FINAL DAYS TO REGISTER

AUGUST 31 - SEPTEMBER 4, 2020 | Eastern Time

2020 CONFERENCE PROGRAMS

- ENGINEERING
- ONCOLOGY
- IMMUNOTHERAPY
- CELL-BASED IMMUNOTHERAPIES
- ANALYTICAL
- EXPRESSION
- IMMUNOGENICITY & BIOASSAYS
- BIOCONJUGATES
- EMERGING THERAPEUTICS AND TECHNOLOGIES
- SC SHORT COURSES

SPONSOR & EXHIBIT OPPORTUNITIES

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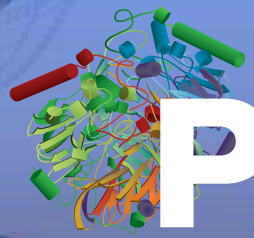

16th Annual

PEGS BOSTON

VIRTUAL CONFERENCE & EXPO

The Essential Protein Engineering & Cell Therapy Summit

22 CONFERENCES

350+ SPEAKERS

1,500+ DELEGATES

A DYNAMIC ONLINE LEARNING & NETWORKING ENVIRONMENT

- **INSPIRING** KEYNOTES
- **RESEARCH** POSTERS
- INTERACTIVE **NETWORKING**
- **SPONSORED** TALKS
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16th Annual
PEGS BOSTON
VIRTUAL CONFERENCE & EXPO
AUGUST 31 - SEPTEMBER 4, 2020 | EASTERN TIME

2020 CONFERENCE PROGRAMS

CONFERENCE AT-A-GLANCE

STAY CONNECTED @PEGSBoston #PEGS20

2020 PROGRAMS

	MONDAY-TUESDAY (AUG. 31-SEPT. 1)	WEDNESDAY-THURSDAY AM (SEPT. 2-3)	THURSDAY PM-FRIDAY (SEPT. 3-4)
ENGINEERING	Display of Antibodies	Engineering Antibodies	Engineering Bispecific Antibodies
ONCOLOGY	Antibodies for Cancer Therapy	Advancing Bispecific Antibodies and Combination Therapy to the Clinic	Clinical Progress of Antibody-Drug Conjugates
IMMUNOTHERAPY	Improving Immunotherapy Efficacy and Safety	CAR Ts, TCRs and TILs	Agonist Immunotherapy Targets
CELL-BASED IMMUNOTHERAPIES	Improving Immunotherapy Efficacy and Safety	CAR Ts, TCRs and TILs	Cell and Gene Therapy Analytics
ANALYTICAL	Characterization for Novel Biotherapeutics	Biophysical Methods	Cell and Gene Therapy Analytics
EXPRESSON	Difficult-to-Express Proteins	Optimizing Protein Expression	Protein Expression System Engineering
IMMUNOGENICITY & BIOASSAYS	Immunogenicity Case Studies and Clinical Management	Immunogenicity Assessment and Regulatory Approval of Biologics	Optimizing Bioassays for Biologics
BIOCONJUGATES		Engineering Antibody-Drug Conjugates	Clinical Progress of Antibody-Drug Conjugates
EMERGING THERAPEUTICS AND TECHNOLOGIES	Emerging Indications for Therapeutic Antibodies	Gene Therapy	
SHORT COURSES (MON., AUG. 31)	SC10: CAR T-Cell Therapy from A-Z SC15: Introduction to Gene Therapy Products Manufacturing and Analytics		

"PEGS has a unique capability to bring together industry experts with most diverse background, accelerating biomedical progress through exchange of ideas."

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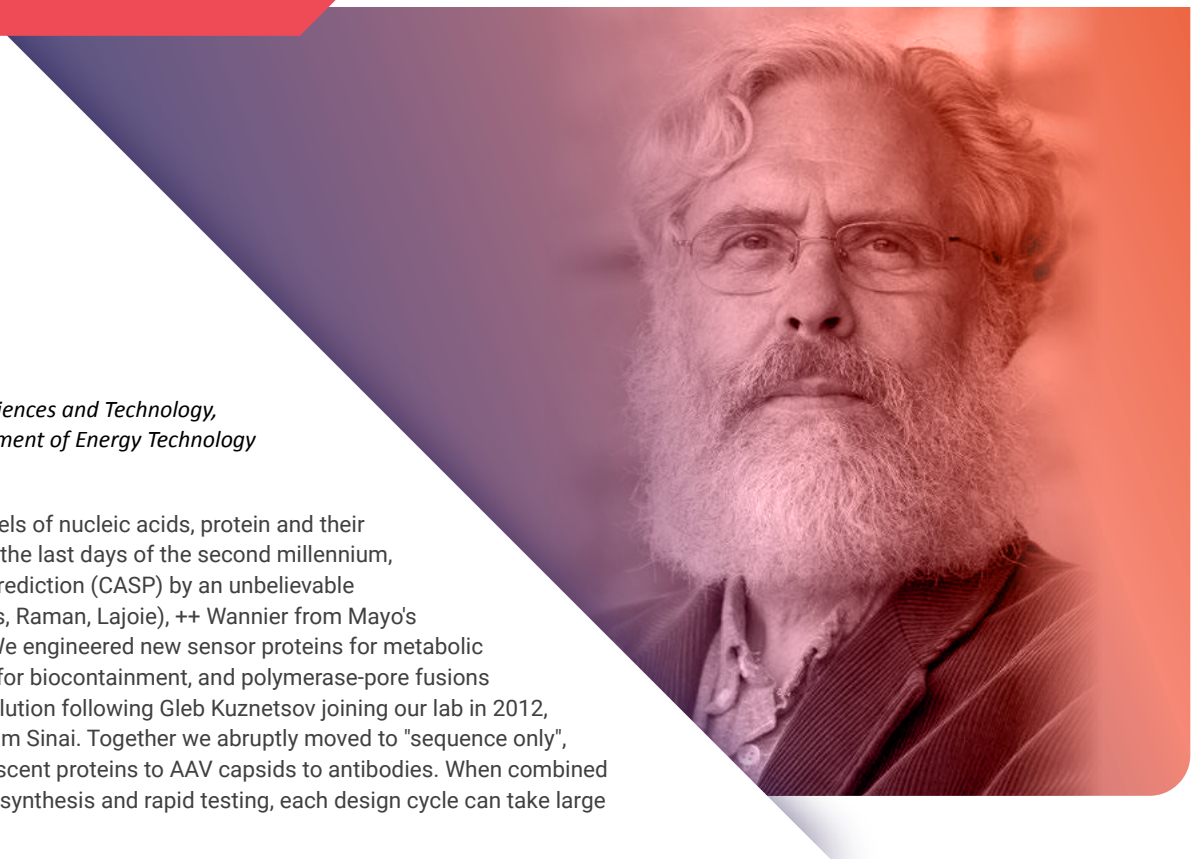
PLENARY KEYNOTE SESSION

MONDAY, AUGUST 31 | 3:25 PM



From Energy to Machine Learning

GEORGE CHURCH, PhD

Professor, Genetics, Harvard Medical School; Professor, Health Sciences and Technology, Massachusetts Institute of Technology (MIT); Director, US Department of Energy Technology Center; Director, NIH Center of Excellence in Genomic Science

In 1974, I adapted energy optimization methods for use in models of nucleic acids, protein and their interactions, and then for use in crystallographic refinement. In the last days of the second millennium, David Baker's team won the Critical Assessment of Structure Prediction (CASP) by an unbelievable margin. Since then, our labs exchanged 3 PhD students (Dantas, Raman, Lajoie), ++ Wannier from Mayo's group, Stranges from Kuhlman, and Mandell from Kortemme. We engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing. None of this prepared us for the revolution following Gleb Kuznetsov joining our lab in 2012, joined soon by Surge Biswas, Pierce Ogden, Ethan Alley, and Sam Sinai. Together we abruptly moved to "sequence only", deep machine learning for protein design -- ranging from fluorescent proteins to AAV capsids to antibodies. When combined with libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

YOUNG SCIENTIST KEYNOTE

The Case for Intelligent Design in Protein Engineering

JAMIE SPANGLER, PhD

Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing a so-called “intelligent design” approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

MONDAY, AUGUST 31 10:00 AM-12:30 PM

SC10: CAR T-Cell Therapy from A-Z

Instructor:
Tara Arvedson, PhD, Executive Director, Oncology Research, Amgen, Inc.

This course will provide an overview of the history of the CAR T cell platform including early successes and failures. It will review learnings from the non-clinical and clinical evaluation of CAR T cells in hematologic malignancies and solid tumors. It will discuss challenges encountered with the current CAR T cell formats and approaches to address these challenges followed by discussion of the next generation CAR T cells including technical improvements and therapeutic opportunities.

MONDAY, AUGUST 31 1:00-3:30 PM

SC15: Introduction to Gene Therapy Products Manufacturing and Analytics

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.

PRESENT A VIRTUAL POSTER

SAVE $50

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the virtual 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 July 10, 2020.

Virtual 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

Cambridge Healthtech Institute is proud to support and recognize the scientists of tomorrow! Full-time graduate students and PhD candidates qualify for the student rate. Students are encouraged to present a research poster and will receive an additional discount off the registration fee. They will also be recognized as a Student Fellow of the event.

Visit PEGSummit.com/posters for more details.

POSTER COMPETITION

Present your virtual poster at PEGS Boston and be automatically entered to win. The winners will be chosen based on clarity of abstract, novelty of data, technology advances and implications of the work presented, visual clarity of PowerPoint presentation, clear and engaging oral explanation.

Reasons you should present your research poster at this conference:

- **Your research will be seen by our international delegation, representing leaders from top pharmaceutical, biotech, academic and government institutions**
- **Discuss your research and collaborate with other attendees during designated chat times**
- **Your poster presentation will be published on our conference platform**
- **Receive $50 off your registration**
- **Automatically entered into the poster competition**

ENGINEERING STREAM

Discovering and Optimizing First-in-Class Biologics

The Engineering stream profiles the rapid advancements in biologic drug development and provides unparalleled knowledge and collaboration opportunities. This year's list of hot topics includes deep sequencing of antibody repertoires, single cell analysis, yeast and phage display for antibody discovery, tools for designing "smart" antibodies including AI and machine learning, improving targeting specificity, overcoming liabilities, next-generation libraries, targeting membrane proteins, engineering bispecific antibodies for oncology and beyond. Plan to attend and learn why this has become the industry's leading event in biotherapeutics.

2020 ENGINEERING STREAM CONFERENCES

AUGUST 31-SEPTEMBER 1
AGENDA Display of Antibodies

SEPTEMBER 2-3
AGENDA Engineering Antibodies

SEPTEMBER 3-4
AGENDA Engineering Bispecific Antibodies

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August 31-September 1 | 22nd Annual

DISPLAY OF ANTIBODIES

Leading the Way for Antibody Drugs of the Future

MONDAY, AUGUST 31

STATE-OF-THE-ART IN ANTIBODY ENGINEERING

9:00 am Chairperson's Opening Remarks
K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

9:05 KEYNOTE PRESENTATION: Design of Bispecific Antibodies: From Heavy/ Light Chain Pairing Preferences to Mitigating High Viscosity
Paul J. Carter, Genentech Fellow, Antibody Engineering, Genentech

This talk offers mechanistic understanding of antibody heavy/light chain pairing preference and application to the efficient production of bispecific IgG in single host cells. The second part of this talk will focus on elevated antibody viscosity at high concentration, which can be limiting for subcutaneous delivery, as well as manufacturing. Specifically, a novel mutational strategy was devised to mitigate high viscosity of monospecific and bispecific antibodies that may complement existing methods.

9:25 Addressing Antibody Developability by Mammalian Display
John D. McCafferty, PhD, CEO & Founder, IONTAS

As well as having appropriate binding affinity, it is important that clinical drug candidates are non-polyreactive and have optimal biophysical properties allowing formulation at high concentrations. Our mammalian display platform has allowed direct selection of antibody variants with reduced polyreactivity and aggregation propensity from large mammalian display libraries. Thus, mammalian display addresses developability issues during the earliest stages of lead discovery and significantly de-risks the future development of antibody drugs.

9:45 Selection and Optimization of Antibodies against Multipass Membrane Proteins *in situ* on Cell Surfaces
Robert Pejchal, PhD, Director, Antibody Engineering, Adimab LLC

Whole cell selections extend discovery of yeast-presented antibodies to integral membrane proteins, such as GPCRs. A case study from initial binder identification to functional characterization of affinity-optimized antagonist leads against a GPCR will be presented. Affinity optimization by selection and high-throughput selection-free screening of antibody variants will be discussed, along with takeaways for leveraging multiple cell lines in NGS-based enrichment analysis of highly diverse library selection outputs.

10:05 Live Q&A: Session Wrap-Up
Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
John D. McCafferty, PhD, CEO & Founder, IONTAS
Robert Pejchal, PhD, Director, Antibody Engineering, Adimab LLC
Paul J. Carter, Genentech Fellow, Antibody Engineering, Genentech

10:30 Coffee Break - View our Virtual Exhibit Hall

STATE-OF-THE-ART IN ANTIBODY ENGINEERING (CONT.)

10:45 Chairperson's Remarks
K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

10:50 Next-Generation Platforms for Antibody Discovery
Andrew R.M. Bradbury, PhD, CSO, Specifica, Inc.

Antibody display libraries have served as a rich source of therapeutic antibodies. However, antibody leads selected from display libraries usually require downstream affinity and developability optimization, extending lead development timelines and costs. Specifica has established a unique antibody discovery display platform based on natural antibody sequences in which sub-nanomolar antibodies, requiring minimal optimization, are routinely selected.

11:10 Choosing the Right Platform: Applications of *in vivo* and *in vitro* Systems across the Discovery Pipeline
Melissa Geddie, PhD, Principal Scientist, Antibody Discovery, Biogen

Deciding which platforms to use for new campaigns is an important step in the antibody discovery process. Some considerations include the purpose of the antibodies (reagents vs. therapeutics), as well as the difficulty of the target. Recent campaigns at Biogen will be discussed that highlight the advantages and disadvantages of our *in vivo* and *in vitro* platforms.

11:30 Antibody to watch: neutralizing SARS-CoV-2 antibody from recovered COVID-19 patient
Birgit Viira, PhD, Key Account and Technology Officer, Icosagen

We take advantage of our universal HybriFree antibody discovery engine to efficiently discover therapeutic antibody candidates by direct cloning from COVID-19-recovered patients' blood samples. HybriFree method is further powered by our patented QMCF protein expression platform, permitting high-quality recombinant antigen and antibody production for pre-clinical research (including afucosylated antibodies for enhanced ADCC). Both technologies and relevant case studies will be presented, and discussed.

11:55 Live Q&A: Session Wrap-Up
Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
Melissa Geddie, PhD, Principal Scientist, Antibody Discovery, Biogen
Andrew R.M. Bradbury, PhD, CSO, Specifica, Inc.
Birgit Viira, PhD, Key Account and Technology Officer, Icosagen

12:15 pm Lunch Break - View our Virtual Exhibit Hall

NGS AND MACHINE LEARNING IN ANTIBODY DISCOVERY

1:05 Semi-Supervised Machine Learning in the Identification of Antibody Leads from *in vitro* Selections
M. Frank Erasmus, PhD, Head, Bioinformatics, Specifica, Inc.

One important goal of therapeutic selection campaigns is to generate diverse antibody panels that comprehensively explore epitope space. While antibodies with very different sequences are expected to bind different epitopes, it is not clear what constitutes a "different antibody". This seminar will describe a semi-supervised machine learning tool that utilizes low-to-moderate-trained screening data coupled to unsupervised learning built around high-throughput, next-generation sequence information to improve lead prediction accuracy.

1:25 Synthetic DNA Technologies Enable Antibody Discovery and Optimization
Aaron Sato, PhD, CSO, Biopharma, Twist Bioscience

Utilizing its proprietary DNA technology to write synthetic libraries, Twist Biopharma provides end-to-end antibody discovery and optimization solutions for the biotechnology industry. This solution includes (1) a panel of highly diverse synthetic naïve antibody phage display libraries, (2) several target class specific antibody phage display libraries against difficult-to-drug targets, (3) a Twist Antibody Optimization (TAO) platform for antibody affinity and developability optimization and (4) a high-throughput antibody expression service.

1:50 Live Q&A: Session Wrap-Up
Moderator: Andrew R.M. Bradbury, PhD, CSO, Specifica, Inc.
Panelists:
M. Frank Erasmus, PhD, Head, Bioinformatics, Specifica, Inc.
Aaron Sato, PhD, CSO, Biopharma, Twist Bioscience

2:10 Refresh Break - View Our Virtual Exhibit Hall

2:30 Problem Solving Breakout Discussions - Part A

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 1: Can Mammalian Display Compete with Yeast and Phage? Challenges and Benefits of Mammalian Selection Systems for Protein Engineering

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

3:00 Refresh Break - View Our Virtual Exhibit Hall

3:20 Problem Solving Breakout Discussions - Part B

TABLE 2: Enabling Technologies to Enhance Selections Based on Immune Function

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

3:50 Refresh Break - View our Virtual Exhibit Hall

PLENARY KEYNOTE SESSION

4:10 Chairperson's Remarks

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

4:15 KEYNOTE PRESENTATION: From Energy to Machine Learning

George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School

We've engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing, before abruptly moving to "sequence-only" deep machine learning for protein design – from fluorescent proteins to AAV capsids to antibodies. When combined with libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

4:40 KEYNOTE PRESENTATION: The Case for Intelligent Design in Protein Engineering

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

Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing a so-called "intelligent design" approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

5:15 Live Q&A: Session Wrap-Up

Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

5:35 Happy Hour - View our Virtual Exhibit Hall

6:10 Close of Day

TUESDAY, SEPTEMBER 1

PROTEIN STRUCTURE FOR ENGINEERING PROTEINS

9:00 am Chairperson's Remarks

Gregory A. Weiss, PhD, Professor, Chemistry, Pharmaceutical Sciences, Molecular Biology & Biochemistry, University of California, Irvine

9:05 Mammalian Display Platform for Facile, FACS-Based Engineering of Antibodies, T Cell Receptors, and Viral Glycoproteins

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

To streamline engineering of antibodies, related receptors and complex proteins, we developed a mammalian screening platform which allows for variant selection in the manufacturing host with near-native glycosylation. We have used this to identify human T cell receptors with sub-nanomolar affinities and modulate Fc binding to Fc receptors. Efforts to select for SARS-CoV-2 spike variants with increased stability and modified glycosylation sites to focus the immune response will be reported.

9:25 MicroED: Conception, Practice, and Future Opportunities

Emma R Danelius, Postdoctoral Researcher, Biological Chemistry & Physiology, Univ of California Los Angeles

In 2013, we unveiled the cryoEM method, Microcrystal Electron Diffraction (MicroED). The CryoEM is used in diffraction mode for structural-using crystals that are a billion times smaller than what is used for X-ray crystallography. In this seminar, I will describe the basics of this method, from concept to data collection, analysis and structure determination, and illustrate how samples that were previously unattainable can now be studied by MicroED.

9:45 Yeast Display, A powerful modality for high affinity and manufacturable antibody discovery

Syngene

Saurabh Joshi, Phd, Associate Research Director, Discovery Biology, Syngene International Ltd

Syngene provides a one-stop solution for large molecule discovery and development using multiple modalities such as classical hybridoma, phage display, and yeast display. Yeast display combines the advantages of both hybridoma and phage methods viz. ease of identification of high affinity, manufacturability, and a higher number of sequences. Our novel methodologies to generate the desired immune response in animals and expertise in yeast display has yielded great success in antibody discovery/development for various disease condition.

10:10 Live Q&A: Session Wrap-Up

Moderator: Gregory A. Weiss, PhD, Professor, Chemistry, Pharmaceutical Sciences, Molecular Biology & Biochemistry, University of California, Irvine
Panelists:
Emma R Danelius, Postdoctoral Researcher, Biological Chemistry & Physiology, Univ of California Los Angeles
Jennifer A. Maynard, PhD, Henry Beckman Professor, McKetta Department of Chemical Engineering, Cockrell School of Engineering, University of Texas Austin
Saurabh Joshi, Phd, Associate Research Director, Discovery Biology, Syngene International Ltd

10:30 Coffee Break - View our Virtual Exhibit Hall

NGS AND MACHINE LEARNING IN ANTIBODY DISCOVERY

10:50 Structure-Guided Design of Immunogens Based on Flavivirus Glycoprotein E Domain III (EDIII)

Jonathan R. Lai, PhD, Professor, Biochemistry, Albert Einstein College of Medicine

We have utilized structure-based protein engineering and phage display to mask unproductive epitopes of flavivirus E glycoprotein domain III (EDIII) by mutation while maintaining neutralizing epitopes. We have engineered these "resurfaced" EDIIIs from both DENV and ZIKV. Furthermore, we have developed protein nanoparticles containing EDIIIs from DENV and ZIKV using Spycatcher/Spytag conjugation technology. We will describe these design strategies and their potential for development of novel subunit vaccines.

11:10 Combining Machine Learning and Antibody Discovery

Simon Friedensohn, Researcher, Biosystems Science & Engineering, ETH Zurich

We present a deep learning model that can be used to extract antigen-specific sequence patterns, that act as highly accurate, immunological

biomarkers. Besides its diagnostic value, we show how this model not only facilitates antibody discovery, but also generates a large amount of rationally designed, novel *in silico* variants which can be used to identify promising lead candidates at an early stage during drug discovery.

11:30 Live Q&A: Session Wrap-Up
Moderator: Andrew R.M. Bradbury, PhD, CSO, Specifica, Inc.
Panelists:
Jonathan R. Lai, PhD, Professor, Biochemistry, Albert Einstein College of Medicine
Simon Friedensohn, Researcher, Biosystems Science & Engineering, ETH Zurich

11:50 Lunch Break - View Our Virtual Exhibit Hall

PHAGE AND YEAST DISPLAY FOR EMERGING AND CHALLENGING TARGETS

12:55 pm Chairperson's Remarks
Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University

1:00 KEYNOTE PRESENTATION: Attacking the Cancer Surfaceome with Recombinant Antibodies
James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco
Our lab uses proteomic technologies, both mass spectroscopy-based and a new multiplexed antibody method to systematically understand how cancer cells remodel their membrane proteomes. We then generate recombinant antibodies to detect and then attack these cells by toxifying the antibodies or recruiting immune cells to kill. I will describe our current studies in this area of attacking cancer from the outside.

1:20 Antibody Fragments as Tools to Investigate G Protein-Coupled Receptor Signaling
Andrew C. Kruse, PhD, Associate Professor, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School
G protein-coupled receptors (GPCRs) are critical regulators of most aspects of human physiology, including control of cardiovascular function and metabolic homeostasis. New methods for synthetic antibody fragment discovery allow targeting of GPCRs, offering new insights into receptor structure, function, and signaling. In particular, GPCR-targeted antibodies now enable structural studies of receptor activation mechanisms, revealing in atomic detail how agonists trigger conformational changes and thereby activate cellular signaling pathways.

1:40 Leveraging Next-Generation Yeast Display Libraries for Systems Immunology
Aaron M. Ring, MD, PhD, Assistant Professor, Immunobiology, Yale School of Medicine
Yeast have a remarkable capacity to functionally display a large fraction of the human exoproteome on their surface, including cytokines, growth-factors, and immunoreceptors. Using curated, genetically barcoded yeast libraries of these proteins, we have developed high-throughput approaches for antibody discovery, detection of protein-protein interactions, and characterization of functional humoral responses in patient samples.

2:00 Live Q&A: Session Wrap-Up
Moderator: Jennifer R. Cochran, PhD, Shriram Chair & Professor, Bioengineering & Chemical Engineering, Stanford University
Panelists:
James A. Wells, PhD, Professor, Departments of Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California, San Francisco
Aaron M. Ring, MD, PhD, Assistant Professor, Immunobiology, Yale School of Medicine
Andrew C. Kruse, PhD, Associate Professor, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School

2:25 Refresh Break - View our Virtual Exhibit Hall

2:40 Close of Display of Antibodies

ENGINEERING ANTIBODIES

New Science and Technologies for the Discovery and Engineering of Next-Generation Biotherapeutics

WEDNESDAY, SEPTEMBER 2

APPLICATIONS OF MACHINE LEARNING AND NGS IN BIOTHERAPEUTIC R&D

9:05 am Applying Machine Learning to Improve Protein Expression and Solubility

Erik Vernet, PhD, Director, Protein Engineering, Discovery Biologics, Novo Nordisk Research Center

The elusive relationship between protein sequence, expression, and solubility necessitates costly and time-consuming analogue screening for protein therapeutics R&D. In this presentation, I will share our work on applying machine learning to predict protein expression and to accelerate protein solubility assessment, using internal and publicly available data sources.

9:25 Machine Learning Methods for *de novo* Design of Proteins and Antibodies

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

I will present novel methodologies for the *de novo* design of proteins and antibodies, including a protein design platform based on modern convolutional neural network architectures and methods for *de novo* design of H3 loops.

9:45 Lessons in Generating Monoclonal Antibodies against Multipass Membrane Proteins

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

Integral Molecular has a 95% success rate of discovering high-affinity monoclonal antibodies against multipass membrane proteins despite the structural complexity and low immunogenicity of these targets. Here, we present some of the lessons we have learned to enable discovery campaigns against these historically intractable targets, including GPCRs, ion channels and transporters. Case studies for CB1, P2X7, SLC2A4 and Claudin18.2 will be discussed.

10:10 LIVE Q&A: Session Wrap-Up

Moderator: Philip M. Kim, PhD, Associate Professor, Molecular Genetics & Computer Science, University of Toronto
Panelists:
Erik Vernet, PhD, Director, Protein Engineering, Discovery Biologics, Novo Nordisk Research Center
Ross Chambers, PhD, Vice President, Antibody Discovery, Integral Molecular

10:30 KEYNOTE PRESENTATION: Machine Learning-Based Antibody Discovery

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

We present a machine learning method that optimizes complementarity-determining regions of antibodies drawn from phage display experiments. We discuss how machine learning can improve target specificity by the modular composition of models from different experimental campaigns, enabling a new integrative approach to improving target specificity. We demonstrate how predictive and differentiable models of antibody binding can be learned from high-throughput experimental data without the need for target structural data.

10:50 Session Break

10:55 Next-Generation Technologies for Antibody Genetic and Functional Analysis

Brandon DeKosky, PhD, Assistant Professor, The University of Kansas

We have developed new strategies in library design and screening to enable comprehensive antibody developmental pathway assessment and to survey the entire landscape of possible single mutations. We are also exploring new features related to the genetic regulation of antibody development. We will discuss applications of these technologies to better understand antibody development and to identify improved antibody therapeutics.

11:15 A Novel Mammalian Display Platform for the Engineering of Highly Specific T Cell Receptors

Rodrigo Vazquez-Lombardi, PhD, PostDoc Lab for Systems & Synthetic Immunology, Biosystems Science & Engineering, ETH Zurich

Traditional approaches for engineering T cell receptors (TCR) with increased affinity can be largely unsuitable for T cell therapy applications, as they can yield TCR variants that promote T cell exhaustion, preclude serial TCR triggering and, in some instances, cause fatal cross-reactivity. Using multi-step CRISPR-Cas9 genome editing, we have developed a novel cellular TCR display platform supporting high-throughput selection of optimal TCRs by means of functional screening and deep sequencing.

11:35 Integrated mAb Pipeline from Virtual Machine Learning to Transposon-Mediated Cell Line Development

Claes Gustafsson, Ph.D, Co-Founder and CCO, ATUM

Monoclonal antibodies in their many divergent formats have revolutionized medicine and today represent >$100B/year in pharmaceutical sales. ATUM has built an integrated pipeline from generation of antigens via affinity maturation, developability, engineering, and humanization all the way through scale-up and stable cell line generations. The presentation will include case studies highlighting the process; each step uses technological breakthroughs in synthetic biology, machine learning, LIMS data integration, robotics, and engineered transposases to ensure maximum efficiency.

12:00 pm LIVE Q&A: Session Wrap-Up

Moderator: David K. Gifford, PhD, Professor, Electrical Engineering & Computer Science, Massachusetts Institute of Technology
Panelists:
Brandon DeKosky, PhD, Assistant Professor, The University of Kansas
Rodrigo Vazquez-Lombardi, PhD, PostDoc Lab for Systems & Synthetic Immunology, Biosystems Science & Engineering, ETH Zurich
Claes Gustafsson, Ph.D, Co-Founder and CCO, ATUM

12:20 Lunch Break - View our Virtual Exhibit Hall

IMPROVING TARGET SPECIFICITY

12:45 Design of Exquisite Binding Specificity

Shohei Koide, PhD, Professor, Biochemistry & Molecular Pharmacology, New York University School of Medicine; Perlmutter Cancer Center, NYU Langone Health

There is increasing demand for sophisticated specificity profiles for next-generation biotherapeutics. Gone are the days when we simply needed to generate high affinity to the target of interest. We often need to achieve extremely high specificity, as well as cross-reactivity among relevant targets and epitopes. I will illustrate critical roles that the design of library sorting schemes plays in achieving exquisite binding specificity using several case studies.

1:05 Engineering Acidic pH-Selective mAbs Targeting VISTA

Julie Su, PhD, Principal Scientist, Discovery Biotherapeutics, Bristol Myers Squibb Co

VISTA is a checkpoint inhibitor that preferentially engages T cells at low pH. We engineered potent, acidic pH-selective mAbs that bind to VISTA and block its interaction with the receptor, PSGL-1. Further characterization using revertants, also a structure of VISTA:Fab complex, revealed the mechanism for the acidic pH selectivity. The acidic pH-selective mAbs have improved PK and superior tumor targeting compared to a pH-independent mAb, while retaining *in vivo* efficacy.

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1:25 Amplifying Antibody Diversity: Single-Cell Screening Combined with Repertoire Sequencing from Humanized Mice

Kevin Heyries, PhD, Co-Found and Head, Business Development, AbCellera

We identified hundreds of target-specific antibodies using high-throughput, single-cell screening from humanized mice. To reveal greater diversity, we sequenced the immunoglobulin repertoire of immunized animals and superimposed validated single-cell-derived sequences using bioinformatics to reconstruct clonal trees. This versatile approach dramatically expands the total available number of fully human, *in vivo*-generated antibodies against any therapeutic target.

1:50 LIVE Q&A: Session Wrap-Up

Moderator: Shohei Koide, PhD, Professor, Biochemistry & Molecular Pharmacology, New York University School of Medicine; Perlmutter Cancer Center, NYU Langone Health
Panelists:
Julie Su, PhD, Principal Scientist, Discovery Biotherapeutics, Bristol Myers Squibb Co
Kevin Heyries, PhD, Co-Found and Head, Business Development, AbCellera

2:10 Refresh Break - View our Virtual Exhibit Hall

SUBCELLULAR & INTRACELLULAR TARGETING

2:25 Subcellular Trafficking Pathways as Targets for the Design of Therapies for Autoimmunity and Cancer

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

The presentation will describe how analyses of the Fc receptor, FcRn, using a combination of protein engineering, cellular biological studies, and mouse disease models, have been used to design therapeutics to modulate the dynamic behavior of antibodies. The generation of engineered antibody-drug conjugates that are designed to deliver their cytotoxic payload more efficiently through altered subcellular trafficking behavior to tumor cells will also be discussed.

2:45 Developing Therapeutics for Intracellular Targets

Francois-Thomas Michaud, PhD, CEO, Feldan Therapeutics

To allow biologics to reach intracellular targets, we generated peptides that can deliver proteins, peptides, and protein complexes in cells. Using intranasal instillations, Feldan and collaborators showed that these carrier peptides ("Feldan Shuttles") efficiently deliver CRISPR complexes in lungs, leading to genetic modifications of epithelial cells *in vivo*. This proves the therapeutic interest of the Shuttle platform for pulmonary diseases by showing that it can lead to functional changes in lungs.

3:05 Function vs. Force: Accelerated Identification of Relevant Antibody Candidates in the Modern Discovery Landscape

Colby Souders, PhD, CSO, Abveris

As the complexity of therapeutic targets continues to evolve, more efficient and predictive identification of pertinent antibody candidates becomes increasingly valuable. Incorporating state-of-the-art, high-resolution characterization tools and methods into discovery workflows enables rapid and reliable selection of lead candidates more effectively than traditional techniques. The presentation will focus on elucidating function early during screening and development to enhance candidate triage, as opposed to relying on brute-force methods to characterize large panels containing primarily non-functional clones.

3:30 LIVE Q&A: Session Wrap-Up

Moderator: Francois-Thomas Michaud, PhD, CEO, Feldan Therapeutics
Panelists:
E. Sally Ward, PhD, Director, Translational Immunology; Professor, Molecular Immunology, Centre for Cancer Immunology, University of Southampton
Colby Souders, PhD, CSO, Abveris

3:50 Refresh Break - View Our Virtual Exhibit Hall

4:10 Problem-Solving Breakout Discussions Part A - View our Virtual Exhibit Hall

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 14: Mammalian Cell Display for High-Throughput Engineering of Immune Receptors

Rodrigo Vazquez-Lombardi, PhD, PostDoc Lab for Systems & Synthetic Immunology, Biosystems Science & Engineering, ETH Zurich

TABLE 15: Modulating the Dynamic and Subcellular Trafficking Behavior of Antibodies for Therapy

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

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem-Solving Breakout Discussions Part B - View our Virtual Exhibit Hall

TABLE 16: Big Data Challenges in Protein Engineering

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

5:30 Close of Day

THURSDAY, SEPTEMBER 3

CHALLENGES & SOLUTIONS

9:05 am Molecular Design Intent in Early Drug Discovery

Carlos Rodrigues dos Reis, PhD, Group Leader, Biopharm Discovery, GlaxoSmithKline

The early selection of biotherapeutics requires the meticulous assessment of a variety of molecule properties. The increased complexity of non-standard formats requires further molecular design and engineering strategies to optimize their properties, as well as new screening approaches to select the best candidate molecules. In this presentation, I will discuss applications and current engineering challenges to optimize the developability profile of molecules during early discovery and accelerate their development.

9:25 Presentation of Non-Germline Residues and Clinical Consequences: A Case Study

Nicoletta Bivi, PhD, Director, Assay Development, Immunogenicity and Immunoassays, Laboratory for Experimental Medicine (LEM), Eli Lilly and Company

The anti-PCSK9 antibody, Bococizumab, was terminated after Phase 3 due to high immunogenicity. We assessed its intrinsic immunogenicity risk using our current tools, consisting of *in silico* analyses, MAPPS, and T cell activation. We observed significant presentation of non-germline residues and Bococizumab-driven T cell activation in 90% and 56% of donors, respectively. In contrast, anti-PCSK9 antibodies with low immunogenicity demonstrated low-to-moderate presentation of non-germline residues and no T cell activation.

9:45 Accelerating Antibody Engineering with Structured Data and Insights

Prem Mohanty, Product Marketing Manager, Marketing, Benchling

Antibody engineering is now more streamlined than ever, but several factors contribute to its complexity such as concerns around immunogenicity, increasing diversity of antibody formats, and the need for comprehensive characterization. I will highlight how Benchling provides a modern and fully configurable informatics platform to address complex antibody R&D needs.

9:58 Leveraging Recombinant Patient Antibodies in Therapeutic Applications

Anthony Stajduhar, Business Development Manager, Sales, Rapid Novor, Inc

Rapid Novor has perfected the art of monoclonal antibody sequencing, and is now ready to demonstrate its ability to sequence mAbs from polyclonal mixtures. Further, they have coupled this technology with the ability to track the relative abundance of these antibodies over time using NovorIg™ to profile the immune response.

10:10 LIVE Q&A: Session Wrap-Up
Moderator: Nicoletta Bivi, PhD, Director, Assay Development, Immunogenicity and Immunoassays, Laboratory for Experimental Medicine (LEM), Eli Lilly and Company
Panelists:
Carlos Rodrigues dos Reis, PhD, Group Leader, Biopharm Discovery, GlaxoSmithKline
Prem Mohanty, Product Marketing Manager, Marketing, Benchling
Anthony Stajduhar, Business Development Manager, Sales, Rapid Novor, Inc

10:30 Antibody Engineering and Vaccine Design Based on Proteomic Profiling of Antibody Repertoire
Jiwon Lee, PhD, Assistant Professor, Engineering, Dartmouth College
Antibody molecules circulating in blood and neutralizing different pathogens is a key element of the immune system. Combining high-resolution proteomics with Next-Gen sequencing of B cell receptor transcripts, we have developed a quantitative approach for delineating and characterizing the antigen-specific antibody repertoire. Here, I will present insights gained from characterizing serological repertoires and highlight recent work demonstrating how this knowledge can guide the engineering efforts for next-generation therapeutics and vaccines.

