mass MS in characterization of protein therapeutics and non-biological complex drugs. In many cases, this problem can be effectively addressed using novel chromatographic methods coupled with online MS detection and by supplementing MS measurements with tools from the arsenal of gas phase ion chemistry. These approaches will be illustrated using extensively glycosylated proteins, synthetic vaccines, and large immune complexes.

2:55 Mass Spectrometry and Development of Biologics for Diagnostic Assays

Jeffrey R. Fishpaugh, PhD, Senior Principal Research Scientist, Analytical Chemistry R&D, Abbott Laboratories

We use mass spectrometry (MS) to collaborate and support assay development of new immunoassays. Our efforts support development of proteins for small molecule (vitamin D) and large molecule (HIV, SARS-CoV-2) assays. This talk will explore recent efforts and approaches used to facilitate protein development in R&D phases of immunoassay development with an array of mass spectrometers and techniques as well as recent progress on quality assurance MS testing.

3:25 Hassle-Free Protein Interaction Analysis of Your Most Challenging Targets

Fluidic Analytics

Molly Coseno, Dr, Field Applications Specialist, Sales and Business Development, Fluidic Analytics

Introducing Microfluidic Diffusional Sizing (MDS) Technology which brings a new tool to the analytical characterization toolbox: a different approach that enables the analysis of protein interactions close to ***in vivo*** conditions.

3:55 Ice Cream Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 Fully Automating MS Analytics of Next-Generation Protein Therapeutics: From Sample to Report

Miroslav Nikolov, PhD, Senior Scientist & Laboratory Head, Roche, Germany

I will present an end-to-end automated MS analytics workflow developed at Roche Innovation Center Munich. It covers all aspects of the protein MS analytics, starting with sample registration, wet lab processing, and MS measurement, as well as data analysis, management, and reporting applied on heterogeneous antibody-based drug candidate samples. Data and metadata are ultimately consolidated and stored in a way that enables mining and efficient and informed decision-making.

STRUCTURAL ANALYSIS

5:00 Deep Learning Methods for Protein Structure Prediction

Sergey Ovchinnikov, PhD, John Harvard Distinguished Science Fellow, Harvard University

The presentation will summarize current progress, compare the arc of developing the deep learning approaches with the conventional methods, and describe concepts behind current strategies that may lead to potential future opportunities. For the presentation I'll dive into the details of how methods including RoseTTAFold, AlphaFold and recent large language models work.

5:30 Applications of Cryo-EM in Antibody Characterization

Xinchao Yu, PhD, Director, Structural Chemistry, Gilead Sciences

Cryo-EM has become a powerful technique to speed up pharmaceutical discovery in the past few years. As a direct visualization technology that can reach atomic resolution, cryo-EM has broad applications in antibody research. Here we provide examples of utilizing EM to characterize antibodies and complexes, to provide key information for epitope mapping, cross-linking, and oligomerization. Therefore, cryo-EM demonstrates strong potential in antibody engineering by generating information that was previously intractable.

6:00 Networking Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Biophysical Methods

SUNDAY, MAY 1

2:00 pm Recommended Pre-Conference Short Course*

SC2: Introduction to Lipid Nanoparticle Characterization and Formulation

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

TUESDAY, MAY 3

6:30 pm Recommended Dinner Short Course*

SC6: Introduction to Gene Therapy Product Manufacturing and Analytics

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

THURSDAY, MAY 5

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 302

EARLY-STAGE EVALUATIONS

8:25 Chairperson's Opening Remarks

Kruti Soni, PhD, Scientist, Technical Development, Biogen

8:30 Opportunities and Challenges for the Clinical Translation of Structured DNA Assemblies as Gene Therapeutic Delivery and Vaccine Vectors

Mark Bathe, PhD, Professor, Biological Engineering, Massachusetts Institute of Technology

Synthetic nucleic acids can be formulated as virus-like particles (VLPs) for vaccines or gene therapeutic delivery vectors. These VLPs can be used to display variable copy numbers and types of peptide and protein antigens, as well as sugars and small molecules for programmable immune cell targeting and stimulation. I will present our work on design and fabrication of DNA-based VLPs for application to subunit vaccines for COVID-19 and AIDS.

