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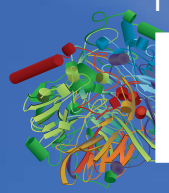

14th Annual

PEGS BOSTON

April 30 - May 4, 2018
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Boston, MA

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The Essential Protein Engineering Summit

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SUNDAY (APRIL 29)	MONDAY - TUESDAY (APRIL 30 – MAY 1)		WEDNESDAY-THURSDAY AM (MAY 2-3)		THURSDAY PM - FRIDAY (MAY 3-4)
Pre - Conference Short Courses	Display of Antibodies	Tuesday Dinner Short Courses	Engineering Antibodies	Thursday Dinner Short Courses	Engineering Bispecific Antibodies
	Antibodies for Cancer Therapy		Advancing Bispecific Antibodies & Combination Therapy to the Clinic		Clinical Progress of Antibody-Drug Conjugates
	Improving Immunotherapy Efficacy and Safety		CAR Ts, TCRs and TILs		Agonist Immunotherapy Targets
	Difficult to Express Proteins		Optimizing Protein Expression		Protein Expression System Engineering
	Characterization of Biotherapeutics		Biophysical Analysis of Biotherapeutics		Protein Aggregation and Stability
	Immunogenicity Case Studies and Clinical Management		Immunogenicity Assay Assessment		Bioassays for Biologics
	Fusion Protein Therapeutics		Engineering Antibody-Drug Conjugates		Clinical Progress of Antibody-Drug Conjugates
	Emerging Indications for Therapeutic Antibodies		CRISPR for Genome Engineering		Nanotechnology in Medicine
	Training SEMINARS By Cambridge Healthtech Institute Intro to Protein Engineering Intro to Structure-Based Drug Design and Development Intro to Bioprocessing Intro Design of Experiments for Bioassay Development		Training SEMINARS By Cambridge Healthtech Institute Next Generation Sequencing for Antibody Discovery and Engineering Immunology for Drug Discovery Scientists		Training SEMINARS By Cambridge Healthtech Institute Introduction to Immunogenicity

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PRESENT A POSTER AND SAVE $50

PRESENT YOUR POSTER TO 2,300 PROTEIN ENGINEERING RESEARCHERS

REASONS YOU SHOULD PRESENT YOUR RESEARCH POSTER AT THIS CONFERENCE:

- Your poster will be seen by our international delegation, representing leaders from top pharmaceutical, biotech, academic and government institutions
- Receive $50 off your registration
- Your poster abstract will be published in our conference materials
- Automatically entered into poster competition

POSTER COMPETITION

Two poster awards will be given at the conference for a cash prize for best poster.

Present your poster at PEGS and be automatically entered to win. One winner from each poster session will be chosen based on visual appearance of poster, clarity of concepts presented, audience engagement, technology advances and implications of the work presented.

SPECIAL POSTER DEADLINES APPLY.

To secure a poster board and inclusion in specific conference materials, your abstract must be submitted, approved and your registration paid in full by the following deadlines: March 9, 2018 Printed Program Guide and Electronic Program Materials; March 30, 2018 Electronic Program Materials only;
All poster abstracts are due no later than March 30, 2018.

STUDENT FELLOWSHIPS

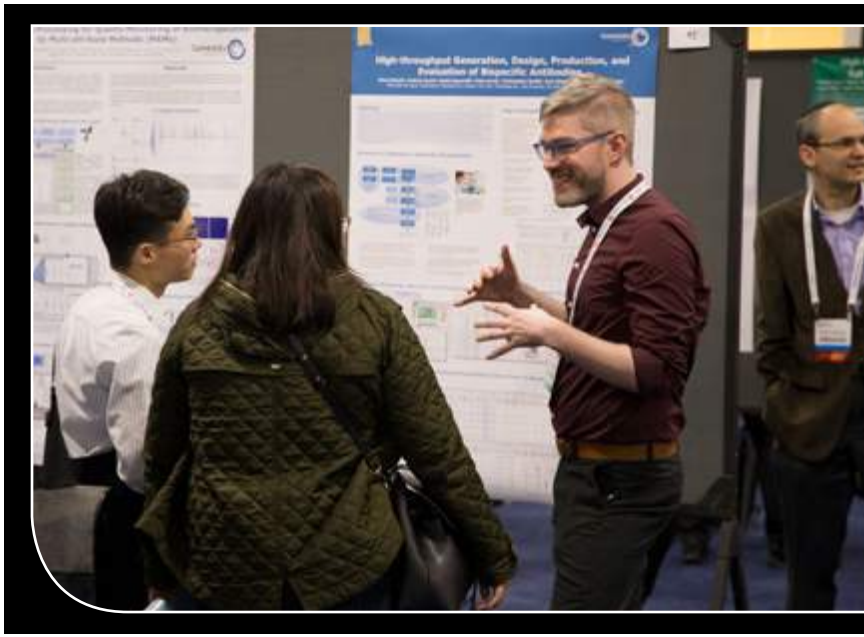
PEGS SUMMIT IS PROUD TO SUPPORT AND RECOGNIZE THE SCIENTISTS OF THE TOMORROW!

Full-time graduate students and PhD candidates are encouraged to apply for the PEGS conference Student Fellowship. Fellows will receive a poster presentation slot and a savings of over $900 on their registration fee. Applications are due by March 30, 2018.

STUDENT FELLOWSHIP DETAILS:

- Receive a poster presentation slot and a savings of over $900 on their registration fee
- Present your research poster to an international delegation of nearly 2,300 posters
- Meet face-to-face with potential employers and contacts to further your research and form collaborations
- Be entered in the Poster Competition – with cash prizes!

Fellowship are limited to 25 students and submission deadlines must be met. Special pricing is available for students without a poster presentation. See the event website for details.



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PLENARY KEYNOTE SESSION

MONDAY, APRIL 30 | 4:00 PM

CHALLENGES AND OPPORTUNITIES IN ENGINEERING PROTEIN BIOPHARMACEUTICALS

K. DANE WITTRUP, PHD

C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)

Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

Professor K. Dane Wittrup is the Carbon P. Dubbs Professor of Chemical Engineering and Biological Engineering at the Massachusetts Institute of Technology, and the Associate Director of the Koch Institute for Integrative Cancer Research. From 1989 to 1999, he was Assistant Professor, Associate Professor, and then J. W. Westwater Professor of Chemical Engineering, Bioengineering, and Biophysics at the University of Illinois in Champaign/Urbana. Prof. Wittrup received a BS in Chemical Engineering Summa cum Laude in 1984 from the University of New Mexico, and a PhD in Chemical Engineering from the California Institute of Technology in 1988 under the thesis direction of Prof. James Bailey. Following a year of postdoctoral research at Amgen (Thousand Oaks, CA), Dr. Wittrup joined the faculty at the University of Illinois. Wittrup's research program is focused on protein engineering of biopharmaceutical proteins by directed evolution. Areas of interest include: pretargeted radioimmunotherapy, biological response modification of EGFR, and immunotherapy of cancer via engineered cytokines and vaccines.

YOUNG SCIENTIST KEYNOTE
THE NEXT GENERATION OF CANCER IMMUNOTHERAPY: TARGETING MYELOID IMMUNE CHECKPOINTS

KIPP WEISKOPF, MD, PHD

Resident Physician, Internal Medicine, Brigham and Women's Hospital

Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

Kipp Weiskopf, MD, PhD, is a resident physician in Internal Medicine at Brigham and Women's Hospital in Boston, MA. He completed his training in the Medical Scientist Training Program at Stanford University. His research focuses on the development of novel cancer immunotherapies, particularly those that activate innate immune cells to attack cancer. In the laboratory of Irving Weissman, MD, he studied the interaction between CD47 and SIRPα, which acts as a myeloid-specific immune checkpoint. He developed novel therapies that disrupt the CD47-SIRPa interaction and stimulate macrophage phagocytosis of cancer cells. He has over 10 patent applications related to this work and was a winner of the 2013 Collegiate Inventors Competition at the US Patent and Trademark Office. He is a co-Founder of Alexo Therapeutics, a biotech company formed to develop these therapeutics. He has also been the recipient of a Winston Churchill Scholarship, an NCI Ruth L. Kirschstein NRSA Fellowship, the Harold M. Weintraub Graduate Student Award from the Fred Hutchinson Cancer Research Center, and the Joanna M. Nicolay Melanoma Foundation Research Scholar Award.

THE PEGS YOUNG SCIENTIST KEYNOTE

The PEGS Boston Young Scientist Keynote recognizes a rising star in the field of protein science who is current in a postdoc program or who has completed a postdoc in the last five years. Nominations of candidates for this role were solicited from leading industry and academic research labs in the fall of 2017, and the final selection was made on the basis of votes from a 15-person group of scientific advisors.

CHI's Young Scientist Keynotes join the company's Student Fellowships and Featured Poster Presentations as ways of supporting the increased visibility of those new to our field. Please visit the PEGS website following the 2018 meeting for details on how you can nominate a candidate for the 2019 meeting.