10:50 A High-Throughput Production Workflow for Complex-Format Therapeutic Molecules
Avinash Gill, PhD, Senior Scientific Manager, Antibody Engineering, Genentech Inc.
A high-throughput, automated platform for production of large molecules makes it feasible to generate purified, high-quality material for screening potential therapeutic candidates in assays. We have developed a highly productive, preparative HPLC workflow to rapidly purify complex-engineered, antibody-like molecules for use in assays designed to evaluate novel large-molecule formats for desired functionality, thereby overcoming some of the limitations of traditional purification techniques.

10:10 LIVE Q&A: Session Wrap-Up
Moderator: Nicoletta Bivi, PhD, Director, Assay Development, Immunogenicity and Immunoassays, Laboratory for Experimental Medicine (LEM), Eli Lilly and Company

11:10 LIVE Q&A: Session Wrap-Up
Moderator: Avinash Gill, PhD, Senior Scientific Manager, Antibody Engineering, Genentech Inc.
Panelists:
Jiwon Lee, PhD, Assistant Professor, Engineering, Dartmouth College
Carlos Rodrigues dos Reis, PhD, Group Leader, Biopharm Discovery, GlaxoSmithKline

11:30 Close of Engineering Antibodies

September 3-4 | 11th Annual

ENGINEERING BISPECIFIC ANTIBODIES

Designing New Off-the-Shelf Antibody Therapies

THURSDAY, SEPTEMBER 3

BISPECIFIC ANTIBODIES FOR CO-STIMULATION AND CANCER IMMUNOTHERAPY

12:30 pm Chairperson's Opening Remarks
Jonathan H. Davis, PhD, Head, Innovation, Invenra, Inc.

12:35 KEYNOTE PRESENTATION: Co-Stimulatory Bispecific Antibodies for Combination Cancer Immunotherapy
Dimitris Skokos, PhD, Senior Director, Cancer Immunology, Regeneron Pharmaceuticals

Tumor-specific antigen (TSAxCD3) bispecifics have demonstrated promising anti-tumor efficacy in cancer patients, but the opportunity to optimize T cell activity further remains. We introduce a novel class of bispecific antibodies mimicking "signal 2", by bridging a TSA to a co-stimulatory receptor on T cells. Combining this novel class of co-stimulatory bispecific antibodies with the emerging class of TSAxCD3 bispecifics may provide well-tolerated, "off-the-shelf" antibody therapies with potentially enhanced anti-tumor efficacy.

12:55 T Cell-Engaging Bispecific Antibodies: Comparing Pfizer's Platforms
Javier Chaparro-Riggers, PhD, Executive Director, Biomedicine Design, Pfizer

T cell-engaging bispecific antibodies are a promising therapeutic approach for the treatment of multiple cancer types. Many formats are currently being tested in the clinic. Pfizer has developed several Fc-containing T cell-engaging bispecific antibody platforms, which increase the half-life and allow for conventional dosing. These platforms are currently being evaluated in the clinic. Here, we will compare these platforms, and the challenges and opportunities of each platform will be highlighted.

1:25 Dealing with the Combinatorial Complexity of Protein Engineering: Bi- and Multi-Specifics, TCRs, and CAR Ts
Amanda Fitzgerald, PhD, Senior Scientific Consultant, Biologics, Genedata

We present a new technology platform to fully automate both molecular design, as well as the integrated assessment of potency, efficacy, and developability profiling of large panels of bispecific candidates. We will present use cases showing how the platform allows for the systematic cloning, expression, purification, and characterization of complex multi-specific, CAR T and TCR modalities, with a focus on immuno-oncology applications.

1:50 A Bispecific SNIPER™ Demonstrates Preclinical Efficacy through the Selective Elimination of Tumor Tregs
Jonathan H. Davis, PhD, Head, Innovation, Invenra, Inc.

Antibodies for immune checkpoint blockade have revolutionized cancer therapy but their use is oftentimes limited by toxicity, particularly when used in combination. The next generation of immunotherapies must address these toxicities to enable more potent combination therapies. Here, we describe a bispecific SNIPER™ antibody that selectively targets intratumoral regulatory T cells (Treg), diminishing the immunosuppressive tumor microenvironment without the toxicity associated with systemic Treg depletion.

2:10 Refresh Break - View our Virtual Exhibit Hall

2:30 Close of Day

FRIDAY, SEPTEMBER 4

MULTISPECIFICITY AND COMBINATION STRATEGIES

9:00 am Chairperson's Opening Remarks
Mahiuddin Ahmed, PhD, President and CSO, VITRUVIAE

9:05 Rational Combinatorial CAR Designs for Effective Immunotherapy
Mohamad Hamieh, PhD, Research Associate, Center for Cell Engineering, Memorial Sloan Kettering Cancer Center

Despite remarkable complete response rates observed with patients suffering from B cell malignancies, relapses occur in a large fraction of patients, some of which are antigen-negative and others antigen-low. We explored multiple strategies of antigen dual targeting to improve chimeric antigen receptor (CAR) design with target-adapted co-stimulatory domains to prolong functional CAR T cell persistence and mitigate the risk of antigen escape.

9:25 Novel Insights into Immune Cell-Mediated Killing of Tumor Cells
Stephen J. Demarest, PhD, Senior Research Fellow, Eli Lilly and Company

Using computational modeling and protein engineering, we generated novel agents to redirect T cells to fight cancer. The designs provide for robust production of these novel agents. Impacts on epitope, affinity, and geometry will be discussed.

9:45 Platformization of Multi-Specific Protein Engineering: Learning from High-Throughput Screening Data
Norbert Furtmann, PhD, Section Head Data Science & Computational Design, Biologics Research Germany, Sanofi

Our novel, automated high-throughput engineering platform enables fast generation of large panels of multi-specific variants (up to 10.000) giving rise to large data sets (more than 100.000 data points). We report on our visualization and data analysis workflows to improve understanding of our complex molecules and guide the engineering process.

10:10 Live Q&A: Session Wrap-Up
Moderator: Mahiuddin Ahmed, PhD, President and CSO, VITRUVIAE
Panelists:
Mohamad Hamieh, PhD, Research Associate, Center for Cell Engineering, Memorial Sloan Kettering Cancer Center
Stephen J. Demarest, PhD, Senior Research Fellow, Eli Lilly and Company
Norbert Furtmann, PhD, Section Head Data Science & Computational Design, Biologics Research Germany, Sanofi

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

CLINICAL VALIDATION OF PLATFORMS

11:00 Chairperson's Remarks
G. Jonah Rainey, PhD, Vice President, Antibody Therapeutics, Gritstone Oncology

11:05 T Cell Therapeutics to Address Hematological Malignancies and Solid Tumors
Tara Arvedson, PhD, Executive Director, Oncology Research, Amgen, Inc.

T cell therapeutics have demonstrated clinical benefit in hematological malignancies and there is growing evidence of activity in solid tumors. This presentation will describe key findings from recent trials along with observations from nonclinical studies that inform on mechanism of action and approaches to address clinically observed challenges.

11:25 Live Q&A: Session Wrap-Up
Moderator: G. Jonah Rainey, PhD, Vice President, Antibody Therapeutics, Gritstone Oncology
Panelists:
Tara Arvedson, PhD, Executive Director, Oncology Research, Amgen, Inc.

*** Presentations delivered via a live, interactive video conferencing platform. ***

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12:15 pm Lunch Break - View Our Virtual Exhibit Hall

TUNING SPECIFICITY – BALANCING POTENCY VS. SIDE-EFFECTS

12:30 Chairperson's Remarks
Eugene A. Zhukovsky, PhD, CSO, Biomunex Pharmaceuticals

12:35 A Novel Bispecific Antibody Platform that Elicits Efficient Tumor Lysis with Minimal Cytokine Release in Liquid and Solid Tumors
Nathan D. Trinklein, PhD, CTO, TeneoBio Inc.
Using a unique sequence-based discovery approach, we have created a large collection of fully human anti-CD3 antibodies with diverse T cell-agonist activities. Using machine learning tools, we were able to rapidly establish sequence-activity relationships and identify key residues in antibody sequences that had desired agonist behavior. We have created a platform for tunable immune activation at the site of the tumor that works with a variety of tumor antigens.

12:55 Optimizing Cytolytic Activity and Cytokine Release via Affinity Modulation of CD3-Engaging DART® Molecules for Redirected T Cell Killing
Gundo Diedrich, PhD, Senior Director, Antibody Engineering, MacroGenics, Inc.
CD3-engaging bispecifics mediate potent, redirected T cell killing and anti-tumor activity. However, their dosing is limited by systemic cytokine release. While cytokine release effects can be mitigated, an expansion of the therapeutic window of CD3-engaging bispecifics is desirable. Our studies suggest that modulating the affinity of CD3 engagement can reduce systemic cytokine secretion without compromising anti-tumor efficacy, and therefore might improve the activity and safety profile of next-generation CD3-engaging DART molecules.

1:15 Activating and Recruiting T Cells with Bispecific Antibodies and Potency-Optimized Cytokines
John R. Desjarlais, PhD, CSO, Xencor, Inc.
Xencor has developed a robust platform for the creation of bispecific antibodies that recruit and activate immune cells to destroy tumors. This platform, importantly, includes the ability to explore different valencies and CD3 affinities to maximize selectivity and therapeutic index. We have also applied our platform to create novel, reduced-potency IL15-Fc fusions with superior pharmacodynamic properties and improved therapeutic index.

1:35 Close of Summit

ONCOLOGY STREAM

Advancing Antibody Therapeutics to the Clinic

The Oncology Stream at PEGS is back to share what is new in the fight against cancer, and the antibody developments that are leading the charge. Drug discovery in oncology has relied on antibodies as a tool to determine therapeutic success. Bispecific antibodies and cell engagers, as well as antibody-drug conjugates are all utilized to improve targeted therapy and drug delivery. This year, we will look at how these impact the clinical journey from discovery to trials, whether as a single agent or in combinations. We will investigate the role of the tumor microenvironment and microbiome, and what is next on the horizon in biologic development in oncology.

PEGSBOSTON

CONFERENCE STREAMS

- ENGINEERING
- ■ ONCOLOGY
- IMMUNOTHERAPY
- CELL-BASED IMMUNOTHERAPIES
- ANALYTICAL
- EXPRESSION
- IMMUNOGENICITY & BIOASSAYS
- BIOCONJUGATES
- EMERGING THERAPEUTICS AND TECHNOLOGIES

2020 ONCOLOGY STREAM CONFERENCES

AUGUST 31-SEPTEMBER 1

AGENDA Antibodies for Cancer Therapy

SEPTEMBER 2-3

AGENDA Advancing Bispecific Antibodies and Combination Therapy to the Clinic

SEPTEMBER 3-4

AGENDA Clinical Progress of Antibody-Drug Conjugates

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August 31-September 1 | 10th Annual

ANTIBODIES FOR CANCER THERAPY

Introducing and Optimizing Breakthrough Therapies

MONDAY, AUGUST 31

IMPROVEMENTS IN TARGETING AND DELIVERY

9:00 am Chairperson's Opening Remarks
Daniel A. Vallera, PhD, Lion Scholar and Professor; Director, Section on Molecular Cancer Therapeutics; Professor, Therapeutic Radiology, University of Minnesota Masonic Cancer Center

9:05 Optimization of Antibody Half-Life for Cancer Therapeutics
Donald J. Buchsbaum, PhD, Professor & Director, Division of Radiation Biology, Department of Radiation Oncology, University of Alabama, Birmingham

There are many approaches to the use of monoclonal antibodies in cancer therapy. A factor associated with efficacy and toxicity is the circulation half-life, which relates to antibody size (intact vs. fragments), glycosylation, humanization, pegylation, albumin binding, coupling to nanoparticles, and use of a masking domain to protect the antibody from an antigen sink. Half-life is important for direct antibody therapeutics and cytotoxic antibody conjugates. Examples will be discussed.

9:25 NK Cells as Immune Engagers: A Focus on TriKES
Daniel A. Vallera, PhD, Lion Scholar and Professor; Director, Section on Molecular Cancer Therapeutics; Professor, Therapeutic Radiology, University of Minnesota Masonic Cancer Center

TriKEs are trispecific natural killer (NK) cell engagers and novel immunotherapeutic drugs consisting of two antibody scFV fragments; one recognizing NK cells, the other tumor markers, both cross-linked with cytokine IL-15. The talk will focus on improvements to the platform made using camelid technology, clinical progress against liquid tumors, prospects for solid tumor trials, and prospects for adverse reactions. We will discuss xenograft studies and their relevancy to clinical translation.

9:45 Accelerating Therapeutic Antibody Discovery with Three Distinct Humanized Mouse Models
Qingcong Lin, PhD, CEO, Biocytogen Boston Corp.

With a robust immune response, RenMab™ Mouse produces fully-human antibodies with high specificity and diverse epitopes. To identify leads, Biocytogen has created a catalog of target-humanized mouse models, allowing to conduct high throughput *in vivo* hit screening. Lastly, to further select for drug candidates with best clinical translation potential, Biocytogen offers immune-cell humanized mouse models for preclinical pharmacology evaluation. Biocytogen integrates these three mouse models to catalyze the process from target validation to IND application.

10:10 Panel Discussion: What is the Best?
Moderator: Daniel A. Vallera, PhD, Lion Scholar and Professor; Director, Section on Molecular Cancer Therapeutics; Professor, Therapeutic Radiology, University of Minnesota Masonic Cancer Center

- Best target for solid tumors
- Best route of delivery
- Best way of minimizing adverse reactions
- Best way of prolonging half-life of therapeutics

Panelists:
Donald J. Buchsbaum, PhD, Professor & Director, Division of Radiation Biology, Department of Radiation Oncology, University of Alabama, Birmingham
Qingcong Lin, PhD, CEO, Biocytogen Boston Corp.

10:30 Coffee Break - View our Virtual Exhibit Hall

12:05 pm Lunch Break - View our Virtual Exhibit Hall

BISPECIFIC ANTIBODIES AND IMMUNOTHERAPY COMBINATIONS

12:40 Chairperson's Remarks
Horacio G Nastri, PhD, Senior Director, Antibody Discovery, Incyte Corporation

12:45 Multispecifics Platform for IO: Challenges and Opportunities
Maria Wendt, PhD, Head, Biologics Research US, Sanofi

1:05 Assessing Immune Oncology Combinations with Common Light Chain Bi-/Tri-Specific Antibodies
Simon Plyte, PhD, Vice President, Immune Oncology, Merus NV

The Merus Biclonics® and Triclonics™ platforms utilize proprietary common light chain technologies to rapidly generate panels of multi-specific antibodies. Using unbiased screening approaches, large numbers of multi-specific antibodies can be tested in relevant biological assays to identify those with the strongest or even new biological responses. Case studies will be presented demonstrating the application of the these platforms in immuno-oncology.

1:50 Live Q&A: Session Wrap-Up
Moderator: Horacio G Nastri, PhD, Senior Director, Antibody Discovery, Incyte Corporation
Panelists:
Maria Wendt, PhD, Head, Biologics Research US, Sanofi
Simon Plyte, PhD, Vice President, Immune Oncology, Merus NV

2:10 Refresh Break - View Our Virtual Exhibit Hall

2:30 Problem Solving Breakout Discussions - Part A
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 3: What is the Best?
Daniel A. Vallera, PhD, Lion Scholar and Professor; Director, Section on Molecular Cancer Therapeutics; Professor, Therapeutic Radiology, University of Minnesota Masonic Cancer Center

3:00 Refresh Break - View Our Virtual Exhibit Hall

3:20 Problem Solving Breakout Discussions - Part B

3:50 Refresh Break - View our Virtual Exhibit Hall

PLENARY KEYNOTE SESSION

4:10 Chairperson's Remarks
K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

4:15 KEYNOTE PRESENTATION: From Energy to Machine Learning
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School

We've engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing, before abruptly moving to "sequence-only" deep machine learning for protein design – from fluorescent proteins to AAV capsids to antibodies. When combined with libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

4:40 KEYNOTE PRESENTATION: The Case for Intelligent Design in Protein Engineering
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing

*** Presentations delivered via a live, interactive video conferencing platform. ***

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a so-called "intelligent design" approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

5:15 Live Q&A: Session Wrap-Up

Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

5:35 Happy Hour - View our Virtual Exhibit Hall

6:10 Close of Day

TUESDAY, SEPTEMBER 1

BISPECIFIC ANTIBODIES AND IMMUNOTHERAPY COMBINATIONS (CONT.)

9:20 am Chairperson's Remarks
Horacio G Nastri, PhD, Senior Director, Antibody Discovery, Incyte Corporation

9:25 Combinatorial Approaches to Enhance Bispecific Anti-Tumor Efficacy
Eric Smith, PhD, Senior Director, Bispecifics, Regeneron Pharmaceuticals, Inc.
This presentation will describe Regeneron's bispecific platform and present preclinical data on REGN4018, a clinical-stage, T cell-engaging, bispecific-targeting Muc16 for solid tumor indications. In addition, status updates on Regeneron's other clinical-stage bispecific antibodies (REGN1979, REGN5458, REGN5678) will be presented, as well as a discussion of new combinatorial approaches being taken to enhance bispecific anti-tumor efficacy.

9:45 AlivaMab® Mouse and AlivaMab Discovery Services: AMMPD-DNA Immunization to Meet the Antibody TPP for a Toxic Target
Larry Green, Ph.D., CEO, Ablexis, LLC
John "Lippy" Lippincott, Ph.D., Vice President of Research, AlivaMab Discovery Services, LLC
An ADS client project presented the dual challenges of generating low picomolar neutralizing antibodies against a toxic target. ADS overcame these challenges in an exceptionally fast timeline by using Ablexis' AlivaMab Mouse and a novel application of its proprietary AMMPD-DNA immunization coupled with a direct function-first screening paradigm. Together, AlivaMab Mouse and ADS' robust suite of proprietary processes put projects on the fastest and most de-risked path from discovery through development and to market.

10:10 Live Q&A: Session Wrap-Up
Moderator: Horacio G Nastri, PhD, Senior Director, Antibody Discovery, Incyte Corporation
Panelists:
Eric Smith, PhD, Senior Director, Bispecifics, Regeneron Pharmaceuticals, Inc.
Larry Green, Ph.D., CEO, Ablexis, LLC
John "Lippy" Lippincott, Ph.D., Vice President of Research, AlivaMab Discovery Services, LLC

10:30 Coffee Break - View our Virtual Exhibit Hall

TARGETING B7-H3: BRINGING IT FORWARD TO CLINICAL APPLICATION

10:40 Chairperson's Remarks
Soldano Ferrone, PhD, Professor-in-Residence, Surgery, Massachusetts General Hospital

10:45 Targeting B7-H3 with Multiple Therapeutic Modalities
Ezio Bonvini - MacroGenics, Inc.
B7-H3 expression has been associated with cancer progression and poor prognosis. While its immunological function is unclear, B7-H3 remains an attractive target for tumor-directed interventions, owing to its broad cancer-associated overexpression. We have developed an Fc-enhanced mAb (enoblituzumab), CD3 bispecific DART® molecule (MGD009) and ADC (MGC018) to target NK cells, T cells, or direct a cytotoxic payload to B7-H3. The strategic rationale and development update will be presented.

11:05 B7-H3 Targeted Antibody-Based Combinatorial Immunotherapy for the Treatment of Solid Tumors
Soldano Ferrone, PhD, Professor-in-Residence, Surgery, Massachusetts General Hospital
Strategies will be described to eliminate both differentiated cancer cells and cancer initiating cells, utilizing both our B7-H3-specific mAb 376.96 and Fc receptors. In addition, approaches which upregulate B7-H3 expression on tumor cells and recover "exhausted" T cells will be shown to enhance the antitumor activity of antibody-based strategies which target B7-H3.

11:30 Use of Mammalian Virus Display to Select Antibodies Specific for Complex Membrane Antigens
Ernest Smith, Senior Vice President, Research & CSO, Vaccinex, Inc.
We have developed a technology to enable direct incorporation of multipass membrane proteins, such as GPCRs and ion channels, into the membrane of a mammalian virus. Antigen-expressing virus can be readily purified and used for antibody selection using either vaccinia, phage, or yeast display methods. This method is rapid, does not require any detergents or refolding, and can be applied to multiple cell types in order to provide properly folded protein.

11:55 Live Q&A: Session Wrap-Up
Moderator: Soldano Ferrone, PhD, Professor-in-Residence, Surgery, Massachusetts General Hospital
Panelists:
Ezio Bonvini - MacroGenics, Inc.
Ernest Smith, Senior Vice President, Research & CSO, Vaccinex, Inc.

12:15 pm Lunch Break - View Our Virtual Exhibit Hall

EMERGING TARGETS

12:45 Chairperson's Remarks
Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH

12:50 BCMA-Directed CAR T Cells for Myeloma: What Have We Learned?
Nina Shah, Associate Professor, Medicine, University of California, San Francisco
Chimeric antigen receptor (CAR) T cells have given new hope to patients with multiple myeloma. In this session, we will review the rationale behind BCMA-CAR T therapy. We will also review clinical data on efficacy and toxicity. Finally, we will discuss the unmet needs in this space. We will explore new avenues, including cell culture, cell engineering and patient selection, being explored to enhance the success of this promising therapy.

1:10 CAR T Cells Targeting CD123 or Other Targets
M. Eric Kohler, PhD, Instructor, Blood & Marrow Transplant & Cellular Therapeutics, Children's Hospital Colorado
Relapse after lineage-targeted immunotherapy for B cell leukemia associated with antigen loss is a relatively frequent occurrence. Phenotypic heterogeneity in AML suggests that this may also emerge as a pattern following targeted immunotherapy for this disease. Approaches to reduce the emergence of resistant leukemia associated with CAR T cell therapy for leukemia will be discussed.

1:30 Session Wrap-Up
Moderator: Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH
Panelists:
Nina Shah, Associate Professor, Medicine, University of California, San Francisco
M. Eric Kohler, PhD, Instructor, Blood & Marrow Transplant & Cellular Therapeutics, Children's Hospital Colorado

2:25 Refresh Break - View our Virtual Exhibit Hall

EMERGING TARGETS (CONT.)

2:30 Chairperson's Remarks
Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH

2:35 Development of Cancer-Reactive Antibodies Focused to the 287-302 Amino Acid Loop of the Human Epidermal Growth Factor Receptor
David J. FitzGerald, PhD, Chief, Biotherapy Section, Laboratory of Molecular Biology, CCR, National Cancer Institute, NIH
The 287-302 loop from EGFR is exposed on EGFRvIII (deletion of exons 2-7), partially exposed on some cancers, but cryptic on cells expressing WT EGFR. Seven antibodies to this loop reacted with EGFRvIII, but not EGFR WT. One antibody, 40H3, also exhibited binding to MDA-468 and A431 cells, but not to non-cancerous WI-38 cells. The 40H3 antibody was engineered as a potent recombinant immunotoxin for treating tumors with abnormal EGFR.

2:50 Glypicans as Emerging CAR T Cell Therapy Targets: GPC3 and Beyond
Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH
We have studied the role of GPC3 in regulating Wnt signaling, and developed antibody therapeutics including CAR T cells, antibody-drug conjugates, and immunotoxins for treating liver cancer. In recent years, we applied what we learned from GPC3 biology to explore the roles of other glypicans in solid tumors, and established GPC2 and GPC1 as new targets of CAR T cell therapy for neuroblastoma and pancreatic cancer, respectively.

3:10 Session Wrap-Up
Moderator: Mitchell Ho, PhD, Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute, NIH
Panelists:
David J. FitzGerald, PhD, Chief, Biotherapy Section, Laboratory of Molecular Biology, CCR, National Cancer Institute, NIH

3:40 Close of Antibodies for Cancer Therapy

September 2-3 | 8th Annual

ADVANCING BISPECIFIC ANTIBODIES AND COMBINATION THERAPY TO THE CLINIC

Creating the Killer Combo

WEDNESDAY, SEPTEMBER 2

INNOVATION IN IMMUNO-ONCOLOGY BISPECIFIC ANTIBODIES

9:05 am Current Status of Bispecifics Biologics and Combination Biologics Therapies

Rakesh Dixit, PhD, President & CEO, Bionavigen

In this talk, we will discuss next-generation bispecifics biologics, including IgG antibody, BiTE, CAR T cells, CD-3 T cells and enhanced TCR-based bispecifics. We'll continue into the clinical landscape of bispecifics and learnings from the successful and failed bispecifics, as well as combinations biologics, and whether we should consider them friends or foes.

9:50 Session Break

9:55 Session Wrap-Up

Moderator: Rakesh Dixit, PhD, President & CEO, Bionavigen

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

INNOVATION IN IMMUNO-ONCOLOGY BISPECIFIC ANTIBODIES (CONT.)

10:50 Chairperson's Remarks

Rakesh Dixit, PhD, President & CEO, Bionavigen

10:55 REGN4018 Is a Mucin 16 Bispecific T Cell-Engaging Antibody for the Treatment of Ovarian Cancer

Alison Crawford, PhD, Senior Staff Scientist, Oncology & Angiogenesis, Regeneron Pharmaceuticals

REGN4018 binds both MUC16 and CD3. REGN4018 inhibited growth of human tumors in a xenogenic model and murine tumors expressing human MUC16. Combination with an anti-PD-1 antibody enhanced this efficacy. Immuno-PET imaging demonstrated localization of REGN4018 in MUC16-expressing tumors, as well as in T cell-rich organs. Toxicology studies in cynomolgus monkeys showed minimal and transient increases in serum cytokines, and C-reactive protein following REGN4018 administration with no overt toxicity.

11:15 Combinatorial Immune Checkpoint Blockade Using Clinical Stage Bispecific DART® Molecules MGD013 and MGD019

Alexey Berezhnoy, PhD, Scientist III, MacroGenics, Inc.

This talk will dive into an investigation of co-expression of multiple immune checkpoint receptors by tumor-infiltrating lymphocytes, whose co-blockade provides additional benefits in immunotherapy. We will also discuss selection and format optimization of bispecific molecules for simultaneous blockade of two checkpoint pathways, in addition to discussing MGD013 and MGD019 preclinical pharmacology, IND enabling studies and clinical trial design.

11:35 Session Wrap-Up

Moderator: Rakesh Dixit, PhD, President & CEO, Bionavigen
Panelists:
Alison Crawford, PhD, Senior Staff Scientist, Oncology & Angiogenesis, Regeneron Pharmaceuticals
Alexey Berezhnoy, PhD, Scientist III, MacroGenics, Inc.

12:20 pm Lunch Break - View our Virtual Exhibit Hall

INNOVATION IN IMMUNO-ONCOLOGY BISPECIFIC ANTIBODIES (CONT.)

12:40 Chairperson's Remarks

Frank Comer, PhD, Associate Principal Scientist, AstraZeneca

12:45 Tumor-Targeted 4-1BB Activation with PRS-343, a HER2/4-1BB Antibody-Anticalin Bispecific

Ingmar Bruns, MD, PhD, Senior Vice President & Head, Clinical Development, Pieris Pharmaceuticals GmbH

In this talk, we will share comprehensive clinical experience gained from interim analyses of the PRS-343 trials, and provide an overview about the broader Pieris pipeline of 4-1BB targeting antibody-anticalin bispecific molecules.

1:05 Development of CDX-527, a Novel Bispecific-Immune Modulating Antibody Targeting PD-L1 and CD27

Joel Goldstein, Senior Director, R&D, Celldex Therapeutics

Antibodies blocking the PD-1 signaling pathway has led to a tremendous effort in combinations and bispecifics to further improve outcomes in cancer. CD27 is a costimulatory molecule providing a complementary target to the PD-1/PD-L1 axis on T cells. A tetravalent format was selected for CDX-527, that along with potent PD-1 blockade, provides efficient cross-linking, which is important for CD27 agonistic activity by allowing interaction with both Fc-receptor and PD-L1-bearing cells.

1:25 Blockade of Glycol-Immune Checkpoints (Siglecs) Using Bifunctional EAGLE for Cancer Immunotherapy

Li Peng, PhD, Senior Vice President, Research & Early Product Development, Palleon Pharmaceuticals

The Siglec/sialoglycan axis has recently emerged as a new mechanism of cancer immune evasion. We engineered a human sialidase and developed a bifunctional antibody-sialidase platform named EAGLE to inhibit this axis. EAGLE showed enzyme-dependent, robust monotherapy efficacy with complete regressions and immune memory in preclinical tumor models. We further demonstrated EAGLE's mechanism of modulating innate and adaptive antitumor responses, and identified correlative pharmacodynamic biomarkers to EAGLE treatment in preclinical models.

1:45 Session Wrap-Up

Moderator: Frank Comer, PhD, Associate Principal Scientist, AstraZeneca
Panelists:
Ingmar Bruns, MD, PhD, Senior Vice President & Head, Clinical Development, Pieris Pharmaceuticals GmbH
Joel Goldstein, Senior Director, R&D, Celldex Therapeutics
Li Peng, PhD, Senior Vice President, Research & Early Product Development, Palleon Pharmaceuticals

2:10 Refresh Break - View our Virtual Exhibit Hall

4:10 Problem Solving Breakout Discussions - Part A

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem Solving Breakout Discussions - Part B

TABLE 17: Pre-Clinical Mouse Models to Examine Immunotherapeutics

Alison Crawford, PhD, Senior Staff Scientist, Oncology & Angiogenesis, Regeneron Pharmaceuticals

5:30 Close of Day

THURSDAY, SEPTEMBER 3

NOVEL MODALITIES AND NOVEL BIOLOGY: MAXIMIZING THE POTENTIAL OF BISPECIFIC TARGETING

9:00 am Chairperson's Remarks
Frank Comer, PhD, Associate Principal Scientist, AstraZeneca

9:05 KEYNOTE PRESENTATION: Bispecific Antibody Drug Development
Paul Parren, PhD, Executive Vice President & Head, Lava Therapeutics

Currently more than 20 different commercialized technology platforms are available for bsAb creation and development, two bsAbs are marketed and over 85 are in clinical development. A defining bsAb feature is their potential for novel functionalities – activities that do not exist in mixtures of the parental or reference antibodies. This presentation provides insights in the design and function of these so-called obligate bsAb and their potential in drug development.

9:25 Oncolytic Adenoviruses Armed with BiTEs and BiKEs
Ramon Alemany, PhD, Scientist, ProCure and Oncobell Programs, Catalan Institute of Oncology - IDIBELL

Oncolytic viruses replicate and induce lymphocyte infiltration in tumors. However, the infiltrating T cells target exclusively virus-infected cells due to the immunodominance of viral antigens. BiTEs and BiKEs secreted from the oncolytic virus offer a unique opportunity to retarget T cells or NKs towards non-infected bystander tumor or stromal cells. Further, selective expression in tumors reduces the potential systemic toxicity of these engagers. Results on this strategy will be presented.

9:45 Panel Discussion: Session Wrap-Up
Moderator: Frank Comer, PhD, Associate Principal Scientist, AstraZeneca
Panelists:
Ramon Alemany, PhD, Scientist, ProCure and Oncobell Programs, Catalan Institute of Oncology - IDIBELL
Paul Parren, PhD, Executive Vice President & Head, Lava Therapeutics

10:30 Coffee Break - View our Virtual Exhibit Hall

NOVEL MODALITIES AND NOVEL BIOLOGY: MAXIMIZING THE POTENTIAL OF BISPECIFIC TARGETING (CONT.)

10:45 Chairperson's Remarks
Frank Comer, PhD, Associate Principal Scientist, AstraZeneca

10:50 A Comprehensive Immunotherapy Strategy for Solid Cancers
Jogender Tushir-Singh, PhD, Assistant Professor, Biochemistry & Molecular Genetics, UVA Cancer Center, University of Virginia School of Medicine

Since a larger ovarian cancer population highly overexpresses cancer antigen-125, we argue that ADCC-based approaches are not clinically feasible options. Therefore, to achieve a clinically applicable and patient centered approach, we hypothesize enhancing farletuzumab's anti-tumor activity beyond and independent of the ADCC function. If successful, our approach will significantly improve the survival of ovarian cancer patients with desirable clinical safety.

11:10 T Cells Redirected with Modular Biepitopic and Bispecific Antibody Mimic Receptors
Rihe Liu, PhD, Associate Professor, Chemical Biology & Medicinal Chemistry, Eschelman School of Pharmacy, University of North Carolina, Chapel Hill

We used single-domain antibody mimics with small size, simple structure, and high stability that can be modularly engineered on the surface of immune cells to acquire multifunctional TAA recognition. We demonstrated that protein domains targeting EGFR and HER2 of the ErbB family can be assembled into antibody mimic receptor (amR) molecules, and efficiently redirect T cells for biepitopic or bispecific TAA recognition *in vitro* and *in vivo*.

11:30 Selective Blockade of the Immune Checkpoint CD47 Using Bi- and Multi-Specific Antibodies
Nicolas Fischer, PhD, CEO, Light Chain Bioscience

Safe and selective blockade of the innate immune checkpoint CD47 can be achieved using bispecific antibodies (bsAb) having two arms with different affinities. This dual targeting concept has been validated in different preclinical models of human cancer and is now being explored in patients with a bsAb generated using our kappa-lambda body platform.

11:50 Close of Advancing Bispecific Antibodies and Combination Therapy to the Clinic

September 3-4 | 10th Annual

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

Clinical Updates and Lessons Learned

Part of BIOCONJUGATES STREAM

THURSDAY, SEPTEMBER 3

12:40 pm Antibody-Drug Conjugates Industry Overview
John M Lambert, PhD, Independent Consultant

LESSONS LEARNED FROM PAST ADC PROGRAMS AND RELATED FIELDS - PART I

12:45 KEYNOTE PRESENTATION: Ugly Ducklings: Why Clinically Effective Antibody-Drug Conjugates May Not Look that Pretty (at First)…And How to Spot Them
Greg M. Thurber, PhD, Assistant Professor, Chemical Engineering & Biomedical Engineering, University of Michigan
Here, I present a 'systems' approach for designing ADCs and describe when the most potent ADC *in vitro*, the most effective ADC *in vivo*, and/or the least toxic ADC in animal models may not be the most effective drug in the clinic. This 'systems' approach can help ensure the most clinically effective agents, often 'ugly ducklings' in the pipeline, thrive in the end.

1:05 Microdistribution of Antibody Distribution in Clinical Trials Using Fluorescently Labeled Anti-EGFR Antibody in Multiple Tumor Types
Eben L. Rosenthal, MD, John and Ann Doerr Medical Director, Stanford University
Systemically-administered labeled antibodies in cancer patients prior to surgery has allowed us to successfully measure antibody concentration in normal and tumor tissues. The biggest impact of this strategy is the ability to localize the antibody within tissues at the cellular level. We hypothesize that near-infrared, fluorescently labeled antibodies can be leveraged to estimate the dose at which the antibody reaches maximal tumor saturation, most notably for antibody-drug conjugates.

1:25 Modeling Target-Mediated Drug Disposition to Design More Effective Therapeutics
Donald E. Mager, PharmD, PhD, Professor & Vice Chair, Pharmaceutical Sciences, SUNY Buffalo
Target-mediated drug disposition (TMDD) is a case in which binding of a drug to its pharmacological target influences the pharmacokinetics of the drug. This phenomenon represents a major distribution/elimination process for many antibody-based constructs. This talk will review the basic tenets of TMDD, highlight how computational modeling of TMDD is being used to guide the design and development of antibodies and antibody-drug conjugates, and potential clinical implications of TMDD.

1:50 Refresh Break - View our Virtual Exhibit Hall

LESSONS LEARNED FROM PAST ADC PROGRAMS AND RELATED FIELDS - PART II

2:30 A New Mechanism of Malignant Cell Resistance to Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)
Louis M. Weiner, MD, Professor & Director, Oncology, Lombardi Comprehensive Cancer Center, Georgetown University
ADCC provides a model for uncovering immune resistance mechanisms. We have continuously exposed different cancer cell lines to KIR-deficient NK92-CD16V effector cells and ADCC-promoting monoclonal antibodies. We show that the induction of ADCC resistance involves genetic and epigenetic changes that lead to a general loss of target cell adhesion properties required for the establishment of an immune synapse, killer cell activation, and target cell cytotoxicity.

2:50 Radiohapten Capture Radioimmunotherapy for Cures of Human Tumor Xenografts in Mice
Steven M. Larson, MD, Donna & Benjamin M. Rosen Chair, Lab Head, Molecular Pharmacology, Memorial Sloan Kettering Cancer Center
We have developed an antibody-based platform approach for parenterally targeted radiotherapy with a goal of cures without histologic evidence of radiotoxicity in laboratory models of highly radioresistant solid tumors. Using a radiohapten capture system developed in collaboration with the Wittrup Laboratory of MIT, we have demonstrated proof of principle with beta- and alpha-emitting radionuclides in 3 solid tumors (antigen targets): neuroblastoma (GD2), breast cancer (Her 2), and colon cancer (A33).