9:00 KEYNOTE PRESENTATION: Begin with the End in Mind – Rethink the Early-Stage Analytics for the Development of AAV Gene Therapy Products

Xiaohui Lu, PhD, Director, Analytical Development, Ultragenyx Pharmaceutical

Gene therapy programs are advancing through research and development at record speed. Late-stage clinical development is often hampered by deficiencies in analytical method and potential quality issues. Recent learnings from late-stage development can be applied to the upcoming clinical candidates. Selective critical quality attributes can be assessed in early-stage development by adopting new analytical platforms. Revamped early-stage analytics will significantly boost the development of gene therapy products.

9:30 A Systems Model of Gene Therapy for Sickle Cell Disease

Raibatak Das, PhD, Principal Scientist, Applied BioMath

Sickle cell disease (SCD) is an inherited genetic disease of the blood with no known cure. Stem cell gene therapy is an emerging experimental therapy for SCD with the potential for lifelong cure, but it is an expensive multi-step treatment regimen. We developed a quantitative systems pharmacology model to predict how varying treatment will affect post-treatment hemoglobin and red blood cell dynamics after autologous stem cell gene therapy.

10:00 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

ANALYTICAL SUPPORT FOR DRUG PRODUCT DEVELOPMENT

10:40 Understanding Degradation and Stabilization of AAV

Matthew Petroff, PhD, High-Throughput Process Development Lead, Spark Therapeutics, Inc.

Adeno-associated viral vectors present key challenges in formulation development, including high molecule complexity and limited material for development. This talk will discuss several high-throughput strategies to overcome those challenges. Results will include case studies for engineered AAV capsids and common drug-product impurities.

11:10 Challenges in Fill-Finish Process for Gene Therapy Drug Product

Kruti Soni, PhD, Scientist, Technical Development, Biogen

Gene Therapy fill-finish operations present control strategy challenges related to the small volumes of solution being processed. Requirements tied to specific routes of administration of the gene therapy drug product may impose additional challenges. Formulation and drug delivery case studies will be shared that highlight these challenges. These examples show the importance of an integrated, end-to-end approach when developing a gene therapy drug product manufacturing process.

11:40 Selected Poster Presentation: Microfluidic Electrophoresis-Based Assessment of Adeno-Associated Virus Purity in Terms of Full and Empty Capsids

Adriana Coll De Pena, Graduate Student, Biomedical Engineering, Tripathi Lab, Brown University

AAV has shown great potential as a gene delivery vehicle; however, the lack of rapid, high-throughput analytical platforms to assess sample purity of in terms of full and empty capsids creates a major bottleneck in the large-scale manufacturing of AAV. We propose a novel high-throughput methodology, which integrates a microfluidic electrophoresis platform with a mathematical model for the rapid assessment of AAV samples. This research was funded by Perkin Elmer.

12:10 pm Luncheon in the Exhibit Hall and Last Chance for Poster Viewing (Exhibit Hall A & B)

DEVELOPMENT OF ESSENTIAL ASSAYS

1:15 Chairperson's Remarks

Diana Colleluori, PhD, MBA, Consultant, CMC Analytical, Biologics Consulting Group

1:20 Microfluidic Resonator Approaches for Quality Control of Recombinant Adeno-Associated Virus-Based Gene Therapies

Georgios Katsikis, PhD, Postdoctoral Associate, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

Recombinant Adeno-Associated Viruses (rAAVs) deliver therapeutic DNA for gene therapy. However, rAAV manufacturing is imperfect, producing mostly defective capsids without the complete therapeutic gene. Here, we used microfluidic resonators for biophysical measurements of both rAAV and rAAV-producing cells. We juxtapose our approach with ddPCR measurements, and modelling efforts

to identify correlations between biophysical measurements and genome and functional titers, towards rapid quality control of rAAV-based gene therapies.