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SHORT COURSES

SUNDAY, APRIL 29

MORNING, 10:00 AM – 1:00 PM

SC1: Preclinical and Clinical Assessment of Immunogenicity: Multidomain Therapeutics and New Modalities, Including Gene Therapy and CAR T

Darshana Jani, MS, Senior Manager, Pfizer, Inc.
Seema Kumar, PhD, Associate Director, Quantitative Pharmacology & Drug Disposition (QPD), R&D Global Early Development (GED), EMD Serono, a business of Merck KGaA, Darmstadt, Germany
Magdalena Tary-Lehmann, MD, PhD, CSO, Cellular Technology Limited (CTL); Adjunct Associate Professor of Pathology, Case Western Reserve University (CWRU)
Ravi Shankar Singh, PhD, Associate Director, Clinical Pharmacology, Pfizer
Ben Hock, PhD, Director, Immunogenicity, BioMarin Pharmaceuticals

SC2: Translational Considerations for Development of Monoclonal Antibodies and Emerging Constructs: Part I: Focus on Construct Design

Glareh Azadi, PhD, Senior Scientist, Translational PKPD, Merck Research Laboratories
Gadi Bornstein, PhD, Senior Director, Biologics Discovery, TESARO, Inc.
Veronica Juan, PhD, Principal Scientist, Protein Sciences, Merck Research Labs
Scott L. Klakamp, PhD, Vice President of Chemistry and Biochemistry, Bioptix
Mohammad Tabrizi, PhD, Director Biologics Discovery, Merck Research Laboratories Palo Alto

SC3: The Life Science Executive's Fundraising Manifesto

Dennis Ford, Founder and CEO, Life Science Nation

SC4: Selection, Screening and Engineering for Affinity Reagents

Jonas V. Schaefer, PhD, Lab Head/Investigator II, Novartis Institutes for BioMedical Research (NIBR)
Christian Kunz, PhD., Associate Director, MorphoSys AG

AFTERNOON, 2:00 – 5:00 PM

SC5: *In silico* Immunogenicity Predictions (Hands-On) Workshop

Vinodh B. Kurella, PhD, Senior Scientist, Protein Engineering, Immuno-Oncology Division, Intrexon Corp.
Eliud Oloo, PhD, Senior Principal Scientist, Schrodinger

SC6: Practical Considerations for Biomarker Bioanalysis

Darshana Jani, MS, Senior Manager, Pfizer, Inc.
Paul Rhyne, PhD., VP, Biological Development Services
Tim Sikorski, PhD., Investigator, Exploratory Biomarkers, GlaxoSmithKline

SC7: Translational Considerations for Development of Monoclonal Antibodies and Emerging Constructs: Part 2: Focus on Preclinical Development

Glareh Azadi, PhD, Senior Scientist, Translational PKPD, Merck Research Laboratories
Gadi Bornstein, PhD, Senior Director, Biologics Discovery, TESARO, Inc.
Veronica Juan, PhD, Principal Scientist, Protein Sciences, Merck Research Labs
Scott L. Klakamp, PhD, Vice President, Chemistry and Biochemistry, Bioptix
Mohammad Tabrizi, PhD, Director, Biologics Discovery, Merck Research Laboratories Palo Alto

TUESDAY, MAY 1

DINNER, 6:00 – 8:30 PM

SC8: Introduction to Biophysical Analysis for Biotherapeutics: Discovery & Development Applications

Christine P. Chan, PhD, Principal Scientist, Global Manufacturing Science & Technology, Sanofi

SC9: CAR T Cell Therapy for Solid Tumors

Soldano Ferrone, MD, PhD, Division of Surgical Oncology, Surgery, Massachusetts General Hospital, Harvard Medical School
Moonsoo M. Jin, PhD, Associate Professor, Molecular Imaging Innovations Institute, Radiology, Weill Cornell Medical College
Tara Arvedson, PhD, Director, Oncology Research, Amgen

THURSDAY, MAY 3

DINNER, 5:45 – 8:15 PM

SC10: Critical Considerations for the Design and Development of Antibody-Drug Conjugates

Isabel Figueroa, PhD, Scientist, PTPK, Genentech, Inc.
Shawn Owen, PhD, Assistant Professor, Pharmaceutics and Pharmaceutical Chemistry, University of Utah

SC11: Strategic/Modular Bioassay Design and Analysis

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

SC13: Sub Visible Protein Particles in Immunogenicity: Measurement, Characterization and Impact

Björn Boll, PhD, Head, Particle Lab and Higher Order Structure Protein Analytics, Physical Chemical Analytics, Novartis Pharma AG
Anacelia Ríos Quiroz, PhD, Scientist, Group Leader Particle Lab, Pharma Technical Development Europe (Biologics) Analytics (PTDE-A), F. Hoffmann-La Roche Ltd.

DINNER, 5:45 – 8:45 PM

SC12: Transient Protein Production in Mammalian Cells

Richard Altman, MS, Scientist, Protein Technologies, Amgen
Henry C. Chiou, PhD, Associate Director, Cell Biology, Life Science Solutions, Thermo Fisher Scientific
Bojiao Yin, PhD, Scientist, Protein Technologies, Amgen

Training SEMINARS
By Cambridge Healthtech Institute

Cambridge Healthtech Institute Training Seminars offer real-life case studies, problems encountered and solutions applied, along with extensive coverage of the academic theory and background. Each training seminar offers a mix of formal lecture and interactive discussions and activities to maximize the learning experience. These training seminars are led by experienced instructors who will focus on content applicable to your current research and provide important guidance to those new to their fields.

MONDAY, APRIL 30 - TUESDAY, MAY 1

DAY 1
8:30 am – 12:30 pm ..... Training Seminars in Session
12:30 ..... Lunch on Your Own
2:20 – 7:15 ..... Breakout Discussions, Plenary Keynote Session, Welcome Reception

DAY 2
8:30 am - 5:25 pm ..... Training Seminars in Session
Refreshment breaks and exhibit hall viewing hours also provided.

TS9A: Introduction to Protein Engineering

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

Instructor:

David Bramhill, PhD, Founder, Bramhill Biological Consulting, LLC

TS10A: Introduction to Structure-Based Drug Design and Development

CHI's Introduction to Structure-Based Drug Design and Development offers an introduction to the concepts, strategies and tools of structure-based drug design, optimization and development. The seminar consists of presentations and live demonstrations of some of the common computational tools used in the field. We will cover techniques to triage therapeutics sequences, modulate affinity, create novel constructs (such as Fc-fusions, bispecifics, protein traps) along with increasing the manufacturability of a biologic. The class is directed at scientists new to the industry, academic scientists and career protein engineers wanting an introduction into how structure can aid in guiding experimental design.

Instructors:

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

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

TS11A: Introduction to Bioprocessing

CHI's Introduction to Bioprocessing training seminar offers a comprehensive survey of the steps needed to produce today's complex biopharmaceuticals, from early development through commercial. The seminar begins with a brief introduction to biologic drugs and the aspects of protein science that drive the intricate progression of analytical and process steps that follows. We then step through the stages of bioprocessing, beginning with the development of cell lines and ending at scaling up for commercial production. The seminar also explores emerging process technologies, facility design considerations, and the regulatory and quality standards that govern our industry throughout development. The important roles of analytical methods at all stages of development as well as formulation and stability assessments in developing and gaining approval for a biopharmaceutical are also examined. This 1.5-day class is directed to attendees working in any aspect of industry, including scientific, technical, business, marketing or support functions, who would benefit from a detailed overview of this field.

Instructors:

Sheila G. Magil, PhD, Senior Consultant, BioProcess Technology Consultants, Inc.

Frank J. Riske, PhD, Senior Consultant, BioProcess Technology Consultants, Inc.

TS12A: Introduction to Design of Experiments for Bioassay Development

This 1.5-day lecture-based seminar is an introduction course to the concept of Design of Experiments (DoE) for bioassay lifecycle management. First, trainees will learn, using a simple example, the value of DoE and how it can drastically increase the amount of information provided by each experiment. Then, we'll discuss how to choose the appropriate design for different assay development situations. Trainees will have an overview of the DoE catalog, including the advantage of each type of design (Screening designs, Factorial designs, Response-surface designs, Optimal designs). Finally, attendees will gain an appreciation for the many ways output can be used to better understand and optimize processes.

Instructor:

Perceval Sondag, Senior Manager, Statistics, PharmaLex

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TRAINING SEMINARS

Cambridge HEALTHTECH Institute
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WEDNESDAY, MAY 2 - THURSDAY, MAY 3

DAY 1
8:30 am – 5:45 pm ..... Training Seminars in Session
12:25 - 2:10 pm ..... Lunch Provided
5:45 – 7:00 ..... Networking Reception

DAY 2
8:30 am – 12:30 pm ..... Training Seminars in Session
12:35 pm ..... Lunch in the Exhibit Hall with Poster Viewing
Refreshment breaks and exhibit hall viewing hours also provided.

TS9B: Next-Generation Sequencing for Antibody Discovery and Engineering

In this training seminar, participants will learn about Next-Generation Sequencing (NGS) of antibody repertoires. Part 1 will provide an introduction to the antibody repertoires, consisting of genetic background, generation of diversity, sequencing technologies and a hands-on session on the computational tools available for the analysis antibody repertoire NGS data. Part 2 will focus on the preprocessing and analysis of data. Each step of the preprocessing will be elucidated using the programming platforms of R and Python, along with existing bioinformatics pipelines available. Repertoire analysis content will provide statistical quantification and visualization of high-dimensional data. The course will be fully interactive with case studies; participants will be able to download data and example scripts. Please bring your computer.

Instructors:

Simon Friedensohn, MSc, Research Assistant; Biosystems Science and Engineering, ETH Zurich, Switzerland

Enkelejda Miho, Research Assistant, Biosystems Science and Engineering, ETH Zürich, Switzerland

TS10B: Immunology for Drug Discovery Scientists

This 1.5-day seminar will cover the fundamentals of human immunology for an audience of scientists across different backgrounds working in pharmaceutical and biotech organizations in programs related to immuno-therapy. The course will cover a historical perspective, basic mechanisms, fundamental concepts and practical approaches to developing therapeutics and their combinations to modulate the immune system. Additionally, the class will offer perspectives on how immune responses can be monitored by assessment of biomarkers and modulated through biopharmaceutical intervention. Through group activities, attendees will actively review immunological concepts as well as design functional immunological assays and read-outs.