3:10 Live Q&A: Q&A and Session Wrap-Up
Moderator: Greg M. Thurber, PhD, Assistant Professor, Chemical Engineering & Biomedical Engineering, University of Michigan
Panelists:
Eben L. Rosenthal, MD, John and Ann Doerr Medical Director, Stanford University
Louis M. Weiner, MD, Professor & Director, Oncology, Lombardi Comprehensive Cancer Center, Georgetown University
Steven M. Larson, MD, Donna & Benjamin M. Rosen Chair, Lab Head, Molecular Pharmacology, Memorial Sloan Kettering Cancer Center
Donald E. Mager, PharmD, PhD, Professor & Vice Chair, Pharmaceutical Sciences, SUNY Buffalo

3:40 Close of Day

FRIDAY, SEPTEMBER 4

PROGRESS FROM THE CLINIC - PART I

9:05 am Belantamab Mafodotin – Driving Innovation for Next-Generation Therapy in Multiple Myeloma
Axel Hoos, PhD, Senior Vice President, Therapeutic Area Head, Oncology, GSK
BCMA has become the leading new target for multiple myeloma with several BCMA-targeting agents in clinical development. GSK's belantamab mafodotin is an antibody-drug conjugate which has recently completed a pivotal study in 4th line of treatment in patients with multiple myeloma. This presentation provides an update on the pivotal data and overall clinical program of belantamab mafodotin.

9:25 TRPH-222: A Next-Generation ADC Targeting CD22
Nancy J. Levin, PhD, Vice President, Development, Triphase Accelerator Corp.
TRPH-222 is a CD22-directed ADC, constructed via a novel, site-specific (SMARTag™) conjugation approach, resulting in highly controlled and reproducible drug loading. TRPH-222 is being studied in relapsed and/or refractory B cell lymphoma patients in a phase 1 clinical trial (NCT03682796); currently, the trial is enrolling patients in the dose-escalation phase, with promising tolerability, PK, and PD, as well as early signs of clinical efficacy in this single agent study.

9:45 Live Q&A: Q&A and Session Wrap-Up
Moderator: John M Lambert, PhD, Independent Consultant
Panelists:
Axel Hoos, PhD, Senior Vice President, Therapeutic Area Head, Oncology, GSK
Nancy J. Levin, PhD, Vice President, Development, Triphase Accelerator Corp.

10:10 Session Break

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

PROGRESS FROM THE CLINIC - PART II

10:50 ZW49: Combining Zymeworks' Platforms to Expand the Therapeutic Window of ADCs in HER2-Positive Cancer

Rupert Davies, PhD, Director, Translational Sciences, Zymeworks Biopharmaceuticals Inc.

HER2-targeted therapies have transformed the treatment of patients, but there remains a need for well tolerated and effective treatments across a range of HER2 expression levels. ZW49 is a bispecific antibody-drug conjugate that combines the ZymeLink™ linker-payload with the unique mechanisms of action of a biparatopic, anti-HER2 Azymetric antibody. ZW49 has the potential to address the unmet medical need across a range of HER2-expressing cancers.

11:10 Combining ADCs and Immunotherapy: Mechanistic Insights and Clinical Observations

Nancy C. Whiting, PhD, Executive Vice President, Development, Seattle Genetics, Inc.

MMAE-based ADCs have demonstrated the potential to change the natural history of multiple cancers. MMAE, the cytotoxic payload, has been shown to induce immunogenic cell death. Combining MMAE-based ADCs with immunotherapy has the promise of augmenting the benefit of each of these therapies.

11:30 Antibody-Drug Conjugates: Are We There Yet?

Anthony W. Tolcher, MD, FRCPC, FACP, CEO & Founder, NEXT Oncology

If success is measured by regulatory approval, then 2019 and 2020 were successful years for antibody drug conjugates. With the approvals of enfortumab vedotin-ejfv, polatuzumab vedotin-piiq, fam-trastuzumab deruxtecan-nxki, and more recently, sacituzumab govitecan-hziy, by the Food and Drug Administration, the past 18 months exemplifies how the platform has evolved over the last 25 years. I will review the clinical lessons learned and opportunities to broaden the field.

11:50 Q&A and Session Wrap-Up

Moderator: Nancy C. Whiting, PhD, Executive Vice President, Development, Seattle Genetics, Inc.

12:15 pm Close of Summit

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IMMUNOTHERAPY STREAM

Developing Next-Generation Targeted Cancer Immunotherapies

The Immunotherapy stream focuses on the latest science, modalities and targeting strategies driving the development of immunotherapies for solid and liquid tumors. Part One examines strategies for demonstrating T cell activity, combinations, preventing toxicology, dosing, and targeting the tumor microenvironment. Part Two focuses on developing and engineering adoptive cell therapies for solid and liquid tumors, especially CAR Ts, TCRs, NKs, and TILs, as well as new targets of interest. Finally, Part Three examines new clinical and preclinical data in agonist immunotherapy targets, as well as the biology and mechanisms of these emerging therapies of interest. Together, these three units will provide a focused look at how industry is applying new science and technology in developing the next generation of targeted cancer immunotherapies.

PEGS BOSTON

CONFERENCE STREAMS

- ENGINEERING
- ONCOLOGY
- IMMUNOTHERAPY
- CELL-BASED IMMUNOTHERAPIES
- ANALYTICAL
- EXPRESSION
- IMMUNOGENICITY & BIOASSAYS
- BIOCONJUGATES
- EMERGING THERAPEUTICS AND TECHNOLOGIES

2020 IMMUNOTHERAPY STREAM CONFERENCES

AUGUST 31-SEPTEMBER 1

AGENDA Improving Immunotherapy Efficacy and Safety

SEPTEMBER 2-3

AGENDA CAR Ts, TCRs and TILs

SEPTEMBER 3-4

AGENDA Agonist Immunotherapy Targets

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August 31-September 1 | 5th Annual

IMPROVING IMMUNOTHERAPY EFFICACY AND SAFETY

Engineering the Next Generation of Immunotherapies

MONDAY, AUGUST 31

IMPROVING IMMUNOTHERAPY OUTCOMES AND TARGET IDENTIFICATION

9:05 am FEATURED PRESENTATION: Therapeutic Manipulation of the Tumor Microenvironment to Enhance Response to Immunotherapy

Allison Betof Warner, MD, PhD, Assistant Attending Physician, Memorial Sloan Kettering Cancer Center

Tumors are not simply collections of cancer cells; they are complex structures composed of blood vessels, immune cells, and supporting structures that interact, consume oxygen and other nutrients, and produce waste. Changing a tumor's environment can have profound impacts on the efficacy of antitumor therapy. I will discuss the influence of microenvironmental modulators on immunobiology and our group's approach to harness these interactions to improve therapeutic outcomes.

9:25 *In vivo* T Cell CRISPR Screen for Immunotherapy Target Discovery

Sidi Chen, PhD, Assistant Professor, Department of Genetics and Systems Biology Institute, Yale University; Member, Yale Cancer Center and the Yale Stem Cell Center

T cells have become the central focus of new cancer therapeutics. We recently performed *in vivo* CRISPR screens in CD8 cytotoxic T cells in tumor models of immunotherapy, which rediscovered prime immunotherapy targets, such as PD-1, TIM-3, LAG3, and previously undocumented targets. Other novel immunotherapy modalities will also be discussed.

9:45 Predicting NCE/NBE outcome screens with Human derived Tissueoids using AXTEX-4D™ platform

Prabuddha Kundu, PhD, Co-founder and Managing Director, Premas Biotech Pvt Ltd.

Evaluation of a new chemical/biological entities (NCE/NBE) in tumor targeting therapies takes 5-12 years for development while only a few candidates reach clinics. One bottleneck is the absence of a reliable human model with an intact tumor micro-environment & data consistency. AXTEX-4D™ seals this gap and offer a suitable alternative. Drug-Tissueoid interactions, T cell migration, and validation of the tumor characteristics like necrosis, angiogenesis, EMT etc., broaden its scope in the modern discovery landscape.

10:10 Session Wrap-Up

Moderator: Oliver Hill, PhD, Vice President, Drug Discovery, Apogenix AG
Panelists:
Sidi Chen, PhD, Assistant Professor, Department of Genetics and Systems Biology Institute, Yale University; Member, Yale Cancer Center and the Yale Stem Cell Center
Allison Betof Warner, MD, PhD, Assistant Attending Physician, Memorial Sloan Kettering Cancer Center
Prabuddha Kundu, PhD, Co-founder and Managing Director, Premas Biotech Pvt Ltd.

10:30 Coffee Break - View our Virtual Exhibit Hall

IMPROVING IMMUNOTHERAPY TARGET IDENTIFICATION

10:50 Understanding Tumor-Reactive T Cells by Repertoire and Gene Expression Analysis

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

Although T cells can be isolated directly from tumor-infiltrating lymphocyte (TIL) specimens, recent work has questioned whether T cells are tumor-reactive or specific for viral or other antigens. We've looked across tumor indications at patients to identify whether T cell receptor clonality and TIL gene expression analysis can identify tumor-reactive T cells. Using a yeast-display system, antigen specificities of T cell populations can be identified and linked to the tumor.

AGONIST IMMUNOTHERAPY

11:10 IL-15-Based Trifunctional Antibody-Fusion Proteins with Costimulatory TNF-Superfamily Ligands for Cancer Immunotherapy

Dafne Müller, PhD, Group Leader, Institute of Cell Biology and Immunology, University of Stuttgart

In order to support the generation and efficacy of an antitumor response, we have designed trifunctional antibody-fusion proteins for tumor-directed combined delivery of IL-15 and costimulatory members of the TNF-superfamily, demonstrating enhanced immune responsiveness *in vitro* and antitumor activity in a mouse model *in vivo*.

11:30 HERA-GITRL: A Unique Hexavalent GITR Agonist for Cancer Immunotherapy

Oliver Hill, PhD, Vice President, Drug Discovery, Apogenix AG

HERA-GITRL is a member of a novel class of hexavalent TNFR superfamily agonists that share the natural ligand conformation. The biological activities of HERA-GITRL, boosting antigen-specific T cell response and anti-tumor efficacy in mouse models, are crosslinking independent. As the Fc-mediated mixed mode of actions observed for antibodies are avoided, HERA-GITRL is an excellent candidate for further development into a next-generation GITR agonistic immuno-oncology drug.

11:55 Session Wrap-Up

Moderator: Adam Adler, Professor, Department of Immunology, UConn Health School of Medicine
Panelists:
Dafne Müller, PhD, Group Leader, Institute of Cell Biology and Immunology, University of Stuttgart
Oliver Hill, PhD, Vice President, Drug Discovery, Apogenix AG
Marvin Gee, PhD, Co-Founder & Head, Target Discovery, 3T Biosciences

12:15 pm Lunch Break - View our Virtual Exhibit Hall

IMPROVING CAR-T EFFICACY AND SAFETY

12:45 CAR T Cells for T Cell Malignancies

Maksim Mamonkin, PhD, Assistant Professor, Center for Cell and Gene Therapy, Baylor College of Medicine

Development of effective CAR T cells targeting widely pan-T cell antigens for T cell leukemia and lymphoma has been hindered by frequent self-targeting of CAR T cells and possible induction of prolonged T cell aplasia. We developed fratricide-resistant, CD5 CAR T cells that produce high anti-tumor activity in patients with refractory or relapsed T cell malignancies, without eliminating healthy endogenous T cells.

1:05 Cytokine Storm after COVID-19: Lessons Learned from CAR T Cell Therapy

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

Despite the unprecedented activity of CAR T cell therapy, the wider application is limited by the development of life-threatening toxicities of cytokine release syndrome and neurotoxicity. Here we will review new insights into the mechanisms of these toxicities and novel strategies to enhance CAR T cell safety.

1:25 Preclinical Mouse Model to Evaluate Efficacy of Chimeric Antigen Receptor (CAR) T Cell Therapy in Immuno-Oncology

Basile Siewe, Director, Business Development-JAX Services, The Jackson Laboratory

1:50 Session Wrap-Up
Moderator: Adam Adler, Professor, Department of Immunology, UConn Health School of Medicine
Panelists:
Saad Kenderian, PhD, Assistant Professor, Medicine and Oncology, Mayo Clinic College of Medicine
Maksim Mamonkin, PhD, Assistant Professor, Center for Cell and Gene Therapy, Baylor College of Medicine
Basile Siewe, Director, Business Development-JAX Services, The Jackson Laboratory

2:10 Refresh Break - View Our Virtual Exhibit Hall

2:30 Problem Solving Breakout Discussions - Part A
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 4: CAR T Safety
Saad Kenderian, PhD, Assistant Professor, Medicine and Oncology, Mayo Clinic College of Medicine

3:00 Refresh Break - View Our Virtual Exhibit Hall

3:20 Problem Solving Breakout Discussions - Part B

3:50 Refresh Break - View our Virtual Exhibit Hall

PLENARY KEYNOTE SESSION

4:10 Chairperson's Remarks
K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

4:15 KEYNOTE PRESENTATION: From Energy to Machine Learning
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
We've engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing, before abruptly moving to "sequence-only" deep machine learning for protein design – from fluorescent proteins to AAV capsids to antibodies. When combined with libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

4:40 KEYNOTE PRESENTATION: The Case for Intelligent Design in Protein Engineering
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University
Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing a so-called "intelligent design" approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

5:15 Live Q&A: Session Wrap-Up

Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

5:35 Happy Hour - View our Virtual Exhibit Hall

6:10 Close of Day

TUESDAY, SEPTEMBER 1

ADVANCING NK-BASED THERAPIES

9:05 am KEYNOTE PRESENTATION: 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
NK cells can achieve complete remission in patients with refractory AML. Limitations of current NK cell strategies include single donor products, allogeneic persistence, and tumor specificity. To enhance specificity, trispecific killer engagers can be used alone or with adoptive transfer. NK cell multi-dosing will be achieved with off-the-shelf, genetically modified, induced pluripotent stem cells overexpressing CD16 or CAR with an endogenous IL-15 signal to enhance persistence.

9:25 Leveraging NK Cells in IO Combinations for Treatment of Solid Tumors
Alicja J Copik, PhD, Asst Scholar & Core Mgr, Univ of Central Florida

9:45 Accelerate Antibody Drug Discovery with Single B Cell Technology
Tina Kang, Senior Scientist, Discovery, GenScript ProBio
Antibody drug discovery is as arduous and strenuous as finding a needle in a haystack. Single B cell technology (SBCT) is indispensable for accessing a large antibody repertoire of an immune-experienced animal and the ability to interrogate each individual cells, rather than to measure the average of a cell pool. In this talk, we will: 1) introduce the general approaches of SBCT; 2) GenScript offerings with case study; 3) summarize the advantages of SBCT screening.

10:10 am Session Wrap Up
Moderator: Conrad Russell Y. Cruz, PhD, Director, Translational Research Labs; Assistant Professor, Center for Emerging Technologies Immune Cell Therapy, Children's National Health System
Panelists:
Jeffrey Miller, MD, Professor of Medicine, Deputy Director, Masonic Cancer Center, Division of Hematology, Oncology and Transplantation, University of Minnesota
Alicja J Copik, PhD, Asst Scholar & Core Mgr, Univ of Central Florida
Tina Kang, Senior Scientist, Discovery, GenScript ProBio

10:30 Coffee Break - View our Virtual Exhibit Hall

ADVANCES IN NK/GAMMA DELTA CELL-BASED THERAPY

11:10 Cord-Blood-Derived NK Cells
Conrad Russell Y. Cruz, PhD, Director, Translational Research Labs; Assistant Professor, Center for Emerging Technologies Immune Cell Therapy, Children's National Health System
This presentation will discuss the technical considerations when developing cord blood NKs, alongside frequent obstacles, gene modification protocols, and potential applications.

11:30 Accelerated Disc of anti-hPDL1 Antibodies by B Cell Cloning on Beacon® using Trianni Mice®
Shireen Khan, PhD, Senior Director of Biologics, Biologics Discovery, ChemPartner
In this talk, we will discuss combining multiple methods, including immunization strategy, single plasma B cell cloning on the Beacon platform and the use of transgenic animals to significantly reduce the cycle times while rapidly identifying high affinity functional antibodies.

11:55 Session Wrap-Up
Moderator: Lawrence Lamb, Jr., PhD, Executive Vice President & CSO, Incysus Therapeutics, Inc.
Panelists:
Conrad Russell Y. Cruz, PhD, Director, Translational Research Labs; Assistant Professor, Center for Emerging Technologies Immune Cell Therapy, Children's National Health System
Shireen Khan, PhD, Senior Director of Biologics, Biologics Discovery, ChemPartner
Linda Masat, V.P. Business Development, Business Development, Trianni Inc.

12:15 pm Lunch Break - View Our Virtual Exhibit Hall

ADVANCING GAMMA DELTA-BASED THERAPIES

12:50 BTN3A and BTN2A are New Immune-Checkpoint-Targeting Vg9Vd2 T Cell Functions against Cancer Cells
Daniel Olive, MD, PhD, Head, Tumor Immunology, Marseille Cancer Research Center
Vγ9Vδ2 T cell activation leads to broad functional activities against tumors. Tumor-infiltrating γδ T cells are the most significant favorable cancer-wide prognostic signature. Anti-tumoral response of Vγ9Vδ2 T cells requires sensing of phosphoantigens accumulated through binding of butyrophilin 3A(BTN3A) expressed in tumors. We identified butyrophilin 2A (BTN2A) as a requirement for BTN3A-mediated, Vγ9Vδ2 T cell cytotoxicity against cancer cells.

1:10 Development of a Next-Generation Anti-Cancer Immunotherapy: A Humanized anti-BTN3A Antibody that Activates Gamma-Delta (Vg9-Vd2) T Cells
Alem Truneh, PhD, Co-Founder & CTO, ImCheck Therapeutics SAS
ImCheck Therapeutics is developing a first-in-class activating, humanized antibody to butyrophilin 3A for treatment of cancer. ICT01 binds to BTN3A and primes a broad range of tumor cells for killing by gamma-delta T cells. ICT01 has entered early-stage clinical trials in solid tumors and hematological malignancies. Therapeutic antibodies targeting several novel butyrophilins are currently in preclinical development. This could potentially usher in a novel avenue for next-generation cancer immunotherapy.

1:30 De-Risking Antibody Lead Selection: Is Your Antibody as Specific as You Think?
Benjamin Doranz, PhD, MBA, President and CEO, Integral Molecular
The Membrane Proteome Array (MPA) platform de-risks lead selection by testing biotherapeutics for specificity and off-target binding. This platform contains over 6,000 human membrane proteins, each expressed in live cells in their native conformation. In the process of testing hundreds of antibodies, we found up to 20% of antibodies exhibit off-target binding. We used our high-resolution Shotgun Mutagenesis epitope mapping platform to understand these observations and explain how some mAbs can bind completely unrelated proteins.

1:55 LIVE Q&A: Session Wrap-up
Moderator: Alem Truneh, PhD, Co-Founder & CTO, ImCheck Therapeutics SAS
Panelists:
Daniel Olive, MD, PhD, Head, Tumor Immunology, Marseille Cancer Research Center
Benjamin Doranz, PhD, MBA, President and CEO, Integral Molecular

2:15 Refresh Break - View our Virtual Exhibit Hall

NOVEL APPLICATIONS OF CELL-BASED THERAPIES

2:35 Engineering Novel Targeted Cell Therapies for the Treatment of Immune Disorders
Anthony Conway, PhD, Associate Director, Cell Therapy, Sangamo Therapeutics
Sangamo Therapeutics is a clinical-stage genomic medicine company focused on gene therapy, cell therapy, and *in vivo* genome editing and gene regulation. This presentation will highlight preclinical data for several technology platforms and therapeutic programs.

2:55 Engineering Cell Therapy against Alloimmunity
Feiyan Mo, Graduate Student, Baylor College of Medicine
Pathologies produced by activated alloimmune T cells are a major cause of morbidity and mortality in patients following allogeneic bone marrow or solid organ transplant. We have developed engineered T cells that selectively recognize and eliminate pathogenic lymphocytes, and prevent disease progression without producing systemic T cell elimination.

3:15 LIVE Q&A: Session Wrap-up
Moderator: Alem Truneh, PhD, Co-Founder & CTO, ImCheck Therapeutics SAS
Panelists:
Anthony Conway, PhD, Associate Director, Cell Therapy, Sangamo Therapeutics
Maksim Mamonkin, PhD, Assistant Professor, Center for Cell and Gene Therapy, Baylor College of Medicine
Feiyan Mo, Graduate Student, Baylor College of Medicine

3:35 Close of Improving Immunotherapy Efficacy and Safety

WEDNESDAY, SEPTEMBER 2

CAR T INDUSTRY OVERVIEW

9:00 am Industry Overview: Maximizing the Potential of T Cell Therapy Based on Lessons Learned in Clinical Studies and the Real World

Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company

CAR TS IN THE CLINIC

9:05 KEYNOTE PRESENTATION: Development, Clinical Results and Translational Analysis of CAR T Cell Products for Non-Hodgkin's Lymphomas

Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company

Axi-cel, a first in class anti-CD19 CAR T cell product for lymphoma, has been approved to date for treatment of r/r DLBCL patients post third line therapy. In addition to summarizing key development translational findings to date, we will showcase novel data speaking to the efficacy and toxicities of Axi-cel in DLBCL at 3 years follow up, and of a similar product in Mantle cell lymphoma patients post BTKi treatment failure.

TARGETING SOLID TUMORS

9:25 Engineering CARs for Solid Tumors

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

We developed a new second generation CAR comprising a truncated human CD34, a scFV directed to Lewis Y, and endodomains CD28-CD3zeta in T cells that were enriched for 'early' T cells (stem cell and central memory-like). These "early" CAR T had enhanced proliferation, generating diverse progeny with increased cytotoxic function increased cytokine/chemokine secretion, and better *in vivo* therapy responses.

9:45 Cell Avidity – The Best Predictor for Clinical Efficacy of T-Cell Therapy? LUMICKS

Rogier Reijmers, PhD, Principal Scientist, Immuno Oncology Department, LUMICKS

The overall binding strength (avidity) between cells is a crucial parameter for developing new immune cell therapies. An important obstacle is the lack of a fast and accurate technology to assess cellular binding avidity. The z-Movi® is a novel and unique instrument for direct measurement of cell–cell binding avidity using acoustic forces. We demonstrate that binding avidity of CAR and TCR transgenic T cells to tumor cells strongly correlates with *in vitro* functionality.

10:10 LIVE Q&A: Session Wrap-up

Moderator: Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Panelists:
Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company
Paul Neeson, PhD, Associate Professor, Cancer Immunoloy Research, Peter MacCallum Cancer Centre
Rogier Reijmers, PhD, Principal Scientist, Immuno Oncology Department, LUMICKS

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

TARGETING SOLID TUMORS

10:55 KEYNOTE PRESENTATION: Progress in Solid Tumors: CAR T Therapy in Mesothelioma

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

Malignant pleural disease (MPD) from primary malignant pleural mesothelioma (MPM) or secondary metastatic disease (lung and breast cancers) affects more than 150,000 patients a year in the US alone. We developed chimeric antigen receptors (CARs) to target mesothelin (MSLN), a cell-surface antigen that we have shown is highly expressed in MPD, is associated with aggressiveness and poor survival, and has low expression in normal tissues.

11:15 Enhancing CAR T cell therapy by enabling CAR T cell interaction with antigen-presenting cells (APCs)

Clare Y. Slaney, PhD, Senior Research Officer, Peter MacCallum Cancer Centre

We generated novel bispecific proteins to mediate the interaction between APCs and CAR T cells. We termed these bispecifics "Bispecific Engagers of APCs and T cells (BEATs)". CAR T cell proliferation and function was significantly enhanced by BEATs in the presence of APCs *in vitro* and *in vivo*. Importantly, murine syngeneic and human xenograft solid tumor growth was significantly inhibited when CAR T cells were administered in combination with BEATs.

11:35 Genetically-Engineered Immuno-oncology Cell Lines and Services for Early Drug Discovery Research and Preclinical Mfg MilliporeSigma

Stephanie Scherer, Principle R&D Scientist, Advanced Genetic and Cell Technologies / Cell Design Studio, MilliporeSigma

Gene editing experts within MilliporeSigma's Cell Design Studio™ provide custom cell line engineering services to create and deliver unique cell-based assays tailored for drug discovery and preclinical manufacturing. Our cellular models have been used for applications such evaluating efficacy of CAR-T cells, screening candidate checkpoint inhibitors, and generating potency assays for therapeutic testing. In this presentation, we will discuss the technology of these lines, their utility in immuno-oncology and novel therapeutic testing.

12:00 pm LIVE Q&A: Session Wrap-up

Moderator: Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Panelists:
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
Clare Y. Slaney, PhD, Senior Research Officer, Peter MacCallum Cancer Centre
Stephanie Scherer, Principle R&D Scientist, Advanced Genetic and Cell Technologies / Cell Design Studio, MilliporeSigma

12:20 Lunch Break - View our Virtual Exhibit Hall

ENGINEERING ALLOGENEIC CAR T CELLs

12:45 Engineering of Allogeneic CAR T cells

Tom Van Blarcom, PhD, Senior Director, Head of Protein Engineering, Allogene Therapeutics

Allogeneic CAR T cells have shown encouraging preliminary Phase I clinical data demonstrating the potential promise of this therapy for more patients. This talk will highlight the critical areas that need to be addressed to maximize the dissemination of allogeneic CAR T cells and our approach to engineer optimal CARs that specifically targets tumors across a range of hematological malignancies and solid tumors.

1:05 Engineering Gene-Edited Off-the-Shelf CAR T Cells to Reduce Immunogenicity and Improve Activity
Daniel T. MacLeod, PhD, Senior Director, Cell Therapy Discovery, Precision BioSciences
Gene editing can be used to generate off-the-shelf allogeneic CAR T cell products and to impart desirable features to improve their function. For our next generation of therapeutics, we are exploring gene knockout and incorporation of RNAi cassettes to modulate gene expression, with the goal of avoiding rejection, reducing T cell exhaustion, and enhancing function in the suppressive tumor microenvironment.

1:25 New Bioluminescent Tools for the Development of TCR-Redirected Therapies
Julia Gilden, Sr Research Scientist, Integrated Biology, Research & Development, Promega Corporation
This presentation will discuss new bioluminescent tools to expedite the development of T cell-redirecting cancer therapies. First, we will describe two NanoBiT-based assay platforms that can quantitatively measure the potency of CD3 bispecific antibodies or BiTEs to induce T cell-dependent target cell killing and cytokine production. Next, we will describe TCRαβ-null reporter cell lines that can be used to screen transgenic TCRs against specific tumor antigen targets.

1:50 LIVE Q&A: Session Wrap-up
Moderator: Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Panelists:
Daniel T. MacLeod, PhD, Senior Director, Cell Therapy Discovery, Precision BioSciences
Tom Van Blarcom, PhD, Senior Director, Head of Protein Engineering, Allogene Therapeutics
Julia Gilden, Sr Research Scientist, Integrated Biology, Research & Development, Promega Corporation

2:10 Refresh Break - View our Virtual Exhibit Hall

ENGINEERING ALLOGENEIC CAR T CELLs

2:25 Gene Edited Off-the-Shelf Immunotherapies
Laurent Poirot, PhD, Vice President, Immunology, Cellectis
CAR T cells have proven successful in B cell malignancies but the unmet needs are still high in oncology. TALEN-mediated gene editing is highly efficacious, precise and specific. We are leveraging our expertise in gene editing to tailor properties of CAR T cells towards increasing their potency, rendering them resistant to tumor microenvironment while maintaining safety.

2:45 Non-Gene Edited Allogeneic CAR T Cells: Maximizing Safety and Persistence
Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Targeting of CD3ζ by shRNA leads to efficient knockdown of the TCR complex, inhibiting GvHD *in vivo* and, importantly, allowing for increased persistence of T cells. Celyad's "plug & play" shRNA allogeneic platform will be presented. Implementation of a T cell inhibitory peptide in the NKG2D CAR vector (CYAD-101) leads to blunting TCR activity and preventing GvHD. Clinical testing of CYAD-101 showed no significant toxicity and no GvHD.

3:05 LIVE Q&A: Session Wrap-up
Moderator: Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Panelists:
Laurent Poirot, PhD, Vice President, Immunology, Cellectis
Prem Mohanty, Product Marketing Manager, Marketing, Benchling

3:25 Session Break

3:50 Refresh Break - View Our Virtual Exhibit Hall

4:10 Problem Solving Breakout Discussions - Part A
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 18: Mirror, Mirror on the Wall, Who Is the Finest CAR T Phenotype of Them All?
Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem Solving Breakout Discussions - Part B

TABLE 19: Present and Future of Genetically Engineered T Cells in Oncology
Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company

5:30 Close of Day

THURSDAY, SEPTEMBER 3

ADVANCES IN TCRs AND TILs

9:05 am CAR T: Mechanisms and Novel Therapeutic Strategies
Marco Ruella, MD, Assistant Professor of Medicine, Scientific Director, Lymphoma Program, Division of Hematology and Oncology and Center for Cellular Immunotherapies, University of Pennsylvania
This presentation will provide an overview of the mechanisms of resistance to CAR T immunotherapy and strategies to develop rationally designed, next-generation immunotherapies.

9:25 TCR-Engaging Strategies to Eliminate Tumor Cells
Rajkumar Ganesan, PhD, Director, Antibody Engineering, Bispecifics and CAR T, Janssen
Redirecting the cytotoxicity of T cells by CD3-bispecific antibodies has resulted in remarkable clinical activity, albeit often accompanied by immune-related adverse events. IRAE is due to robust activation of T cells via CD3 rapid signaling, leading to severe cytokine storm that limits the dose of the drug, resulting in a narrow therapeutic index. To mitigate, a plethora of TCR-engaging strategies, such as modulating the affinity and epitope, are being explored.

9:45 LIVE Q&A: Session Wrap-Up
Moderator: Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company
Panelists:
Rajkumar Ganesan, PhD, Director, Antibody Engineering, Bispecifics and CAR T, Janssen
Marco Ruella, MD, Assistant Professor of Medicine, Scientific Director, Lymphoma Program, Division of Hematology and Oncology and Center for Cellular Immunotherapies, University of Pennsylvania

10:30 Coffee Break - View our Virtual Exhibit Hall

ADVANCES IN TILs

10:50 Advancements in Tumor-Infiltrating Lymphocytes in Treatment of Solid Tumors
Cecile Chartier, PhD, VP, Research, Iovance Biotherapeutics
TIL therapy uses a patient's own immune cells to attack cancer. Iovance is currently conducting pivotal studies in patients with metastatic melanoma and advanced cervical cancer. In addition, the company's TIL therapies are being investigated for the treatment of patients with locally advanced, recurrent or metastatic cancers including head and neck and non-small cell lung cancer.

11:10 Tumor-Infiltrating Lymphocytes Therapy for Solid Tumors
Chantale Bernatchez, PhD, Assistant Professor, Department of Melanoma Medical Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center
In TIL therapy T cells are grown from solid tumor samples and expanded to large numbers *ex vivo* to be infused back to the patient. The therapy has been very successful in metastatic melanoma with a 42% clinical response rate at our institution and others with most of the responses being durable. We are at this point investigating why the other half of the patients would not respond.

11:30 Session Wrap-Up
Moderator: Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company
Panelists:
Cecile Chartier, PhD, VP, Research, Iovance Biotherapeutics
Chantale Bernatchez, PhD, Assistant Professor, Department of Melanoma Medical Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

11:50 Close of CAR Ts, TCRs and TILs

AGONIST IMMUNOTHERAPY TARGETS

Priming the Immune System with Costimulatory Agents

THURSDAY, SEPTEMBER 3

ADVANCES IN ICOS AGONISTS

12:45 pm KEYNOTE PRESENTATION: ICOS Agonism – The Next Generation of Immune Checkpoint Modulation for Cancer

Axel Hoos, PhD, Senior Vice President, Therapeutic Area Head, Oncology, GSK

GSK3359609 is a non-T cell depleting ICOS costimulatory receptor agonist antibody. In non-clinical systems, it enhances immune-stimulatory and anti-tumor properties as monotherapy and in combination with other anti-cancer agents. INDUCE-1 study has demonstrated the pharmacology and anti-cancer properties of GSK3359609 including clinical activity as monotherapy and in combination with PD1 blockade in r/mHNSCC warranting randomized trials to evaluate overall survival.

1:05 Reverse Translational Approaches in Development of ICOS Agonist Vopratelimab

Elizabeth Tréhu, MD, CMO, Jounce Therapeutics Inc.

Vopratelimab is an investigational ICOS agonist monoclonal antibody that results in activation and proliferation of CD4 T effector cells with high levels of ICOS. In the ICONIC trial, emergence of these cells was associated with improved ORR, PFS, and OS. An RNA signature in baseline tumor samples appears to predict for emergence of ICOS high CD4 T cells and improved clinical outcomes.

1:25 LIVE Q&A: Session Wrap-up

Moderator: Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB
Panelists:
Axel Hoos, PhD, Senior Vice President, Therapeutic Area Head, Oncology, GSK
Elizabeth Tréhu, MD, CMO, Jounce Therapeutics Inc.

1:45 Refresh Break - View our Virtual Exhibit Hall

ADVANCES IN CD137 AGONISTS

2:30 A CD137 Antibody with Differential Agonist Properties that Promotes Antitumor Immunity

Helen Kotanides, PhD, Senior Research Advisor, Oncology Biologics Discovery, Loxo Oncology at Lilly

We developed the CD137 agonist, 7A5, a fully human IgG1 Fc effector null monoclonal antibody, and characterized its biological properties. 7A5 binds CD137, and the binding epitope overlaps with the CD137L binding site. 7A5 engages the CD137 receptor in cell-based function assays and inhibits tumor growth in human tumor xenograft mouse models reconstituted with human immune cells. Collectively, the preclinical data support further development of 7A5 as a cancer immunotherapy.

2:50 A CD137 Bispecific Antibody Targeting the Tumor Microenvironment

Patrick Mayes, PhD, Executive Director, Head, IO Antibody Research, Incyte

We have identified a CD137xPD-L1 bispecific antibody (MCLA-145) which drives transactivation of CD137, specifically in the vicinity of cells expressing PD-L1. MCLA-145 treatment resulted in significant immune cell activation in primary human immune cell assays as well as antitumor immune responses in two separate humanized mouse tumor models. These data support the clinical evaluation of MCLA-145 as a novel, PD-L1 dependent CD137 agonist immune therapy and clinical studies are ongoing (NCT03922204).

3:10 IGM Antibodies with Very Potent Agonism to DR-5 Induced Apoptosis and as Anti-Tumor Agents

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

3:30 LIVE Q&A: Session Wrap-up

Moderator: Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB
Panelists:
Helen Kotanides, PhD, Senior Research Advisor, Oncology Biologics Discovery, Loxo Oncology at Lilly
Patrick Mayes, PhD, Executive Director, Head, IO Antibody Research, Incyte
Bruce Keyt, PhD, CSO, R&D, IGM Biosciences, Inc.

3:50 Close of Day

FRIDAY, SEPTEMBER 4

ADVANCES IN OX-40, 4-1BB, CD40 AGONISTS

9:05 am Overcoming the Resistance to Agonist Immunotherapy

Bin Zhang, PhD, Professor, Department of Medicine, Division of Hematology/Oncology Department of Microbiology-Immunology Director, Cancer Immunotherapy Initiative Co-Director, Immune Assessment Core Facility Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine

The underlying mechanisms of agonist immunotherapy remain incompletely understood. We recently demonstrated an inhibitory role of ecto-enzyme CD73 (generating extracellular adenosine) for agonistic anti-4-1BB/CD137 Ab therapy. In particular, the TGF-β-rich tumor milieu confers resistance to anti-4-1BB therapy by sustaining CD73 expression primarily on infiltrating CD8+ T cells across several tumor models. Thus, our findings identify a novel resistance mechanism targeting of 4-1BB and other costimulatory molecules.

9:25 Elucidating How Nonlinked CD4+ Help Augment OX40 plus 4-1BB Agonist Immunotherapy

Adam Adler, Professor, Department of Immunology, UConn Health School of Medicine

Engaging tumor-unrelated CD4 T cells can boost the efficacy of costimulatory receptor agonist immunotherapy through a previously uncharacterized process termed "nonlinked help". The ability of the unrelated CD4 T cells to provide nonlinked help appears to be conferred via a TCR-independent, "innate-like" response that involves stimulation with a JAK/STAT activating cytokine plus an IL-1 family member.

9:45 Fc-Silenced Bispecific Antibodies Targeting PD-L1 and 4-1BB Combine Checkpoint Blockade and T Cell Co-Stimulation to Promote Anti-Tumor Activity

Alexander Muik, PhD, Head, Immunomodulators, BioNTech SE

DuoBody®-PD-L1x4-1BB [GEN1046] was designed to combine ICB and conditional T cell co-stimulation through dual targeting of PD-L1 and 4-1BB. This distinctive mechanism of action triggers potent anti-tumor immunity without inducing hepatotoxicity in mice. Correspondingly, the clinical candidate, DuoBody®-PD-L1x4-1BB, enhances human primary T cell function and TIL expansion.