1:50 Emerging Methods for the Characterization and Quantitation of High Molecular Weight Species and Particles in AAV Products

George Bou-Assaf, PhD, Scientist, Analytical Development – Product & Technology Development, Biogen

The smaller manufacturing scales of AAV-based products make it particularly challenging to develop methods with very limited sample availability. Use of traditional methods for the separation and quantitation of high molecular weight (HMW) species is challenging given their larger size. This talk focuses on enumerating existing methods for HMW and particle characterization and their limitations. In addition, emerging methods and their advantages over existing ones will be described.

2:20 Mass-Photometry: The New Kid on the Block for Quantifying AAV Empty-Full Ratios

Gael Nicolas, Technical Sales Specialist, Sales, Refeyn

Mass photometry is a novel, easy-to-use bioanalytical technology that measures the empty-full AAV capsid ratio in minutes using minimal sample amounts and without the need of sample preparation. Circumventing the requirement of large capital expense and skilled operators, it can be employed throughout the manufacturing process. We present a novel mass photometry instrument dedicated to the challenges of AAV characterization.

2:35 Sponsored Presentation *(Opportunity Available)*

2:50 Networking Refreshment Break (Hynes Main Lobby)

3:20 Lessons Learned: Potency Assay Strategy, Selection, and Development

Diana Colleluori, PhD, MBA, Consultant, CMC Analytical, Biologics Consulting Group

The assessment of product potency is required for both investigational and licensed cell and gene therapy products. Due to the complexity of cell and gene therapy products, significant challenges and obstacles will be encountered during potency assay selection and development. While the assessment of potency may change throughout product development, it is imperative that potency assays are developed incrementally and in parallel with clinical development activities.

3:50 Standardization of Biophysical Tests for AAV

Lake Paul, PhD, President, BioAnalysis LLC

With the importance of biophysical methods such as SV-AUC in the gene therapy space, standardization of the experimental design, analysis, software and the inclusion of reference material is critical. SV-AUC is the gold standard in the determination of the empty, intermediate/partial, and full capsids of rAAV. In this talk, the implementation of standard procedures in the QC environment (SV-AUC data collection, software, and data analysis) will be discussed.

4:20 Close of Day

FRIDAY, MAY 6

7:00 Registration and Morning Coffee (Hynes Main Lobby)

7:30 Interactive Discussions with Continental Breakfast (Ballroom Pre-Function)

Grab your breakfast and Coffee and join a Discussion Group. 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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 9: Towards Real-Time Characterization of Viral Vectors During Biomanufacturing: Emerging Technologies and Challenges

Georgios Katsikis, PhD, Postdoctoral Associate, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

TABLE 10: Directions for Handling and Administration Studies for GeneTherapy Products

Kruti Soni, PhD, Scientist, Technical Development, Biogen

ROOM LOCATION: 302

MASS SPEC APPLICATIONS

8:25 Chairperson's Remarks

Wei-Chiang Chen, PhD, Associate Director, BioProcess Analytics, Genomic Medicine Unit, Sanofi

8:30 LC-MS-Based Characterization of AAV Capsid Under Denaturing and Native Conditions

Shunhai Wang, PhD, Associate Director, Analytical Chemistry, Regeneron Pharmaceuticals, Inc.

LC-MS-based characterization assays have been increasingly applied to support AAV-based gene therapy programs. Under denaturing conditions, the constituent capsid proteins can be analyzed to achieve serotype identification, global PTM characterization, and stoichiometry assessment. Under near-native conditions, the intact capsid ensemble can be analyzed to quantify empty, partial, and full capsids. In this presentation, we will discuss some emerging LC-MS techniques for AAV attribute characterization.

9:00 Intact Particle Characterization with Charge Detection Mass Spectrometry

Benjamin Draper, PhD, Director, Gene Therapy Analysis, Megadalton Solutions

Because of its sensitivity, dynamic range, selectivity, and speed, mass spectrometry (MS) is the gold standard for biomolecule analysis. However, the ~1 megadalton (MDa) mass limit of conventional instruments limits applications to larger species. Simultaneous measurement of m/z and z by charge detection (CD) MS enables analysis of gene therapies (revealing full and empty capsids, multimers, aggregates, intact and partial genomes) and other large assemblies (e.g., viruses, exosomes, nanoparticles).