Instructors:

Masha Fridkis-Hareli, MSc, PhD, Founder and President, ATR, LLC

Tatiana Novobrantseva, PhD, Co-Founder, Head of Research and Development, Verseau Therapeutics

THURSDAY, MAY 3 - FRIDAY, MAY 4

DAY 1
1:40 pm – 5:20 pm ..... Training Seminars in Session
12:35 pm ..... Lunch in the Exhibit Hall with Poster Viewing

DAY 2
8:30 am – 3:40 pm ..... Training Seminars in Session
12:35 pm ..... Lunch Provided

TS9C: Introduction to Immunogenicity

All protein drugs generate an immunogenic response. This 1.5-day training seminar provides a practical, comprehensive overview of immunogenicity – the causes, how to assess, predict and prevent, and what to do if you observe immunogenicity during preclinical, clinical and post-market approval. The seminar begins by detailing the science behind immunogenicity, the latest international guidances, followed by assay and bioanalytical assessment strategies for traditional and emerging biologics. Other topics include predictive models and how to report immunogenicity incidents both internally and externally.

Instructor:

Bonnie Rup, PhD, Independent Consultant

Each CHI Training Seminar offers 1.5 days of instruction with start and stop times for each day shown above and on the Event-at-a-Glance published in the onsite Program & Event Guide. Training Seminars will include morning and afternoon refreshment breaks, as applicable, and lunch will be provided to all registered attendees on the full day of the class.

Each person registered specifically for the training seminar will be provided with a hard copy handbook for the seminar in which they are registered. A limited number of additional handbooks will be available for other delegates who wish to attend the seminar, but after these have been distributed, no additional books will be available.

Though CHI encourages track hopping between conference programs, we ask that Training Seminars not be disturbed once they have begun. In the interest of maintaining the highest quality learning environment for Training Seminar attendees, and because Seminars are conducted differently than conference programming, we ask that attendees commit to attending the entire program, and not engage in track hopping, as to not disturb the hands-on style instruction being offered to the other participants.

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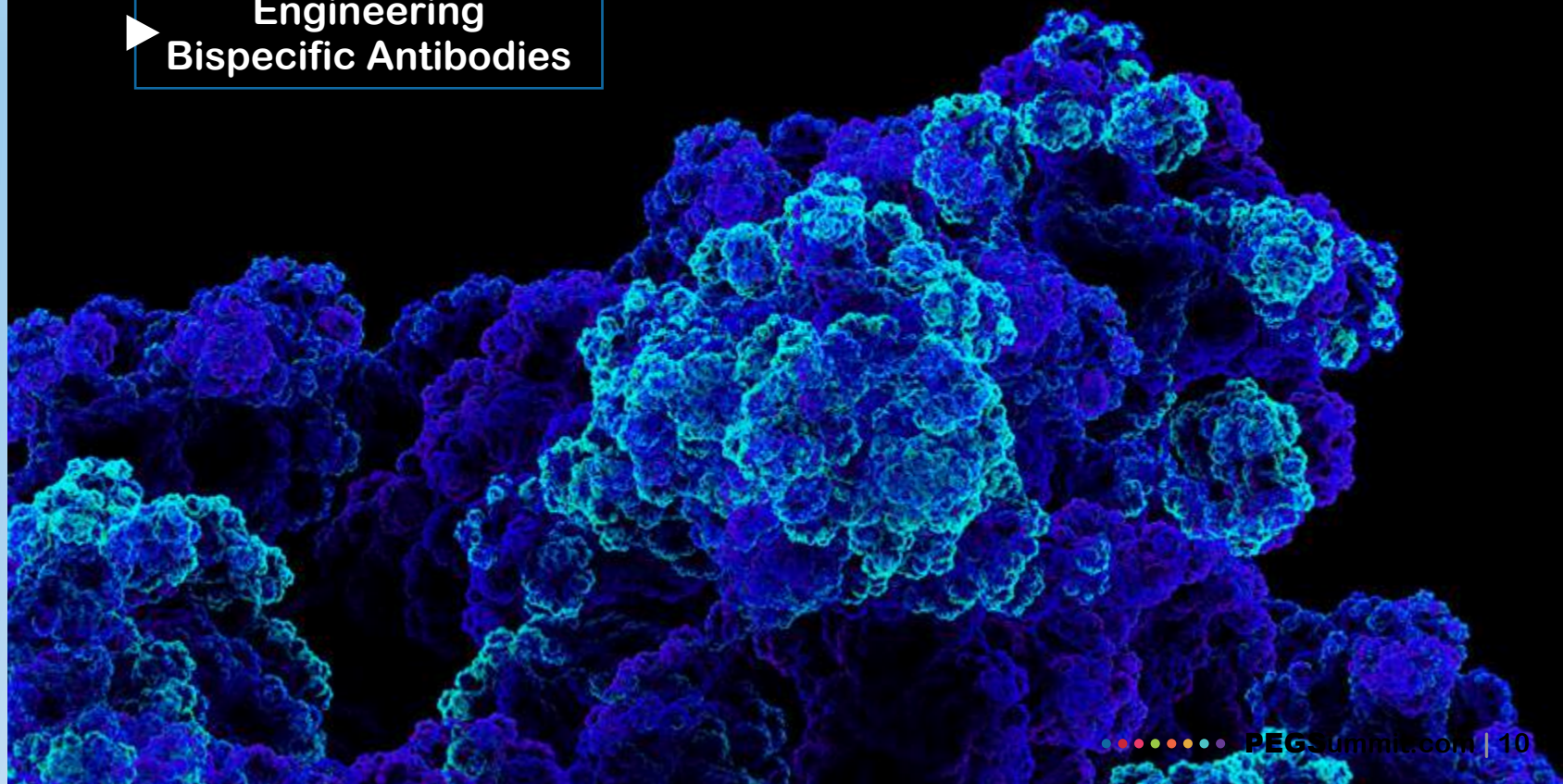
ENGINEERING STREAM

- Display of Antibodies
- Engineering Antibodies
- Engineering Bispecific Antibodies

Leading Innovation in Engineering Novel First-in-Class Biologics

Creating new platforms, formats, activation, and delivery methods for the next generation of drug candidates demands a high degree of innovation to address hard to reach and difficult targets. The PEGS Engineering stream provides knowledge and collaboration opportunities for scientists in this highly competitive field. Display and engineering of antibodies will be highlighted along with applications in oncology, immunotherapy, infectious disease, inflammation and autoimmune disorders.



Twentieth Annual

DISPLAY OF ANTIBODIES

New Tools for Creating Novel Biologics

SUNDAY, APRIL 29

RECOMMENDED SHORT COURSE(S)*

SC4: Selection, Screening and Engineering for Affinity Reagents

SC6: Practical Considerations for Biomarker Bioanalysis

**Separate registration required, please see page 6 for course details.*

MONDAY, APRIL 30

7:00 am Registration and Morning Coffee

PHAGE AT WORK

8:30 Chairperson's Remarks
Andrew M. Bradbury, PhD, MB BS, CSO, Specifica, Inc.

8:40 KEYNOTE PRESENTATION: Phages and the Human Microbiome
Frederic D. Bushman, PhD, Chair and Professor, Microbiology, University of Pennsylvania
Humans harbor enormous communities of viruses that are important in health and disease. Many viral groups, particularly phage, are poorly represented in genome databases, and so difficult to recognize in sequence data. Metagenomic methods, however, allow these viral communities to be reconstructed and genomes tracked, permitting longitudinal quantification, analysis of variation over time, and tracking transfer during transplantation between human individuals. Results from recent studies will be presented.

9:10 Use of Engineered Phage in Cancer Therapy and Tissue Regeneration
Chuanbin Mao, PhD, Professor, Chemistry and Biochemistry, University of Oklahoma
Phages are biological nanostructures that can serve as therapeutics. They can be engineered to display functional peptides. As a result, they can target tumors and inhibit tumor growth when tumor-homing and inhibiting peptides are displayed. They can also instruct the stem cells to differentiate into functional bone forming cells and induce bone tissue formation when differentiation-inducing peptides are displayed.

9:40 A Phage Virus-Like Particle Display Platform for Identifying Vaccines for Chronic and Infectious Disease
Bryce Chackerian, PhD, Professor, Molecular Genetics and Microbiology, University of New Mexico School of Medicine
Display of antigens on virus-like particles (VLPs) is a valuable technique for enhancing the immunogenicity of targets that are poorly immunogenic in their native context. In this talk, I'll describe how bacteriophage VLPs can be engineered to target molecules that play important roles in two chronic diseases, cardiovascular disease and Alzheimer's.

10:10 Networking Coffee Break

10:50 Single Domain Antibodies Targeting Membrane-Bound Glypicans in Cancer
Mitchell Ho, PhD, Senior Investigator, National Cancer Institute, NIH
The Ho laboratory studies cancer cell surface proteins, focusing primarily on the role of glypicans including GPC2 and GPC3 as a new family of tumor antigens, and designs 'single domain antibodies' that modulate Wnt and other glypican signaling processes responsible for the development of cancer. The talk will also include an update on new phage-displayed shark and camel single domain antibody libraries.

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11:20 Deep Sequencing of Phage-Displayed Random Sequence and Genome-Derived Peptide Libraries for Norovirus Detection and Epitope Mapping

Timothy Palzkill, PhD, Professor, Chair, Pharmacology and Chemical Biology, Baylor College of Medicine

Norovirus infections are the leading cause of non-bacterial gastroenteritis, and there is a need for diagnostic tools to detect virus. In this study, a combination of phage display, deep sequencing, and computational analysis was used to identify peptides with specific binding to norovirus. In addition, deep sequencing and computational analysis of phage display libraries derived from norovirus genomic DNA was used to map antibody binding sites on norovirus proteins.