10:05 LIVE Q&A: Session Wrap-up

Moderator: Adam Adler, Professor, Department of Immunology, UConn Health School of Medicine
Panelists:
Bin Zhang, PhD, Professor, Department of Medicine, Division of Hematology/Oncology Department of Microbiology-Immunology Director, Cancer Immunotherapy Initiative Co-Director, Immune Assessment Core Facility Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine
Alexander Muik, PhD, Head, Immunomodulators, BioNTech SE

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

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ADVANCES IN OX-40, 4-1BB, CD40 AGONISTS

10:50 Developing Novel Combinations to Enhance the Therapeutic Efficacy of OX40 Agonists

William Redmond, PhD, Associate Member and Director, Immune Monitoring Laboratory, Earle A. Chiles Research Institute, Providence Cancer Institute

Novel combinatorial approaches are needed to improve the efficacy of immunotherapy. We investigated the efficacy of combined therapy with pegzilarginase, a human arginase 1 enzyme engineered to have superior stability and enzymatic activity relative to native human arginase 1, plus anti-PD-L1 or agonist anti-OX40 mAb. Combined pegzilarginase/immunotherapy induced robust anti-tumor immunity characterized by increased intratumoral CD8+ T cells and M1-polarization of tumor-associated macrophages.

11:10 CD40 Enhances Type I Interferon Responses Downstream of CD47 Blockade to Bridge Innate and Adaptive Immunity

Taylor H. Schreiber, PhD, CEO, Shattuck Labs Inc.

CD47/SIRPa blockade enhances macrophage-mediated phagocytosis of tumor cells that are dying, or have been tagged with an ADCP-competent antibody, however this event does not enhance anti-tumor immunity in the absence of antigen presentation to CD8+ T cells. SIRPa-Fc-CD40L (SL-172154) links these two mechanisms via a Type I interferon response, and has shown profound activity in both mouse and non-human primate studies.

11:30 Targeting CD40 to Unleash Dendritic Cells in Immuno-Oncology – Expanding the Tumor Specific T Cell Repertoire

Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB

Tumors that lack tumor infiltrating T cells, cold tumors, do not respond to checkpoint therapies. In many cases, the lack of T cell infiltration is a result of insufficient activation of dendritic cells. Alligator Bioscience develops therapies targeting CD40, including the Phase II ready CD40 agonistic antibody that activates dendritic cells. Activation of dendritic cells can increase the frequency and activation of tumor infiltrating T cells resulting in anti-tumor responses.

11:50 LIVE Q&A: Session Wrap-up

Moderator: Adam Adler, Professor, Department of Immunology, UConn Health School of Medicine
Panelists:
Taylor H. Schreiber, PhD, CEO, Shattuck Labs Inc.
Peter Ellmark, PhD, Vice President, Discovery, Alligator Bioscience AB
William Redmond, PhD, Associate Member and Director, Immune Monitoring Laboratory, Earle A. Chiles Research Institute, Providence Cancer Institute

12:15 pm Lunch Break - View our Virtual Exhibit Hall

1:35 Close of Summit

CELL-BASED IMMUNOTHERAPIES STREAM

New for 2020

The Cell-Based Immunotherapy stream focuses on the latest protein engineering, clinical and analytical strategies driving the development of cell-based immunotherapies such as CAR Ts, TCRs, TILs and NKs, for the treatment of cancer and immune disorders. Topics include improving target identification, optimizing product design, specificity, safety, characterization and analytics.

PEGS BOSTON

CONFERENCE STREAMS

- ENGINEERING
- ONCOLOGY
- IMMUNOTHERAPY
- **CELL-BASED IMMUNOTHERAPIES**
- ANALYTICAL
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- IMMUNOGENICITY & BIOASSAYS
- BIOCONJUGATES
- EMERGING THERAPEUTICS AND TECHNOLOGIES

2020 CELL-BASED IMMUNOTHERAPIES STREAM CONFERENCES

AUGUST 31-SEPTEMBER 1

AGENDA Improving Immunotherapy Efficacy and Safety

SEPTEMBER 2-3

AGENDA CAR Ts, TCRs and TILs

SEPTEMBER 3-4

AGENDA Cell and Gene Therapy Analytics

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IMPROVING IMMUNOTHERAPY EFFICACY AND SAFETY

Engineering the Next Generation of Immunotherapies

Part of IMMUNOTHERAPY STREAM

MONDAY, AUGUST 31

IMPROVING IMMUNOTHERAPY OUTCOMES AND TARGET IDENTIFICATION

9:05 am FEATURED PRESENTATION: Therapeutic Manipulation of the Tumor Microenvironment to Enhance Response to Immunotherapy

Allison Betof Warner, MD, PhD, Assistant Attending Physician, Memorial Sloan Kettering Cancer Center

Tumors are not simply collections of cancer cells; they are complex structures composed of blood vessels, immune cells, and supporting structures that interact, consume oxygen and other nutrients, and produce waste. Changing a tumor's environment can have profound impacts on the efficacy of antitumor therapy. I will discuss the influence of microenvironmental modulators on immunobiology and our group's approach to harness these interactions to improve therapeutic outcomes.

9:25 *In vivo* T Cell CRISPR Screen for Immunotherapy Target Discovery

Sidi Chen, PhD, Assistant Professor, Department of Genetics and Systems Biology Institute, Yale University; Member, Yale Cancer Center and the Yale Stem Cell Center

T cells have become the central focus of new cancer therapeutics. We recently performed *in vivo* CRISPR screens in CD8 cytotoxic T cells in tumor models of immunotherapy, which rediscovered prime immunotherapy targets, such as PD-1, TIM-3, LAG3, and previously undocumented targets. Other novel immunotherapy modalities will also be discussed.

9:45 Predicting NCE/NBE outcome screens with Human derived Tissueoids using AXTEX-4D™ platform

Prabuddha Kundu, PhD, Co-founder and Managing Director, Premas Biotech Pvt Ltd.

Evaluation of a new chemical/biological entities (NCE/NBE) in tumor targeting therapies takes 5-12 years for development while only a few candidates reach clinics. One bottleneck is the absence of a reliable human model with an intact tumor micro-environment & data consistency. AXTEX-4D™ seals this gap and offer a suitable alternative. Drug-Tissueoid interactions, T cell migration, and validation of the tumor characteristics like necrosis, angiogenesis, EMT etc., broaden its scope in the modern discovery landscape.

10:10 Session Wrap-Up

Moderator: Oliver Hill, PhD, Vice President, Drug Discovery, Apogenix AG
Panelists:
Sidi Chen, PhD, Assistant Professor, Department of Genetics and Systems Biology Institute, Yale University; Member, Yale Cancer Center and the Yale Stem Cell Center
Allison Betof Warner, MD, PhD, Assistant Attending Physician, Memorial Sloan Kettering Cancer Center
Prabuddha Kundu, PhD, Co-founder and Managing Director, Premas Biotech Pvt Ltd.

10:30 Coffee Break - View our Virtual Exhibit Hall

IMPROVING IMMUNOTHERAPY TARGET IDENTIFICATION

10:50 Understanding Tumor-Reactive T Cells by Repertoire and Gene Expression Analysis

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

Although T cells can be isolated directly from tumor-infiltrating lymphocyte (TIL) specimens, recent work has questioned whether T cells are tumor-reactive or specific for viral or other antigens. We've looked across tumor indications at patients to identify whether T cell receptor clonality and TIL gene expression analysis can identify tumor-reactive T cells. Using a yeast-display system, antigen specificities of T cell populations can be identified and linked to the tumor.

AGONIST IMMUNOTHERAPY

11:10 IL-15-Based Trifunctional Antibody-Fusion Proteins with Costimulatory TNF-Superfamily Ligands for Cancer Immunotherapy

Dafne Müller, PhD, Group Leader, Institute of Cell Biology and Immunology, University of Stuttgart

In order to support the generation and efficacy of an antitumor response, we have designed trifunctional antibody-fusion proteins for tumor-directed combined delivery of IL-15 and costimulatory members of the TNF-superfamily, demonstrating enhanced immune responsiveness *in vitro* and antitumor activity in a mouse model *in vivo*.

11:30 HERA-GITRL: A Unique Hexavalent GITR Agonist for Cancer Immunotherapy

Oliver Hill, PhD, Vice President, Drug Discovery, Apogenix AG

HERA-GITRL is a member of a novel class of hexavalent TNFR superfamily agonists that share the natural ligand conformation. The biological activities of HERA-GITRL, boosting antigen-specific T cell response and anti-tumor efficacy in mouse models, are crosslinking independent. As the Fc-mediated mixed mode of actions observed for antibodies are avoided, HERA-GITRL is an excellent candidate for further development into a next-generation GITR agonistic immuno-oncology drug.

11:55 Session Wrap-Up

Moderator: Adam Adler, Professor, Department of Immunology, UConn Health School of Medicine
Panelists:
Dafne Müller, PhD, Group Leader, Institute of Cell Biology and Immunology, University of Stuttgart
Oliver Hill, PhD, Vice President, Drug Discovery, Apogenix AG
Marvin Gee, PhD, Co-Founder & Head, Target Discovery, 3T Biosciences

12:15 pm Lunch Break - View our Virtual Exhibit Hall

IMPROVING CAR-T EFFICACY AND SAFETY

12:45 CAR T Cells for T Cell Malignancies

Maksim Mamonkin, PhD, Assistant Professor, Center for Cell and Gene Therapy, Baylor College of Medicine

Development of effective CAR T cells targeting widely pan-T cell antigens for T cell leukemia and lymphoma has been hindered by frequent self-targeting of CAR T cells and possible induction of prolonged T cell aplasia. We developed fratricide-resistant, CD5 CAR T cells that produce high anti-tumor activity in patients with refractory or relapsed T cell malignancies, without eliminating healthy endogenous T cells.

1:05 Cytokine Storm after COVID-19: Lessons Learned from CAR T Cell Therapy

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

Despite the unprecedented activity of CAR T cell therapy, the wider application is limited by the development of life-threatening toxicities of cytokine release syndrome and neurotoxicity. Here we will review new insights into the mechanisms of these toxicities and novel strategies to enhance CAR T cell safety.

1:25 Preclinical Mouse Model to Evaluate Efficacy of Chimeric Antigen Receptor (CAR) T Cell Therapy in Immuno-Oncology

Basile Siewe, Director, Business Development-JAX Services, The Jackson Laboratory

1:50 Session Wrap-Up
Moderator: Adam Adler, Professor, Department of Immunology, UConn Health School of Medicine
Panelists:
Saad Kenderian, PhD, Assistant Professor, Medicine and Oncology, Mayo Clinic College of Medicine
Maksim Mamonkin, PhD, Assistant Professor, Center for Cell and Gene Therapy, Baylor College of Medicine
Basile Siewe, Director, Business Development-JAX Services, The Jackson Laboratory

2:10 Refresh Break - View Our Virtual Exhibit Hall

2:30 Problem Solving Breakout Discussions - Part A
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 4: CAR T Safety
Saad Kenderian, PhD, Assistant Professor, Medicine and Oncology, Mayo Clinic College of Medicine

3:00 Refresh Break - View Our Virtual Exhibit Hall

3:20 Problem Solving Breakout Discussions - Part B

3:50 Refresh Break - View our Virtual Exhibit Hall

PLENARY KEYNOTE SESSION

4:10 Chairperson's Remarks
K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

4:15 KEYNOTE PRESENTATION: From Energy to Machine Learning
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
We've engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing, before abruptly moving to "sequence-only" deep machine learning for protein design – from fluorescent proteins to AAV capsids to antibodies. When combined with libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

4:40 KEYNOTE PRESENTATION: The Case for Intelligent Design in Protein Engineering
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University
Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing a so-called "intelligent design" approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

5:15 Live Q&A: Session Wrap-Up

Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

5:35 Happy Hour - View our Virtual Exhibit Hall

6:10 Close of Day

TUESDAY, SEPTEMBER 1

ADVANCING NK-BASED THERAPIES

9:05 am KEYNOTE PRESENTATION: 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
NK cells can achieve complete remission in patients with refractory AML. Limitations of current NK cell strategies include single donor products, allogeneic persistence, and tumor specificity. To enhance specificity, trispecific killer engagers can be used alone or with adoptive transfer. NK cell multi-dosing will be achieved with off-the-shelf, genetically modified, induced pluripotent stem cells overexpressing CD16 or CAR with an endogenous IL-15 signal to enhance persistence.

9:25 Leveraging NK Cells in IO Combinations for Treatment of Solid Tumors
Alicja J Copik, PhD, Asst Scholar & Core Mgr, Univ of Central Florida

9:45 Accelerate Antibody Drug Discovery with Single B Cell Technology
Tina Kang, Senior Scientist, Discovery, GenScript ProBio
Antibody drug discovery is as arduous and strenuous as finding a needle in a haystack. Single B cell technology (SBCT) is indispensable for accessing a large antibody repertoire of an immune-experienced animal and the ability to interrogate each individual cells, rather than to measure the average of a cell pool. In this talk, we will: 1) introduce the general approaches of SBCT; 2) GenScript offerings with case study; 3) summarize the advantages of SBCT screening.

10:10 am Session Wrap Up
Moderator: Conrad Russell Y. Cruz, PhD, Director, Translational Research Labs; Assistant Professor, Center for Emerging Technologies Immune Cell Therapy, Children's National Health System
Panelists:
Jeffrey Miller, MD, Professor of Medicine, Deputy Director, Masonic Cancer Center, Division of Hematology, Oncology and Transplantation, University of Minnesota
Alicja J Copik, PhD, Asst Scholar & Core Mgr, Univ of Central Florida
Tina Kang, Senior Scientist, Discovery, GenScript ProBio

10:30 Coffee Break - View our Virtual Exhibit Hall

ADVANCES IN NK/GAMMA DELTA CELL-BASED THERAPY

11:10 Cord-Blood-Derived NK Cells
Conrad Russell Y. Cruz, PhD, Director, Translational Research Labs; Assistant Professor, Center for Emerging Technologies Immune Cell Therapy, Children's National Health System
This presentation will discuss the technical considerations when developing cord blood NKs, alongside frequent obstacles, gene modification protocols, and potential applications.

11:30 Accelerated Disc of anti-hPDL1 Antibodies by B Cell Cloning on Beacon® using Trianni Mice®
Shireen Khan, PhD, Senior Director of Biologics, Biologics Discovery, ChemPartner
In this talk, we will discuss combining multiple methods, including immunization strategy, single plasma B cell cloning on the Beacon platform and the use of transgenic animals to significantly reduce the cycle times while rapidly identifying high affinity functional antibodies.

11:55 Session Wrap-Up
Moderator: Lawrence Lamb, Jr., PhD, Executive Vice President & CSO, Incysus Therapeutics, Inc.
Panelists:
Conrad Russell Y. Cruz, PhD, Director, Translational Research Labs; Assistant Professor, Center for Emerging Technologies Immune Cell Therapy, Children's National Health System
Shireen Khan, PhD, Senior Director of Biologics, Biologics Discovery, ChemPartner
Linda Masat, V.P. Business Development, Business Development, Trianni Inc.

12:15 pm Lunch Break - View Our Virtual Exhibit Hall

ADVANCING GAMMA DELTA-BASED THERAPIES

12:50 BTN3A and BTN2A are New Immune-Checkpoint-Targeting Vg9Vd2 T Cell Functions against Cancer Cells
Daniel Olive, MD, PhD, Head, Tumor Immunology, Marseille Cancer Research Center
Vγ9Vδ2 T cell activation leads to broad functional activities against tumors. Tumor-infiltrating γδ T cells are the most significant favorable cancer-wide prognostic signature. Anti-tumoral response of Vγ9Vδ2 T cells requires sensing of phosphoantigens accumulated through binding of butyrophilin 3A(BTN3A) expressed in tumors. We identified butyrophilin 2A (BTN2A) as a requirement for BTN3A-mediated, Vγ9Vδ2 T cell cytotoxicity against cancer cells.

1:10 Development of a Next-Generation Anti-Cancer Immunotherapy: A Humanized anti-BTN3A Antibody that Activates Gamma-Delta (Vg9-Vd2) T Cells
Alem Truneh, PhD, Co-Founder & CTO, ImCheck Therapeutics SAS
ImCheck Therapeutics is developing a first-in-class activating, humanized antibody to butyrophilin 3A for treatment of cancer. ICT01 binds to BTN3A and primes a broad range of tumor cells for killing by gamma-delta T cells. ICT01 has entered early-stage clinical trials in solid tumors and hematological malignancies. Therapeutic antibodies targeting several novel butyrophilins are currently in preclinical development. This could potentially usher in a novel avenue for next-generation cancer immunotherapy.

1:30 De-Risking Antibody Lead Selection: Is Your Antibody as Specific as You Think?
Benjamin Doranz, PhD, MBA, President and CEO, Integral Molecular
The Membrane Proteome Array (MPA) platform de-risks lead selection by testing biotherapeutics for specificity and off-target binding. This platform contains over 6,000 human membrane proteins, each expressed in live cells in their native conformation. In the process of testing hundreds of antibodies, we found up to 20% of antibodies exhibit off-target binding. We used our high-resolution Shotgun Mutagenesis epitope mapping platform to understand these observations and explain how some mAbs can bind completely unrelated proteins.

1:55 LIVE Q&A: Session Wrap-up
Moderator: Alem Truneh, PhD, Co-Founder & CTO, ImCheck Therapeutics SAS
Panelists:
Daniel Olive, MD, PhD, Head, Tumor Immunology, Marseille Cancer Research Center
Benjamin Doranz, PhD, MBA, President and CEO, Integral Molecular

2:15 Refresh Break - View our Virtual Exhibit Hall

NOVEL APPLICATIONS OF CELL-BASED THERAPIES

2:35 Engineering Novel Targeted Cell Therapies for the Treatment of Immune Disorders
Anthony Conway, PhD, Associate Director, Cell Therapy, Sangamo Therapeutics
Sangamo Therapeutics is a clinical-stage genomic medicine company focused on gene therapy, cell therapy, and *in vivo* genome editing and gene regulation. This presentation will highlight preclinical data for several technology platforms and therapeutic programs.

2:55 Engineering Cell Therapy against Alloimmunity
Feiyan Mo, Graduate Student, Baylor College of Medicine
Pathologies produced by activated alloimmune T cells are a major cause of morbidity and mortality in patients following allogeneic bone marrow or solid organ transplant. We have developed engineered T cells that selectively recognize and eliminate pathogenic lymphocytes, and prevent disease progression without producing systemic T cell elimination.

3:15 LIVE Q&A: Session Wrap-up
Moderator: Alem Truneh, PhD, Co-Founder & CTO, ImCheck Therapeutics SAS
Panelists:
Anthony Conway, PhD, Associate Director, Cell Therapy, Sangamo Therapeutics
Maksim Mamonkin, PhD, Assistant Professor, Center for Cell and Gene Therapy, Baylor College of Medicine
Feiyan Mo, Graduate Student, Baylor College of Medicine

3:35 Close of Improving Immunotherapy Efficacy and Safety

September 2-3 | 7th Annual

CAR Ts, TCRs AND TILs

Engineering Clinically Relevant Adoptive T Cell Therapies

Part of IMMUNOTHERAPY STREAM

WEDNESDAY, SEPTEMBER 2

CAR T INDUSTRY OVERVIEW

9:00 am Industry Overview: Maximizing the Potential of T Cell Therapy Based on Lessons Learned in Clinical Studies and the Real World

Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company

CAR TS IN THE CLINIC

9:05 KEYNOTE PRESENTATION: Development, Clinical Results and Translational Analysis of CAR T Cell Products for Non-Hodgkin's Lymphomas

Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company

Axi-cel, a first in class anti-CD19 CAR T cell product for lymphoma, has been approved to date for treatment of r/r DLBCL patients post third line therapy. In addition to summarizing key development translational findings to date, we will showcase novel data speaking to the efficacy and toxicities of Axi-cel in DLBCL at 3 years follow up, and of a similar product in Mantle cell lymphoma patients post BTKi treatment failure.

TARGETING SOLID TUMORS

9:25 Engineering CARs for Solid Tumors

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

We developed a new second generation CAR comprising a truncated human CD34, a scFV directed to Lewis Y, and endodomains CD28-CD3zeta in T cells that were enriched for 'early' T cells (stem cell and central memory-like). These "early" CAR T had enhanced proliferation, generating diverse progeny with increased cytotoxic function increased cytokine/chemokine secretion, and better *in vivo* therapy responses.

9:45 Cell Avidity – The Best Predictor for Clinical Efficacy of T-Cell Therapy?

Rogier Reijmers, PhD, Principal Scientist, Immuno Oncology Department, LUMICKS

The overall binding strength (avidity) between cells is a crucial parameter for developing new immune cell therapies. An important obstacle is the lack of a fast and accurate technology to assess cellular binding avidity. The z-Movi® is a novel and unique instrument for direct measurement of cell–cell binding avidity using acoustic forces. We demonstrate that binding avidity of CAR and TCR transgenic T cells to tumor cells strongly correlates with *in vitro* functionality.

10:10 LIVE Q&A: Session Wrap-up

Moderator: Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Panelists:
Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company
Paul Neeson, PhD, Associate Professor, Cancer Immunoloy Research, Peter MacCallum Cancer Centre
Rogier Reijmers, PhD, Principal Scientist, Immuno Oncology Department, LUMICKS

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

TARGETING SOLID TUMORS

10:55 KEYNOTE PRESENTATION: Progress in Solid Tumors: CAR T Therapy in Mesothelioma

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

Malignant pleural disease (MPD) from primary malignant pleural mesothelioma (MPM) or secondary metastatic disease (lung and breast cancers) affects more than 150,000 patients a year in the US alone. We developed chimeric antigen receptors (CARs) to target mesothelin (MSLN), a cell-surface antigen that we have shown is highly expressed in MPD, is associated with aggressiveness and poor survival, and has low expression in normal tissues.

11:15 Enhancing CAR T cell therapy by enabling CAR T cell interaction with antigen-presenting cells (APCs)

Clare Y. Slaney, PhD, Senior Research Officer, Peter MacCallum Cancer Centre

We generated novel bispecific proteins to mediate the interaction between APCs and CAR T cells. We termed these bispecifics "Bispecific Engagers of APCs and T cells (BEATs)". CAR T cell proliferation and function was significantly enhanced by BEATs in the presence of APCs *in vitro* and *in vivo*. Importantly, murine syngeneic and human xenograft solid tumor growth was significantly inhibited when CAR T cells were administered in combination with BEATs.

11:35 Genetically-Engineered Immuno-oncology Cell Lines and Services for Early Drug Discovery Research and Preclinical Mfg

Stephanie Scherer, Principle R&D Scientist, Advanced Genetic and Cell Technologies / Cell Design Studio, MilliporeSigma

Gene editing experts within MilliporeSigma's Cell Design Studio™ provide custom cell line engineering services to create and deliver unique cell-based assays tailored for drug discovery and preclinical manufacturing. Our cellular models have been used for applications such evaluating efficacy of CAR-T cells, screening candidate checkpoint inhibitors, and generating potency assays for therapeutic testing. In this presentation, we will discuss the technology of these lines, their utility in immuno-oncology and novel therapeutic testing.

12:00 pm LIVE Q&A: Session Wrap-up

Moderator: Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Panelists:
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
Clare Y. Slaney, PhD, Senior Research Officer, Peter MacCallum Cancer Centre
Stephanie Scherer, Principle R&D Scientist, Advanced Genetic and Cell Technologies / Cell Design Studio, MilliporeSigma

12:20 Lunch Break - View our Virtual Exhibit Hall

ENGINEERING ALLOGENEIC CAR T CELLs

12:45 Engineering of Allogeneic CAR T cells

Tom Van Blarcom, PhD, Senior Director, Head of Protein Engineering, Allogene Therapeutics

Allogeneic CAR T cells have shown encouraging preliminary Phase I clinical data demonstrating the potential promise of this therapy for more patients. This talk will highlight the critical areas that need to be addressed to maximize the dissemination of allogeneic CAR T cells and our approach to engineer optimal CARs that specifically targets tumors across a range of hematological malignancies and solid tumors.

1:05 Engineering Gene-Edited Off-the-Shelf CAR T Cells to Reduce Immunogenicity and Improve Activity
Daniel T. MacLeod, PhD, Senior Director, Cell Therapy Discovery, Precision BioSciences
Gene editing can be used to generate off-the-shelf allogeneic CAR T cell products and to impart desirable features to improve their function. For our next generation of therapeutics, we are exploring gene knockout and incorporation of RNAi cassettes to modulate gene expression, with the goal of avoiding rejection, reducing T cell exhaustion, and enhancing function in the suppressive tumor microenvironment.

1:25 New Bioluminescent Tools for the Development of TCR-Redirected Therapies
Julia Gilden, Sr Research Scientist, Integrated Biology, Research & Development, Promega Corporation
This presentation will discuss new bioluminescent tools to expedite the development of T cell-redirecting cancer therapies. First, we will describe two NanoBiT-based assay platforms that can quantitatively measure the potency of CD3 bispecific antibodies or BiTEs to induce T cell-dependent target cell killing and cytokine production. Next, we will describe TCRαβ-null reporter cell lines that can be used to screen transgenic TCRs against specific tumor antigen targets.

1:50 LIVE Q&A: Session Wrap-up
Moderator: Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Panelists:
Daniel T. MacLeod, PhD, Senior Director, Cell Therapy Discovery, Precision BioSciences
Tom Van Blarcom, PhD, Senior Director, Head of Protein Engineering, Allogene Therapeutics
Julia Gilden, Sr Research Scientist, Integrated Biology, Research & Development, Promega Corporation

2:10 Refresh Break - View our Virtual Exhibit Hall

ENGINEERING ALLOGENEIC CAR T CELLs

2:25 Gene Edited Off-the-Shelf Immunotherapies
Laurent Poirot, PhD, Vice President, Immunology, Cellectis
CAR T cells have proven successful in B cell malignancies but the unmet needs are still high in oncology. TALEN-mediated gene editing is highly efficacious, precise and specific. We are leveraging our expertise in gene editing to tailor properties of CAR T cells towards increasing their potency, rendering them resistant to tumor microenvironment while maintaining safety.

2:45 Non-Gene Edited Allogeneic CAR T Cells: Maximizing Safety and Persistence
Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Targeting of CD3ζ by shRNA leads to efficient knockdown of the TCR complex, inhibiting GvHD *in vivo* and, importantly, allowing for increased persistence of T cells. Celyad's "plug & play" shRNA allogeneic platform will be presented. Implementation of a T cell inhibitory peptide in the NKG2D CAR vector (CYAD-101) leads to blunting TCR activity and preventing GvHD. Clinical testing of CYAD-101 showed no significant toxicity and no GvHD.

3:05 LIVE Q&A: Session Wrap-up
Moderator: Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad
Panelists:
Laurent Poirot, PhD, Vice President, Immunology, Cellectis
Prem Mohanty, Product Marketing Manager, Marketing, Benchling

3:25 Session Break

3:50 Refresh Break - View Our Virtual Exhibit Hall

4:10 Problem Solving Breakout Discussions - Part A
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 18: Mirror, Mirror on the Wall, Who Is the Finest CAR T Phenotype of Them All?
Peggy Sotiropoulou, PhD, Head, Research & Development, Celyad

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem Solving Breakout Discussions - Part B

TABLE 19: Present and Future of Genetically Engineered T Cells in Oncology
Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company

5:30 Close of Day

THURSDAY, SEPTEMBER 3

ADVANCES IN TCRs AND TILs

9:05 am CAR T: Mechanisms and Novel Therapeutic Strategies
Marco Ruella, MD, Assistant Professor of Medicine, Scientific Director, Lymphoma Program, Division of Hematology and Oncology and Center for Cellular Immunotherapies, University of Pennsylvania
This presentation will provide an overview of the mechanisms of resistance to CAR T immunotherapy and strategies to develop rationally designed, next-generation immunotherapies.

9:25 TCR-Engaging Strategies to Eliminate Tumor Cells
Rajkumar Ganesan, PhD, Director, Antibody Engineering, Bispecifics and CAR T, Janssen
Redirecting the cytotoxicity of T cells by CD3-bispecific antibodies has resulted in remarkable clinical activity, albeit often accompanied by immune-related adverse events. IRAE is due to robust activation of T cells via CD3 rapid signaling, leading to severe cytokine storm that limits the dose of the drug, resulting in a narrow therapeutic index. To mitigate, a plethora of TCR-engaging strategies, such as modulating the affinity and epitope, are being explored.

9:45 LIVE Q&A: Session Wrap-Up
Moderator: Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company
Panelists:
Rajkumar Ganesan, PhD, Director, Antibody Engineering, Bispecifics and CAR T, Janssen
Marco Ruella, MD, Assistant Professor of Medicine, Scientific Director, Lymphoma Program, Division of Hematology and Oncology and Center for Cellular Immunotherapies, University of Pennsylvania

10:30 Coffee Break - View our Virtual Exhibit Hall

ADVANCES IN TILs

10:50 Advancements in Tumor-Infiltrating Lymphocytes in Treatment of Solid Tumors
Cecile Chartier, PhD, VP, Research, Iovance Biotherapeutics
TIL therapy uses a patient's own immune cells to attack cancer. Iovance is currently conducting pivotal studies in patients with metastatic melanoma and advanced cervical cancer. In addition, the company's TIL therapies are being investigated for the treatment of patients with locally advanced, recurrent or metastatic cancers including head and neck and non-small cell lung cancer.

11:10 Tumor-Infiltrating Lymphocytes Therapy for Solid Tumors
Chantale Bernatchez, PhD, Assistant Professor, Department of Melanoma Medical Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center
In TIL therapy T cells are grown from solid tumor samples and expanded to large numbers *ex vivo* to be infused back to the patient. The therapy has been very successful in metastatic melanoma with a 42% clinical response rate at our institution and others with most of the responses being durable. We are at this point investigating why the other half of the patients would not respond.

11:30 Session Wrap-Up
Moderator: Adrian Bot, PhD, Vice President, Translational Medicine, Kite Pharma, a Gilead Company
Panelists:
Cecile Chartier, PhD, VP, Research, Iovance Biotherapeutics
Chantale Bernatchez, PhD, Assistant Professor, Department of Melanoma Medical Oncology - Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

11:50 Close of CAR Ts, TCRs and TILs

September 3-4 | Inaugural

CELL AND GENE THERAPY ANALYTICS

A Best Practices Exchange for Essential Assays and Product and Process Quality Strategies

Part of ANALYTICAL STREAM

THURSDAY, SEPTEMBER 3

CHARACTERIZATION ASSAYS

12:45 pm Characterization of Gene Therapies by Charge Detection Mass Spectrometry

Martin Jarrold, PhD, Professor, Chemistry, Indiana University

Conventional mass spectrometry is usually limited to masses less than a Megadalton because of heterogeneity. Charge detection mass spectrometry (CDMS) can overcome this limitation and extend accurate mass measurements into the Gigadalton regime. Recent technical advances have dramatically improved the sensitivity of CDMS. Applications of CDMS to the analysis of complex biopharmaceuticals, including gene therapy products and vaccines, will be presented.

1:05 Assay Development for Emerging Single-Cell Platforms

Eric S. Alonzo, PhD, Senior Scientist, Cell Analytics, bluebird bio

Clinical-grade CAR T cell drug products contain a heterogenous mixture of phenotypically and functionally distinct cells. Such heterogeneity necessitates innovative and comprehensive strategies to characterize CAR T cell therapy investigational drug products. Here, we present how high-dimensional single-cell analytics in CAR T manufacturing and beyond can be used to resolve drug product complexity and identify potentially key clinical correlates.

1:25 A Platform Approach for Analytical Methods to Support Adeno-Associated Virus (AAV) Gene Therapy Products

charles river

Michael Hantman, Associate Director, Methods Development, Biologics, Charles River

Recombinant adeno-associated virus (rAAV) vectors have been widely used for *in vivo* gene therapy with commercial products approved by FDA. Charles River Laboratories (CRL) PA Biologics has established a platform approach for rAAV vector genome titer quantification, residual host cell DNA quantification and sizing evaluation, and replication competent virus (rcAAV) detection, by adopting real-time PCR as well as ddPCR technologies and using reference materials available from ATCC or biological materials created at CRL.

1:50 LIVE Q&A: Session Wrap-Up

Moderator: Eric S. Alonzo, PhD, Senior Scientist, Cell Analytics, bluebird bio
Panelists:
Martin Jarrold, PhD, Professor, Chemistry, Indiana University
Michael Hantman, Associate Director, Methods Development, Biologics, Charles River

2:10 Refresh Break - View our Virtual Exhibit Hall

STANDARDS AND REGULATORY CONSIDERATIONS

2:25 Chairperson's Remarks

Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP

2:30 Principles and Practices for Bioassay Standards

Tim Schofield, Owner & Consultant, CMC Sciences LLC

Standards are essential to the development and control of biological products. Considering their importance, there is no consensus on the source of a standard, the basis and means of standard qualification, and stability evaluation. This talk will discuss principles and practices related to standards used to report potency of biological products and propose strategies. Those proposals will borrow from practices related to quality by design, highlighting fitness-for-use of a standard.

2:50 Current Efforts in Bioassay Standardization

Dawn Henke, PhD, Senior Technical Program Manager, Standards Coordinating Body

This discussion will cover standards for regenerative medicine products. Discussion will focus on standards for bioassays, published standards and how to implement these standards be addressed. An overview of current standards under development and how to get involved, as well as a forum for questions will be provided.

3:10 Panel Discussion : Standards and Regulatory Considerations

Moderator: Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP

- Setting standards for new bioassay modalities including cell & gene therapies and immunotherapies
- Developing standards and using already-established standards
- Getting involved with standard-setting organizations
- Qualification of standards
- Correction of relative potency when changing standards

Panelists:
Dawn Henke, PhD, Senior Technical Program Manager, Standards Coordinating Body
Tim Schofield, Owner & Consultant, CMC Sciences LLC

3:50 Close of Day

FRIDAY, SEPTEMBER 4

INCREASING ANALYTICAL DEPTH AND THROUGHPUT

9:05 am Overcoming the Barriers of Biophysics in Gene Therapy

Lake Paul, President, BioAnalysis LLC

Currently the gene therapy space is under utilizing the power of biophysics, specifically Analytical Ultracentrifugation (AUC). Besides the quantitation of empty capsids, AUC can also be used to evaluate the physicochemical properties, higher-order structures, and other pertinent properties. The EMA and FDA are seeing QC release specifications based on AUC, therefore it is paramount that AUC methods are fully realized and meticulously developed.

9:25 Understanding Structure-Function Relationship on AAV Capsid Proteins in Gene Therapy Products

Lin Liu, PhD, CMC Dossier Development & Coordination, Sanofi

Viral capsid proteins play an important role in cellular targeting and trafficking as part of the viral infection cycle, and thus changes in the viral capsid protein sequence or post-translational modifications (PTMs) might impact viral targeting and infectivity. We evaluated the role of AAV capsid protein PTMs on AAV transduction potential by generating AAV2 and AAV5 capsid mutants and performing a stress study.

9:45 See your capsids leak and pop: AAV genome ejection and capsid stability on Uncle

UNCHAINED LABS

Kevin Lance, PhD, Marketing Manager, Marketing, Unchained Labs

When thermally stressed AAV genomes leak out from their capsids, and do it before proteins melt. However, methods that look only at protein unfolding don't track DNA, so you're not getting the whole story. This talk will show Uncle's insight on AAV stability by monitoring DNA ejection from capsids, and how to look at quantifying encapsulated DNA and particle titer.

10:10 LIVE Q&A: Session Wrap-Up

Moderator: Lake Paul, President, BioAnalysis LLC
Panelists:
Lin Liu, PhD, CMC Dossier Development & Coordination, Sanofi
Kevin Lance, PhD, Marketing Manager, Marketing, Unchained Labs

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

ANALYTICAL CHALLENGES

10:50 Evaluating a Control Strategy for an Autologous Cell Therapy for Risk to Patients

Ken Riker, Director Product Quality, Product Quality, Celgene Corp.

An integrated control strategy was developed for a late-phase CAR-T cell therapy product based on our current understanding of the product quality attributes, the manufacturing process, and analytical capability. Based on this comprehensive assessment, the overall risk of drug product to patient safety and product efficacy was determined to be low, demonstrating that the combined operational and testing controls are suitable to ensure product quality from the proposed commercial process.

11:10 Machine Learning for the Rapid Classification of Flow Imaging to Characterize Cell Therapies

Amber H. Fradkin, PhD, Director, Particle Characterization Core Facility, KBI Biopharma

We used a very common analytical method to characterize subvisible particles in biologics (Micro-Flow Imaging) and applied the technique to cell therapy products. We have developed customized machine learning algorithms specific to cell therapy MFI data for rapid classification of images to establish particle profiles. The method has overwhelming potential to monitor cell particle size distributions, cell debris, cell agglomerates, as well as extrinsic material from batch to batch.