PROBLEMS AND SOLUTIONS

9:30 Release Kinetics of DNA from Viral Capsids for Gene Therapy Using Total Intensity Light Scattering

Wayne F. Reed, PhD, Professor, Physics, Tulane University

We studied degradation of an engineered AAV serotype at physiological pH and ionic strength. Solutions with mixed full and empty AAV were held between 30-53oC, with molecular weight changes monitored versus time by total light scattering intensity. Results demonstrate fundamental differences in degradation behavior between full and empty AAV, revealing interactions between viral capsids and their cargo that should be understood when designing a storage strategy of an AAV drug.

10:00 Modernize Your Gene Therapy Analytics with Automated Tools from Bio-Techne

bio-techne

Peter Johnson, FAS Manager, Customer Care, Bio-Techne

Innovative analytical tools from Bio-Techne can support gene therapy workflows from discovery to quality control and address certain critical quality attributes of your therapeutic. Today's presentation will explore the many ways viral vector analysis is streamlined with ProteinSimple instruments and how our products improve line-of-sight across the development process.

10:30 Networking Coffee Break (Hynes Main Lobby)

GENE THERAPY R&D ANALYTICS | CONTINUED

11:00 Monitoring Adeno-associated Virus (AAV) Capsid Purity, Ratio, and Identity In-process with a High Throughput CE-SDS Platform

Wei-Chiang Chen, PhD, Associate Director, BioProcess Analytics, Genomic Medicine Unit, Sanofi

Conserved profiles can be used to distinguish product-specific capsid proteins from unwanted process impurities, and the variation in these capsid profiles and ratios can provide a specific capsid "fingerprint" to determine capsid serotype. We present the work on developing a high throughput CE-SDS platform to screen samples from process development and manufacturing control for AAV capsid purity profiles as well as capsid ratios for several different capsid serotypes.

11:30 Best Practices for Gene Therapy IND Submissions

Nicole Lowe Gallo, RAC, Associate Principal Consultant, Regulatory Affairs, The Halloran Consultant Group

The drastic advancements of human cell and gene therapy in recent years has opened the door to new treatments, paving the way towards cures of diseases once considered incurable. However, this development is not without pitfalls. This talk will address common oversights sponsors make leading up to an IND submission and key factors to consider as you are preparing your IND submission.

12:00 Overcoming Low Throughput Testing Issues of AAV Characterization Using SECMALS

Vikas Bhat, PhD, Associate Director, Process Development, BioMarin Pharmaceutical, Inc.

Size exclusion chromatography (SEC) coupled to multiangle light scattering (MALS) offers a straightforward approach to comprehensively characterize AAV capsids. The method can be used for detailed AAV characterization, including but not limited to aggregation profile, size-distribution, capsid content, capsid molar mass, encapsulated DNA molar mass, and total capsid and vector genome titer. These applications make this a powerful tool for gene therapy product development and process analytics.

12:30 pm Close of PEGS Summit

IMMUNOGENICITY STREAM
CONFERENCE

MAY 2-3

Introduction to Immunogenicity

AGENDA Training SEMINAR

MAY 3-4

Immunogenicity Assessment and Management

AGENDA

MAY 5-6

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

AGENDA Training SEMINAR

IMMUNOGENICITY STREAM

Ensuring the Safety and Efficacy of Biologics

This year's Immunogenicity Stream focuses on the latest science, technologies and strategies to ensure the safety and efficacy of biologics, with particular focus on novel modalities including cell & gene therapies, bispecifics, trispecifics, immunotherapies and ADCs. The *Immunogenicity Assessment and Management* conference presents case studies on assay development and validation, clinical relevance, drug and target interference, risk assessment and recent advances with predictive studies and tools. The conference is preceded by an in-depth introduction to immunogenicity training seminar and followed by an introduction to bioassay design and analysis.