11:50 Identification of High Affinity HER2 Binding Fab Antibodies Using CHO Surface Display

Jennifer Maynard, PhD, Associate Professor, Chemical Engineering, University of Texas at Austin

Discovery of new antibodies is most commonly performed using phage or yeast display, but mammalian cells are used for large-scale production because of the complex antibody structure, including multiple disulfide bonds and a key glycosylation required for function. To circumvent problems associated with changing hosts, we developed a plasmid-based Fab screening platform on CHO cells which allows for antibody selection in the same host used for manufacturing. We further show that this method is generalizable to engineering other cell surface receptors, including T cell receptors and chimeric antigen receptors.

12:20 pm Further Advancement for Human Antibody Discovery

Vera Molkenthin, PhD, Chief Scientist, AbCheck s.r.o.

AbCheck has developed Mass Humanization to generate humanized libraries. This approach utilizes batch cloning of CDR3 immune repertoires from immunized rabbits into selected human frameworks containing specifically diversified CDR1 and CDR2 regions. For selecting high affinity binders from the resulting, highly diverse library, AbCheck routinely applies Phage or Yeast Display under various conditions. In this talk, AbCheck will present new technological developments regarding its human antibody discovery and optimization platform.

12:50 Discovery of Potent, Functional Anti-TIGIT Antagonists from Three Different Phage Display Platforms

Sponsored by LakePharma

Aaron Sato, PhD, CSO, Antibody Center, LakePharma

In a head-to-head study, we compared the performance of a synthetic scFv (Distributed Bio), a naïve Fab (XOMA), and an antigen-specific mouse immune library. Each library was panned against TIGIT (T cell immunoreceptor with Ig and ITIM domains) and screened using our high-throughput HighRes Biosolutions ELISA deck. All IgGs were tested for affinity, competition with TIGIT's ligands, cell binding, and functional activity. Some commonalities as well as some striking differences amongst the leads were discovered.

1:20 Luncheon Presentation: Use of Mammalian Virus Display to Select Antibodies Specific for Complex Membrane Antigens

Sponsored by VACCINEX

Ernest Smith, CSO & Senior Vice President, Research, 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. This method is rapid, does not require any detergents or refolding, and can be applied to multiple cell types in order to maximize protein expression and to provide properly folded protein that is necessary for antibody selection.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 Challenges and Opportunities in Engineering Protein Biopharmaceuticals

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)

Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk, I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

4:55 The Next Generation of Cancer Immunotherapy: Targeting Myeloid Immune Checkpoints

Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital

Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

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

Sponsored by PRECISION FOR MEDICINE
THE FUTURE OF MEDICINE IS PRECISION

7:15 End of Day

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

TUESDAY, MAY 1

8:00 am Registration and Morning Coffee

NOVEL TECHNOLOGIES

8:25 Chairperson's Remarks
Jennifer Cochran, PhD, Chair, Bioengineering, Stanford University School of Medicine and School of Engineering; Chief Scientist, Lagunita Biosciences

8:30 Inefficient Ribosomal Skipping for Simultaneous Cell Surface Display and Soluble Secretion of Proteins in Yeast
Balaji M. Rao, PhD, Associate Professor, Chemical and Biomolecular Engineering, North Carolina State University
We have developed a system for simultaneous cell surface display and soluble secretion of proteins in yeast *Saccharomyces cerevisiae*, based on inefficient ribosomal skipping. Application of this system to efficiently isolate and characterize binding proteins isolated from combinatorial protein libraries will be discussed.

9:00 Engineering Peptides and Peptidomimetics for Non-Invasive Disease Screening and Treatment Monitoring
Greg M. Thurber, PhD, Assistant Professor, Chemical Engineering and Biomedical Engineering, University of Michigan
Peptides hold a unique position between small molecule agents (less than 500 Da) and proteins (larger than ~5 kDa), endowing them with optimal properties for imaging agent development. However, their lack of structure and poor stability often result in low affinity and rapid clearance. Using bio-orthogonal chemistry and physicochemical property manipulation, we demonstrate how novel structures can be identified for non-invasive screening and disease monitoring.

9:30 Mammalian Display Platform Yields Cysteine-Dense Peptide that Blocks the Oncogenic YAP:TEAD Interaction with High Affinity
James M. Olson, MD, PhD, Sarah Hughes Chair for Pediatric Oncology; Member, Fred Hutchinson Cancer Research Center; Attending Physician, Seattle Children's Hospital; Professor of Pediatrics, University of Washington
The hippo pathway drives proliferation during embryogenesis and, aberrantly, in some cancers. The hippo pathway's YAP:TEAD interaction has eluded drug discovery efforts. Noting that some cysteine dense peptides (CDPs) act intracellularly despite the reducing environment and that CDPs naturally have other ideal properties for mid-sized medicines, we created and used a mammalian display platform which we used to select and evolve candidate therapeutics, ultimately yielding a 300 pM KD antagonist.

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

IMPROVING SELECTION WITH NGS

Chairperson's Remarks
Andrew M. Bradbury, PhD, MB BS, CSO, Specifica, Inc.

10:50 KEYNOTE PRESENTATION: Protein Engineering and Evolution to Create Base Editors for Precision Genome Editing without Double-Stranded DNA Breaks
David R. Liu, PhD, Richard Merkin Professor, Director, Merkin Institute of Transformative Technologies in Healthcare, Broad Institute Core Institute Member, Vice-Chair, Faculty, Director of the Chemical Biology and Therapeutic Sciences Program, Howard Hughes Medical Institute Investigator, Professor, Chemistry and Chemical Biology, Harvard University
In this lecture, I will describe the use of protein engineering and protein evolution to create base editing, a new approach to genome editing that enables programmable correction of point mutations efficiently without requiring DNA backbone cleavage or donor DNA templates. Base editing has the potential to advance the scope and effectiveness of genome editing of point mutations, which represent the substantial majority of known human genetic variants associated with disease but are difficult to correct cleanly and efficiently using standard genome editing methods.

11:20 Leveraging Next-Generation Sequencing to Understand and Improve Antibody Libraries, and Selections from Them
Andrew M. Bradbury, PhD, MB BS, CSO, Specifica, Inc.
Early selection experiments indicated that antibody libraries yield 1-5 specific antibodies for a diversity of 107- in line with theoretical calculations. However, as antibody libraries got larger, the number of selected antibodies per target did not proportionately keep pace. This suggests either that libraries are not as diverse as claimed, or that commonly used selection methods are unable to tap the full diversity. We use next-generation sequencing to answer these questions, as well as to design and construct phage antibody libraries of maximum diversity.

11:50 Deep Sequencing Analysis of Phage Selection Outputs: Leaving Conventional Screening Behind
Stefan Ewert, PhD, Senior Investigator, NIBR Biologics Center, Novartis Pharma AG
We will show adaptations to library design and planning strategies exploiting the full potential of deep sequencing analysis of phage selection output pools to identify high affine antibodies without conventional screening.

Sponsored by integral molecular

12:20 pm Luncheon Presentation I: Discovery of Antagonist mAbs against the GPCR CB1 for Treating NASH
Ross Chambers, PhD, Vice President, Antibody Discovery, Integral Molecular
CB1 is a therapeutic target for non-alcoholic steatohepatitis (NASH), a metabolic disease with no approved treatment. Integral Molecular has

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discovered potent antagonist antibodies against this challenging GPCR using its MPS Antibody Discovery Engine. This approach yielded a large panel of CB1-reactive antibodies with diverse epitopes, increasing the likelihood of discovering rare antagonist antibodies. Lead candidates were affinity matured, resulting in high affinity, exquisite specificity, and potent inhibition of CB1 signaling.

High-Resolution Epitope Mapping and Specificity Profiling of MAbs Targeting Complex Proteins

Duncan Huston-Paterson, DPhil, Project Leader, Integral Molecular

Integral Molecular specializes in characterizing antibodies against structurally-complex targets, including GPCRs, ion channels, and immuno-oncology targets. Our Shotgun Mutagenesis technology maps conformational antibody epitopes at single-amino acid resolution with >95% success, generating critical intellectual property and detailed mechanistic insights. Our Membrane Proteome Array enables safety analysis of antibodies by testing each antibody against an expression array of 5,300 structurally-intact membrane proteins, providing a comprehensive assessment of off-target antibody interactions.

Sponsored by isogenica

12:50 Luncheon Presentation II: Design and Validation of Isogenica's Fully Synthetic Human Fab Library

Guy Hermans, PhD, CSO, Isogenica Ltd.

We will present validation data on our recently developed fully synthetic human Fab library. The diverse set of heavy and light chain germlines, combined with the fully synthetic nature of the randomized CDR1, -2 and -3 regions ensures many issues with immune and naïve libraries can be overcome. Use of Colibra™ DNA library build technology allowed for the removal of CMC liability motifs from both the framework as well as CDR regions.

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

DISPLAY AS A TOOL FOR DISCOVERY

2:00 Chairperson's Remarks

K. Dane Wittrup, PhD, J.R. Mares Professor, Chemical Engineering & Bioengineering, Massachusetts Institute of Technology

2:05 High-Throughput Synthetic Antibody Discovery at the Institute for Protein Innovation (IPI)

Joseph Jardine, PhD, Head, Antibody Discovery, Institute for Protein Innovation

The mission statement for the Institute for Protein Innovation is to produce high quality, highly validated open source antibodies against human cell surface proteins. We are building high-throughput pipelines for mammalian protein production, yeast Fab display for antibody selection and receptor-ligand deorphaning for novel target identification, details of which will be presented in this talk.

2:35 Multi-Tasking for Multi-Specific Targets at Sanofi

Leila Sevigny, PhD, Senior Scientist, Sanofi Genzyme

In the present case study, we show how Sanofi increased the efficiency of bi- and multi-specific screening, antigen creation and engineering. We show how we have benefited from the use of the fully integrated workflow platform, Genedata Biologics, which enables molecule, sample and assay data tracking from generation to final candidates. Not only does the underlying database system provide a shared repository to track all the pertinent data associated with the project from start to finish, but it also allows us to draw conclusions from the cross-project data mining and learn from our experience for future multi-specific antibody discovery and optimization campaigns.