11:30 Development and Qualification of a Cell Counting Assay for Dose Determination

Michele Perry, Lead Microbiology Associate, Analytical Development, Synlogic, Inc.

Live bacterial products (LBP) are novel therapeutics with the potential to treat unmet needs in rare genetic diseases, such as phenylketonuria. Viability is a critical aspect of LBPs and traditionally determined through colony-forming unit methods. Another approach to determining viability is automated cell counting. When the methods were compared, the cell counting results were more indicative of *in vivo* activity of the LBPs and is now used to determine dose.

11:50 LIVE Q&A: Session Wrap-Up

Moderator: Ken Riker, Director Product Quality, Product Quality, Celgene Corp.
Panelists:
Amber H. Fradkin, PhD, Director, Particle Characterization Core Facility, KBI Biopharma
Michele Perry, Lead Microbiology Associate, Analytical Development, Synlogic, Inc.

12:10 pm Close of Summit

ANALYTICAL STREAM

Best Practices and Solutions for Analytical Characterization of Novel Biologics, New Biophysical Methods and Cell/Gene Therapy Analytics

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 2020, this three-meeting stream offers comprehensive individual programs focused on novel therapeutic modalities, biophysical methods and the rapidly expanding challenges of cell and gene therapy analytics. The more than forty conference speakers in this stream will be augmented by focused short courses and hosted roundtable discussions on themes related to this field.

PEGSBOSTON

CONFERENCE STREAMS

- ENGINEERING
- ONCOLOGY
- IMMUNOTHERAPY
- CELL-BASED IMMUNOTHERAPIES
- ■ ANALYTICAL
- EXPRESSION
- IMMUNOGENICITY & BIOASSAYS
- BIOCONJUGATES
- EMERGING THERAPEUTICS AND TECHNOLOGIES

2020 ANALYTICAL STREAM CONFERENCES

AUGUST 31-SEPTEMBER 1

AGENDA Characterization for Novel Biotherapeutics

SEPTEMBER 2-3

AGENDA Biophysical Methods

SEPTEMBER 3-4

AGENDA Cell and Gene Therapy Analytics

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CHARACTERIZATION FOR NOVEL BIOTHERAPEUTICS

Exploring the Analytical Challenges of Emerging Modalities

MONDAY, AUGUST 31

TRANSITIONING FROM THERAPEUTIC PROTEINS TO CELL AND GENE THERAPIES

9:05 am Key Assays and Methods for Generation, In-Process Testing and Characterization, towards CMC of AAV Vectors

Stefan Seeber, PhD, Sr Principal Scientist, Cell Line & Molecule Dev, Roche Innovation Ctr Penzberg

As AAV-based gene therapy is coming of age with clinical success and increasing numbers of market entries, the industry has set out to develop AAV vector production protocols according to CMC standards. We are leveraging our expertise in CMC for therapeutic proteins to adopt existing and integrate new protocols for AAV vector generation, purification, and quality control. A case study will be presented to illustrate the differences between therapeutic modalities.

9:25 KEYNOTE PRESENTATION: Expanding Analytical Capabilities from Protein Biologics to Gene Therapy Products

Julia Ding, PhD, Director, Global Process Analytical Development Network Lead, Bristol Myers Squibb Co.

With the advance of modern analytical technologies, protein biologics are well characterized at the molecular level. Product critical quality attributes are assessed through a structure-functional relationship and controlled throughout process and product development. Analytical paradigm of gene therapy products has brought significant challenges in analytical standardization and control strategy. Case studies in adapting and advancing analytical capability in support of viral vector development will be presented.

9:45 Protein or Not? Advanced High-Throughput Aggregate Analysis with the Aura

halo labs

Rick Gordon, PhD, VP of Sales, Halo Labs

Distinguishing aggregated API from other particle types is important for understanding the root cause of instability. Existing methods are unreliable, too cumbersome and difficult to use in many workflows. With Aura, you can now finally count, size, and characterize aggregates and identify them as proteins, non-proteins, or other molecules.

10:10 The Experience of a Protein Biochemist Transitioning to Gene Therapy

George Bou-Assaf, PhD, Scientist, Analytical Development – Product & Technology Development, Biogen

Gene therapy products comprise a protein capsid and a nucleic acid packaged inside. We describe how analytical tools traditionally employed by biochemists for protein therapeutics are applied as is, or are adapted to GT products. We highlight similarities between gene therapy and protein-based products and discuss specific examples related to their critical quality attributes. We describe challenges unique to gene therapy products and how they were overcome with new methods.

10:30 LIVE Q&A: Session Wrap-Up

Moderator: George Bou-Assaf, PhD, Scientist, Analytical Development – Product & Technology Development, Biogen
Panelists:
Julia Ding, PhD, Director, Global Process Analytical Development Network Lead, Bristol Myers Squibb Co.
Stefan Seeber, PhD, Sr Principal Scientist, Cell Line & Molecule Dev, Roche Innovation Ctr Penzberg
Rick Gordon, PhD, VP of Sales, Halo Labs

BISPECIFIC AND MULTISPECIFIC ANTIBODIES

10:50 Analysis of Peptide-Exchanged MHCI Complexes by Native Mass Spectrometry

Wendy Sandoval, Principal Scientist, Genentech, Inc.

Immune monitoring provides insight into a patient's immune response over the course of treatment. The challenge lies in making peptide MHCI complexes, since HLA are highly polymorphic. To successfully produce libraries, highly sensitive assays are necessary to validate peptide exchanges. Here, we describe a robust SEC-MS method and also a sensitive and high-throughput assay using capillary zone electrophoresis coupled to a high-resolution mass spectrometer for characterizing peptide-exchanged MHCIs under native conditions.

11:10 Bispecific Molecules and Characterization for Pharmacokinetics Studies

Mei Han, Principal Scientist, Pharmacokinetics & Drug Metabolism, Amgen Inc.

The sophistication required for proper molecular design causes the manufacturing and development of bispecific antibodies to be complex. Monitoring structural stability is critical for retention of the favorable drug distribution and pharmacokinetic of the antibody format. Classic ligand binding assays have limited resolution to capture some structural modifications in bispecifics. Here we will discuss characterization of bispecific molecules from pre-dose and post-dose pharmacokinetic samples.

11:30 LIVE Q&A: Session Wrap-Up

Moderator: Wendy Sandoval, Principal Scientist, Genentech, Inc.
Panelists:
Mei Han, Principal Scientist, Pharmacokinetics & Drug Metabolism, Amgen Inc.

11:50 Session Break

12:15 pm Lunch Break - View our Virtual Exhibit Hall

12:45 Session Break

DRUG COMBINATIONS

1:05 Use of 2D Liquid Chromatography to Characterize Aggregates in Co-Formulated Drug Products

Xiaoqing Hua, PhD, Senior Scientist, Bioprocess, Merck Research Labs

Co-formulated monoclonal antibodies pose challenges for characterization due to their complexity. Aggregation is a common degradation pathway for mAbs and is often monitored under native state with size exclusion chromatography (SEC); for co-formulation, new challenges appear due to similar size and shape of individual mAbs. A 2D-LC approach with orthogonal methods to SEC was adopted to improve knowledge of single mAb profile in co-formulation and characterize aggregation in co-formulated DPs.

1:25 Physicochemical Characterization of Antibody Drug Conjugates

Waters
THE SCIENCE OF WHAT'S POSSIBLE.

Shawn C. Owen, PhD, Assistant Professor, Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah, College of Pharmacy

Antibodies are the most rapidly growing form of therapeutic. High-throughput methods of characterization are essential as companies and researchers develop new candidates. Dr. Owen discusses advanced characterization techniques to assess antibody-drug conjugates. For ADCs, the level of payload and site of conjugation are determined using LC/MS. Thermal stability and binding affinity are characterized using DSC, IR, and ITC. These methods can be used for the in-depth analysis of these biologics and for routine product validation.

1:50 LIVE Q&A: Session Wrap-Up

Moderator: Xiaoqing Hua, PhD, Senior Scientist, Bioprocess, Merck Research Labs
Panelists:
Shawn C. Owen, PhD, Assistant Professor, Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah, College of Pharmacy

2:10 Refresh Break - View Our Virtual Exhibit Hall

2:30 Problem-Solving Breakout Discussions Part A - View our Virtual Exhibit Hall

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 5: Co-Formulation of Therapeutic Proteins
Dennis Krieg, Graduate Student, Pharmacy, Ludwig Maximilians University

3:00 Refresh Break - View Our Virtual Exhibit Hall

3:20 Problem-Solving Breakout Discussions Part B - View our Virtual Exhibit Hall

TABLE 6: Challenges Associated with Analytical Method Development for the Characterization of AAV-Based Therapeutics
George Bou-Assaf, PhD, Scientist, Analytical Development – Product & Technology Development, Biogen

3:50 Refresh Break - View our Virtual Exhibit Hall

PLENARY KEYNOTE SESSION

4:10 Chairperson's Remarks
K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

4:15 KEYNOTE PRESENTATION: From Energy to Machine Learning
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School

We've engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing, before abruptly moving to "sequence-only" deep machine learning for protein design – from fluorescent proteins to AAV capsids to antibodies. When combined with libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

4:40 KEYNOTE PRESENTATION: The Case for Intelligent Design in Protein Engineering
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing a so-called "intelligent design" approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

5:15 Live Q&A: Session Wrap-Up

Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

5:35 Happy Hour - View our Virtual Exhibit Hall

6:10 Close of Day

TUESDAY, SEPTEMBER 1

EMERGING MODALITIES

9:05 am siRNA-mAb Conjugate Analysis: To Ioinise in Positive or Negative ESI Mode, That Is the Question
Iain Campuzano, Principal Scientist, Discovery Attribute Sciences, Amgen

Antibody-drug conjugates are important classes of molecules currently being used to treat multiple diseases. Advances in small-interfering RNA (siRNA) technology result in numerous RNAi-based therapies being pursued in clinical trials. Herein we present how native nESI-MS, in both positive and negative polarities, is the only bona fide analytical method for accurate intact MW and RAR (RNA-to-antibody ratio) calculation for siRNA-mAb conjugates.

9:25 Characterization of Conditionally Activating Biologics
Wendy Ritacco, Principal Research Scientist I, Global Biologics, AbbVie Bioresearch Center

Bispecific conditional dual variable domain immunoglobulins (cDVD-Igs) are targeted and locally activated biologics that offer new prospects for engineering efficacy, while minimizing systemic side effects. We will describe preclinical examples of tissue targeting and activation in *in vivo* disease models as part of a new generation of locally acting "regio-specific" biologics therapies.

9:45 Overcoming Challenges in Co-Formulation of Therapeutic Proteins with Contradicting Stability Profiles
Dennis Krieg, Graduate Student, Pharmacy, Ludwig Maximilians University

In this talk, we present our work on co-formulation of the model proteins, EPO and G-CSF, which are interesting from both clinical and physicochemical perspectives. These cytokines differ a lot in their structure and respective stability profile, so obtaining a stable co-formulation of both proteins in one solution is challenging. We present a systematic approach to study and stabilize these two physicochemical, very different therapeutic proteins in one formulation.

10:10 LIVE Q&A: Session Wrap-Up
Moderator: Iain Campuzano, Principal Scientist, Discovery Attribute Sciences, Amgen
Panelists:
Dennis Krieg, Graduate Student, Pharmacy, Ludwig Maximilians University
Wendy Ritacco, Principal Research Scientist I, Global Biologics, AbbVie Bioresearch Center

10:30 Coffee Break - View our Virtual Exhibit Hall

DEVELOPABILITY ANALYSIS

11:10 Developability As A Tool For Risk Mitigation In Early Drug Discovery
Christina G. Palmer, Scientist I, Antibody Discovery, Biogen

We will present several case studies following the developability assessment of our preclinical to commercial pipeline. These case studies will illustrate how the evolving field of developability can help inform antibody selection and progression through development. We will highlight several examples of red flags and red herrings in developability and shed light on some of the underlying mechanisms and how they relate to antibody development.

11:30 CO-PRESENTATION: In-Depth Peptide Mapping Profiling of Multispecific Antibodies Using Genedata Expressionist

Genedata solutions in silico

Arnd Brandenburg, PhD, Head, Professional Services, Genedata Expressionist, Genedata
Soraya Hoelper, PhD, Lab Head, Mass Spectrometry, Protein Therapeutics, Research & Development, Biologics, Germany, Sanofi-Aventis Deutschdland GmbH

At Sanofi, we use peptide mapping to perform deep characterization of innovative multispecific biotherapeutics. We developed a custom data processing workflow that enables us to extract the maximum amount of molecular information from our biotherapeutic candidate molecules and created a knowledge base that allows us to leverage the insights gained throughout a molecule's lifecycle for future analyses and development.

11:55 LIVE Q&A: Session Wrap-Up
Moderator: Christina G. Palmer, Scientist I, Antibody Discovery, Biogen
Panelists:
Arnd Brandenburg, PhD, Head, Professional Services, Genedata Expressionist, Genedata
Soraya Hoelper, PhD, Lab Head, Mass Spectrometry, Protein Therapeutics, Research & Development, Biologics, Germany, Sanofi-Aventis Deutschdland GmbH

12:15 pm Lunch Break - View Our Virtual Exhibit Hall

2:45 Close of Characterization for Novel Biotherapeutics

BIOPHYSICAL METHODS

Characterizing and Optimizing the Physical Properties of Proteins in the Research and Development of Next-Generation Biologics

WEDNESDAY, SEPTEMBER 2

AUTOMATION, MODELING AND HIGH-THROUGHPUT ANALYSIS

9:05 am Discovery Developability Workflow to Utilize Machine Learning Algorithms for Biologics Optimization

Marc Bailly, PhD, Principal Scientist, Merck Research Labs

The current race to develop better drugs faster has led biopharmaceutical companies into optimizing all drug discovery and development processes. As part of this effort, machine learning algorithms are being developed to identify correlations between amino acid sequences and physicochemical properties observed during drug development. Here, we describe our ongoing efforts aiming at benchmarking such machine learning algorithms to facilitate our drug discovery process.

9:25 KEYNOTE PRESENTATION: Machine Learning Applications for Analysis of Process-Induced Protein Aggregates

Theodore Randolph, PhD, Professor, Chemical and Biological Engineering, University of Colorado

Protein aggregates can be produced in almost any processing step and should be carefully monitored and controlled. Recent advances in flow imaging microscopy provide rich data sets of images of particles produced within protein formulations. Machine learning techniques can be exploited to analyze large collections of flow microscope images of aggregates in order to detect process upsets and perform root-cause analyses of process-induced aggregate populations.

9:45 Stunner is ready for anything: UV/Vis quantification and DLS for upstream and downstream needs

Kevin Lance, PhD, Marketing Manager, Marketing, Unchained Labs

Choosing one protein quantification tool that spans upstream and downstream workflows means that sample volume, throughput, and accuracy are all critical. Stunner delivers fast, automation-compatible protein quantification to within 2% accuracy and 1% precision on 2 µL of sample. And when moving downstream, Stunner will ace the USP and Ph. Eur. standards for UV/Vis.

10:10 Modeling and Experimental Investigation of Avidity-Driven Bispecific Antibody-Antigen Binding Interactions

John J. Rhoden, PhD, Director, Preclinical Development, Fusion Pharmaceuticals Inc.

Multivalent binding of antibodies and bispecifics to cell surface targets can be strongly modulated by leveraging avidity to affect target antigen binding. Avidity-driven target engagement can be exploited to improve properties, such as drug potency and target-cell or tissue selectivity. We demonstrate examples utilizing mathematical modeling as a powerful tool to make mechanistically driven predictions and guide experiments to optimize multivalent proteins, guide dosing, and select desirable targets.

10:30 LIVE Q&A: Session Wrap-Up

Moderator: John J. Rhoden, PhD, Director, Preclinical Development, Fusion Pharmaceuticals Inc.
Panelists:
Marc Bailly, PhD, Principal Scientist, Merck Research Labs
Theodore Randolph, PhD, Professor, Chemical and Biological Engineering, University of Colorado
Kevin Lance, PhD, Marketing Manager, Marketing, Unchained Labs

10:55 Combining Experimental and Computational Methods to Identify Antibody Variants with Drug-Like Biophysical Properties

Peter M. Tessier, PhD, Albert M. Mattocks Professor, Pharmaceutical Sciences & Chemical Engineering, University of Michigan

Monoclonal antibodies display variable and difficult-to-predict levels of nonspecific and self-interactions that lead to various drug development challenges, including antibody aggregation, abnormally high viscosity, and fast antibody clearance. In this presentation, we will report experimental and computational methods for identifying, engineering, and predicting antibody variants with drug-like biophysical properties for diverse panels of preclinical and clinical antibodies.

11:15 Utilizing High-Throughput Differential Scanning Fluorimetry (DSF) to Inform Protein Engineering Decisions

Andrew K. Urick, PhD, Senior Scientist, AbbVie

As the initial stages of biologics discovery become geared toward generating large numbers of small quantities of material, there is increasing need for sensitive and high-throughput structural assays. Thermostability is an important property for therapeutic proteins, particularly for new biologics formats of increasing complexity. We will describe our implementation of differential scanning fluorimetry to interrogate thermostability in both our protein production and protein engineering workflows.

11:35 High-throughput stability characterization to support the entire biologic development process

Charles Heffern, PhD, Product Manager, Research & Development, NanoTemper Technologies

Automated and high-throughput analysis of biologic stability spans the entire workflow of biologic development, from early stage developability assessments through protein engineering to formulation and manufacturing decisions. The necessity for high-quality data to inform modeling and pipeline decisions is pervasive. Here we discuss how Prometheus empowers organizations to improve their biologic development through the use of high-quality data to make better decisions.

12:00 pm LIVE Q&A: Session Wrap-Up

Moderator: Andrew K. Urick, PhD, Senior Scientist, AbbVie
Panelists:
Peter M. Tessier, PhD, Albert M. Mattocks Professor, Pharmaceutical Sciences & Chemical Engineering, University of Michigan
Charles Heffern, PhD, Product Manager, Research & Development, NanoTemper Technologies

12:20 Lunch Break - View our Virtual Exhibit Hall

EMERGING METHODS AND INSTRUMENTS

1:05 High-Throughput Investigation of Protein Energy Landscapes in Non-Antibody Scaffolds

Gabriel J. Rocklin, PhD, Assistant Professor, Pharmacology, Northwestern University

An ideal therapeutic scaffold should possess both high folding stability and minimal conformational fluctuations, but to date it has not been possible to measure conformational fluctuations on a large scale. We developed a multiplexed hydrogen-deuterium exchange mass spectrometry-based approach for measuring stability and conformational fluctuations for thousands of designed protein scaffolds in parallel. These data should reveal the structural determinants of conformational fluctuations and enable the design of optimized scaffolds.

12:45 Membrane Mimetic FACS to Facilitate Antibody Screening

Christy A. Thomson, PhD, Senior Scientist, Amgen, Inc.

The ability to identify and characterize therapeutic antibodies targeting multi-pass membrane proteins is hampered by the often difficult expression and purification of membrane proteins in their native conformation. We examined the utility of novel methods for membrane

protein stabilization, including SMALPs, nanodiscs, and amphipols, to isolate a model multi-pass membrane protein. Following successful incorporation into the membrane mimetics, we evaluated their utility in FACS to facilitate lead identification.

1:25 Get ahead in the screening race, catch the WAVE!

Rony Nehmé, Dr, Application Scientist, Creoptix AG

In this presentation, we will discuss the benefits of early stage kinetic characterization from crude samples ranging from peptides to membrane proteins and relevant clinical samples.

Save time, work with suboptimal assay conditions and validate your ELISA data.

1:50 LIVE Q&A: Session Wrap-Up

Moderator: Christy A. Thomson, PhD, Senior Scientist, Amgen, Inc.
Panelists:
Gabriel J. Rocklin, PhD, Assistant Professor, Pharmacology, Northwestern University
Rony Nehmé, Dr, Application Scientist, Creoptix AG

2:10 Session Break

3:50 Refresh Break - View Our Virtual Exhibit Hall

4:10 Problem-Solving Breakout Discussions Part A - View our Virtual Exhibit Hall

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 20: High-Throughput (HT) Analytical Data Management to Enable Machine Learning

Marc Bailly, PhD, Principal Scientist, Merck Research Labs

TABLE 21: Biophysical Methods to Drive Protein Decisions: What Matters and How Do We Measure It?

Andrew K. Urick, PhD, Senior Scientist, AbbVie

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem-Solving Breakout Discussions Part B - View our Virtual Exhibit Hall

TABLE 22: The Role of Denaturing and Native-MS in Pharma: From mAbs to Membrane Proteins and Beyond

Wendy Sandoval, Principal Scientist, Genentech, Inc.
Iain Campuzano, Principal Scientist, Discovery Attribute Sciences, Amgen

5:30 Close of Day

THURSDAY, SEPTEMBER 3

NEW APPLICATIONS FOR MASS SPECTROMETRY

9:05 am Automating Protein A through Tryptic Digest LC-MS/MS for Looking at Post-Translational Modifications on mAbs and Multi-Specifics

Stephen D'Eri, Scientist, Sanofi

Rapid technological growth in analytical instrumentation and data processing has enabled researchers to develop powerful new methods for use in the biopharmaceutical industry. Unfortunately, sample preparation methods have progressed at a much slower rate, leading to a bottleneck in high-throughput analytics. By incorporating automation into our sample preparation and data analysis methods, we address the bottleneck issue while supporting harmonization of workflows across multiple sites.

9:25 Probing the Interactions of BBB-Crossing Antibodies with IGF1R Using HDX-MS

John Kelly, PhD, Senior Research Officer, Mass Spectrometry, National Research Council Canada

NRC has developed nanobodies that act as carriers to shuttle therapeutic payloads across the blood-brain barrier. The antibodies bind to IGF1R on the surface of brain endothelial cells and trigger transcytosis. HDX-MS, integrated with NMR and imaging based structural techniques, is being deployed to better understand the mechanisms by which these antibodies bind to IGF1R and how this differs from interactions with its endogenous ligand, IGF-1.

9:45 New Mid-IR Liquid Analyzer for Protein Characterization

Craig Magee, PhD, Director, Business Development, Life Sciences, DRS Daylight Solutions

We will introduce an entirely new class of high-sensitivity, inline mid-IR liquid analyzers. Based on ultra-high-brightness tunable quantum cascade lasers (QCL), this new platform technology offers fast scan rates, a large dynamic range and an ability to easily measure small sample volumes. We will present the physical operating principles of these new analyzers and provide several application examples including their use in fractionated HPLC measurements and chemical and biologic reactor monitoring.

10:10 Gas-Phase Structural Biology: New Tools for the Rapid Assessment of Protein Sequence, Structure and Stability

Daniel D. Vallejo, Graduate Student Researcher, Chemistry, University of Michigan

The next generation of medicines depends upon our ability to quickly assess the structures and stabilities of protein and protein complexes, as well as protein-based biotherapeutics. Such endeavors are nearly insurmountable with current tools without exhaustive orthogonal experimentation. In this presentation, we will discuss recently developed ion mobility-mass spectrometry tools aimed at bridging this gap in basic technology to characterize novel biotherapeutics and their generic analogs (biosimilars).

10:30 Transforming Biomolecular Characterization with Digital Microfluidics and Artificial Intelligence

Ryan Denomme, CEO, Nicoya

In-depth, quantitative characterization of protein interactions is crucial in engineering and optimizing new biologics that can act as effective therapeutics. Among the many biophysical techniques that have accelerated this process for scientists, surface plasmon resonance (SPR) is an industry standard that is both sensitive and powerful, enabling rapid and label-free detection of a wide range of molecular interactions. Yet, there has been minimal innovation in SPR platforms to date, considerably limiting their use and accessibility. Join us as we discuss how we've integrated digital microfluidics technology and AI-powered intelligence with SPR, and how this will eliminate challenges in efficiency and optimization to help you go-to-market faster with your biotherapeutics.

10:50 LIVE Q&A: Session Wrap-Up

Moderator: John Kelly, PhD, Senior Research Officer, Mass Spectrometry, National Research Council Canada
Panelists:
Stephen D'Eri, Scientist, Sanofi
Ryan Denomme, CEO, Nicoya
Craig Magee, PhD, Director, Business Development, Life Sciences, DRS Daylight Solutions
Daniel D. Vallejo, Graduate Student Researcher, Chemistry, University of Michigan

11:10 Close of Biophysical Methods

September 3-4 | Inaugural

CELL AND GENE THERAPY ANALYTICS

A Best Practices Exchange for Essential Assays and Product and Process Quality Strategies

Part of CELL-BASED IMMUNOTHERAPIES STREAM

THURSDAY, SEPTEMBER 3

CHARACTERIZATION ASSAYS

12:45 pm Characterization of Gene Therapies by Charge Detection Mass Spectrometry

Martin Jarrold, PhD, Professor, Chemistry, Indiana University

Conventional mass spectrometry is usually limited to masses less than a Megadalton because of heterogeneity. Charge detection mass spectrometry (CDMS) can overcome this limitation and extend accurate mass measurements into the Gigadalton regime. Recent technical advances have dramatically improved the sensitivity of CDMS. Applications of CDMS to the analysis of complex biopharmaceuticals, including gene therapy products and vaccines, will be presented.

1:05 Assay Development for Emerging Single-Cell Platforms

Eric S. Alonzo, PhD, Senior Scientist, Cell Analytics, bluebird bio

Clinical-grade CAR T cell drug products contain a heterogenous mixture of phenotypically and functionally distinct cells. Such heterogeneity necessitates innovative and comprehensive strategies to characterize CAR T cell therapy investigational drug products. Here, we present how high-dimensional single-cell analytics in CAR T manufacturing and beyond can be used to resolve drug product complexity and identify potentially key clinical correlates.

1:25 A Platform Approach for Analytical Methods to Support Adeno-Associated Virus (AAV) Gene Therapy Products

charles river

Michael Hantman, Associate Director, Methods Development, Biologics, Charles River

Recombinant adeno-associated virus (rAAV) vectors have been widely used for *in vivo* gene therapy with commercial products approved by FDA. Charles River Laboratories (CRL) PA Biologics has established a platform approach for rAAV vector genome titer quantification, residual host cell DNA quantification and sizing evaluation, and replication competent virus (rcAAV) detection, by adopting real-time PCR as well as ddPCR technologies and using reference materials available from ATCC or biological materials created at CRL.

1:50 LIVE Q&A: Session Wrap-Up

Moderator: Eric S. Alonzo, PhD, Senior Scientist, Cell Analytics, bluebird bio
Panelists:
Martin Jarrold, PhD, Professor, Chemistry, Indiana University
Michael Hantman, Associate Director, Methods Development, Biologics, Charles River

2:10 Refresh Break - View our Virtual Exhibit Hall

STANDARDS AND REGULATORY CONSIDERATIONS

2:25 Chairperson's Remarks

Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP

2:30 Principles and Practices for Bioassay Standards

Tim Schofield, Owner & Consultant, CMC Sciences LLC

Standards are essential to the development and control of biological products. Considering their importance, there is no consensus on the source of a standard, the basis and means of standard qualification, and stability evaluation. This talk will discuss principles and practices related to standards used to report potency of biological products and propose strategies. Those proposals will borrow from practices related to quality by design, highlighting fitness-for-use of a standard.

2:50 Current Efforts in Bioassay Standardization

Dawn Henke, PhD, Senior Technical Program Manager, Standards Coordinating Body

This discussion will cover standards for regenerative medicine products. Discussion will focus on standards for bioassays, published standards and how to implement these standards be addressed. An overview of current standards under development and how to get involved, as well as a forum for questions will be provided.

3:10 Panel Discussion : Standards and Regulatory Considerations

Moderator: Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP

- Setting standards for new bioassay modalities including cell & gene therapies and immunotherapies
- Developing standards and using already-established standards
- Getting involved with standard-setting organizations
- Qualification of standards
- Correction of relative potency when changing standards

Panelists:
Dawn Henke, PhD, Senior Technical Program Manager, Standards Coordinating Body
Tim Schofield, Owner & Consultant, CMC Sciences LLC

3:50 Close of Day

FRIDAY, SEPTEMBER 4

INCREASING ANALYTICAL DEPTH AND THROUGHPUT

9:05 am Overcoming the Barriers of Biophysics in Gene Therapy

Lake Paul, President, BioAnalysis LLC

Currently the gene therapy space is under utilizing the power of biophysics, specifically Analytical Ultracentrifugation (AUC). Besides the quantitation of empty capsids, AUC can also be used to evaluate the physicochemical properties, higher-order structures, and other pertinent properties. The EMA and FDA are seeing QC release specifications based on AUC, therefore it is paramount that AUC methods are fully realized and meticulously developed.

9:25 Understanding Structure-Function Relationship on AAV Capsid Proteins in Gene Therapy Products

Lin Liu, PhD, CMC Dossier Development & Coordination, Sanofi

Viral capsid proteins play an important role in cellular targeting and trafficking as part of the viral infection cycle, and thus changes in the viral capsid protein sequence or post-translational modifications (PTMs) might impact viral targeting and infectivity. We evaluated the role of AAV capsid protein PTMs on AAV transduction potential by generating AAV2 and AAV5 capsid mutants and performing a stress study.

9:45 See your capsids leak and pop: AAV genome ejection and capsid stability on Uncle

UNCHAINED LABS

Kevin Lance, PhD, Marketing Manager, Marketing, Unchained Labs

When thermally stressed AAV genomes leak out from their capsids, and do it before proteins melt. However, methods that look only at protein unfolding don't track DNA, so you're not getting the whole story. This talk will show Uncle's insight on AAV stability by monitoring DNA ejection from capsids, and how to look at quantifying encapsulated DNA and particle titer.

10:10 LIVE Q&A: Session Wrap-Up

Moderator: Lake Paul, President, BioAnalysis LLC
Panelists:
Lin Liu, PhD, CMC Dossier Development & Coordination, Sanofi
Kevin Lance, PhD, Marketing Manager, Marketing, Unchained Labs

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

ANALYTICAL CHALLENGES

10:50 Evaluating a Control Strategy for an Autologous Cell Therapy for Risk to Patients

Ken Riker, Director Product Quality, Product Quality, Celgene Corp.

An integrated control strategy was developed for a late-phase CAR-T cell therapy product based on our current understanding of the product quality attributes, the manufacturing process, and analytical capability. Based on this comprehensive assessment, the overall risk of drug product to patient safety and product efficacy was determined to be low, demonstrating that the combined operational and testing controls are suitable to ensure product quality from the proposed commercial process.

11:10 Machine Learning for the Rapid Classification of Flow Imaging to Characterize Cell Therapies

Amber H. Fradkin, PhD, Director, Particle Characterization Core Facility, KBI Biopharma

We used a very common analytical method to characterize subvisible particles in biologics (Micro-Flow Imaging) and applied the technique to cell therapy products. We have developed customized machine learning algorithms specific to cell therapy MFI data for rapid classification of images to establish particle profiles. The method has overwhelming potential to monitor cell particle size distributions, cell debris, cell agglomerates, as well as extrinsic material from batch to batch.

11:30 Development and Qualification of a Cell Counting Assay for Dose Determination

Michele Perry, Lead Microbiology Associate, Analytical Development, Synlogic, Inc.

Live bacterial products (LBP) are novel therapeutics with the potential to treat unmet needs in rare genetic diseases, such as phenylketonuria. Viability is a critical aspect of LBPs and traditionally determined through colony-forming unit methods. Another approach to determining viability is automated cell counting. When the methods were compared, the cell counting results were more indicative of *in vivo* activity of the LBPs and is now used to determine dose.

11:50 LIVE Q&A: Session Wrap-Up

Moderator: Ken Riker, Director Product Quality, Product Quality, Celgene Corp.
Panelists:
Amber H. Fradkin, PhD, Director, Particle Characterization Core Facility, KBI Biopharma
Michele Perry, Lead Microbiology Associate, Analytical Development, Synlogic, Inc.

12:10 pm Close of Summit

EXPRESSION STREAM

Increasing Productivity, Ensuring Quality

The intrinsic nature of proteins poses endless challenges. Meeting industry's growing demands requires next-gen strategies, breakthrough research, and applying cutting-edge tools and technologies. Synthetic biology, genetic engineering, Cryo-EM, crystallography and production system research are revolutionizing protein expression and leading the field into a new age of designer cells and cell lines. The week-long Expression Stream explores 'Difficult-to-Express' proteins, including membrane and other especially troublesome proteins. "Optimizing Protein Expression" examines production strategies, as well as protein expression systems, including CHO and *E. coli.* And finally, the "Protein Expression System Engineering" conference looks at the foundations of protein expression and the breakthrough research that is innovating protein production.

2020 EXPRESSION STREAM CONFERENCES

AUGUST 31-SEPTEMBER 1
AGENDA Difficult-to-Express Proteins

SEPTEMBER 2-3
AGENDA Optimizing Protein Expression

SEPTEMBER 3-4
AGENDA Protein Expression System Engineering

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MONDAY, AUGUST 31

OVERCOMING PRODUCTION CHALLENGES

9:05 am Harnessing Synthetic Biology to Produce Difficult-to-Express-Proteins

Shlomo Zarzhitsky, PhD, Research Associate, Chemistry, Princeton University

Biotech scientists often get mixed results when using fusion proteins to attempt high yield production of difficult-to-express proteins. We developed a new kind of fusion tag – synthetic, custom, and optimized for the protein of interest. Using this novel tag, we observed an increase in expression yields of notoriously difficult-to-express targets like amyloid beta and a designed membrane pore peptide, 2 and 10 fold, respectively when compared to SUMO.

9:25 Strategies to Improve Single-Chain Fvs as Crystallization Chaperones

Susanne Gräslund, PhD, Principal Investigator, Structural Genomics Consortium, Karolinska Institute

Antibody fragments such as scFvs have great potential as crystallization chaperones for structural biology due to their ability to stabilise targets, trap certain conformations and/or promote crystal packing. Here we present a few examples of using scFvs to determine 3D structures through X-ray crystallography and discuss properties of the molecule that could be improved for higher success rates. Furthermore, production of biotinylated antigens and scFvs have also been optimized.

9:45 Addressing Complex Protein Challenges with Lonza's GS Xceed® Toolbox Lonza Pharma & Biotech

Alison Porter, Head, Expression Systems Sciences, Lonza Pharma & Biotech

-Although antibodies still predominate in the clinic, there is a shift in drug development pipelines towards more complex, next generation biologics (NGBs)

-Such NGBs often do not express well in traditional expression platforms

-In this presentation, we will discuss two solutions which are included in our GS toolbox and are designed to especially help overcome challenges with NGBs: GS® pXC Multigene Vectors and GS piggyBac®.

10:10 LIVE Q&A: Session Wrap-Up

Moderator: Rana Sidhu, PhD, Protein Expression Lead, Early Solutions, UCB, Inc.
Panelists:
Shlomo Zarzhitsky, PhD, Research Associate, Chemistry, Princeton University
Susanne Gräslund, PhD, Principal Investigator, Structural Genomics Consortium, Karolinska Institute

10:30 Coffee Break - View our Virtual Exhibit Hall

BREAKTHROUGH TECHNOLOGIES TO ANALYZE & EXPRESS DTEPs

10:50 Cryo-EM Guided Reconstitution System Optimization for Challenging Membrane Proteins towards High Conformational Stability

Xinchao Yu, PhD, Senior Scientist, Molecular Engineering, Amgen, Inc.

Cryo-EM has demonstrated great potential to elucidate high-resolution structures of challenging membrane protein targets with fast turnaround time. In the current study, we utilized cryo-EM as a major tool to identify the optimal reconstitution systems for two difficult membrane proteins. Our results indicated that even though these membrane proteins showed decent biophysical properties, only through high-resolution cryo-EM structural studies were we able to identify conditions that confer the greatest stability.

11:10 Native Ion Mobility Mass Spectrometry of Intact Membrane Protein Complexes

Arthur Laganowsky, PhD, Associate Professor, Chemistry, Texas A&M University

Native ion mobility mass spectrometry (IM-MS) is an emerging biophysical technique to probe membrane protein complexes and their interactions with lipids and other small molecules. I will demonstrate how IM-MS can be used as an invaluable method to optimize purification of target proteins. I will then highlight our work using native IM-MS to not only determine binding thermodynamics but also cooperative and allosteric mechanisms for membrane protein-ligands interactions.