CONFERENCE STREAMS

ENGINEERING | ONCOLOGY | BISPECIFICS | IMMUNOTHERAPY | EXPRESSION | ANALYTICAL | IMMUNOGENICITY

PEGS BOSTON

DAY 1: MONDAY MAY 2 – 8:30AM-4:00PM | DAY 2: TUESDAY, MAY 3 – 8:30AM-12:30PM

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:

Bonnie Rup, PhD, Biotechnology Consultant, Bonnie Rup Consulting

Sofie Pattijn, Founder & CTO, ImmunXperts SA

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

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.

CHI's Mandatory COVID-19 Vaccination Policy - Your Safety is Our Top Priority

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Our Code of Conduct

All in-person attendees must agree to CHI's Code of Conduct

TUESDAY, MAY 3

1:40 pm Dessert Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

ROOM LOCATION: 102

IMMUNOGENICITY EVALUATION OF NEW MODALITIES

2:15 Chairperson's Opening Remarks

Kate Peng, PhD, Director/Principle Scientist, BioAnalytical Sciences, Genentech

2:20 Evaluation of the Humoral Response to AAV-Based Gene Therapy Modalities Using Total Antibody Assays

Boris Gorovits, PhD, Vice President, in vitro Pharmacology, Biomarker Discovery and Bioanalysis, Sana Biotechnology

Many viral vector-based gene therapies (GTx) therapeutics are adeno-associated virus-based (AAV) based. Pre-existing humoral immunity against AAV presents a significant concern as it is expected to impact treatment safety and/or efficacy. Patients are screened for anti-AAV antibodies in either neutralizing (NAb) or total antibody (TAb) assays. This presentation will review current opinions on value of TAb vs. NAb assays, recommendations for development and validation of TAb methods

2:50 Investigating the Clinical Impact of the Immunogenicity for a Bispecific Antibody

Wenyu Liu, PhD, Scientist, Bioanalysis, Genentech, Inc.

Immunogenicity assessment is an integral part of biotherapeutics development. Anti-drug antibody (ADA) measurements inform the host responses against the biotherapeutics treatment, and interpretation of ADA results should be performed within the relevant clinical context. This presentation highlights a case study for a bispecific therapeutic with a focus on bioanalytical strategy considerations and analysis of ADA impact on other clinical endpoints.

3:20 Multiplexed Immunospot Assays Enable Detailed Assessment of Antigen-Specific B Cell Frequency, Class Usage and Functional Affinity

Greg A. Kirchenbaum, PhD, Senior Staff Scientist, Cellular Technology Limited

3:50 Refreshment Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

OPTIMIZING PATIENT OUTCOMES AND SETTING SPECIFICATIONS

4:30 KEYNOTE PRESENTATION: Optimizing Patient Outcome with Prevention and Mitigation Strategies for Immunogenicity of Therapeutic Proteins

Amy Rosenberg, MD, Senior Director of Immunology and Protein Therapeutics, Epivax

The development of immune responses to protein, gene and cell therapies can be devastating. This seminar will discuss both prevention and mitigation strategies and the deimmunization of protein therapeutics as a preventive strategy, and immune tolerance induction as a preventive and mitigation strategy. Significant advances in both areas will be presented that clearly poise us to take advantage of these modalities to improve patient outcome for the most devastating diseases.

5:00 Application of Predictive Technologies to Assess Risk of Critical Quality Attributes to Justify Safe Specifications for Patients

Marisa Joubert, PhD, Scientific Director and Group Leader, Amgen

Several case studies will be discussed that explore the utilization of predictive data for assessing immunogenicity risk to justify the setting or widening of safe specifications for patients in regulatory filings.