Sponsored by ttplabtech

3:05 Screening Smarter to Derive Data Driven Decisions Faster

Ben Schenker, Director, TTP Labtech Inc.

There's a smart way to increase the pace of therapeutic antibody and vaccine discovery. Derive data driven decisions faster with no-wash, cell, or bead-based immunoassay screening workflows that can be multiplexed to combine hit identification with selectivity, species cross-reactivity, viability, infectivity, or titer for accelerated decision making.

3:20 Sponsored Presentation *(Opportunity Available)*

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:25 Engineering Alternative Scaffolds via Yeast Display

Benjamin Hackel, PhD, Associate Professor, Chemical Engineering and Materials Science, University of Minnesota

Small protein scaffolds provide an efficient basis for ligand discovery with potential advantages in molecular imaging, *ex vivo* diagnostics, and multi-functional protein fusions. We have merged computational analysis of scaffold biophysical properties, yeast display sorting of scaffold libraries, and deep sequencing of phenotypic populations to discover novel scaffolds and elucidate the characteristics that dictate evolvability. The discovery platform and case studies will be presented.

4:55 Identification and Development of Variable Lymphocyte Targeting Ligands for Glioblastoma

Benjamin Umlauf, PhD, Post-Doctoral Fellow, Chemical and Biological Engineering Department, University of Wisconsin

The median survival for patients presenting with the brain tumor Glioblastoma Multiforme (GBM) remains less than two years despite clinical intervention. Here we present a screening paradigm, identification of lead candidates, and a functional application for identifying Variable Lymphocyte Receptors that serve as targeting ligands for GBM therapies by binding to pathologically exposed brain extracellular matrix.

5:25 End of Display of Antibodies

5:30 Registration for Dinner Short Courses*

****Separate registration required, please see page 6 for course details.***

Nineteenth Annual

ENGINEERING ANTIBODIES

New Science and Technologies for the Selection, Engineering and Targeting of Next Generation Therapeutic Antibodies and Biotherapeutics

RECOMMENDED SHORT COURSE(S)*

SC8: Introduction to Biophysical Analysis for Biotherapeutics: Discovery & Development Applications

**Separate registration required, please see page 6 for course details.*

WEDNESDAY, MAY 2

7:30 am Registration and Morning Coffee

ANTIBODIES AGAINST DIFFICULT TARGETS

8:30 Chairperson's Remarks
Jonas V. Schaefer, PhD, Lab Head/Investigator II, Novartis Institutes for BioMedical Research (NIBR)

8:40 Anti-RAS DARPins as Multipurpose Tools to Investigate Its Versatile Functions and to Design Novel Approaches to Make It a Druggable Target
Jonas V. Schaefer, PhD, Lab Head/Investigator II, Novartis Institutes for BioMedical Research (NIBR)
Even after decades of research, a direct inhibition of the high-priority anticancer drug target KRAS with small molecules has been extremely challenging. Therefore, DARPins – very potent proteinaceous binders with highly beneficial properties – were generated to bind to various sites of oncogenic Ras mutants, thus efficiently interfering with the numerous interactions with their effector proteins. These DARPins might therefore help to investigate various approaches to attack this so far 'undruggable' target.

9:10 New Strategies to Identify Functional Antibodies against Complex Membrane Proteins
JT Koerber, PhD, Scientist, Antibody Engineering, Genentech
Integral membrane proteins comprise a large untapped target space for therapeutic antibodies, but the discovery of functional antibodies against this class of proteins remains a challenge. The dynamic nature of these targets coupled with complex functional assays can limit the efficiency of all project stages from initial discovery to ultimately characterization of lead antibodies. I will discuss our efforts towards addressing these challenges.

9:40 Distinct 4-1BB Binding Properties of Therapeutic Utomilumab and Urelumab Antibodies
Andy Yeung, PhD, Associate Research Fellow, Rinat, Oncology R&D, Pfizer, Inc.
Agonistic anti-human 41BB (CD137) antibodies, utomilumab (PF-05082566) and urelumab (BMS-663513) showed distinctive therapeutic efficacy and toxicity profiles in clinical trials. To gain insight into their binding modes, we solved structures of the human 4-1BB receptor-ligand complex and the 4-1BB receptor bound to either utolilumab or urelumab. We also compared their binding epitopes to that of surrogate anti-m41BB antibodies. Our work provide insight into the future development of 4-1BB targeted biologics.

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

DISCOVERY OF UNIQUE ANTIBODIES

10:55 Structure-Function Analysis to Identify Rare Epitopes with Unique Binding Properties
Bruno Correia, PhD, Professor, Protein Design and Immunoengineering, EPFL Zurich, Switzerland
We developed a computational design strategy with the ultimate goal of designing accurate epitope mimics for the development of novel vaccine candidates. Recently, a first proof of principle has shown that a computationally designed protein presenting the Respiratory Syncytial Virus (RSV) Motavizumab epitope elicited potent neutralizing antibodies in nonhuman primates. We have extended this approach to several epitopes in RSV, and I will present biochemical, biophysical and immunological characterization of the computationally designed immunogens.

11:25 Discovery of High-Affinity Human PD-1 and LAG-3 Antibodies Using Novel Microfluidic and Molecular Genomic Methods
David S. Johnson, PhD, CEO, GigaGen
Conventionally, mouse hybridomas or well-plate screening are used to identify therapeutic monoclonal antibody candidates. We have developed a novel alternative to hybridoma-based discovery that combines microfluidics, yeast single chain variable fragment (scFv) display, and deep sequencing. We have used our technology to rapidly discover thousands of checkpoint inhibitor candidates against sixteen targets, in less than six months. In this talk, we will specifically focus on our PD-1 and LAG-3 programs.

11:55 KEYNOTE PRESENTATION: Engineering Antibodies to Modulate Antibody Dynamics

E. Sally Ward, Ph.D., Professor, Molecular and Cellular Medicine, Texas A&M Health Science Center

There have been multiple developments in the engineering of FcRn-IgG interactions to modulate the *in vivo* dynamics of antibodies and their target antigens. In parallel, analyses of the behavior of FcRn and its ligands at the subcellular level can be used to inform the design of therapeutics. The presentation will cover recent progress in these areas.

12:25 pm Engineering SURE CHO-M Cell Lines for Optimized and Customized Solutions to Therapeutics Production

Sponsored by SELEXIS

Valerie Le Fourn, PhD, Research & Development Cell Culture Director, Selexis SA

New complex biotherapeutics molecules are increasingly being developed resulting in new manufacturing challenges for CHO cell lines. To address these challenges, we developed the SUREtechnology platform. Using our CHO-M cell line genomics/transcriptomics data, we have improved our understanding of endogenous pathways regulating the expression of recombinant proteins. I will describe case studies with customized solutions for Difficult-to-Express Proteins to generate CHO cell lines with high productivities while maintaining product quality.

12:55 Luncheon Presentation I: Rapid Purification, Concentration, and Characterization of Antibodies and Proteins: Capturem High-Capacity Membranes

Sponsored by TaKaRa (Clontech TaKaRa cellartis)

Tim Larson, PhD, Marketing Specialist I, Marketing, Takara Bio USA

We have developed Capturem technology, a novel, nylon membrane-based system with an extremely fast workflow that can be completed in 5–20 minutes, with the added benefit of resulting in an exceptionally pure and concentrated eluate in single column and high-throughput formats. We have also demonstrated trypsin and pepsin-functionalized membranes for rapid protein digestion for downstream analysis. Capturem membranes can dramatically speed up product development by eliminating the long incubation times required with traditional workflows.

1:25 Computationally Optimized SuperHuman Library Generates 100,000 Unique Antibodies Against 24 Immune Targets in Weeks

Sponsored by distributed bio

Jacob Glanville, PhD, Co-Founder & CSO, Distributed Bio

Here we describe a computational antibody library design that was optimized for both sequence diversity, engineering fitness and speed through the analysis of 1000's of human antibody repertoires. This diversity has resulted in a uniquely engineered library that generates over 5000 unique antibodies saturating all epitopes in all 24 tested antigens. This library can be panned under aggressive conditions, recovering picomolar binders, and isolating multi-species cross-reactive members against target homologs without additional engineering.

1:55 Session Break

ENGINEERING FOR SELECTIVE BINDING

2:10 Chairperson's Remarks

Danlin Yang, PhD, Scientist, Biotherapeutics Discovery, Boehringer Ingelheim

2:15 Receptor Engineering and Strategies for Selective Binding

Joel Cohen-Solal, PhD, Senior Research Scientist, Global Protein Sciences, AbbVie Bioresearch Center

Binding studies of IgG-based biologics to Fc Receptors carried out by cell-based assays are valuable to better characterize the interactions in physiologic-like settings and to identify parameters for selective binding.

2:45 Maximizing *in vivo* Target Clearance by Design of pH-Dependent Target Binding Antibodies with Altered Affinity to FcRn

Danlin Yang, PhD, Scientist, Biotherapeutics Discovery, Boehringer Ingelheim

In the past five years, the concept of recycling and sweeping antibodies has emerged in the literature. These antibodies have demonstrated potential success in reducing target levels compared to conventional antibodies. Here we present the groundwork on how to maximize target reduction through the optimal design of binding kinetics and pH-dependence to both antigen and FcRn in the therapeutic candidate, potentially providing a path to greater patient dosing convenience.