11:30 Utilizing Expi-CHO-S™ Cells to Combat the COVID-19 Pandemic: Optimized Production of the SARS-CoV-2 S Protein and Downstream Biological and Clinical Applications ThermoFisher SCIENTIFIC

Natalia Herrera, Graduate Student/ PhD Candidate, Albert Einstein College of Medicine
Nicholas Morano, Graduate Student, Albert Einstein College of Medicine

COVID-19 is a global health crisis caused by SARS-CoV-2, and there is a critical need to produce large quantities of high-quality SARS-CoV-2 Spike (S). We characterize the production of the SARS-CoV-2 S protein in ExpiCHO-S Cells™, and highlight downstream biological and clinical uses of purified recombinant S protein. These include examining interactions with proposed binding partners within the human secretome, analysis of S protein glycosylation patterns, the development of clinical assays to detect SARS-CoV-2 antibodies, and analysis of the innate and humoral immune responses to SARS-CoV-2.

11:55 LIVE Q&A: Session Wrap-Up

Moderator: Rana Sidhu, PhD, Protein Expression Lead, Early Solutions, UCB, Inc.
Panelists:
Xinchao Yu, PhD, Senior Scientist, Molecular Engineering, Amgen, Inc.
Arthur Laganowsky, PhD, Associate Professor, Chemistry, Texas A&M University
Natalia Herrera, Graduate Student/ PhD Candidate, Albert Einstein College of Medicine
Nicholas Morano, Graduate Student, Albert Einstein College of Medicine

12:15 pm Lunch Break - View our Virtual Exhibit Hall

INNOVATING SOLUTIONS

12:45 Tailoring HDL Mimetics to Deliver mRNA for *in vivo* Protein Expression

Wei He, PhD, Biomedical Scientist, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory

Manufacturing of protein therapeutics, such as biologics, antibodies and subunit vaccines, is often hindered by difficulties in recombinant protein production, especially for membrane-bound proteins. Messenger RNA therapeutics harness the body's own cells to produce and deliver therapeutic protein molecules. We have successfully developed a platform using HDL mimetics (termed nanolipoprotein particles, NLPs) to deliver self-amplifying mRNA constructs *in vivo* and achieve robust expression efficiency.

1:05 Driving Biological Discovery: An Expanding Toolkit for Affinity Proteomics

John LaCava, PhD, Group Leader, Laboratory of Macromolecules and Interactomes, European Research Institute for the Biology of Aging, University Medical Center Groningen

It remains challenging to transfer intact physiological macromolecules from their native sources into suitably stabilizing *in vitro* environments. To address this, we developed an interactome capture platform that is akin to a crystallographic screen. The approach will be summarized in this talk. Our long-term objective is to enable robust, tunable transfer of target endogenous macromolecules from their *in vivo* milieus into test tubes, for biochemical, structural, and mechanistic studies.

1:25 The Optimization of Recombinant Protein Expression

Rob Burgess, Chief Business Officer, Sino Biological Inc

Sino Biological is a global leader in development and manufacturing of ISO9001 and ISO13485-certified reagents, including recombinant proteins and antibodies. An overview of the company's state-of-the-art technologies for optimizing protein expression will be given addressing production challenges as well as key influencing factors and will include several example case studies.

1:50 LIVE Q&A: Session Wrap-Up
Moderator: Wei He, PhD, Biomedical Scientist, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory
Panelists:
John LaCava, PhD, Group Leader, Laboratory of Macromolecules and Interactomes, European Research Institute for the Biology of Aging, University Medical Center Groningen
Rob Burgess, Chief Business Officer, Sino Biological Inc

2:10 Refresh Break - View Our Virtual Exhibit Hall

2:30 Problem Solving Breakout Discussions - Part A
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 7: Experiences with Using Different Binder Types as Crystallization Chaperones or Cryo-EM Handles
Susanne Gräslund, PhD, Principal Investigator, Structural Genomics Consortium, Karolinska Institute

3:00 Refresh Break - View Our Virtual Exhibit Hall

3:20 Problem Solving Breakout Discussions - Part B

TABLE 8: Cell-Free Approaches to Difficult Proteins
Matthew Coleman, PhD, Senior Scientist & Group Leader, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory

3:50 Refresh Break - View our Virtual Exhibit Hall

PLENARY KEYNOTE SESSION

4:10 Chairperson's Remarks
K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

4:15 KEYNOTE PRESENTATION: From Energy to Machine Learning
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
We've engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing, before abruptly moving to "sequence-only" deep machine learning for protein design – from fluorescent proteins to AAV capsids to antibodies. When combined with libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

4:40 KEYNOTE PRESENTATION: The Case for Intelligent Design in Protein Engineering
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University
Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing a so-called "intelligent design" approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

5:15 Live Q&A: Session Wrap-Up



Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

5:35 Happy Hour - View our Virtual Exhibit Hall

6:10 Close of Day

TUESDAY, SEPTEMBER 1

EXPRESSING MEMBRANE PROTEINS & UTILIZING NANODISCS

9:05 am Large Nanodiscs Going Viral
Mahmoud Nasr, PhD, RPh, Group Leader, Medicine, Brigham and Women's Hospital, Harvard Medical School
Covalently circularized nanodiscs and DNA-corralled nanodiscs have opened up the possibility of engineering large nanodiscs up to 90 nm. These large nanodiscs are extending the applicability of nanodisc technology from studying small membrane proteins to acting as a surrogate membrane to investigate structural and functional aspects of viral entry. We will present the recent technical developments leading to construction of large nanodiscs and show some of the viral entry applications.

9:25 Cell-Free Co-Translational Approaches for Producing Mammalian Receptors Using Nanolipoproteins (Nanodisc)
Matthew Coleman, PhD, Senior Scientist & Group Leader, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory
Employing nanolipoprotein particles (NLPs), aka nanodiscs, to yield membrane proteins in stable, native-like states has become common practice to facilitate biochemical and biophysical characterization. Our approach involves utilizing cell-free expression systems in the presence of NLPs or using co-translation techniques. We show how cell-free reactions can be modified to render control over nanoparticle size, monodispersity and complex organization in support of producing functional membrane proteins.

10:10 LIVE Q&A: Session Wrap-Up
Moderator: Matthew Coleman, PhD, Senior Scientist & Group Leader, Biosciences and Biotechnology Division, Lawrence Livermore National Laboratory
Panelists:
Mahmoud Nasr, PhD, RPh, Group Leader, Medicine, Brigham and Women's Hospital, Harvard Medical School

10:30 Coffee Break - View our Virtual Exhibit Hall

EXPRESSING MEMBRANE PROTEINS

10:50 Recombinant Production of a G-Protein Coupled Receptor Using an *Escherichia coli* Cell-Free Expression System
Ho Leung Ng, PhD, Associate Professor, Biochemistry & Molecular Biophysics, Kansas State University
G-protein coupled receptors (GPCRs) are the largest family of drug targets and the targets of >35% of all drugs. Biochemical and structural studies of GPCRs have been hampered by the difficulty of recombinantly producing and purifying GPCRs. I provide an overview of using cell-free expression systems to produce GPCRs. I also describe our lab's success with producing the GPCR, G-protein coupled estrogen receptor, for the first published biochemical binding assays.

11:10 Expression of Thermostable Human Cannabinoid Receptor CB2 in Mammalian Cell Cultures and Its Biophysical Characterization
Alexei Yeliseev, PhD, Staff Scientist, Group Leader, LMBB, NIH/NIAAA
Our work focuses on human cannabinoid receptor CB2, an important regulator of inflammatory pathways. To obtain thermostable variants of this receptor we expressed it and purified using protocols developed in our laboratory. The mammalian cell-expressed receptor was functionally active and homogenous. The detergent-solubilized receptor is stable at 15 oC for several days which enables its characterization by solution-state NMR; post-translational modifications of this protein likely determine its structural stability.

11:30 Shake Flask Off-Gas Measurement and Scale-up to Single Use Orbital Bioreactors

Thariska Tharmakulasingam, Specialist, Orbital Bioreactors, Kuhner Shaker AG

Off-gas measurement from shake flasks will facilitate a fundamental understanding of upstream processes and enable reliable scale-up into larger-scale bioreactors. Combining this powerful technology with the proven scale-up benefits of orbital-shaken bioreactors offers fast and reproducible results. Here we introduce the new Kuhner TOM instrument for off-gas analysis online in parallel shake flasks and highlight its use to scale into large-scale shaken bioreactors - focusing on recent successes at the 10L scale.

11:55 LIVE Q&A: Session Wrap-Up

Moderator: Ho Leung Ng, PhD, Associate Professor, Biochemistry & Molecular Biophysics, Kansas State University
Panelists:
Alexei Yeliseev, PhD, Staff Scientist, Group Leader, LMBB, NIH/NIAAA
Thariska Tharmakulasingam, Specialist, Orbital Bioreactors, Kuhner Shaker AG

12:15 pm Lunch Break - View Our Virtual Exhibit Hall

STRATEGIES FOR OPTIMIZING DTEP EXPRESSION

12:50 Strategies for Optimizing Challenging-to-Express Protein Targets

Rana Sidhu, PhD, Protein Expression Lead, Early Solutions, UCB, Inc.

The Protein Expression group within the Early Solutions team at UCB generates protein targets for gene to structure analysis and biochemical assays. Case studies will be presented describing the expression and process optimization of challenging-to-express proteins.

1:10 Utilizing Randomized Configuration Targeted Integration (RCTI) Cell Line Development (CLD) Approach for Expression of Difficult or Complex Therapeutic Proteins

Shahram Misaghi, PhD, Senior Scientist, Cell Culture and Bioprocess Operations (CCBO), Genentech, Inc.

Randomized configuration targeted integration (RCTI) CLD approach allows simultaneous transfection of multiple configurations of transgenes encoding a complex protein to generate a plurality of clones each with a unique transgene configuration, specific folding, and product quality. Screening RCTI single cell clones allows seamless isolation of clones with comparable titers and product quality attributes to that of several parallel standard CLDs, significantly reducing resources needed to express difficult or complex molecules.

1:55 LIVE Q&A: Session Wrap-Up

Moderator: Mahmoud Nasr, PhD, RPh, Group Leader, Medicine, Brigham and Women's Hospital, Harvard Medical School
Panelists:
Rana Sidhu, PhD, Protein Expression Lead, Early Solutions, UCB, Inc.
Shahram Misaghi, PhD, Senior Scientist, Cell Culture and Bioprocess Operations (CCBO), Genentech, Inc.

2:15 Close of Difficult-to-Express Proteins

OPTIMIZING PROTEIN EXPRESSION

Enhancing Expression Systems

WEDNESDAY, SEPTEMBER 2

PROTEIN EXPRESSION STRATEGIES

9:05 am KEYNOTE PRESENTATION: Cell and Process Optimization Strategies to Improve Biologics Manufacturing

Stefan R. Schmidt, MBA, PhD, COO & Head, Operations, BioAtrium AG

In the last decades, a tremendous productivity increase of bioprocessing was observed. Three different innovations drive this evolution: molecular design of expression constructs, engineering of host cell lines, and optimization of cultivation processes. These different strategies are used either as standalone, or in combination, to multiply the cellular output. This presentation gives a comprehensive overview on where and how to implement these approaches, based on successful examples and case studies.

9:25 Recombinant Protein Production Strategies for Multi-Protein Complexes in Drug Discovery

Saleha Patel, PhD, Senior Research Scientist, Protein Science, Discovery Biology, AstraZeneca

The increasing complexity of drug targets, many of which are multi-protein complexes, provides a challenge for successful reagent generation for drug discovery. Whilst there have been advances in the downstream analytical technologies (such as cryo-EM) the ways in which recombinant proteins are produced remains largely unchanged. However, to ensure the protein reagents are fit for purpose, for these novel technologies, new strategies are required within the protein production workflow.

9:45 GPEx® Boost: A Novel Approach for High-Expressing CHO Cell Line Engineering

Gregory Bleck, Global Head of R&D, Biologics, Catalent

10:10 Session Wrap-Up

Moderator: William Gillette, PhD, Principal Scientist, Protein Expression Laboratory, Leidos Biomedical Research
Panelists:
Saleha Patel, PhD, Senior Research Scientist, Protein Science, Discovery Biology, AstraZeneca
Stefan R. Schmidt, MBA, PhD, COO & Head, Operations, BioAtrium AG
Gregory Bleck, Global Head of R&D, Biologics, Catalent

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

CHO CELL EXPRESSION

10:50 Multi-Omics Investigation of Hyper Productivity in CHO Cells: Gaining New Insights into the Role of Nuclear Proteomics in Enhancing Cellular Productivity

Hussain Nuruddin Dahodwala, PhD, Director, Upstream Process Development, NIIMBL

IgG-producing cell clones were analyzed using a combination of transcriptomic, proteomic, phosphoproteomic, and chromatin immunoprecipitation (ChIP) techniques. Our data suggested increased *in vivo* CMV promoter-transcription factor interaction in the higher producing cell line. We show here that the nuclear proteome and phosphoproteome have an important role in regulating final productivity of recombinant proteins from CHO cells.

11:10 Physiological Responses to Increased Productivity: A Transcriptomic and Proteomic Study

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

In this study, we compare a parental cell line and its DHFR-amplified progeny using RNA-Seq and proteomic analysis. A wide range of cellular processes are altered in response to increased productivity, including the protein processing machinery and primary metabolism. These changes provide insights into the use of CHO cells for recombinant protein production and strategies for cell engineering for improved productivity.

11:35 Novel Solution for High Throughput Antibody and Protein Purification using Magnetic Beads

Sean Taylor, Ph.D., Field Application Scientist Manager, Catalog Products, GenScript Inc. USA

With the ever increasing demand for antibody and protein-based therapeutics, a flexible purification platform that can handle low to high sample volumes and expression levels is critical for screening. Protein purification using traditional chromatography is limited by throughput, time-consuming, and involves labor-intensive sample preparation processes. Magnetic beads-based purification permits the incubation of the beads directly into culture soups. The tools/ application to simplify and significantly augment protein purification and screening cost-effectively will be described.

12:00 pm Investigation of Gene Expression Patterns in Stable and Unstable Clonally Derived CHO Cell Lines

Theodore Peters, PhD, Sr Scientist, Cell Line Dev, Seattle Genetics

Development of biologic-producing CHO clones in accelerated timelines is encumbered by demonstrating production stability in candidate cell lines. Screening out unstable lines earlier in development could mitigate the risk of advancing unstable candidates. Our work reveals significant phenotypic heterogeneity in clonal populations by characterizing subclones from stable and unstable clones. This highlights the prevalence of phenotypic drift in clonal cell lines providing a basis for investigating gene expression patterns.

12:20 Lunch Break - View our Virtual Exhibit Hall

PROTEIN PRODUCTION ADVANCES

12:45 Using Recoded Organisms for the Expression of Post-Translationally Modified Proteins: Leveraging the Benefits while Avoiding the Pitfalls

Richard B. Cooley, PhD, Assistant Professor, Biochemistry & Biophysics, Oregon State University

To increase yields and mitigate premature termination, organisms in which UAG codons have no functional assignment are gaining widespread use as GCE expression hosts. However, heterogeneously modified proteins are often obtained with these systems. Here, we develop GCE systems for homogenous, multi-site incorporation of phosphoserine and nitro-tyrosine in recoded organisms, and demonstrate their benefits for accessing biologically relevant post-translationally modified proteins.

1:05 Integrating Vibrio Natriegens into a Protein Production Workflow

William Gillette, PhD, Principal Scientist, Protein Expression Laboratory, Leidos Biomedical Research

Vibrio natriegens offers an alternative host to express recombinant proteins. Although there are some minor differences in basic *E. coli* protocols, much, including expression constructs, is bifunctional across the two systems. Case studies that cover how the system has improved some aspects of protein production will be presented.

1:25 GlycoExpress® – An Alternative Host for Difficult to Express Proteins

Lars Stöckl, PhD, Doctor, Glycotope Service Division, Glycotope GmbH

The era of classical IgG molecules in bio-pharma development is shifting rapidly to more challenging complex biopharmaceuticals. With CHO being a good production cell line for IgG molecules, they might fail to produce more challenging candidates. The GlycoExpress (GEX®) system represents an ideal alternative for the production these difficult to express protein molecules and will provide case studies which demonstrate the superiority in productivity and product quality vs. CHO cell expression.

1:50 LIVE Q&A: Session Wrap-Up
Moderator: Hussain Nuruddin Dahodwala, PhD, Director, Upstream Process Development, NIIMBL
Panelists:
Susan Sharfstein, PhD, Professor, Nanobioscience, Nanoscale Science and Engineering, SUNY Polytechnic Institute
Theodore Peters, PhD, Sr Scientist, Cell Line Dev, Seattle Genetics
William Gillette, PhD, Principal Scientist, Protein Expression Laboratory, Leidos Biomedical Research
Richard B. Cooley, PhD, Assistant Professor, Biochemistry & Biophysics, Oregon State University
Lars Stöckl, PhD, Doctor, Glycotope Service Division, Glycotope GmbH
Sean Taylor, Ph.D., Field Application Scientist Manager, Catalog Products, GenScript Inc. USA

2:10 Refresh Break to View our Virtual Exhibit Hall

FEATURED SESSION: BACULOVIRUS

2:25 FEATURED PRESENTATION: Vectors for Baculo-Insect and BacMam Protein Expression
Frederick Boyce, MD, PhD, Assistant Professor, Neurology, and Director, MGH Gene Delivery Technology Core, Massachusetts General Hospital and Harvard Medical School
The popular pFastBac vectors for baculovirus expression have remained relatively unchanged since their publication by Luckow in 1993. We will discuss improvements that we and others have made to these workhorse vectors for protein expression for use in either insect (BEVS) or mammalian (BacMam) systems. Modern versions of these vectors allow more facile and efficient production of recombinant viruses, enabling high-throughput applications, and can also lead to increased protein expression.

2:45 FEATURED PRESENTATION: New Avenue for COVID-19 Antivirals: MultiBac Enables Discovery of a Druggable Pocket in SARS-CoV-2 Spike Protein
Imre Berger, PhD, Director, Max Planck Centre for Minimal Biology, University of Bristol
The MultiBac BEVS platform proved central to the COVID-19 response at University and Medical School in Bristol, UK, underpinning serology testing, drug discovery and vaccine candidate production. SARS-CoV-2, the virus causing COVID-19, exposes a glycoprotein called Spike, the predominant COVID-19 antigen. MultiBac production and Cryo-EM revealed an unexpected druggable pocket in the SARS-CoV-2 Spike. Avenues to combat COVID-19 by exploiting the pocket we discovered, will be discussed.

3:05 His-tag vs. Strep-tag®: A Benchmarking Study for Purification from Expi Supernatants
Dennis Karthaus, MSc, Director Protein Products & Assays, IBA Lifesciences
New expression systems enable high titer production while simultaneously reducing the expression volume and time. Here we compare the efficiency of the purification of Strep-tagged versus His-tagged proteins from different Expi supernatants. Furthermore, Strep-Tactin®XT can be used in combination with IMCSTips for high throughput purification from automated systems.

3:18 Accelerating Process Development and Tech Transfer for a Biosimilar
Steven Lang, VP, Biologics, Aragen Bioscience
We demonstrate a platform-based upstream process development plan of a biosimilar protein that delivers reduced timelines to GMP manufacturing and consistent product quality. This method can be applied to ensure timely success of CHO biomanufacturing.

3:30 LIVE Q&A: Session Wrap-Up
Moderator: Frederick Boyce, MD, PhD, Assistant Professor, Neurology, and Director, MGH Gene Delivery Technology Core, Massachusetts General Hospital and Harvard Medical School
Panelists:
Imre Berger, PhD, Director, Max Planck Centre for Minimal Biology, University of Bristol
Dennis Karthaus, MSc, Director Protein Products & Assays, IBA Lifesciences
Steven Lang, VP, Biologics, Aragen Bioscience

3:50 Refresh Break - View Our Virtual Exhibit Hall

4:10 Problem Solving Breakout Discussions - Part A
This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 23: Prepping Endogenous Protein Complexes for Downstream Analysis
John LaCava, PhD, Group Leader, Laboratory of Macromolecules and Interactomes, European Research Institute for the Biology of Aging, University Medical Center Groningen

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem Solving Breakout Discussions - Part B

TABLE 24: Non-Standard Amino Acid Incorporation in Recombinant Proteins
Jesse Rinehart, PhD, Associate Professor, Cellular & Molecular Physiology, Systems Biology Institute, Yale University School of Medicine

TABLE 25: Challenges in Cell Therapy Manufacturing Development
Zhimei Du, PhD, Director, Process Development, Merck and Co., Inc.

5:30 Close of Day

THURSDAY, SEPTEMBER 3

ESCHERICHIA COLI

9:05 am Large-Scale Synthetic Human Phosphoproteomes to Decode Novel Protein-Protein Interaction Networks in *E. coli*
Jesse Rinehart, PhD, Associate Professor, Cellular & Molecular Physiology, Systems Biology Institute, Yale University School of Medicine
We have developed technologies that enable site-specific incorporation of phosphorylated amino acids into proteins by expanding the genetic code of *Escherichia coli*. I will describe our new capability to synthesize and observe phosphoproteome-scale libraries of human phosphoproteins that enable answers to systems level questions. Our work has also advanced the protein-protein interaction field by enabling the first system for large-scale genetic screening of phosphorylation-dependent protein-protein interactions.

9:25 Continuous Production with *E. coli* – USP Concepts and Strategies
Gerald Striedner, PhD, Associate Professor, Biotechnology, University of Natural Resources & Life Sciences, Vienna (BOKU)
Genetic stability of *E. coli* expression systems represents the major barrier in context with development of continuous production processes. In this talk, data from successful solutions, comprising host cell engineering (genome integrated plasmid free systems, growth decoupled systems) and USP process design strategies (multistage cultivation) will be presented and aspects for further improvements will be discussed.

9:45 Engineering *E. coli* Strains for Recombinant Protein Production
Jan-Willem de Gier, PhD, Professor, Biochemistry and Biophysics, Stockholm University
My laboratory has been using an engineering approach to create *E. coli* strains with improved properties for recombinant protein production. This will be illustrated by showing examples of the construction of strains for the production of proteins in the periplasm and in inclusion bodies in the cytoplasm.

10:10 LIVE Q&A: Session Wrap-Up
Moderator: Jesse Rinehart, PhD, Associate Professor, Cellular & Molecular Physiology, Systems Biology Institute, Yale University School of Medicine
Panelists:
Jan-Willem de Gier, PhD, Professor, Biochemistry and Biophysics, Stockholm University
Gerald Striedner, PhD, Associate Professor, Biotechnology, University of Natural Resources & Life Sciences, Vienna (BOKU)

10:30 Coffee Break - View our Virtual Exhibit Hall

ENGINEERING CHO

10:50 S-CHOice : Accelerated, High-performing Cell Line Development

John Gill, Director, CDO R&D Team, Cell Line Development, Samsung Biologics

It can be a critical decision by any institution to select right host cell line; it can impact quality, cost of goods and timeline. The presentation describes development studies of S-CHOice, Samsung's proprietary cell line, which can help achieve high quality product, adding value to Samsung's one-stop CDMO capability.

11:15 Multi-Omics Analysis of CHO Cell Lines Reveals Differences in Energy Metabolism and ER Stress

Krishnakumar Malu, PhD, Senior Engineer I, Biogen

Chinese hamster ovary cells are widely used in manufacturing monoclonal antibodies. Cellular energy metabolism and endoplasmic reticulum stress are known to greatly impact cell growth, productivity, and structure of the biotherapeutics. However, molecular mechanisms responsible for these changes are not fully understood. Here, we use multi-omics analysis to investigate differences between cell lines and gain an in-depth understanding of the biological differences that can be exploited to improve the bioprocess.

11:35 LIVE Q&A: Session Wrap-Up

Moderator: Jan-Willem de Gier, PhD, Professor, Biochemistry and Biophysics, Stockholm University
Panelists:
Krishnakumar Malu, PhD, Senior Engineer I, Biogen
John Gill, Director, CDO R&D Team, Cell Line Development, Samsung Biologics

11:55 Close of Optimizing Protein Expression

PROTEIN EXPRESSION SYSTEM ENGINEERING

Gene to Cell Line

THURSDAY, SEPTEMBER 3

HARNESSING OMICS

12:45 pm Product Quality Control Strategy Development for Non-mAb Complex Modalities by Using Combinatorial Cell Engineering and OMICS Screening Tools

Amit Kumar, PhD, Senior Scientist, Merck Research Labs

To improve understanding and increase options in developing a successful production cell line with desired product quality profile, it is important to develop diversified CHO host lineages with differences in cell growth and protein production in responding to medium and process conditions. In addition, developing predictive OMICS tools and integrating into quality control strategy are highly useful in selecting highly productive recombinant cell lines with the desired protein quality profile.

1:05 Application of Multi-Omics Analyses to Guide Rational Process Development for Recombinant Protein Expression

Hima Yalamanchili, PhD, Postdoctoral Fellow, Cell Line Development, Biogen

In biologics manufacturing, cell culture process development is conventionally driven by empirical studies and thus requires significant resources. We established a cross-program multi-omics platform that enables cross-dataset comparisons and integrated computational analyses. By incorporating multi-omics analyses into routine bioprocess development proactively, we established biological understandings of Biogen's platform cell lines and processes, and further applied the knowledge to monitor process trends, identify cell engineering targets, and guide process optimizations.

1:25 LIVE Q&A: Session Wrap-Up

Moderator: Stefan R. Schmidt, MBA, PhD, COO & Head, Operations, BioAtrium AG
Panelists:
Amit Kumar, PhD, Senior Scientist, Merck Research Labs
Hima Yalamanchili, PhD, Postdoctoral Fellow, Cell Line Development, Biogen

1:45 Session Break

2:10 Refresh Break - View our Virtual Exhibit Hall

CELL-FREE STRATEGIES

2:30 KEYNOTE PRESENTATION: New Methods for Cell-Free Presentation of Proteins for Functional Analysis

Joshua LaBaer, Executive Director, Arizona State University Biodesign Institute

Self-assembling protein microarrays made through cell-free synthesis have been used widely to study protein interactions with drugs and other proteins, to search for enzyme substrates, and to find disease biomarkers. Recent methodological advances now enable new types of studies including highly multiplexed analysis, testing the effects of post-translational changes on protein interactions and providing highly quantitative readouts with significantly reduced background noise.

2:50 Cell-Free Based Approach for Genetic Encoding of Unnatural Chemistries

Zhenling Cui, PhD, CTCB, Research Associate, Science and Engineering, Chemistry, Physics, Mechanical Engineering, Energy and Process Engineering, Queensland University of Technology (QUT)

Genetic code expansion holds the promise to revolutionize the life science and biomedicine through expanding macromolecular chemical diversity outside the natural space. We developed an engineered *Escherichia coli* cell-free system which allows rapid sequestration of selected native tRNA isoacceptors and subsequent reassignment of the liberated sense codons to unnatural amino acids. This represents a powerful tool for numerous practical applications including production of constrained peptides, antibody-drug conjugates and novel enzymes.

3:10 Co-Translational Insertion of Challenging Membrane Proteins into Nanomembranes by Cell-Free Expression

Julija Mezhyrova, MSc, Scientist, Institute of Biophysical Chemistry, Goethe University

Cell-free expression systems became key tools for the production of membrane proteins and other challenging targets. We have developed protocols to insert membrane proteins already co-translationally into supplied nanomembranes of defined composition. The generated protein/nanoparticles are suitable for biochemical and structural studies and contacts with detergents or other artificial environments are avoided. The strategy is exemplified with membrane-inserted phage toxins currently being explored as potential inhibitors of bacterial cell-wall formation.

3:30 LIVE Q&A: Session Wrap-Up

Moderator: Stefan R. Schmidt, MBA, PhD, COO & Head, Operations, BioAtrium AG
Panelists:
Joshua LaBaer, Executive Director, Arizona State University Biodesign Institute
Zhenling Cui, PhD, CTCB, Research Associate, Science and Engineering, Chemistry, Physics, Mechanical Engineering, Energy and Process Engineering, Queensland University of Technology (QUT)
Julija Mezhyrova, MSc, Scientist, Institute of Biophysical Chemistry, Goethe University

3:50 Close of Day

FRIDAY, SEPTEMBER 4

BREAKTHROUGH ADVANCES

9:05 am A General Approach to *in vitro* Protein Folding Using Nanoencapsulation

Chester Drum, MD, PhD, Assistant Professor, Translational Innovation, National University of Singapore

A novel nanoparticle can encapsulate, fold and release proteins of a wide range of sizes, charges, and disulfide content to produce improved yields and improved specific activity. Our index manuscript (Nature Communications | 8: 1442) described the concept and we have a much larger manuscript under review now which we fully expect to be published this year.

9:25 Elevating the Science via a Novel Pipetting Algorithm, 3D-Printing Technology and a Next-Generation Advanced Control Machine

Idris Mustafa, CEO & Chief Engineer, Idris Dot Solutions LLC

TipSort technology (an advanced, in-house robot pipetting algorithm) optimizes pipetting throughout a dynamic 96-position plate or tip tray. In-house CAD design married to 3D-printing fuels the crafting of custom lab inventions, spawning innovation and saving dollars. A fully-loaded Hamilton Vantage Robot enhanced with custom configuration/integrations and a built-in machine learning driven scheduler will support the future of small-scale protein expression analysis in the laboratory.

9:45 DirectedLuck transposase and gentle single cell cloning in Nanowells

ProBioGen Intelligent Biopharmaceutical Solutions

Volker Sandig, Chief Scientific Officer, ProBioGen AG

ProBioGen's travel equipment for the shortest journey to even higher mountains of cell productivity (with a high elevation base camp at pool stage)

In this talk we will assess consecutive advancements of the transposon system: genome targeting, activity and template recognition and show how this optimized system combined with the a refined ALS CellCelector platform affects the cell line development workflow and its outcome for antibodies, proteins and viral vectors.

10:10 LIVE Q&A: Session Wrap-Up

Moderator: William C.W. Chen, MD, PhD, Research Scientist, Massachusetts Institute of Technology
Panelists:
Chester Drum, MD, PhD, Assistant Professor, Translational Innovation, National University of Singapore
Idris Mustafa, CEO & Chief Engineer, Idris Dot Solutions LLC
Volker Sandig, Chief Scientific Officer, ProBioGen AG

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

APPLYING NEXT-GEN TECHNOLOGIES

10:50 The Predictive Cellular and Protein Effects of Glycoengineering

Nathan Lewis, PhD, Associate Professor, Pediatrics, University of California, San Diego (UCSD)

With most top blockbuster drugs therapeutics being glycoproteins, there is a growing interest in engineering their glycan structures for improved safety, efficacy, and manufacturing. Using our systems biology approaches, we can predict the modifications needed to effectively glycoengineer proteins. We further have explored the more global impacts glycoengineering has on the host cell, thus helping to define the design space of CHO-produced glycoproteins.

11:10 Codon and Codon-Pair Usage Tables (CoCoPUTs): Facilitating Genetic Variation Analyses and Recombinant Gene Design

Chava Kimchi-Sarfaty, PhD, Deputy Associate Director for Research, Office of Tissues and Advanced Therapies, CBER, FDA

A novel public resource that presents all codon usage, codon-pair usage and human tissue specific codon usage and codon-pair usage will be discussed. Examples of investigation areas which could greatly benefit from this resource will be provided, such as biotherapeutic development, tissue-specific genetic engineering and genetic disease prediction.

11:30 Engineering Protein Disaggregases to Counter the Protein Misfolding that Underpins Neurodegeneration

Meredith Jackrel, PhD, Assistant Professor, Department of Chemistry, Washington University in St. Louis

There are no therapies that reverse the proteotoxic misfolding events that underpin neurodegenerative diseases including amyotrophic lateral sclerosis (ALS) and Parkinson's disease (PD). Hsp104, a hexameric AAA+ protein from yeast, solubilizes disordered aggregates and amyloid but has only limited activity against human neurodegenerative disease proteins. Here I will describe approaches we have employed to re-engineer Hsp104. The engineered variants can dissolve aggregates, restore protein localization, suppress proteotoxicity, and attenuate dopaminergic neurodegeneration in animal models.

11:55 LIVE Q&A: Session Wrap-Up

Moderator: William C.W. Chen, MD, PhD, Research Scientist, Massachusetts Institute of Technology
Panelists:
Nathan Lewis, PhD, Associate Professor, Pediatrics, University of California, San Diego (UCSD)
Chava Kimchi-Sarfaty, PhD, Deputy Associate Director for Research, Office of Tissues and Advanced Therapies, CBER, FDA
Meredith Jackrel, PhD, Assistant Professor, Department of Chemistry, Washington University in St. Louis

ADVANCING MAMMALIAN CELL ENGINEERING

12:15 pm Lunch Break - View Our Virtual Exhibit Hall

12:35 Advanced Synthetic Biology Tools to Accelerate Mammalian Protein Expression System Engineering

William C.W. Chen, MD, PhD, Research Scientist, Massachusetts Institute of Technology

Conventional mammalian protein expression strategies using transient expression or random genome integration with gene of interest, followed by high-throughput colony screening and expansion, are laborious and/or time-consuming. To address those issues, we have developed a series of synthetic biology toolkits to transform mammalian protein expression system engineering. Our powerful platform technologies are versatile and can be adapted to different mammalian cell types and biomanufacturing settings to optimize complex protein production.

12:55 Exploitation of a Ribosomal Protein Mutation to Enhance Recombinant Protein Production

Kim De Keersmaecker, PhD, Research Professor, Oncology – Laboratory for Disease Mechanisms in Cancer, Katholieke Universiteit Leuven

A mutation in a ribosomal protein that we discovered in cancer cells enhances the levels of ribosomal protein translation and its fidelity and reduces cellular proteasome activity in lymphoid cell models. To validate these findings in mammalian cell lines that are commonly used in protein production, we engineered the ribosomal mutation into CHO and HEK293 cells. A 69-155% increase in production of 3 recombinant proteins was confirmed in HEK293 cells.

1:15 LIVE Q&A: Session Wrap-Up

Moderator: Amr Ali, PhD, Sr. Scientist II, Protein Analytics, Science & Technology Biologics, AbbVie
Panelists:
William C.W. Chen, MD, PhD, Research Scientist, Massachusetts Institute of Technology
Kim De Keersmaecker, PhD, Research Professor, Oncology – Laboratory for Disease Mechanisms in Cancer, Katholieke Universiteit Leuven

1:30 Close of Summit

IMMUNOGENICITY & BIOASSAYS STREAM

Ensuring the Safety and Efficacy of Biologics

This year's Immunogenicity & Bioassays Stream focuses on the latest science, technologies and strategies to ensure the safety and efficacy of novel biologics, with particular focus on new drug modalities including antibody therapies, immunotherapies, and cell & gene therapies. Part One looks at new case studies and how to use immunogenicity data in clinical settings; Part Two examines immunogenicity assessment for novel biologics such as ADCs, bispecifics, CAR-T and mAbs along with an emphasis on new regulatory guideline for cell and gene therapies; and Part Three will showcase emerging technologies and strategies for day-to-day challenges when developing bioassays to evaluate potency, function and robustness of novel biologics.

PEGS BOSTON

CONFERENCE STREAMS

2020 IMMUNOGENICITY & BIOASSAYS STREAM CONFERENCES

AUGUST 31-SEPTEMBER 1

AGENDA — Immunogenicity Case Studies and Clinical Management

SEPTEMBER 2-3

AGENDA — Immunogenicity Assessment and Regulatory Approval of Biologics

SEPTEMBER 3-4

AGENDA — Optimizing Bioassays for Biologics

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August 31-September 1 | 13th Annual

IMMUNOGENICITY CASE STUDIES AND CLINICAL MANAGEMENT

Interpretation and Mitigation Strategies in Clinical Settings

MONDAY, AUGUST 31

CLINICAL STUDIES AND MANAGEMENT

9:05 am Benefits of Prophylactic Short-Course Immunomodulation in Patients with Infantile Pompe Disease: Demonstration of Long-Term Safety and Efficacy in a Large Cohort

Ankit Desai, MBBS, Senior Research Associate, Duke University Medical Center

We have previously demonstrated that immunomodulation with a short-course of rituximab, methotrexate, and IVIG is successful in achieving immune tolerance in a large cohort of IPD patients from various treatment centers. Data presented will support this carefully planned short-course of prophylactic immunomodulation is safe and efficacious in inducing immune tolerance to ERT.

9:25 Immunogenicity Profile of Subjects Receiving 60 Mg/Day Maintenance Dose of Pegvaliase

Johanna Abend, Senior Scientist I, Immunogenicity, Translational Sciences, BioMarin Pharmaceutical, Inc.

Pegvaliase, a PEGylated bacterially-derived enzyme substitution therapy received approval from the Food and Drug Administration (FDA) for maintenance dosages up to 40 mg/day in adult patients with PKU. We will provide comprehensive immunogenicity analyses in subjects receiving 60 mg/day maintenance doses including antibody responses, circulating immune complex levels, and complement (C3 & C4) levels to support the inclusion of doses up to 60 mg/day of pegvaliase.