CRITICAL REAGENT CONSIDERATIONS IN IMMUNOGENICITY ASSAY DEVELOPMENT

5:30 From Critical Reagent Characterization to Immunogenicity Assay Development

Krisna C. Duong-Ly, PhD, Assoc Principal Scientist, Regulated Bioanalytic, Merck Research Labs

While critical reagents are the basis for immunogenicity assays, few characterization guidelines have been provided by regulatory agencies. In addition to determining quality attributes, reagent characterization can enable assay development by guiding reagent selection and assay design to meet sensitivity, drug tolerance, and other criteria. Here, we will describe several reagent characterization approaches and provide examples of how the resultant data have been used to develop and optimize immunogenicity assays.

6:00 Close of Day

6:00 Dinner Short Course Registration (Hynes Main Lobby)

6:30 Recommended Dinner Short Course*

**Short Courses will be offered in-person only. Separate registration required. See short course page for details.*

WEDNESDAY, MAY 4

7:30 Registration and Morning Coffee (Hynes Main Lobby)

ROOM LOCATION: 102

PREDICTIVE TOOLS FOR CANDIDATE SELECTION AND IMMUNOGENICITY RISK ASSESSMENT

8:25 Chairperson's Remarks

Boris Gorovits, PhD, Vice President, in vitro Pharmacology, Biomarker Discovery and Bioanalysis, Sana Biotechnology

8:30 Preclinical Immunogenicity Risk Assessment of Biologics Using CD4 T Cell Proliferation Assays

Robin E. Walsh, MS, Senior Principal Toxicologist, ImmunoToxicology, Eli Lilly & Co.

Immune responses to biologics can change or reduce their efficacy and may increase adverse events. Anti-drug antibodies are associated with clinical immunogenicity. CD4 T cell epitopes contained within the sequences of biologics are the key drivers of immunogenicity. This presentation will address CD4 T cell assays to assess control biologics to demonstrate how T cell dependent immune responses are important in the overall strategy in immunogenicity risk assessment.

9:00 *In silico* and *in vitro* T Cell Assay to Predict Immunogenicity of Biotherapeutic Products

Sivan Cohen, PhD, Scientist, Genentech

Immune responses to biotherapeutics have the potential to affect pharmacokinetics, pharmacodynamics, safety, and efficacy of the product. To ensure product quality and reduce the risks of unwanted immunogenicity, it is imperative to properly assess and mitigate the immunogenicity risk of biotherapeutics. This talk will focus on ***in silico*** and ***in vitro*** T cell assays to characterize the immunogenic potential of different biotherapeutics and their correlation to the clinically observed outcome

9:30 Thoughts Around Immunogenicity Risk Assessment & Mitigation Strategies for Low to Moderate Risk Biotherapeutics

Seema Kumar, PhD, Director & Head, Clinical Bioanalytical Sciences, EMD Serono, Inc.

In the early stages of drug discovery and development, we consider the immunogenicity risk of our biotherapeutics, working cross-functionally to ensure we are de-risking our molecules in advance of clinical studies. Through ***in silico*** and ***in vitro*** approaches we assess the likelihood for development of anti-drug antibodies in a future patient population. This presentation will focus on those approaches and strategies we implement in support of each lead candidate.

10:00 Deep Sea Diving with Proteomics to Find Powerful Antibodies

Anthony Stajduhar, Director Global Business Development, Rapid Novor

Polyclonal antibodies are widely used reagents in biotech and pharmaceutical industries due to their excellent performance characteristics and robust stability, but suffer from limited supply and batch-to-batch variability. Similarly, convalescent or vaccinated patient plasma has recently received much attention but met similar reproducibility challenges in clinical applications. Rapid Novor's REpAb sequencing has overcome many of these challenges through the sequencing and recombinant expression of mAbs found directly from pAb mixtures.

10:15 Cellular Immunogenicity for Gene & Cell Therapies: Understanding Complex Immune Responses to Complex Therapeutics

Amanda Hays, Ph.D., Scientific Officer, BioAgilytix

It is important to understand the immune response elicited from cell and gene therapies. For most protein biotherapeutics, humoral immunogenicity is assessed using standard bridging anti-drug antibody assays. However, there has been a greater interest in characterizing cellular immunogenicity responses that has coincided with development of more advanced modalities, requiring the use of an array of different platforms. In this presentation, bioanalytical assays for understanding cellular immunogenicity will be discussed.