3:15 Advances in Computational Approaches to Antibody Engineering

Sponsored by SCHRÖDINGER

Christopher Negron, PhD, Senior Scientist, Schrödinger

Experimental techniques for discovering and optimizing antibodies with high affinity for a target have matured significantly. However, the discovery and optimization of other "drug-like" properties for antibodies remain challenging. We describe a computational workflow for identifying and removing those liabilities. Beyond this, we will describe computational approaches for predicting changes in protein stability and binding affinity using a rigorous physics-based approach, free energy perturbation (FEP).

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem-Solving Breakout Discussions

5:45 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

Cambridge HEALTHTECH Institute
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THURSDAY, MAY 3

8:00 am Morning Coffee

ENGINEERING ANTIBODIES FOR IMPROVED PROPERTIES

8:30 Chairperson's Remarks
Caroline Colley, PhD, Associate Director, Antibody Discovery and Protein Engineering, MedImmune, United Kingdom

8:35 Agonizing the TNFR Superfamily for Cancer Immunotherapy
Greg Lazar, PhD, Director, Antibody Engineering, Genentech
Multiple technology platforms have been explored to enable antibodies to mediate receptor agonist activity without relying on Fc receptor-mediated crosslinking. 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 as they relate to cancer immunotherapy.

9:05 Strategies for Identifying Biologics with Specific Mechanisms of Action
Caroline Colley, PhD, Associate Director, Antibody Discovery and Protein Engineering, MedImmune, United Kingdom
In biologics discovery, assay cascades can be designed from the outset to triage thousands of antibodies for the desired function, specificity and affinity. While early functional screening is paramount, it is also important to understand the mechanism of action through which an antibody mediates its effects (e.g. competitive, allosteric), to ensure appropriate target suppression. Using case studies, strategies and learnings for identifying antibodies with the desired mechanism will be highlighted.

Sponsored by AbCellera

9:35 Overcoming Tolerance by Deep Mining of Natural Immune Repertoires
Carl Hansen, PhD, CEO, AbSCellera
AbCellera has developed an end-to-end antibody discovery platform for deep screening of natural immune responses. Our microfluidic platform supports a broad array of assay formats, enabling discovery against any target class at a throughput of millions of single cells per run. Here we show that ultra-deep screening of multiple immune tissues can be used to overcome challenges of immune tolerance, generating diverse panels of hundreds of lead candidates against targets with 100% homology.

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

11:05 Fc Engineering for Complement-Mediated Effector Function and FcRn-Mediated Pharmacokinetics
Chang-Han Lee, PhD, Postdoctoral Researcher, Georgiou Lab, The University of Texas at Austin
Engineered Fc domains, which have an asymmetric structure and completely selective binding to C1q without any concomitant FcγR engagement, were used to demonstrate that CDCC and CDCP of therapeutic antibodies mediate removal of target cells with equivalent kinetics and potency as FcγR-dependent ADCC and ADCP mechanisms *in vitro* and in mouse models. In another engineered Fc domain, it showed enhanced serum half-life in several hFcRn mouse models and is applicable for IgG subclasses.

11:35 Engineering Antibodies for Tissue Specific Inhibition
Abhishek Datta, Ph.D., Director, Antibody Discovery and Engineering, Scholar Rock
Traditional therapeutic approaches directly target a growth factor or its receptor everywhere in the body, not only shutting down its harmful function in disease, but also potentially causing undesirable side effects arising from the inherent biology of growth factors. Individual growth factors occur as members of larger families of structurally related proteins, and a single growth factor can lead to a different biological effect in different tissues. By intervening in supracellular activation, our medicines target growth factors in their latent, inactive forms to selectively and locally modulate growth factor activity.

12:05 pm Designer Proteins: Targeting Protein-Pathogen Interactions
Eva-Maria Strauch, PhD, Research Assistant Professor, Biochemistry, University of Washington
Many viral surface glycoproteins and cell surface receptors are homo-oligomers, and hence can potentially be targeted by geometrically matched homo-oligomers. I will describe a general strategy for the computational design of homo-oligomeric protein assemblies with binding functionality precisely matched to homo-oligomeric target sites. I will conclude with how we can take the design of binding proteins to the next level using completely customized, *de novo* designed proteins against pathogens.

12:35 End of Engineering Antibodies

> Well organized, as usual, but particularly in regard to **the breadth of topics covered and the connections made between disciplines was nice to see – very forward looking.**
> - Research Scientist, AbbVie

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Twentieth Annual

ENGINEERING BISPECIFIC ANTIBODIES

Driving Progress in Biologics

THURSDAY, MAY 3

BISPECIFIC VS. CAR T APPROACH: DIRECT COMPARISON

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

G. Jonah Rainey, PhD, Executive Director, Head of Antibody Research, MabVax Therapeutics Holdings, Inc.

1:50 Preventing Antigen Escape with CD19/CD20 Bispecific Chimeric Antigen Receptors

Yvonne Y. Chen, PhD, Assistant Professor, Chemical and Biomolecular Engineering, University of California, Los Angeles

Antigen escape is a major cause of cancer remission in patients treated with CD19 chimeric antigen receptor (CAR)-T cell therapy. Here, we report a bispecific, OR-gate CAR that can trigger robust T cell activation in response to target cells that present either CD19 or CD20, thus preventing malignant B cells from escaping T- cell therapy by simply losing CD19 expression.

2:20 Bispecific CARs Targeting Discreet Conserved Sites on the HIV Env Glycoptoein: Toward a Functional Cure

Edward A. Berger, PhD, Chief, Molecular Structure Section, Laboratory of Viral Diseases, NIAID, National Institutes of Health

To achieve long-term (lifelong?) HIV suppression, CARs must be engineered not only to be highly potent, but also to approach the ideal properties of inescapability and non-immunogenicity. We have designed all-human bispecific CARs targeting containing CD4 linked to a second moiety that targets a highly conserved (essential) site on HIV-gp120. The second moiety enhances potency, and prevents the CD4 from acting as an HIV entry receptor on CD8+ T cells.

2:50 KEYNOTE PRESENTATION: Harnessing T Cells as Cancer Therapeutics: Bispecifics vs. CARs

Stephen Gottschalk, MD, Chair, Bone Marrow Transplantation & Cellular Therapy, St. Jude Children's Research Hospital

Redirecting T cells with bispecifics or CARs has shown impressive clinical results for CD19+ hematological malignancies resulting in their FDA approval. However, for other malignancies, including solid tumors and brain tumors, this therapeutic approach has been less effective. In my talk, I will review pros and cons of bispecifics and CARs, current obstacles, and preclinical efforts to improve their efficacy.

3:20 Industrializing IO Therapeutic Discovery Platforms: Multispecifics, Engineered TCRs and CARs

Maria Wendt, PhD, Head, Science, Biologics, Genedata

Novel classes of bio-molecules are currently evaluated for their use in cancer immunotherapy. Bi- and multi-specific antibodies, Ab-cytokine fusion proteins, non-Ig scaffolds, chimeric antigen receptors (CARs), engineered TCRs and TCR-based bispecific constructs promise significant advantages. However, these highly engineered molecules pose new challenges in design, engineering, cloning, expression, purification, and analytics. We present an infrastructure that addresses these challenges and enables the industrialization of these various novel therapeutic platforms.

3:50 Networking Refreshment Break

ENGINEERING IMPROVEMENTS FOR BISPECIFIC ANTIBODIES

Chairperson's Remarks

Robert Mabry, PhD, VP, Protein Science. Cogen Therapeutics, Inc.

4:20 Immunoglobulin Domain Interface Exchange as a Platform Technology to Engineer Bispecific Antibodies

Stanislas Blein, PhD, Senior Director, Head Antibody Engineering, Biologics Research, Glenmark Pharmaceuticals S.A.

Glenmark Pharmaceuticals' BEAT® platform is a robust and versatile bispecific antibody platform based on heavy chain heterodimerization. The technology relies on biomimicry wherein the protein-protein interfaces of two different immunoglobulin constant domain pairs are exchanged in

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part or fully to design new heterodimeric domains. Using our platform, we have engineered and in-house manufactured two clinical stage bispecific antibodies for cancer therapy. Engineering and Phase I manufacturing data will be presented.

4:50 "In Format" Display, Selection and Screening of Bispecific Antibodies

Nicolas Fischer, PhD, Head of Research, Novimmune

The unique mode of action of bispecific antibodies often requires binding sites in a defined geometry. Rather than randomly combining antibodies into one or multiple bispecific formats and testing of purified bispecific candidates, it would be preferable to screen and even co-select binders that support the desired mode of action. We have developed a dual-display technology allowing 'in format' enrichment of antibody fragments based on target co-engagement. In addition, different modalities to maximize throughput of functional screening for BiAb have been implemented.

5:20 End of Day

5:20 Registration for Dinner Short Courses*

**Separate registration required, please see page 6 for course details.*

FRIDAY, MAY 4

8:00 am Morning Coffee

NEW WAYS OF MAKING BISPECIFIC ANTIBODIES

8:30 Chairperson's Remarks

Christian Klein, PhD, Roche Pharmaceutical Research & Early Development, Oncology Discovery & Translational Area, Cancer Immunotherapy Discovery, Roche Innovation Center Zurich, Roche Glycart AG

8:35 Redirecting T-Cell for Cancer Therapy Using Antibody Circuits

Mark Cobbold, MD, PhD, Cellular Immunotherapy Program, Center for Cancer Immunology, Massachusetts General Hospital; Member of the Faculty of Medicine, Harvard Medical School

Cytotoxic T-cells are amongst the most potent arms of the immune response, and immunotherapies harnessing these exhibit powerful effects against cancer. Separating toxicity from efficacy remains an ongoing challenge for both CAR T and bispecific T-cell engaging biologics. Here we describe a new antibody-based approach to selectively engage T-cells at tumor sites using Boolean operator logic based upon antigen and protease target site expression. By applying logic gating, we obviate many of the current challenges with T-cell engaging antibodies.