9:45 LIVE Q&A: Session Wrap-Up

Moderator: Sandra Garces, MD, PhD, Medical Director, Global Drug Development, Amgen Inc.
Panelists:
Ankit Desai, MBBS, Senior Research Associate, Duke University Medical Center
Johanna Abend, Senior Scientist I, Immunogenicity, Translational Sciences, BioMarin Pharmaceutical, Inc.

10:10 Session Break

10:30 Coffee Break - View our Virtual Exhibit Hall

10:50 KEYNOTE PRESENTATION: Immunogenicity in the Prescription Drug Labeling: Is It Time to Revise?

Sandra Garces, MD, PhD, Medical Director, Global Drug Development, Amgen Inc.

CASE STUDIES OF NEW MODALITIES

11:10 Early Phase Clinical Immunogenicity of Valoctocogene Roxaparvovec, an AAV5-Mediated Gene Therapy for Hemophilia A

Brian Long, PhD, Associate Director, Immunogenicity Assessment, BioMarin Pharmaceutical, Inc.

This presentation describes the clinical immunogenicity profile for Valoctocogene roxaparvovec, an AAV5 mediated gene therapy encoding FVIII for the treatment of Hemophilia A. The development and characterization of assays used to detect pre-existing AAV5 immunogenicity, and to characterize the post-dosing humoral and cellular immune responses will be discussed.

11:30 LIVE Q&A: Session Wrap-Up

Moderator: Sandra Garces, MD, PhD, Medical Director, Global Drug Development, Amgen Inc.
Panelists:
Brian Long, PhD, Associate Director, Immunogenicity Assessment, BioMarin Pharmaceutical, Inc.

11:55 Session Break

12:15 pm Lunch Break - View our Virtual Exhibit Hall

12:45 Immunogenicity Assessments in the Development of AAV Gene Therapies

Mark Milton, PhD, Executive Director, PK Sciences, Global Head Ophthalmology TA, Novartis Institutes for BioMedical Research, Inc.

The assessment of the immunogenicity is a pivotal aspect of the development of AAV-based gene therapies. The humoral and cellular immune responses can have an impact on the efficacy and/or safety of these gene therapies. This presentation will illustrate the challenges that the immune response poses to the safe and effective development of gene therapies and strategies to mitigate the impact of the immune response.

1:05 Approaches to Reduce Target Interference in the Anti-Drug Antibody Assays, a Case Study

Erik Meyer, PhD, Investigator, Bioanalysis, Immunogenicity and Biomarkers (BIB), IVIVT, R&D, GlaxoSmithKline

Once the assay was developed validated, the study results did not correlate with PK profiles and suggested some type of assay interference. Considering more information about the target that was collected during the study, the ADA assay was re-development. With the improved ADA assay and re-analyses of study samples, the results provided a more focused assessment of immunogenicity for the study.

1:25 LIVE Q&A: Session Wrap-Up

Moderator: Mark Milton, PhD, Executive Director, PK Sciences, Global Head Ophthalmology TA, Novartis Institutes for BioMedical Research, Inc.
Panelists:
Erik Meyer, PhD, Investigator, Bioanalysis, Immunogenicity and Biomarkers (BIB), IVIVT, R&D, GlaxoSmithKline

1:50 Session Break

2:10 Refresh Break - View Our Virtual Exhibit Hall

2:30 Problem Solving Breakout Discussions - Part A

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 9: Immunogenicity of PEG: Impact and Analysis

Johanna Abend, Senior Scientist I, Immunogenicity, Translational Sciences, BioMarin Pharmaceutical, Inc.
Madhukar Aryal, MS, Senior Research Associate, BioAnalytical Sciences, BioMarin Pharmaceutical, Inc.

3:00 Refresh Break - View Our Virtual Exhibit Hall

3:20 Problem Solving Breakout Discussions - Part B

TABLE 10: How to Optimize Sample Pretreatment Methods

Lynn Kamen, PhD, Senior Scientist, BioAnalytical Sciences, Genentech Inc.

3:50 Refresh Break - View our Virtual Exhibit Hall

PLENARY KEYNOTE SESSION

4:10 Chairperson's Remarks

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

4:15 KEYNOTE PRESENTATION: From Energy to Machine Learning

George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School

We've engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing, before abruptly moving to "sequence-only" deep machine learning for protein design – from fluorescent proteins to AAV capsids to antibodies. When combined with

libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

4:40 KEYNOTE PRESENTATION: The Case for Intelligent Design in Protein Engineering

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

Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing a so-called "intelligent design" approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

5:15 Live Q&A: Session Wrap-Up

Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

5:35 Happy Hour - View our Virtual Exhibit Hall

6:10 Close of Day

TUESDAY, SEPTEMBER 1

CASE STUDIES OF NEW MODALITIES

9:00 am Industry Overview

Darshana Jani, PhD, Director, Global Bioanalysis, Agenus

9:05 Harmonization of Immunogenicity Bioanalytical Reports

Laura Hay, PhD, Associate Director, PPD Inc.

Immunogenicity Bioanalytical Report Harmonization committee has organized to align reporting strategies for clinical immunogenicity studies across industry and regulatory authorities. To comply with regulatory recommendations on anti-drug antibody and neutralizing antibody validations, this team is working to standardize the presentation of bioanalytical immunogenicity data to facilitate filings to health authorities. This AAPS sponsored effort is supported by ~50 industry representatives.

9:25 Characterization of Immune Response to Bispecific Antibody Therapeutics

Kate Peng, PhD, Associate Director/Senior Scientist, BioAnalytical Sciences, Genentech

Bispecific mAbs (bsmAbs) are a novel class of mAbs that aim to improve drug efficacy by simultaneously working on two targets. This is a relatively new approach with limited experiences in clinical development. This presentation will use case studies to discusses our strategy for assessing the anti-drug antibody (ADA) responses to the bsmAb and summarizes the characterization results as well as the clinical impact of ADAs on drug exposure and safety.

9:45 LIVE Q&A: Session Wrap-Up

Moderator: Darshana Jani, PhD, Director, Global Bioanalysis, Agenus
Panelists:
Laura Hay, PhD, Associate Director, PPD Inc.
Kate Peng, PhD, Associate Director/Senior Scientist, BioAnalytical Sciences, Genentech

10:10 Session Break

10:30 Coffee Break - View our Virtual Exhibit Hall

10:50 Insight into Mechanisms of Immunogenicity Following Treatment with Therapeutic Monoclonal Antibodies

Yariv Wine, PhD, Assistant Professor, Molecular Cell Biology and Biotechnology, Tel Aviv University, Israel

Utilising NGS and proteomics we found that the B-cell response following mAb administration is a vaccine-like response that may be induced by immunocomplexes and that the response is diverted to the marginal zone rather to the germinal centers. The data obtained in the study will help to assess the immunogenicity of biologics under development and help to revise treatment strategies that may result in increased drug efficacy.

11:10 Development of a Novel Dendritic Cell-based Antibody Loading Assay to Predict Immunogenicity of Biotherapeutics

Lynn Kamen, PhD, Senior Scientist, BioAnalytical Sciences, Genentech Inc.

A key component of the immune response is the uptake of antibody by antigen presenting cells (APCs) such as dendritic cells. This presentation will highlight the development of a dendritic cell (DC) loading assay that measures antibody internalization and shows that highly immunogenic antibodies are internalized to a higher degree than antibodies with low immunogenicity.

11:30 LIVE Q&A: Session Wrap-Up

Moderator: Darshana Jani, PhD, Director, Global Bioanalysis, Agenus
Panelists:
Yariv Wine, PhD, Assistant Professor, Molecular Cell Biology and Biotechnology, Tel Aviv University, Israel
Lynn Kamen, PhD, Senior Scientist, BioAnalytical Sciences, Genentech Inc.

11:55 Session Break

12:15 pm Lunch Break - View our Virtual Exhibit Hall

IMMUNOGENICITY RISK ASSESSMENT AND MITIGATION

12:50 Increased Immunogenicity Associated with Combination Regimens with Immune Modulatory Biologic

Vibha Jawa, PhD, Director, Predictive & Clinical Immunogenicity, PK PD & Drug Metabolism, Merck & Co., Inc.

The use of immune modulatory biologics to augment functionality of immune cells can also augment the risk of immunogenicity. The quality of such an immune response and its clinical relevance will be explored through this talk. Whether the activation of immune cells can break tolerance to otherwise tolerant sequences will also be explored.

1:10 Preclinical Immunogenicity Risk Assessment and Lead Optimization for Novel Biological Therapeutic Modalities

Jochem Gokemeijer, PhD, Associate Director, Molecular Discovery Technologies, Bristol-Myers Squibb

This talk will describe the drug development workflow and tools to identify and engineer lead therapeutic biologics with reduced immunogenicity risk. Novel biological modalities can have multiple pathways to an anti-therapeutic immune response and that require modification of tools and assays.

1:30 LIVE Q&A: Session Wrap-Up

Moderator: Vibha Jawa, PhD, Director, Predictive & Clinical Immunogenicity, PK PD & Drug Metabolism, Merck & Co., Inc.
Panelists:
Jochem Gokemeijer, PhD, Associate Director, Molecular Discovery Technologies, Bristol-Myers Squibb

1:55 Session Break

2:15 Refresh Break - View our Virtual Exhibit Hall

ASSESSMENT OF PRE-EXISTING REACTIVITY

2:35 Importance of Pre-Existing Abs to the Viral Capsid during Immunogenicity Assessment of Viral Vectors-Based Gene Therapy

Jim McNally, PhD, Principal, McNally Bioanalytical Consulting

This talk will focus on the assessment of pre-existing antibodies to the viral capsid and the implications for their impact on the successful dosing of gene therapy drug candidates. Case studies will show how the

thought process about pre-existing antibodies is evolving. There will be a focus on the tools used to measure pre-existing antibodies against the viral capsid and their utilization as exclusion criteria for entry into clinical studies.

2:55 Investigation of Pre-Existing Reactivity to Biotherapeutics Can Uncover Potential Immunogenic Epitopes and Predict Immunogenicity Risk

Nicoletta Bivi, PhD, Director, Assay Development, Immunogenicity and Immunoassays, Laboratory for Experimental Medicine (LEM), Eli Lilly and Company

In this study, we use ADA assays to measure pre-existing reactivity, i.e. the ability of a molecule to produce an ADA-like response in normal human serum. The magnitude of pre-existing reactivity correlates with clinical immunogenicity. Furthermore, the domain specificity was the same in pre-existing ADA as in TE-ADA. Based on this, magnitude and domain specificity of pre-existing reactivity can be a powerful tool to understand the immunogenic potential of biotherapeutics.

3:15 LIVE Q&A: Session Wrap-Up

Moderator: Vibha Jawa, PhD, Director, Predictive & Clinical Immunogenicity, PK PD & Drug Metabolism, Merck & Co., Inc.
Panelists:
Jim McNally, PhD, Principal, McNally Bioanalytical Consulting
Nicoletta Bivi, PhD, Director, Assay Development, Immunogenicity and Immunoassays, Laboratory for Experimental Medicine (LEM), Eli Lilly and Company

3:35 Close of Immunogenicity Case Studies and Clinical Management

September 2-3 | 13th Annual

IMMUNOGENICITY ASSESSMENT AND REGULATORY APPROVAL OF BIOLOGICS

Establishing Effective Prediction and Validation of Assays

WEDNESDAY, SEPTEMBER 2

DRUG TOLERANCE AND INTERFERENCES

9:25 am Fully Automated Cell-Based Binding Neutralizing Antibody Assay on MSD Platform

Weifeng Xu, PhD, Principal Scientist & Group Leader, PPDM, Merck Research Labs

The newest FDA Immunogenicity Testing Guidance mentioned that LBA could be developed for antagonistic mAb NAb assay. However, in the case of dual-receptors drug target or hard-to-express drug target/ligand, it is also very challenging to have LBA NAb assay. Here, we share a case study of fully automated NAb assay development and validation using a MSD-based cell binding assay.

9:45 Successful Integration of Pre-clinical Immunosafety Risk Assessment into the Drug Development Process

Lonza Pharma & Biotech

Noel Smith, PhD, Head, Immunology, Lonza Biologics

Immunogenicity and Immunotoxicity are common challenges to address during drug development and can impact both the efficacy and safety of the drug. To assess these risks, a variety of tools can be applied during preclinical development. These include a range of different human primary cell assays to assess the innate and adaptive immune response to the drug as well as both target and off-target mediated immune reactions. This presentation will focus on an overview of these human primary cell assays and how studies can be designed and executed for the assessment of immunogenicity and immunotoxicity risk during preclinical development.

10:10 LIVE Q&A: Session Wrap-Up

Moderator: Boris Gorovits, PhD, Senior Director, Pharmacokinetics, Pharmacodynamics & Metabolism, Pfizer Inc.
Panelists:
Weifeng Xu, PhD, Principal Scientist & Group Leader, PPDM, Merck Research Labs
Noel Smith, PhD, Head, Immunology, Lonza Biologics

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

10:55 ADA Analysis Demonstrates the Potential Impact of Insufficient Drug Tolerance

Kelli Phillips, PhD, Associate Director, PPD

An ELISA method with Acid Dissociation was developed for the detection of ADA against a biosimilar therapeutic at PPD (2015). Pre-validation data indicated that the method was able to detect up to 100 ng/mL of the positive control in the presence of 43.3 mcg/mL drug. This degree of drug tolerance was predicted to be fit-for-purpose for sample analysis.

ANTI-DRUG ANTIBODIES – KEEP CALM AND CARRY ON

11:15 Immunogenicity Risk Factors Associated with Multi-Domain Biotherapeutics

Boris Gorovits, PhD, Senior Director, Pharmacokinetics, Pharmacodynamics & Metabolism, Pfizer Inc.

Compounds containing two or more structural domains with a distinct mode of action-relevant functionality have been defined as multi-domain biotherapeutics (MDB). Several modalities, including endogenous protein fusions with Fc fragment or another polypeptide, bispecific antibodies, antibody-drug conjugates, as well as polyethylene glycol conjugates, have been viewed as examples of MDB type.

11:35 LIVE Q&A: Session Wrap-Up

Moderator: Boris Gorovits, PhD, Senior Director, Pharmacokinetics, Pharmacodynamics & Metabolism, Pfizer Inc.
Panelists:
Kelli Phillips, PhD, Associate Director, PPD

12:00 pm Session Break

12:20 Lunch Break - View our Virtual Exhibit Hall

12:45 Evaluation of Statistical Approaches for the Monitoring of Anti-Drug Antibody (ADA) Assay Performance during Clinical Development

Ching-Ha (Vicky) Lai, PhD, Senior Staff Scientist, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.

It is expected that immunogenicity will be monitored throughout the clinical development program of a biotherapeutic. The ADA assay used to monitor immunogenicity is needed to support multiple clinical studies through different development phases, over several years. Thus, it is important to have an assay life cycle management process in place, which monitors assay performance over time and in different clinical indications.

REGULATORY PERSPECTIVES

1:05 FDA Guidance on Bi- and Tri-Platforms

Mark Ma, PhD, Executive Director, Bioanalytical Development, Alexion Pharmaceuticals, Inc.

The FDA has licensed two bispecific antibodies (BsAbs) and the number in clinical development has steadily increased in recent years. I will discuss the current expectation and guideline from the FDA for novel modalities with a focus on bi- and tri-specific antibodies.

1:25 LIVE Q&A: Session Wrap-Up

Moderator: Mark Ma, PhD, Executive Director, Bioanalytical Development, Alexion Pharmaceuticals, Inc.
Panelists:
Ching-Ha (Vicky) Lai, PhD, Senior Staff Scientist, Bioanalytical Sciences, Regeneron Pharmaceuticals, Inc.

1:50 Session Break

2:10 Refresh Break - View our Virtual Exhibit Hall

2:25 KEYNOTE PRESENTATION: New Technologies and Approaches to Assess and Circumvent Immunogenicity

Wojciech Jankowski, PhD, Commissioner's Fellow, CBER, FDA

We will describe examples of the use of novel assays to assess immunogenicity and use the information to de-immunize therapeutic-proteins. I will give examples how we: evaluated and re-designed immunogenic rFVIIa analog (Vatreptacog Alfa); redesigned variants exhibiting both desired functional activity and reduced immunogenicity-risk; evaluated plasma-derived FVIII vs. recombinant FVIII using the MAPPs assay; and gave the explanation for clinical findings.

2:45 Development and Validation of a Sensitive and Drug Tolerant Anti-PEG Antibody Assays

Madhukar Aryal, MS, Senior Research Associate, BioAnalytical Sciences, BioMarin Pharmaceutical, Inc.

In vitro drug tolerance assessments of an anti-PEG antibody assay suggested potential interference from high levels of pegylated therapeutic in serum samples. This presentation will discuss a Biotin-PEG Extraction Acid Dissociation (BEAD) strategy that reduced the concentration of pegylated protein and matrix components in samples before assay, and improved anti-PEG antibody assay drug tolerance.

3:05 LIVE Q&A: Session Wrap-Up

Moderator: Wojciech Jankowski, PhD, Commissioner's Fellow, CBER, FDA
Panelists:
Madhukar Aryal, MS, Senior Research Associate, BioAnalytical Sciences, BioMarin Pharmaceutical, Inc.

3:30 Session Break

3:50 Refresh Break - View Our Virtual Exhibit Hall

4:10 Problem Solving Breakout Discussions - Part A

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem Solving Breakout Discussions - Part B

TABLE 26: Fully Automated Cell-Based Binding Neutralizing Antibody Assay on MSD Platform

Weifeng Xu, PhD, Principal Scientist & Group Leader, PPDM, Merck Research Labs

5:30 Close of Day

THURSDAY, SEPTEMBER 3

PREDICTIVE IMMUNOGENICITY ASSAYS

9:05 am Current Practice in Predicting Immunogenicity of Biopharmaceuticals for Candidate Selection and Risk Management

Timothy Hickling, PhD, Immunogenicity Sciences Lead, Pfizer Inc.

Immunogenicity prediction through *in silico* and *in vitro* assays is widely employed for screening and selection of candidate biopharmaceuticals across our industry. During clinical development, these techniques, together with mathematical modeling and simulation, can help to understand the overall immunogenicity risk, pointing towards immunogenicity risk management strategies. I will review current practice and provide examples across the drug discovery and development pipeline.

9:25 A Case Study on Prediction of Immunogenicity Potential of Therapeutic Proteins

Sivan Cohen, PhD, Scientist, Genentech

Immunogenic response, such as generation of anti-drug antibodies (ADA), against biotherapeutic products can have detrimental effects on drug safety, efficacy, and pharmacokinetics. Therefore, prediction and quantification of the risk for immunogenicity of therapeutic protein drugs before clinical trials is a crucial need.

9:45 Mastering Immunogenicity in Biologics Development

PROIMMUNE www.proimmune.com

Jeremy Fry, Director of Sales, ProImmune

Immunogenicity is one of the most complex issues to address in drug design and development and requires intelligent application of integrated platforms to mitigate the risk to your biologic. In this talk I will present case studies to illustrate the range of solutions that ProImmune provides including DC-T/T cell proliferation assays for lead selection/optimization, MAPPS assays for characterization of antigen presentation; HLA-peptide binding assays to characterize individual epitopes & undiluted whole blood cytokine storm assays.

10:10 LIVE Q&A: Session Wrap-Up

Moderator: Timothy Hickling, PhD, Immunogenicity Sciences Lead, Pfizer Inc.
Panelists:
Sivan Cohen, PhD, Scientist, Genentech
Jeremy Fry, Director of Sales, ProImmune

10:30 Coffee Break - View our Virtual Exhibit Hall

10:50 Learning the Rules of HLA Class II Antigen Presentation from *in-vitro* Binding and MS Eluted Ligand Data: Applications for Epitope Discovery and Immunogenicity Prediction

Morten Nielsen, Professor, PhD, Department of Health Technology, The Technical University of Denmark & Instituto de Investigaciones Biotecnológicas, Universidad Nacional de San Martín, Argentina

11:10 Case Study for In-Study Cut Point Evaluations According to the 2019 FDA Guidance

Megan Wiberg, Associate Director, PPD, Inc.

Validation of immunogenicity assays results in cut points that may or may not be relevant when applied to the study population once the method is implemented for clinical study support. The potential for the validated cut point to be unsuitable during sample analysis should be considered when determining cut point strategies during method validation.

11:30 LIVE Q&A: Session Wrap-Up

Moderator: Timothy Hickling, PhD, Immunogenicity Sciences Lead, Pfizer Inc.
Panelists:
Morten Nielsen, Professor, PhD, Department of Health Technology, The Technical University of Denmark & Instituto de Investigaciones Biotecnológicas, Universidad Nacional de San Martín, Argentina
Megan Wiberg, Associate Director, PPD, Inc.

11:50 Close of Immunogenicity Assessment and Regulatory Approval of Biologics

THURSDAY, SEPTEMBER 3

NOVEL ASSAY TYPES

12:45 pm Bioassay Strategies for Innovative Molecules

Natalia Kozhemyakina, PhD, Head, Bioassay, BIOCAD

It is extremely important to be sure that we create methods that reflect MoA, especially in cases of multiple MoA, and at the same time is accurate. It is well known how potency assay can be variable, laborious, and time consuming with its long multi-stage protocols. The presentation provides case studies of development strategies for innovative molecules and highlights best practices for handling the most common issues in biological assay development.

1:05 Uh-Oh, Our Primary Standard Isn't Stable: What Do We Do Now?

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

Setting: a product with primary standard nearing expiry (pivotal clinical lots and the original standard have expired). Problem: recent confirmation that the primary standard is not stable. How to assign potency to new primary standard? Solution: model potency of all samples in all assays allowing for variation within assay, between assay, between lots, and among degradation rates for lots; use this model to assign the potency of the new standard.

1:25 LIVE Q&A: Session Wrap-Up

Moderator: Kaitlyn Barago, Assoc Dir, Production, Cambridge Healthtech Institute
Panelists:
David Lansky, PhD, President, Precision Bioassay, Inc.
Natalia Kozhemyakina, PhD, Head, Bioassay, BIOCAD

1:45 Refresh Break - View our Virtual Exhibit Hall

STANDARDS AND REGULATORY CONSIDERATIONS

2:25 Chairperson's Remarks

Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP

2:30 Principles and Practices for Bioassay Standards

Tim Schofield, Owner & Consultant, CMC Sciences LLC

Standards are essential to the development and control of biological products. Considering their importance, there is no consensus on the source of a standard, the basis and means of standard qualification, and stability evaluation. This talk will discuss principles and practices related to standards used to report potency of biological products and propose strategies. Those proposals will borrow from practices related to quality by design, highlighting fitness-for-use of a standard.

2:50 Current Efforts in Bioassay Standardization

Dawn Henke, PhD, Senior Technical Program Manager, Standards Coordinating Body

This discussion will cover standards for regenerative medicine products. Discussion will focus on standards for bioassays, published standards and how to implement these standards be addressed. An overview of current standards under development and how to get involved, as well as a forum for questions will be provided.

3:10 Panel Discussion : Standards and Regulatory Considerations

Moderator: Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP

- Setting standards for new bioassay modalities including cell & gene therapies and immunotherapies
- Developing standards and using already-established standards
- Getting involved with standard-setting organizations
- Qualification of standards
- Correction of relative potency when changing standards

Panelists:
Dawn Henke, PhD, Senior Technical Program Manager, Standards Coordinating Body
Tim Schofield, Owner & Consultant, CMC Sciences LLC

3:50 Close of Day

FRIDAY, SEPTEMBER 4

BIOASSAY DEVELOPMENT FOR INSULIN

9:00 am Chairperson's Remarks

Marla Abodeely, PhD, Director of Bioassay, Analytical Sciences & Technology, Sanofi

9:05 FEATURED PRESENTATION: Metabolic Functional Bioassay Development for Monoclonal Antibodies and Insulins

Carole A.C. Sourbier, PhD, Principal Investigator, Office of Biotechnology Products, OPQ, FDA CDER

It is expected that the potency of the insulin and of their associated biosimilars will be assessed quantitatively in a bioassay that represents product MoA. Current recommendations include rabbit bioidentity test to assess the biological activity of insulins. However, it is likely that bioassays will be submitted for assessing the potency of insulins products. This presentation highlights some aspects of metabolic functional assays for development and product characterization for insulin products.

9:25 Development of a Robust Functional Cell-Based Assay for Replacing the Rabbit Blood Sugar Bioidentity Test of Insulin Analog

Junming Yie, PhD, Principal Scientist, Biologics Analytical, Merck

A rabbit blood sugar bioidentity assay is required by the FDA to evaluate biological activity for insulin analogs per USP guideline. Many live animals used, and the method is also highly variable and expensive. A cell-based assay was developed by utilizing insulin's role in regulating hepatic gluconeogenesis pathway. This assay was qualified to demonstrate its performance and was further evaluated on its robustness using DoE approach.

9:45 LIVE Q&A: Session Wrap-Up

Moderator: Marla Abodeely, PhD, Director of Bioassay, Analytical Sciences & Technology, Sanofi
Panelists:
Carole A.C. Sourbier, PhD, Principal Investigator, Office of Biotechnology Products, OPQ, FDA CDER
Junming Yie, PhD, Principal Scientist, Biologics Analytical, Merck

10:05 Session Break

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

CASE STUDIES IN BIOASSAY DEVELOPMENT

10:45 Chairperson's Remarks

Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP

10:50 KEYNOTE PRESENTATION: Best Practices in Bioassay Development to Support Registration of Biopharmaceuticals

Marla Abodeely, PhD, Director of Bioassay, Analytical Sciences & Technology, Sanofi

Developing bioassays is a complex undertaking that needs to address several challenges including modelling all of the MoA associated with the biotherapeutic. Bioassay development is also an exciting and fast evolving field, not only from a scientific, medical and technological point of view, but also in terms of statistical approaches and regulatory expectations. This has led to an industry-wide discussion on the most appropriate ways to develop bioassays throughout the lifecycle.

11:10 Statistical Model Selection Using USP

Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP

Relative potency is a measure obtained from the comparison of a test sample to a standard based on the capacity to produce the expected biological activity. USP presents several different models and suitability criteria to determine the reliability of the estimate. This talk will cover traditional linear and non-linear bioassay models with an emphasis on model suitability including parallelism.

11:30 Measurement Assurance, Control Strategies and Documentary Standards for the Development of Bioassays for Cell Therapy

Sumona Sarkar, PhD, Biomedical Engineer, Biosystems and Biomaterials Division, Biomaterials Group, National Institute of Standards and Technology

11:50 Critical Reagents Characterization Strategy to Support Biologics/Vaccines Projects at Regulated Bioanalysis

Kun Yang, PhD, Associate Principal Scientist, PPDM, Merck Research Labs

At the heart of bioassays for biologics are critical reagents used to directly or indirectly measure biologic markers or signals. A comprehensive analytical toolbox of biochemical, functional and biophysical methods has been developed to evaluate the quality of critical reagents. Several case studies, including reagents, troubleshooting and comparison of small scale hybridoma and large-scale recombinant protein, lifecycle management of biologics, developing reference material, emerging standards and regulatory frameworks, will be presented.

12:10 pm LIVE Q&A: Session Wrap-Up

Moderator: Steven Walfish, Principal Scientific Liaison, Global Science & Standards, USP
Panelists:
Marla Abodeely, PhD, Director of Bioassay, Analytical Sciences & Technology, Sanofi
Sumona Sarkar, PhD, Biomedical Engineer, Biosystems and Biomaterials Division, Biomaterials Group, National Institute of Standards and Technology
Kun Yang, PhD, Associate Principal Scientist, PPDM, Merck Research Labs

12:30 Close of Summit

DISCUSSIONS

Engage in in-depth discussions with industry experts and your peers about the progress, trends and challenges you face in your research!

BIOCONJUGATES STREAM

Ushering in a New Wave of Antibody-Drug Conjugates Therapy

The field of ADCs has experienced its fair share of ups-and-downs on the road to clinic and regulatory approvals. Finally, this year we saw the approval of POLIVY™, with several other ADCs showing big promise on their road to approval. To highlight the dynamic landscape, CHI's Bioconjugates Stream will bring together the movers and shakers of the industry to our 2-part Antibody-Drug Conjugates program:

Part 1: Engineering Antibody-Drug Conjugates invites scientists to discuss novel design strategies to engineer the right ADC components, using novel payloads, alternative antibody effector moiety platforms, and/or creative linker/conjugation technologies.

Part 2: Clinical Progress of Antibody-Drug Conjugates invites investigators to share their latest results from preclinical to clinical trials, lessons learned from past ADC programs and related fields to inform next-gen ADC design, and to develop better predictability for translation from bench to clinic.

PEGS BOSTON

CONFERENCE STREAMS

2020 BIOCONJUGATES STREAM CONFERENCES

SEPTEMBER 2-3

AGENDA Engineering Antibody-Drug Conjugates

SEPTEMBER 3-4

AGENDA Clinical Progress of Antibody-Drug Conjugates

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ENGINEERING ANTIBODY-DRUG CONJUGATES

Innovations in Next-Generation ADC Design

WEDNESDAY, SEPTEMBER 2

PRECLINICAL OUTCOMES AND TRANSLATION TO CLINIC

12:40 pm OPENING REMARKS & KEYNOTE PRESENTATION: Key Learnings from Successful and Failed ADCs

Rakesh Dixit, PhD, President & CEO, Bionavigen

With seven approved ADCs and the great potential of approval of at least 4 additional ADCs in the next 2 years, there is renewed enthusiasm and momentum in the world of oncolytic ADCs. However, the success in oncolytic ADCs has come with high failures. The presentation will provide a comprehensive review of success factors and top 5 lessons learned from the development of ADCs in the past two decades.

1:05 Application of PK/PD M&S for Preclinical-to-Clinical Translation of ADCs

Dhavalkumar K. Shah, PhD, Associate Professor, Pharmaceutical Sciences, State University of New York at Buffalo

This talk will highlight how preclinical experiments can be used in conjunction with PK/PD modeling and simulation to support the discovery, development and preclinical-to-clinical translation of novel ADCs. The talk will also focus on novel P/PD-based strategies to improve the therapeutic index of ADCs.

1:25 MGTA-117: An Anti-CD117 Antibody Drug Conjugate (ADC) Designed for Patient Conditioning for Stem Cell Transplant and Gene Therapy Provides a Broad Therapeutic Window Across Species

Rahul Palchaudhuri, PhD, Senior Scientist, Magenta Therapeutics

Patient outcomes can be greatly improved by a bone marrow transplant in multiple disease settings. Prior to transplant, patients are conditioned by removing their own bone marrow stem cells using poorly tolerated toxic, non-selective chemotherapy and radiation. This presentation will highlight preclinical POC data demonstrating that ADCs may be safer, targeted agents for patient preparation by extending the use of curative bone marrow transplant and improving outcomes for patients.

1:45 Live: Q&A and Session Wrap Up

Moderator: Dhavalkumar K. Shah, PhD, Associate Professor, Pharmaceutical Sciences, State University of New York at Buffalo
Panelists:
Rakesh Dixit, PhD, President & CEO, Bionavigen
Rahul Palchaudhuri, PhD, Senior Scientist, Magenta Therapeutics

2:10 Refresh Break - View our Virtual Exhibit Hall

NEW & SPECIALTY PAYLOADS

2:25 Targeted C'Dot-Drug Conjugates for the Treatment of Cancer

Gregory P Adams, PhD, CSO, Elucida Oncology Inc

C'Dot Drug Conjugates (CDCs) are ultra-small (sub-10nm) targeted organic-silica hybrid bio-material nanodrug conjugates that have a payload capacity 10 times higher than antibodies. The ultra-small size of CDCs facilitates both effective tumor penetration, including the ability to mediate drug delivery across a disrupted blood brain barrier, and efficient systemic elimination which can reduce toxicities associated with prolonged residence in the circulation. Elucida Oncology developmental platform will be presented.

2:45 IMB-213: A Novel Secretome-Targeted Biologic for the Selective Delivery of Immunomodulatory Payloads to Solid Tumors

Anton Neschadim, PhD, MBA, CEO & Director, ImmunoBiochem Corporation

Strategies harnessing the potential of the innate immune system in cancer therapy are yielding promising clinical results. To improve on the current approaches, the targeted delivery of immunomodulatory payloads, such agonists of the (STING) pathway, could yield a tunable platform for achieving increased efficacy and safety. ImmunoBiochem is utilizing its cancer secretome-targeted biologics platform to deliver high-potency immunomodulatory payloads selectively to the immune cells and stroma within the tumor microenvironment.

3:05 Novel SMARTag™ Linkers Enable Better-Tolerated ADCs

Robyn Barfield, PhD, Group Leader, Chemical Biology, Catalent, Biology, Catalent

SMARTag™ technology uses a simple, robust manufacturing process to generate stable, site-specific ADCs. Our RED-106 noncleavable maytansine linker-payload is resistant to P-glycoprotein efflux, offering wider therapeutic windows as compared to other technologies. This advantage is illustrated by our anti-HER2 RED-106 ADC in comparison to the related drug, T-DM1.

3:30 Live Q&A: Q&A and Session Wrap-Up

Moderator: Anton Neschadim, PhD, MBA, CEO & Director, ImmunoBiochem Corporation
Panelists:
Gregory P Adams, PhD, CSO, Elucida Oncology Inc
Robyn Barfield, PhD, Group Leader, Chemical Biology, Catalent, Biology, Catalent

3:50 Refresh Break - View Our Virtual Exhibit Hall

4:10 Problem Solving Breakout Discussions - Part A

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 27: ADC Targets and Payloads: When Friends Become Foes

Rakesh Dixit, PhD, President & CEO, Bionavigen

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem Solving Breakout Discussions - Part B

TABLE 28: Antibody Engineering Approaches to Improve the Therapeutics Index of ADCs

Dhavalkumar K. Shah, PhD, Associate Professor, Pharmaceutical Sciences, State University of New York at Buffalo

5:30 Close of Day

THURSDAY, SEPTEMBER 3

ENGINEERING THE ANTIBODY EFFECTOR MOIETY

9:05 am Antibody Fragment Drug Conjugates (FDCs): Expanding the Target Repertoire

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

Antikor's HER2 FDC (ANT-043) is in advanced development but our toolbox of antibody libraries and linker-payloads have yielded our second new FDC candidate (ANT-045). We will present compelling new discovery data that helps us understand the strengths of our novel platform and tumour cure efficacy data for ANT-045 for gastro-intestinal cancers, with uptake and imaging data to support our technological approach.

9:25 Engineered Avibodies (Enhanced Diabodies) Precisely Loaded with Novel ADC Payloads that Surpass IgG-ADCs in Cancer Therapy

Peter J. Hudson, PhD, Chief Scientist and CSO, Victorian Cancer Biologics Consortium, Avipep Pty Ltd.

Avibodies™ comprise unique surface disulphides for precise loading of drug payloads with superior tumor xenograft regression compared to conventional IgGs (targeting CD30). PK has been demonstrated in a Phase 1 clinical trial. With TagWorks NV2, Avibodies pre-target and upload tumors with the ADC-drug subsequently released by a systemic

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activator. In summary, Avipep's novel Avibody designs enable precise site-specific loading of drug and isotope payloads for cancer imaging and ADC therapy.

9:45 Antibody-Drug Conjugates (ADCs) and Small-Molecule Drug Conjugates (SMDCs): A Comparative Analysis
Dario Neri, PhD, Full Professor, Chemistry & Applied Biosciences, ETH Zurich
Antibody-drug conjugates (ADCs) and small-molecule drug conjugates (SMDCs) represent two conceptually related strategies for the targeted delivery of potent cytotoxic agents to various types of cancer. In this lecture, I will present a comparative analysis of therapy and biodistribution results in mouse models of cancer, as well as clinical data and information on how ADCs and SMDCs can be potentiated using targeted cytokine therapeutics.

10:10 Q&A and Session Wrap-Up
Moderator: Dario Neri, PhD, Full Professor, Chemistry & Applied Biosciences, ETH Zurich

10:30 Coffee Break - View our Virtual Exhibit Hall

SITE-SPECIFIC CONJUGATION & LINKER TECHNOLOGIES

10:50 Conjugating Payloads to Native Antibodies without the Need of Any Prior Antibody Engineering in a Single or Two Steps
Philipp Spycher, PhD, CEO, Araris Biotech AG
We will introduce a new linker antibody-conjugation technology that enables site-specific payload attachment to native antibodies 'off-the-shelf' in one or two steps without prior engineering. Our linkers enable the incorporation of various functional chemistries and a loading of 2, 4 drugs, or even 2 different drugs in one ADC. We found that the resulting ADCs have favorable physicochemical properties and showed very efficient anti-tumor responses in efficacy studies.

11:10 UV-NBS Site-Specific Antibody Conjugation
Nathan J. Alves, PhD, Assistant Professor, Emergency Medicine, Indiana University
Antibody modification is often necessary to endow antibodies with non-native capabilities from antibody-drug conjugates (ADCs) for targeted therapeutics to fluorescent reporter molecules for use in diagnostic or imaging applications. This session will explore site-specific antibody modification through conjugation to the conserved antibody nucleotide binding site (NBS) and will demonstrate how various linkers and conjugation strategies can be utilized to leverage the UV-NBS technology for use in next-gen antibody pharmaceuticals.