10:30 Coffee Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

11:10 Transition to Plenary Keynote

PLENARY KEYNOTE LOCATION: Ballroom B
PLENARY KEYNOTE SESSION

11:20 Plenary Keynote Introduction

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

11:30 KEYNOTE PRESENTATION: Future Directions in Drug Discovery & Development

Roger M. Perlmutter, MD, PhD, Chairman and CEO, Eikon Therapeutics, Inc.

The intrinsic complexity of human physiology has generally defeated attempts to model normal cellular functions, meaning that until recently we have had few tools to disentangle the molecular pathology associated with common illnesses. Now, dramatic improvements in instrumentation, automation, and computing provide ways to measure dynamic responses in living cells, and to use these measurements to identify both new disease targets, and new chemical starting points for future medicines.

12:15 pm Session Break

ROOM LOCATION: 102

12:30 LUNCHEON PRESENTATION: Human *in vitro* Immunosafety Assessment in the Context of the Evolving Regulatory and Technical Landscape

Noel Smith, PhD, Head of Immunology, Early Development Services, Lonza

An understanding of the potential immunogenicity and immunotoxicity risk of your therapeutic candidate is a key part of pre-clinical development. While human primary cell assays can provide vital data to help support this assessment, the design and qualification of such human ***in vitro*** assays is key to generating high quality, reliable data to support both lead selection and regulatory filings.

1:00 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:30 Find Your Table and Meet Your Discussion Moderator

1:35 Interactive Discussions (Exhibit Hall A & B)

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 Discussion page on the conference website for a complete listing of topics and descriptions.

TABLE 10: When Is ADA Assessment Needed?

Seema Kumar, PhD, Director & Head, Clinical Bioanalytical Sciences, EMD Serono, Inc.

- How sensitive does it need to be?
- What's the value of evaluating immunogenicity if you have good PKPD?
- What does it mean when you pick up ADA activity?
- How do you co-relate it with PKPD and clinical impact?

TABLE 11: Considerations of Immunogenicity Assessment for New Modalities

Kate Peng, PhD, Director/Principle Scientist, BioAnalytical Sciences, Genentech

The new modality approaches hold the potential to tackle challenging therapeutic targets and difficult disease indications. However, there are also unforeseen challenges in the development of new modalities, including immunogenicity assessment. In this roundtable session, we would like to discuss considerations of immunogenicity assessment strategy for protein and cell therapeutics, critical reagent generation, data interpretation, and communication with health authorities.

NAb AND ADA ASSAYS - DRUG TOLERANCE AND INTERFERENCES

2:20 Chairperson's Remarks

Bonnie Wu, PhD, Assoc Scientific Dir, Janssen R&D LLC

2:25 Interference in a NAb Assay for a Bispecific mAb from a Prior Therapy and Possible Mitigation Strategy

Susan Irvin, PhD, Staff Scientist, Bioanalytical Strategy, Regeneron

Cell-based assays (CBA) for NAb are notoriously challenging: drug and soluble targets can generate false-positive/negative results even at low concentrations. In a CD20xCD3 bispecific CBA, prior anti-CD20 therapy (e.g., rituximab) was also shown to interfere. This was mitigated by addition of blocking mAbs, but each anti-CD20 therapy requires specific blockers. This highlights challenges with target-based NAb assays, both from exogenous therapies and endogenous anti-target antibodies (e.g., infectious disease).

IMMUNOGENICITY ASSESSMENT & MANAGEMENT | CONTINUED

2:55 When to Extend Monitoring of Anti-Drug Antibodies for High Risk Biotherapeutics in Clinical Trials: An Opinion from the European Immunogenicity Platform

Daniel Kramer, PhD, Global Scientific Advisor, Clinical Immunogenicity, Sanofi Aventis Deutschland GmbH

3:25 An Integrated Approach To Managing Immunogenicity Risk And Optimum Protein Design

Andrew Isidoridy, PhD, Immunology Sales Specialist, ProImmune, Inc.