9:05 Productive Common Light Chain Libraries Yield Diverse Panels of High Affinity Bispecific Antibodies

Thomas J. Van Blarcom, PhD, Associate Research Fellow, Oncology Research and Development, Pfizer, Inc., Rinat Laboratories

Here we describe the design of a synthetic human antibody library based on common light chains to generate antibodies with biochemical and biophysical properties that are indistinguishable to traditional therapeutic monoclonal antibodies. We used this library to generate diverse panels of well-behaved, high affinity antibodies toward a variety of epitopes across multiple antigens including mouse 4-1BB, a therapeutically important T cell costimulatory receptor. This approach allowed us to identify antibodies with a wide range of agonistic activity which are being used to further investigate the therapeutic potential of antibodies targeting one or more epitopes of 4-1BB.

Sponsored by Avacta LIFE SCIENCES

9:35 Affimer Therapeutics: A Novel Human Scaffold for the Generation of Bi-Specific Antibodies

Amrik Basran, PhD, CSO, Avacta Life Sciences

Affimer therapeutics are based on the human protein Stefin A, a small (12kDa) intracellular protease inhibitor. We have built large (1x1010) phage display libraries and generated highly selective Affimer binders to range of therapeutically relevant targets such as PD-L1 and LAG-3. We have shown that the Affimer scaffold can be fused to either the Fc domain or a full antibody to create bispecific molecules that express and are able to engage both target antigens.

10:05 Networking Coffee Break

RAISING THE THERAPEUTIC INDEX: INCREASING THE SAFETY AND EFFICACY OF BISPECIFIC ANTIBODIES

10:35 Chairperson's Remarks

Mahiuddin Ahmed, PhD, CSO, Y-mAbs Therapeutics

10:35 KEYNOTE PRESENTATION: Engineered Antibody Derivatives for Modulation of Pharmacokinetic Properties of Small Molecules and Targeted Payload Delivery

Ulrich Brinkmann, PhD, Roche Pharma Research & Early Development, Large Molecule Research, Roche Innovation Center Munich (RICM), Penzberg, Germany

The presentation covers recent applications of hapten-binding antibodies and engineered derivatives, including modulation of the pharmacokinetic properties of small compounds or peptides. Hapten-binding antibodies can also serve as payload-capture modules of bispecific and/or multifunctional antibody formats. Here they serve as non-covalent or covalent coupling modules to haptenylated compounds, to enable specific delivery to tissues or cells.

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11:05 IL15 Trispecific Killer Engagers (TriKE) Make Natural Killer Cells Specific to CD33+ Targets While Also Inducing Persistence, *in vivo* Expansion, and Enhanced Function

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

The effectiveness of NK cell infusions to induce leukemic remission is limited by lack of both antigen specificity and *in vivo* expansion. To address the first issue, we previously generated a bispecific killer engager (BiKE) containing single-chain scFv against CD16 and CD33 to create an immunologic synapse between NK cells and CD33(+) myeloid targets. We have now incorporated a novel modified human IL15 crosslinker, producing a 161533 trispecific killer engager (TriKE) to induce expansion, priming, and survival, which we hypothesize will enhance clinical efficacy.

11:35 Anti-Tumor x Anti-DOTA Bispecific Antibodies for Pre-Targeted Radioimmunotherapy

Steven M. Larson, MD, FACNM, FACR, Donna and Benjamin M. Rosen Chair, Attending Molecular Imaging and Therapy Service, Radiology; Member and Lab Head, Molecular Pharmacology and Chemistry Program, Sloan Kettering Institute; Professor, Radiology, Weill Cornell University Medical Center, Radioimmunotherapy and Theranostics, Ludwig Center

We recently developed a promising theranostic; treatment of human solid tumors using a pretargeted radioimmunotherapy strategy (DOTAPRIT) based on a tumor antigen-targeting bispecific antibody (bsAb) and a small-molecule radioactive hapten, a complex of lutetium-177 (177Lu) and S-2-(4-aminobenzyl)-1,4,7,10-tetraazacyclododecane tetraacetic acid (177Lu-DOTA-Bn) that leads to high therapeutic index (Tis) for radiosensitive tissues such as blood and kidney. Studies targeting 3 solid tumor human xenografts in mouse models have shown proof of principle.

12:05 pm Trispecific Broadly Neutralizing HIV Antibodies for Prevention and Treatment of HIV-1 Infection

Amarendra Pegu, PhD, Staff Scientist, Laboratory of Virology, Vaccine Research Center, National Institute of Allergy and Infectious Diseases, NIH

We have engineered trispecific antibodies that allow a single molecule to interact with three independent HIV-1 envelope determinants. These trispecific antibodies exhibited higher potency and breadth than any single anti HIV-1 antibody and showed protective efficacy in an animal model of HIV-1 infection. Trispecific antibodies thus constitute a platform to engage multiple therapeutic targets through a single protein, and could be applicable for diverse diseases, including infections, cancer and autoimmunity.

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

1:05 Networking Refreshment Break

ENGINEERING IMPROVEMENTS FOR BISPECIFIC ANTIBODIES

1:35 Chairperson's Remarks

Robert Mabry, PhD, VP, Protein Science. Cogen Therapeutics, Inc.

1:40 A Semi High-Throughput Method for Screening Small Bispecific Antibodies with High Cytotoxicity

Mitsuo Umetsu, PhD, Professor, Biomolecular Engineering, Graduate School of Engineering, Tohoku University

A number of studies on small bispecific T-cell-recruiting antibodies have showed that their cytotoxicity is critically dependent on their structural and functional properties. In this study, we constructed an optimized procedure for identifying highly cytotoxic antibodies from a variety of the T-cell-recruiting antibodies engineered from a series of antibodies against EGFR family and T-cell receptors, demonstrating the synergistic effects between target, epitope, binding affinity, and antibody structure.

2:10 A New Approach for Generating Bispecific Antibodies Based on a Common Light Chain Format and the Stable Architecture of Human Immunoglobulin G1

John de Kruif, PhD, CTO, Merus NV

We describe an approach for generating bispecific antibodies using common light chains and the stable architecture of human immunoglobulin G1. We used iterative experimental validation and computational modeling to identify an Fc variant pair that drives efficient heterodimerization of the antibody heavy chains. Long-term accelerated stability assays confirmed that this molecule is highly stable and has excellent biophysical characteristics. We show how this molecule is integrated in our discovery platform.

2:40 FIT-Ig: A Novel Tetravalent Bispecific Antibody Design without Peptide Linkers and Fc Mutations

Chengbin Wu, PhD, CEO, EpimAb Biotherapeutics

We describe here a new bispecific design, named Fabs-in-tandem immunoglobulin (FIT-Ig), in which two Fabs are fused directly in a crisscross orientation without any mutations or use of peptide linkers. This unique design provides a symmetrical IgG-like bispecific molecule with correct association of 2 sets of VH/VL pairs. In this paper, we show that FIT-Ig molecules exhibit excellent drug-like properties, *in vitro* and *in vivo* functions, as well as manufacturing efficiency for commercial development.

3:10 Chemically-Generated Immunomodulatory Bispecific Antibodies

Yanwen Fu, PhD, Director, Antibody Technology and Chemical Biology, Sorrento Therapeutics

Bispecific antibodies (BsAbs) capable of engaging cytotoxic T lymphocytes for tumor cell lysis are emerging as a new option for cancer treatment. Sorrento has developed a robust platform to generate BsAbs through hetero-dimerization of two chemically-modified antibodies or antibody fragments. Using this approach, we synthesized a variety of immunomodulatory bispecific antibodies. Results from BsAb assembly, biophysical characterization and effector-cell mediated cytotoxicity assays will be presented.

3:40 End of Conference

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

ONCOLOGY STREAM

- Antibodies for Cancer Therapy
- Advancing Bispecific Antibodies and Combination Therapy to the Clinic
- Clinical Progress of Antibody-Drug Conjugates

Advancing Antibody Therapeutics to the Clinic

Antibody-based therapeutics have proved to be promising in the field of targeted therapies for cancer. At this year's PEGS Summit, the oncology stream will focus on target investigation, ADC monotherapies, combination therapies including ADC/Immuno-oncology and bispecific/ADC combinations. All the latest trends and strategies in choosing optimal constructs and combination therapy will be examined at the discovery and later preclinical and clinical stages. This meeting will also provide insights on regulatory and manufacturing considerations to advance antibody-based therapeutics to the clinic for precision targeting of cancer.

Eighth Annual

ANTIBODIES FOR CANCER THERAPY

Winning Strategies for the Next Breakthrough Therapies

SUNDAY, APRIL 29

RECOMMENDED SHORT COURSE(S)*

SC2: Translational Considerations for Development of Monoclonal Antibodies and Emerging Constructs: Part I: Focus on Construct Design

SC7: Translational Considerations for Development of Monoclonal Antibodies and Emerging Constructs: Part 2: Focus on Preclinical Development

**Separate registration required, please see page 6 for course details.*

MONDAY, APRIL 30

7:00 am **Registration and Morning Coffee**

SELECTING EMERGING TARGETS

8:30 **Chairperson's Remarks**
Mitchell Ho, PhD, Senior Investigator, National Cancer Institute, NIH

8:40 **Immunotherapy for Liver Cancer: How and Targeting What?**
Tim F. Greten, MD, Senior Investigator, GI Maligancy Section, Thoracic and GI Oncology Branch, Center for Cancer Research, National Cancer Institute
Hepatocellular carcinoma (HCC) is the sixth most frequent neoplasm and the second leading cause of cancer-related deaths worldwide. HCC typically arises in the context of liver cirrhosis caused by viral infection, environmental factors, toxins, and in rare cases genetic conditions. We have been studying how the tumor microenvironment affects anti-tumor immunity and study novel immune based treatment approaches for the treatment of patients with liver cancer.