11:30 Live Q&A: Q&A and Session Wrap-Up
Moderator: Tony Joseph A. D'Alessio, PhD, Senior Research Investigator/ Lab Head, Oncology Biotherapeutics, Novartis Institutes for BioMedical Research, Inc.
Panelists:
Philipp Spycher, PhD, CEO, Araris Biotech AG
Nathan J. Alves, PhD, Assistant Professor, Emergency Medicine, Indiana University

11:50 Close of Engineering Antibody-Drug Conjugates

September 3-4 | 10th Annual

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

Clinical Updates and Lessons Learned

Part of ONCOLOGY STREAM

THURSDAY, SEPTEMBER 3

12:40 pm Antibody-Drug Conjugates Industry Overview
John M Lambert, PhD, Independent Consultant

LESSONS LEARNED FROM PAST ADC PROGRAMS AND RELATED FIELDS - PART I

12:45 KEYNOTE PRESENTATION: Ugly Ducklings: Why Clinically Effective Antibody-Drug Conjugates May Not Look that Pretty (at First)…And How to Spot Them
Greg M. Thurber, PhD, Assistant Professor, Chemical Engineering & Biomedical Engineering, University of Michigan
Here, I present a 'systems' approach for designing ADCs and describe when the most potent ADC *in vitro*, the most effective ADC *in vivo*, and/or the least toxic ADC in animal models may not be the most effective drug in the clinic. This 'systems' approach can help ensure the most clinically effective agents, often 'ugly ducklings' in the pipeline, thrive in the end.

1:05 Microdistribution of Antibody Distribution in Clinical Trials Using Fluorescently Labeled Anti-EGFR Antibody in Multiple Tumor Types
Eben L. Rosenthal, MD, John and Ann Doerr Medical Director, Stanford University
Systemically-administered labeled antibodies in cancer patients prior to surgery has allowed us to successfully measure antibody concentration in normal and tumor tissues. The biggest impact of this strategy is the ability to localize the antibody within tissues at the cellular level. We hypothesize that near-infrared, fluorescently labeled antibodies can be leveraged to estimate the dose at which the antibody reaches maximal tumor saturation, most notably for antibody-drug conjugates.

1:25 Modeling Target-Mediated Drug Disposition to Design More Effective Therapeutics
Donald E. Mager, PharmD, PhD, Professor & Vice Chair, Pharmaceutical Sciences, SUNY Buffalo
Target-mediated drug disposition (TMDD) is a case in which binding of a drug to its pharmacological target influences the pharmacokinetics of the drug. This phenomenon represents a major distribution/elimination process for many antibody-based constructs. This talk will review the basic tenets of TMDD, highlight how computational modeling of TMDD is being used to guide the design and development of antibodies and antibody-drug conjugates, and potential clinical implications of TMDD.

1:50 Refresh Break - View our Virtual Exhibit Hall

LESSONS LEARNED FROM PAST ADC PROGRAMS AND RELATED FIELDS - PART II

2:30 A New Mechanism of Malignant Cell Resistance to Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)
Louis M. Weiner, MD, Professor & Director, Oncology, Lombardi Comprehensive Cancer Center, Georgetown University
ADCC provides a model for uncovering immune resistance mechanisms. We have continuously exposed different cancer cell lines to KIR-deficient NK92-CD16V effector cells and ADCC-promoting monoclonal antibodies. We show that the induction of ADCC resistance involves genetic and epigenetic changes that lead to a general loss of target cell adhesion properties required for the establishment of an immune synapse, killer cell activation, and target cell cytotoxicity.

2:50 Radiohapten Capture Radioimmunotherapy for Cures of Human Tumor Xenografts in Mice
Steven M. Larson, MD, Donna & Benjamin M. Rosen Chair, Lab Head, Molecular Pharmacology, Memorial Sloan Kettering Cancer Center
We have developed an antibody-based platform approach for parenterally targeted radiotherapy with a goal of cures without histologic evidence of radiotoxicity in laboratory models of highly radioresistant solid tumors. Using a radiohapten capture system developed in collaboration with the Wittrup Laboratory of MIT, we have demonstrated proof of principle with beta- and alpha-emitting radionuclides in 3 solid tumors (antigen targets): neuroblastoma (GD2), breast cancer (Her 2), and colon cancer (A33).

3:10 Live Q&A: Q&A and Session Wrap-Up
Moderator: Greg M. Thurber, PhD, Assistant Professor, Chemical Engineering & Biomedical Engineering, University of Michigan
Panelists:
Eben L. Rosenthal, MD, John and Ann Doerr Medical Director, Stanford University
Louis M. Weiner, MD, Professor & Director, Oncology, Lombardi Comprehensive Cancer Center, Georgetown University
Steven M. Larson, MD, Donna & Benjamin M. Rosen Chair, Lab Head, Molecular Pharmacology, Memorial Sloan Kettering Cancer Center
Donald E. Mager, PharmD, PhD, Professor & Vice Chair, Pharmaceutical Sciences, SUNY Buffalo

3:40 Close of Day

FRIDAY, SEPTEMBER 4

PROGRESS FROM THE CLINIC - PART I

9:05 am Belantamab Mafodotin – Driving Innovation for Next-Generation Therapy in Multiple Myeloma
Axel Hoos, PhD, Senior Vice President, Therapeutic Area Head, Oncology, GSK
BCMA has become the leading new target for multiple myeloma with several BCMA-targeting agents in clinical development. GSK's belantamab mafodotin is an antibody-drug conjugate which has recently completed a pivotal study in 4th line of treatment in patients with multiple myeloma. This presentation provides an update on the pivotal data and overall clinical program of belantamab mafodotin.

9:25 TRPH-222: A Next-Generation ADC Targeting CD22
Nancy J. Levin, PhD, Vice President, Development, Triphase Accelerator Corp.
TRPH-222 is a CD22-directed ADC, constructed via a novel, site-specific (SMARTag™) conjugation approach, resulting in highly controlled and reproducible drug loading. TRPH-222 is being studied in relapsed and/or refractory B cell lymphoma patients in a phase 1 clinical trial (NCT03682796); currently, the trial is enrolling patients in the dose-escalation phase, with promising tolerability, PK, and PD, as well as early signs of clinical efficacy in this single agent study.

9:45 Live Q&A: Q&A and Session Wrap-Up
Moderator: John M Lambert, PhD, Independent Consultant
Panelists:
Axel Hoos, PhD, Senior Vice President, Therapeutic Area Head, Oncology, GSK
Nancy J. Levin, PhD, Vice President, Development, Triphase Accelerator Corp.

10:10 Session Break

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

PROGRESS FROM THE CLINIC - PART II

10:50 ZW49: Combining Zymeworks' Platforms to Expand the Therapeutic Window of ADCs in HER2-Positive Cancer
Rupert Davies, PhD, Director, Translational Sciences, Zymeworks Biopharmaceuticals Inc.
HER2-targeted therapies have transformed the treatment of patients, but

there remains a need for well tolerated and effective treatments across a range of HER2 expression levels. ZW49 is a bispecific antibody-drug conjugate that combines the ZymeLink™ linker-payload with the unique mechanisms of action of a biparatopic, anti-HER2 Azymetric antibody. ZW49 has the potential to address the unmet medical need across a range of HER2-expressing cancers.

11:10 Combining ADCs and Immunotherapy: Mechanistic Insights and Clinical Observations

Nancy C. Whiting, PhD, Executive Vice President, Development, Seattle Genetics, Inc.

MMAE-based ADCs have demonstrated the potential to change the natural history of multiple cancers. MMAE, the cytotoxic payload, has been shown to induce immunogenic cell death. Combining MMAE-based ADCs with immunotherapy has the promise of augmenting the benefit of each of these therapies.

11:30 Antibody-Drug Conjugates: Are We There Yet?

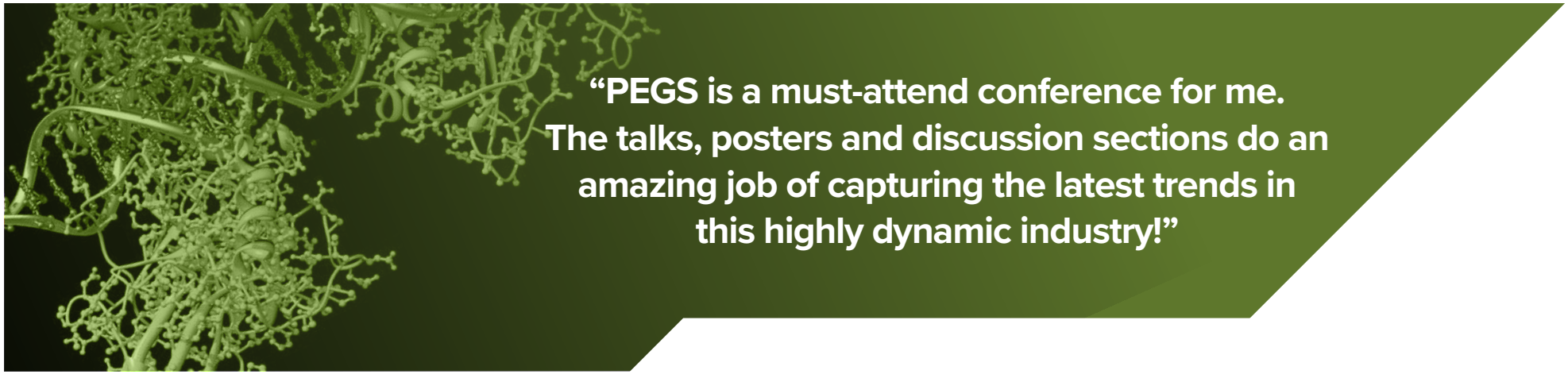
Anthony W. Tolcher, MD, FRCPC, FACP, CEO & Founder, NEXT Oncology

If success is measured by regulatory approval, then 2019 and 2020 were successful years for antibody drug conjugates. With the approvals of enfortumab vedotin-ejfv, polatuzumab vedotin-piiq, fam-trastuzumab deruxtecan-nxki, and more recently, sacituzumab govitecan-hziy, by the Food and Drug Administration, the past 18 months exemplifies how the platform has evolved over the last 25 years. I will review the clinical lessons learned and opportunities to broaden the field.

11:50 Q&A and Session Wrap-Up

Moderator: Nancy C. Whiting, PhD, Executive Vice President, Development, Seattle Genetics, Inc.

12:15 pm Close of Summit



EMERGING THERAPEUTICS & TECHNOLOGIES STREAM

Cutting-Edge Science and Technology to Deliver New Therapeutic Applications

The Emerging Therapeutics & Technologies stream presents three emerging and fast-developing topics, that represent the latest trends and future outlook for many biologics developers. Emerging Indications for Therapeutic Antibodies will reveal new targets and novel mechanisms of actions for development of next-generation therapeutics beyond oncology. Gene Therapy: Advancing from Bench to Clinic will explore the exciting landscape of gene therapy, highlighting regulatory, commercialization and analytical strategies, and showcasing case studies of gene therapies in rare and neurological diseases.

PEGS BOSTON

CONFERENCE STREAMS

- ENGINEERING
- ONCOLOGY
- IMMUNOTHERAPY
- CELL-BASED IMMUNOTHERAPIES
- ANALYTICAL
- EXPRESSION
- IMMUNOGENICITY & BIOASSAYS
- BIOCONJUGATES
- **EMERGING THERAPEUTICS AND TECHNOLOGIES**

2020 EMERGING THERAPEUTICS & TECHNOLOGIES STREAM CONFERENCES

AUGUST 31-SEPTEMBER 1

AGENDA Emerging Indications for Therapeutic Antibodies

SEPTEMBER 2-3

AGENDA Gene Therapy

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August 31-September 1 | 3rd Annual

EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES

R&D Advances in Non-Cancer Indications for Antibodies and Other Biotherapeutics

MONDAY, AUGUST 31

AUTOIMMUNITY & INFLAMMATION

9:05 am Development of a Novel Therapeutic Antibody Drug Conjugate for the Treatment of Autoimmune Disease

Michael McPherson, PhD, Senior Principal Research Scientist, AbbVie

We have developed a plasma-stable antibody drug conjugate (ADC) that has glucocorticoid receptor modulator (GRM) molecules linked to an anti-TNF-α mAb. This ADC is targeted to TNF-α expressing inflammatory cells and internalized into lysosomes where GRM payload is released. This significantly reduces the efficacious GRM dose to below levels that induce undesired side effects. Activity of a surrogate anti-TNF GRM conjugate in inflammatory disease models will be described.

9:25 Engineered Antibody Platforms for Receptor Agonism

Greg A. Lazar, PhD, Director & Senior Scientist, Antibody Engineering, Genentech Inc.

The majority of immune agonist antibodies currently in clinical development rely on extrinsic crosslinking by Fc receptors to enable *in vivo* pharmacologic activity. We have explored multiple technology platforms to enable antibodies to promote receptor signaling without relying on Fc receptor engagement. This talk will describe engineering approaches and considerations, present data demonstrating *in vitro* and *in vivo* proof of concept, and discuss biological and clinical context for immunotherapy.

9:45 Complement Mediation as a Therapeutic Strategy in Autoimmune and Inflammatory Diseases

Claire L. Harris, PhD, Professor Molecular Immunology, Translational & Clinical Research, Newcastle University

The driving role of complement in a single disease, paroxysmal nocturnal hemoglobinuria, provoked the development and FDA approval in 2007 of eculizumab (Soliris™), an anti-C5 antibody. A high attrition rate in complement drug development means that the unmet need for therapy in many complement-driven diseases remains. I will discuss challenges associated with therapeutic inhibition of complement, highlighting lessons learnt and hurdles cleared by various therapeutic approaches.

10:05 Session Break

10:10 LIVE Q&A: Session Wrap-Up

Moderator: Greg A. Lazar, PhD, Director & Senior Scientist, Antibody Engineering, Genentech Inc.
Panelists:
Claire L. Harris, PhD, Professor Molecular Immunology, Translational & Clinical Research, Newcastle University
Michael McPherson, PhD, Senior Principal Research Scientist, AbbVie

10:30 Coffee Break - View our Virtual Exhibit Hall

NEUROLOGY & RARE DISEASES

10:50 Dissecting Anti-Beta-Amyloid Clinical Outcomes; Why Do Some Antibodies Appear to Work while Others Don't?

Charles G. Glabe, PhD, Professor, Molecular Biology & Biochemistry, University of California Irvine

Several active vaccines and mAbs have been tested in human trials and despite removing amyloid deposits, only Aducanumab has been reported to slow cognitive decline. Those that failed in clinical trials target plaques that may represent tombstone markers of antecedent amyloid pathology. Antibodies that target oligomers, but do not bind plaques, have not been fully evaluated yet. Anti-amyloid antibodies with these remain to be tested in human clinical trials.

11:10 KEYNOTE PRESENTATION: Challenges and Opportunities for Biotherapeutics Discovery and Development in Rare Diseases

Madhusudan Natarajan, PhD, Head, Rare Diseases DDU, Takeda

An ongoing biopharma investment in rare disease research, especially in monogenic disorders, coupled with recent advancements and success stories in genetic therapies have fueled a remarkable proliferation of biotherapeutic development at this intersection of therapeutic area and modality. I will showcase examples of opportunities that this intersection provides to "traditional" protein and antibody biotherapeutic development, as well as the associated challenges with these approaches.

11:30 Rapid Human Antibody Discovery

Patricia Odermatt, Senior B Cell Scientist, Antibody Discovery, Aldevron

Genovac Antibody Discovery became the first company to successfully combine three powerful antibody discovery platforms while developing humanized antibodies against SARS-CoV-2 targets. Genovac AbD utilized its proprietary genetic immunization technology, Ligand's OmniRat platform, and Berkeley Lights' Beacon platform to develop high-affinity antibodies that recognize viral proteins and are potentially capable of neutralizing SARS-CoV-2.

11:55 LIVE Q&A: : Session Wrap-Up

Moderator: Madhusudan Natarajan, PhD, Head, Rare Diseases DDU, Takeda
Panelists:
Charles G. Glabe, PhD, Professor, Molecular Biology & Biochemistry, University of California Irvine
Patricia Odermatt, Senior B Cell Scientist, Antibody Discovery, Aldevron

12:15 pm Lunch Break - View our Virtual Exhibit Hall

CARDIOVASCULAR & METABOLIC DISEASES

12:45 The Adipocyte as a Source for Novel Targets for Therapeutic Antibodies for Metabolism, Fibrosis and Cancer

Philipp E Scherer, PhD, Prof & Dir, Touchstone Diabetes Ctr, Univ of Texas Dallas

Adipose tissue dysfunction is at the heart of diabetes, fatty liver disease, organ fibrosis and enhanced growth for invading tumor lesions in a variety of cancers. We have targeted two key players in that area, leptin and endotrophin. Neutralizing antibodies against these factors whose production is enriched in metabolically challenged adipose tissue are highly effective in preclinical settings as anti-obesity, anti-diabetic, anti-fibrotic, and chemosensitizing agents in the breast cancer area.

1:05 Generation of Single-Domain Antibody Antagonists and Agonists to Human Apelin Receptor

MeiYun Zhang, PhD, Principal Scientist, Antibody Discovery, Amgen Asia R&D Center

Developing functional antibodies targeting G-protein-coupled receptors remains challenging. Here we report structure-based and function-based approaches for generating functional single domain antibodies (sdAbs) against human apelin receptor (huAPJ). We co-crystallized an orthosteric sdAb antagonist complexed with huAPJ and converted it into an agonist by structure-guided design. We further developed an HTS method for directly isolating functional antibodies against GPCRs and identified a panel of sdAb antagonists and an agonist to huAPJ.

1:25 LIVE Q&A: Session Wrap-Up

Moderator: Philipp E Scherer, PhD, Prof & Dir, Touchstone Diabetes Ctr, Univ of Texas Dallas
Panelists:
MeiYun Zhang, PhD, Principal Scientist, Antibody Discovery, Amgen Asia R&D Center

1:45 Session Break

2:10 Refresh Break - View Our Virtual Exhibit Hall

2:30 Problem-Solving Breakout Discussions Part A - View our Virtual Exhibit Hall

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 11: Biotherapeutics for Respiratory Indications
Bas van der Woning, PhD, Research Fellow, argenx BVBA

TABLE 12: Antibody Targeting and Delivery Strategies for CNS Indications
Charles G. Glabe, PhD, Professor, Molecular Biology & Biochemistry, University of California Irvine

3:00 Refresh Break - View Our Virtual Exhibit Hall

3:20 Problem-Solving Breakout Discussions Part B - View our Virtual Exhibit Hall

TABLE 13: Strategies for Modulating, Targeting and Directing T Cell Activity for Therapeutic Gain
Elissa Leonard, PhD, Postdoctoral Fellow, Biomedical Engineering, Johns Hopkins University

3:50 Refresh Break - View our Virtual Exhibit Hall

PLENARY KEYNOTE SESSION

4:10 Chairperson's Remarks
K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

4:15 KEYNOTE PRESENTATION: From Energy to Machine Learning
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School

We've engineered new sensor proteins for metabolic engineering, essential proteins with non-standard amino acids for biocontainment, and polymerase-pore fusions for nanopore sequencing, before abruptly moving to "sequence-only" deep machine learning for protein design – from fluorescent proteins to AAV capsids to antibodies. When combined with libraries of millions of designed gene segments from chip-synthesis and rapid testing, each design cycle can take large leaps in sequence space and function space.

4:40 KEYNOTE PRESENTATION: The Case for Intelligent Design in Protein Engineering
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

Directed evolution is in its prime, and it is deepening our understanding of biological systems and empowering therapeutic design. Recent breakthroughs in structural biology, computational design, and high-dimensional data analytics afford us the unprecedented opportunity to apply molecular, structural, and computational principles to guide protein engineering, employing a so-called "intelligent design" approach. This talk will highlight how my lab harnesses this interfacial approach to overcome the deficiencies of natural proteins.

5:15 Live Q&A: Session Wrap-Up

Moderator: K. Dane Wittrup, PhD, CP Dubbs Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology
Panelists:
George M. Church, PhD, Robert Winthrop Professor, Genetics, Harvard Medical School
Jamie B. Spangler, PhD, Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering, Johns Hopkins University

5:35 Happy Hour - View our Virtual Exhibit Hall

6:10 End of Day

TUESDAY, SEPTEMBER 1

INFECTIOUS DISEASES

9:25 am Rapid Capture and Screening of the Native Human Antibody Repertoire for the Discovery of Therapeutic Antibodies
Sarav Rajan, PhD, Senior Scientist, AstraZeneca

The human antibody repertoire is a valuable source of therapeutic grade antibodies. However, identifying the rare B cells expressing these antibodies can be challenging. We have built a platform that uses microfluidics to encapsulate millions of primary B cells into droplets, capturing a paired repertoire that can be screened by phage-display. This presentation will describe the technology and its use in rapidly identifying natively-paired and functional antibodies across multiple campaigns.

9:45 Antibody-Based Scaffolds to Activate T Cells Targeting CMV and EBV
Elissa Leonard, PhD, Postdoctoral Fellow, Biomedical Engineering, Johns Hopkins University

CMV and EBV are pervasive, typically asymptomatic viral infections that can be deadly for immunocompromised individuals. Patients suffering from these infections have been successfully treated with transfer of *ex vivo* expanded virus-specific T cells in clinical trials. This treatment is labor-intensive and highly individualized, limiting broader use. Combining an immunostimulatory IL-2/antibody fusion protein with viral antigens, we are developing an injectable alternative for robust virus-specific T cell activation.

10:05 Session Break

10:10 Engineering Antimicrobial Proteins: Co-Evolutionary Models Aid Molecular Discovery
Benjamin J. Hackel, PhD, Associate Professor, Chemical Engineering & Materials Science, University of Minnesota Twin Cities

Antimicrobial proteins (AMPs) present the opportunity for efficient discovery of potent, selective therapeutics for antibiotic-resistant infection. This presentation will discuss platforms to engineer AMP stability, selectivity, and potency via bioinformatics-guided library design and high-throughput discovery assays. Co-evolutionary models enhanced library strategies to engineer endolysin stability and activity against Clostridium perfringens and Enterococcus. A sequence depletion assay mapped oncocin's sequence-function relationship. These methods are broadly applicable to protein engineering.

10:30 Coffee Break - View our Virtual Exhibit Hall

ANTIBODIES TO TREAT ASTHMA

10:50 Antibody Pliers: A Novel Antibody MOA for Asthma
James T. Koerber, PhD, Senior Scientist, Antibody Engineering, Genentech, Inc.

The serine protease β-tryptase is an important mediator of the allergic inflammatory responses in asthma. Protease inhibitory antibodies employ a mechanism of action (MOA) in which Fab binding directly or allosterically inhibits the protease. I will discuss a novel inhibitory anti-tryptase antibody with a unique bivalent IgG-driven MOA that reveals a new way in which IgGs can inhibit a target and may provide a new strategy for engineering novel antibodies.

11:10 Protein Crystallization Promotes Type 2 Immunity and Is Reversible by Antibody Treatment
Bas van der Woning, PhD, Research Fellow, argenx BVBA

Charcot-Leyden crystals (CLCs) consisting of galectin-10 (Gal10) protein are frequently observed in eosinophilic diseases, such as asthma. We found that CLCs stimulated innate and adaptive immunity and acted as a type-2 adjuvant. Antibodies directed against key epitopes of the CLC crystallization interface dissolved CLCs from patient-derived mucus within hours and reversed crystal-driven inflammation, goblet-cell metaplasia, immunoglobulin E synthesis, and bronchial hyperreactivity in a humanized mouse model of asthma.

11:30 LIVE Q&A: Session Wrap-Up
Moderator: James T. Koerber, PhD, Senior Scientist, Antibody Engineering, Genentech, Inc.
Panelists:
Benjamin J. Hackel, PhD, Associate Professor, Chemical Engineering & Materials Science, University of Minnesota Twin Cities
Elissa Leonard, PhD, Postdoctoral Fellow, Biomedical Engineering, Johns Hopkins University
Sarav Rajan, PhD, Senior Scientist, AstraZeneca
Bas van der Woning, PhD, Research Fellow, argenx BVBA
Jacob Glanville, Founding Partner and CEO, Distributed Bio

11:50 Session Break

12:15 pm Lunch Break - View Our Virtual Exhibit Hall

OTHER EMERGING INDICATIONS

12:50 Identification of Antibodies that Target the Blood-Brain Barrier

Eric V. Shusta, PhD, Professor, Chemical & Biological Engineering, University of Wisconsin Madison

The blood-brain barrier presents a major obstacle to brain drug delivery. We have developed several different enabling platforms for the identification of antibodies against blood-brain barrier resident receptors that could ultimately be used to ferry drug cargo into the brain. Here we will describe our recent efforts to identify such blood-brain barrier-targeting antibodies.

1:10 The Development of Novel WNT Signal Modulating Platforms and their Initial Application to Study Functions of FZDs in Different Tissues

Yang Li, PhD, Vice President, Biology, Surrozen, Inc.

WNT molecules have the potential to induce tissue regeneration and repair. However, their poor biophysical characteristics and lack of selectivity have hindered their application as therapeutics. We have developed a novel antibody based platform for potent, selective WNT surrogate generation, and identified key requirements for maximal signaling.

1:30 LIVE Q&A: Session Wrap-Up

Moderator: Eric V. Shusta, PhD, Professor, Chemical & Biological Engineering, University of Wisconsin Madison
Panelists:
Yang Li, PhD, Vice President, Biology, Surrozen, Inc.

1:55 Close of Emerging Indications for Therapeutics Antibodies

WEDNESDAY, SEPTEMBER 2

CLINICAL DEVELOPMENT & STANDARDIZATION OF GENE THERAPY

9:05 am KEYNOTE PRESENTATION: Clinical Development of Gene Therapies
Mike Singer, MD, PhD, Medical Officer, Division of Clinical Evaluation & Pharmacology, CBER, FDA
The exciting and rapidly-developing field of gene therapy poses unique challenges for FDA in facilitating the timely development and approval of new treatments that are both safe and effective. Clinical development programs for gene therapies differ in some important respects from those used for small molecule drugs. This presentation will discuss these challenges, and the approaches FDA uses to address them.

9:25 An International Collaboration: Towards the Standardisation of Gene Therapy
Yuan Zhao, PhD, Principal Scientist & Leader & Section Head, Gene Therapy, NIBSC
Manufacturing hurdles, including changes in production sites and manufacturing processes, pose challenges regarding reproducibility and comparability for gene therapy. Introduction of an international standard for gene therapy is especially important, given the usually orphan nature of the diseases to be treated. I will discuss challenges and regulatory perspectives in QC and standardization of gene therapy and an international effort in developing the 1st WHO International Standard for gene therapy products.

9:45 AEX membrane for full AAV capsid enrichment


Adam Hejmowski, Research Scientist, Research and Development, Pall Biotech
We have investigated the performance of membrane chromatography as a polishing step for purification of AAV5. We compare the performance for contaminant removal compared to commonly used resin based approaches to show the potential of membrane chromatography as a platform-able polishing step for AAV purification. Membrane chromatography can be loaded 40 times more quickly than conventional chromatography resins, which can lead to much higher productivities and greatly speed the purification step

10:10 Live Q&A: Q&A and Session Wrap-Up
Moderator: Yuan Zhao, PhD, Principal Scientist & Leader & Section Head, Gene Therapy, NIBSC
Panelists:
Mike Singer, MD, PhD, Medical Officer, Division of Clinical Evaluation & Pharmacology, CBER, FDA
Adam Hejmowski, Research Scientist, Research and Development, Pall Biotech

10:30 Speed Networking Coffee Break - View our Virtual Exhibit Hall

COMMERCIALIZATION STRATEGIES AND CHALLENGES BEYOND RARE DISEASES

10:55 Taking Gene Therapy Beyond Rare Diseases
Alexis Bloom, PhD, VP, Regulatory Affairs and Quality Assurance, Gyroscope Therapeutics
To-date, gene therapy development has focused on orphan conditions. This talk will look at both the challenges and opportunities associated with moving gene therapies to large, non-orphan diseases.

11:15 Strategies for the Commercialization of Gene-Modified Cell Therapies
Knut Niss, PhD, CTO, Mustang Bio, Inc.
This presentation will discuss several strategies to commercialize cell and gene therapy products. Particular attention will be given to the manufacturing of these products and how early planning can increase the speed to market and enable lower COGS. Both allogeneic and autologous therapies as well as gene therapy strategies will be discussed.

HARNESSING CRISPR FOR GENE THERAPIES

11:35 Harnessing Novel CRISPR Systems for Genome Engineering
Jonathan S Gootenberg, PhD, McGovern Fellow/Principal Investigator, McGovern Institute, Massachusetts Institute of Technology
Omar Abudayyeh, PhD, McGovern Fellow/Principal Investigator, Massachusetts Institute of Technology
RNA plays important and diverse roles in biology, but molecular tools to manipulate and measure RNA are limited. We demonstrate that RNA-targeting CRISPR effector, Cas13, can be engineered for mammalian cell RNA knockdown, binding, and RNA editing. We also show that both Cas13 and Cas12 can be used for sensitive nucleic acid diagnostics, including COVID-19 detection. Our results establish CRISPR-Cas13 as a flexible platform for studying RNA, diagnostics, and therapeutics.

12:00 pm Live Q&A: Session Wrap-Up
Moderator: Knut Niss, PhD, CTO, Mustang Bio, Inc.
Panelists:
Alexis Bloom, PhD, VP, Regulatory Affairs and Quality Assurance, Gyroscope Therapeutics
Jonathan S Gootenberg, PhD, McGovern Fellow/Principal Investigator, McGovern Institute, Massachusetts Institute of Technology
Omar Abudayyeh, PhD, McGovern Fellow/Principal Investigator, Massachusetts Institute of Technology

12:20 Lunch Break - View our Virtual Exhibit Hall

1:15 Refresh Break - View our Virtual Exhibit Hall

VECTOR DESIGN, DELIVERY AND CHARACTERIZATION

2:25 AI-Powered Design of Synthetic AAV Capsids
Eric Kelsic, PhD, CEO & Co-Founder, Dyno Therapeutics
Pre-existing immunity is a major challenge for AAV gene therapy, preventing many patients from being treated by therapies under development today. Artificial intelligence presents new opportunities for overcoming such challenges, especially when applied to the design of synthetic AAV capsids. I will review the technological advances that are pushing the field of AAV capsid engineering toward AI-powered methods, describe and explore the promise of this approach, and discuss anticipated challenges.

2:45 DNA-Based Nanobody Delivery
Carlo Boutton, PhD, Head, Nanobody Explorative Technologies, Ablynx NV, a Sanofi Company
Small Nanobodies® with their modular design show a different pharmacokinetic profile compared to conventional antibodies. This difference in exposure can be exploited by alternative delivery methods. DNA-based gene transfer of Nanobodies and biopharmaceuticals in general is an appealing alternative to conventional protein therapy. We demonstrate that multivalent Nanobodies encoded as DNA results in a stronger, longer-term and more localized exposure compared to conventional protein therapy.

3:05 The Zetasizer Ultra - A Novel Assay for Measuring Adeno Associated Virus (AAV) Particle Concentration Using MADLS


Jonathan Mehtala, Field Application Scientist, Malvern Panalytical
The high-resolution size capabilities of the Zetasizer Ultra have enabled a new assay to rapidly characterize (AAV) viral concentration. Utilizing (MADLS), Zetasizer Ultra can determine both AAV viral concentration and size in a single measurement that is cuvette-based, rapid, label-free, low volume, and non-destructive.

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3:18 Quantification of the Immune Response to AAV Mediated Gene Therapy

Michael Tovey, PhD, Managing Director, R&D, Svar Life Science

A highly sensitive iLite® reporter assay based on the establishment of a cell line stably transfected with a luciferase reporter-gene placed under the control of an AAV-responsive chimeric promoter, provides a highly sensitive, rapid and precise method for quantifying the immune response to a wide range of recombinant AAV vectors.

3:30 Live Q&A: Q&A and Session Wrap-Up

Moderator: Eric Kelsic, PhD, CEO & Co-Founder, Dyno Therapeutics
Panelists:
Carlo Boutton, PhD, Head, Nanobody Explorative Technologies, Ablynx NV, a Sanofi Company
Jonathan Mehtala, Field Application Scientist, Malvern Panalytical
Michael Tovey, PhD, Managing Director, R&D, Svar Life Science

3:50 Refresh Break - View Our Virtual Exhibit Hall

4:10 Problem Solving Breakout Discussions - Part A

This session provides the opportunity to discuss a focused topic with peers from around the world in an open, collegial setting. Select from the list of topics available and join the moderated discussion to share ideas, gain insights, establish collaborations or commiserate about persistent challenges.

TABLE 29: CQA Identification and Assessment in Gene Therapy Products

Lin Liu, PhD, CMC Dossier Development & Coordination, Sanofi

4:40 Refresh Break - View Our Virtual Exhibit Hall

5:00 Problem Solving Breakout Discussions - Part B

5:30 Close of Day

THURSDAY, SEPTEMBER 3

GENE THERAPY IN CANCER AND NEUROLOGICAL DISEASES

9:05 am Translating Preclinical Responses to Clinical Relevance: Challenges of Gene Therapy

Carl A Morris, PhD, CSO, Solid Biosciences

9:25 Gene and Enzyme Suppression in Cancer Therapy

Brenda Laster, PhD, Prof Nuclear Engineering & Dir, Jerry J Cohen Radiobiology Lab, Ben Gurion Univ of the Negev

We developed an anticancer drug and implanted it directly into solid tumors, suppressing the oncogenes and genes responsible for activation of telomerase. The drug is continuously available in the DNA promoter regions for long periods of time to prevent overexpression and reactivation. In 4 separate experiments, we implanted the drug, using, an intratumoral sustained polymeric system, directly into 100 mouse tumors, reducing the tumor volume 5-fold. Kaplan-Meier p-value was 0.0001.

9:45 Targeted Gene Repression Using Engineered Zinc Finger Protein Transcription Factors as a Novel Therapeutic for Neurodegenerative Disorders

Asa Hatami, PhD, Scientist II, Molecular Biology and Biochemistry, Sangamo Therapeutics

Aggregation of misfolded proteins into toxic species is implicated in pathogenesis of many neurodegenerative proteinopathies, including Alzheimer's disease, Parkinson's disease, and prion disease. Lowering pathogenic protein expression at the DNA level using zinc finger protein transcription factors (ZFP-TFs) has the potential to slow or stop disease progression. We present data from iPSC-derived human neurons, rodents, and nonhuman primates demonstrating durable, highly specific targeted gene regulation following a single ZFP-TF administration.

10:05 Treatment of Neurodegenerative Diseases by Genome Editing Technologies

Thomas Gaj, PhD, Assistant Professor, Bioengineering, University of Illinois Urbana Champaign

Neurodegenerative disorders are the leading cause of disability in the aging population. Our group aims to harness the highly versatile genome-modifying technologies to develop corrective gene therapies for such neurodegenerative conditions. This talk will highlight our most recent efforts on using recently emerged precision gene-editing tools to treat amyotrophic lateral sclerosis and Huntington's disease, two devastating and relentlessly progressing neurodegenerative disorders.

10:30 Coffee Break - View our Virtual Exhibit Hall

10:50 Live Q&A: Q&A and Session Wrap-Up

Moderator: Brenda Laster, PhD, Prof Nuclear Engineering & Dir, Jerry J Cohen Radiobiology Lab, Ben Gurion Univ of the Negev

11:20 Close of Gene Therapy

Live Q&A

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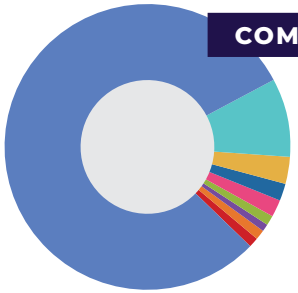

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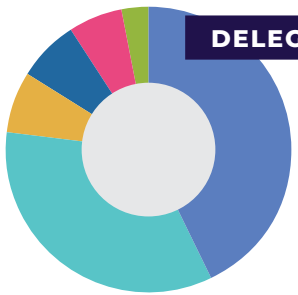

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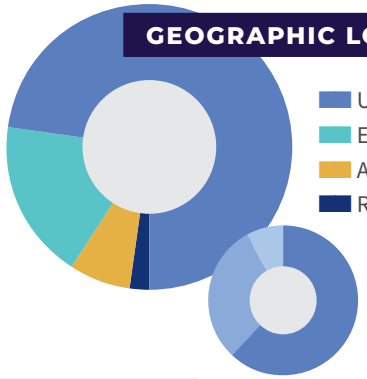

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