Immunogenicity risk assessment is an essential step in bringing therapeutic drugs to the market. ProImmune's risk management tools evaluate immunogenic epitopes and the corresponding functional T cell responses that can lead to unwanted immune responses. Case studies will highlight how the integrated platform is used to address key questions in the drug development phase.

3:55 Ice Cream Break in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

4:30 ADA Characterization for Biotherapeutics: New Methods for the Analysis of the ADA Specificity

Kay-Gunnar Stubenrauch, PhD, Head, Large Molecule Bioanalytical Sciences 1, Roche Diagnostics

The immunogenicity assay package for Biotherapeutics includes screening, confirmation, titer and neutralizing antibody (Nab) assays. Besides such well-known assays, analysis of the ADA specificity might be beneficial in order to understand an immune response and their potential impact. The presentation gives an overview on established and new methods including case studies for illustration of their challenges and chances.

5:00 All We Need Is Screen: Rethinking the Standard Anti-Drug Antibody Tiered Testing Strategy

Daniel J. Baltrukonis, MA, MBA, Senior Director, Biologics Team Lead, Clinical Assay Group, Clinical Pharmacology, Global Product Development, Pfizer Inc.

Over the past 15 years, the assessment of anti-drug antibodies (ADA) to biotherapeutics has predominantly used a tiered testing strategy of screen, confirm, and titer as standard practice. However, simplification of this testing strategy is possible, based on today's improved methodologies and a better understanding of what ADA tiered data provides. Clinical case studies will be presented that support when and why confirmatory and/or titer assays may not be necessary.

6:00 Networking Reception in the Exhibit Hall with Poster Viewing (Exhibit Hall A & B)

7:00 Close of Immunogenicity Assessment & Management

DAY 1: THURSDAY, MAY 5 8:30 AM-4:20 PM | DAY 2: FRIDAY, MAY 6 8:30 AM-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 design of experiments (DOE) to bioassay development, validation, and monitoring. Examples (mostly from cell-based bioassays; some using robotics) will illustrate strategic ways to design bioassays to make it (relatively) easy to use DOE differently in early bioassay development, when measuring the capability of a bioassay, when improving an existing bioassay, and when doing validation. We will cover ways that these strategic assay design considerations, when combined with good assay analysis methods, also support good assay monitoring with graphical and quantitative tools as part of a lifecycle approach.

Instructor:

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

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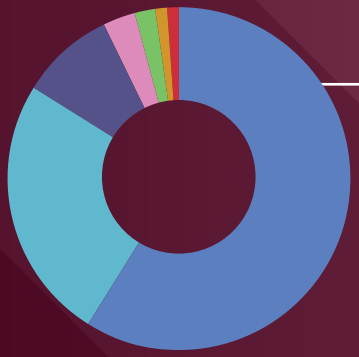

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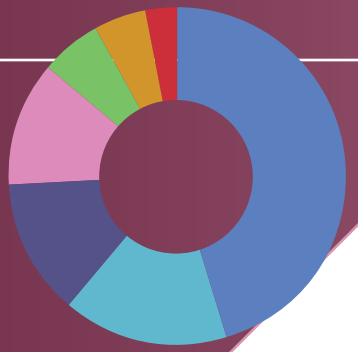

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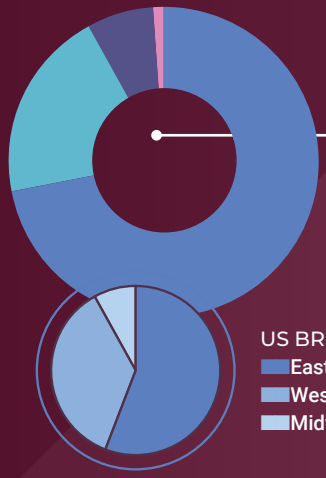

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FOR MORE INFORMATION, PLEASE CONTACT:

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HOTEL & TRAVEL INFORMATION

Conference Venue:
Hynes Convention Center
900 Boylston St,
Boston, MA 02115

Host Hotels:
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