9:10 **Improving Cancer Therapy through Simultaneous Ablation of CD276/B7-H3-Positive Tumor Cells and Tumor Vasculature**
Bradley St. Croix, PhD, Senior Associate Scientist, Head, Tumor Angiogenesis Unit, Mouse Cancer Genetics Program, National Cancer Institute
CD276 is frequently overexpressed in tumors on both tumor cells and tumor infiltrating blood vessels that fuel its growth, making it an alluring dual compartment target for an ADC therapy. The development of anti-CD276 ADCs armed with MMAE or PBD will be discussed, along with the mechanistic basis for the differential efficacy of these agents against tumor-associated stroma and implications for development of other vascular-targeted ADCs.

9:40 **Pharmacological Characterization of Anti-Glypican 3/CD3 Bispecific T Cell-Redirecting Antibody ERY974**
Junichi Nezu, PhD, Senior Specialist, Project & Lifecycle Management Unit, Chugai Pharmaceutical, Co., Ltd.
The bispecific T cell redirecting antibody (TRAB) is a new form of promising immunotherapy. We generated a novel TRAB, ERY974, targeting tumor-specific antigen Glypican-3 (GPC3). Using a mouse model reconstituted with human immune cells, we revealed that ERY974 is highly effective in killing various tumor types including those with non-immunogenic features. In the presentation, combination effect of ERY974 with other anti-cancer agents and its possible mechanism will also be discussed.

10:10 **Networking Coffee Break**

10:45 **Chairperson's Remarks**
Soldano Ferrone, MD, PhD, Surgical Oncology, Surgery, Massachusetts General Hospital

10:50 **KEYNOTE PRESENTATION: Recent Advances in Innovative Engineered Antibodies for Treatment of Cancer**
William R. Strohl, PhD, Owner and President, BiStro Biotech Consulting, LLC
New technologies, including multitargeted bispecific antibodies, T cell redirecting bispecific antibodies, engagement of T cell checkpoint targets, and autologous and allogeneic forms of chimeric-antigen receptor (CAR) T and NK cells, have been employed over the past several years to improve the odds of treating cancer successfully. This presentation will explore the current clinical use of these technologies and will highlight promising new advances that offer hope for future cancer therapy.

Cambridge HEALTHTECH Institute
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11:20 Targeting Netrin-1: From Modulating Cancer Plasticity to Strengthening Immunotherapy

Patrick Mehlen, PhD, CEO Netris Pharma, Centre Léon Bérard

Netrin-1, a secreted cue, has been shown to be up-regulated in a large fraction of human cancers and has been show to promote tumor progression. An anti-netrin-1 mAb called NP137 has been preclinically developed and is currently assessed in a first-in-man-first-in-class Phase I clinical trial. The NP137 shows preclinical efficacy related to a specific effect on cancer plasticity, and preclinical data support the importance of combining NP137 with immune-checkpoint inhibitors. We will present preclinical and preliminary clinical data.

11:50 Antibody Protein Sequencing with Mass Spectrometry

Mingjie Xie, CEO, Rapid Novor, Inc.

Many applications in antibody engineering require the direct sequencing of antibody proteins. At Rapid Novor (rapidnovor.com), we have developed a robust workflow and routinely sequenced antibody proteins. Here we share the success experiences, examine common mistakes novices make, and present our practices to ensure the correctness of every amino acid.

12:20 pm Streamlined Discovery and Production of Antibodies

Sponsored by ICOSAGEN

Sirle Saul, Key Account and Technology Officer, Business Development, Icosagen Technologies, Inc.

Target selection is followed by development and production of monoclonal antibodies. HybriFree technology enables to discover recombinant antibodies by direct cloning from B-cells of immunized rabbits, chicken or from hybridomas. The subsequent production in mammalian cell factories can be done using QMCF technology. This scalable episomal expression system enables to produce up to gram quantities of recombinant antibodies (including non-fucosylated) with low endotoxin levels in few weeks and generate production cell banks in 10 days.

12:50 Luncheon Presentation I: *In Vivo* Platform for Generating Human "Heavy Chain Only" Antibodies for Drug Discovery

Sponsored by HARBOUR BIOMED

Frank Grosveld, PhD, Professor of Cell Biology, Erasmus MC; Founder, Harbour Antibodies BV, Harbour BioMed

The majority of currently approved fully human antibody drugs are generated *in vivo* from transgenic animal platforms. Here we present recent development from Harbour Antibodies utilizing transgenic mice to generate novel "heavy chain only" antibodies (HCAb). The Harbour HCAb platform enables the development of antibody fragment-based therapeutics such as nanobodies, bi-specific or multivalent antibodies and CAR-T with favorable drug-like properties.

1:20 Luncheon Presentation II *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 Challenges and Opportunities in Engineering Protein Biopharmaceuticals

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)

Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk, I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

4:55 The Next Generation of Cancer Immunotherapy: Targeting Myeloid Immune Checkpoints

Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital

Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

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

Sponsored by PRECISION FOR MEDICINE
THE FUTURE OF MEDICINE IS PRECISION

7:15 End of Day

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

TUESDAY, MAY 1

8:00 am Registration and Morning Coffee

B7-H3, AN ATTRACTIVE TARGET FOR ANTIBODY-BASED STRATEGIES: COMPARING DIFFERENT APPROACHES

8:25 Chairperson's Remarks
Soldano Ferrone, MD, PhD, Surgical Oncology, Surgery, Massachusetts General Hospital

8:30 CAR T Cells Targeting B7-H3
Gianpietro Dotti, MD, Lineberger Comprehensive Cancer Center Member, Professor, Microbiology and Immunology; Director, Lineberger Immunotherapy Program, University of North Carolina School of Medicine
The field of chimeric antigen receptors (CARs) in hematologic malignancies has been largely dominated by the adoptive transfer of T cells expressing the CD19-specific CAR for therapy of acute lymphoid leukemia and non-Hodgkin's lymphomas. We generated CAR Ts targeting the B7-H3 antigen that is expressed by many solid tumors. B7-H3.CAR Ts effectively eliminate several solid tumor cells *in vitro*, in PDAC orthotopic and metastatic xenograft NSG mouse models, and patient-derived xenograft (PDX) orthotopic NSG mouse models. B-H3.CAR Ts recognize the murine B7-H3, but we did not observe any decrease in hematopoietic cell numbers in blood, spleen or bone marrow, or significant tissue damage, which further encourage the clinical translation.

9:00 Targeting B7-H3 with Multiple Approaches
Ezio Bonvini, MD, Senior Vice President, Research & CSO, MacroGenics, Inc.
B7-H3 is a member of the B7-family of immune regulators. While its immunological role remains unknown, B7-H3 expression is a negative prognostic factor in cancer and, owing to its limited expression in normal tissues, a suitable tumor target for exploitation by a variety of mechanistic interventions.

9:30 B7-H3 is a potential Antibody Drug Conjugate target for the treatment of solid tumours
Kelli Ryan, PhD, Senior Scientist, Oncology Department, MedImmune
B7H3 is a member of the B7 family of TCR modulatory proteins that is also significantly expressed on the surface of tumor cells and the tumor vasculature, and can be a poor prognostic marker for certain cancers. This presentation will summarize the preclinical data generated upon evaluating ADCs targeting B7H3 with either tubulysin or PBD payloads.

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

EXPLOITING AND POTENTIATING KNOWN TARGETS WITH SECOND GENERATION ANTIBODIES

Chairperson's Remarks
Horacio G. Nastri, PhD, Senior Director, Antibody Biotherapeutics, Incyte Corporation

10:50 Overcoming Resistance to HER2-Targeted Therapy with a Novel HER2/CD3 Bispecific Antibody
Nai-Kong V. Cheung, MD, PhD, Head, Neuroblastoma Program; Enid A. Haupt Endowed Chair, Pediatric Oncology, Memorial Sloan Kettering Cancer Center
HER2 is an established tumor target for breast, ovarian and gastric cancers. We explored a novel HER2/CD3 bispecific antibody (HER2-BsAb) platform which, in addition to preserving the anti-proliferative effects of trastuzumab, recruits and activates circulating T cells, promoting T cell tumor infiltration, as well as ablating HER2(+) tumors resistant to standard HER2-targeted therapies. HER2-BsAb-mediated cytotoxicity is relatively insensitive to PD-1/PD-L1 immune checkpoint inhibition, although the addition of ICI does improve its efficacy.

11:20 Unbiased Functional Screening of Large Bispecific Antibody Panels to Unlock Novel Biology
Mark Throsby, PhD, CSO, Merus NV
The bispecific antibody format represents an emerging therapeutic modality. We have developed a set of robust and validated technologies that permits unbiased in-format functional screening to identify human full-length IgG bispecific antibodies candidates with superior therapeutic properties. Two case studies will be presented where this approach has been successfully employed to discover lead candidates with differentiating properties that are now in clinical development.

11:50 Balancing Selectivity and Efficacy of Bispecific EGFR x c-MET Antibodies and Antibody-Drug Conjugates
Achim Doerner, PhD, Principal Scientist, Protein Engineering and Antibody Technologies, Merck KGaA Darmstadt, Germany
Therapies targeting EGFR often suffer from toxicities due to basal EGFR expression in normal tissue and may face limited efficacy through c-MET activation. Hence, we aim to construct bispecific EGFR x c-MET antibodies employing affinity-optimized binding moieties to balance both high selectivity and anti-tumor efficacy and to evaluate their potential for an innovative antibody-drug conjugate approach.

12:20 pm Luncheon Presentation I: OmniAb Engineered Animals for the Discovery of Fully Human Antibodies
Sponsored by OmniAb
Bill Harriman, PhD, MBA, Vice President, Antibody Discovery Services, Ligand
OmniRat®, OmniFlic®, OmniMouse® and OmniChicken™ use newly patented technology and deliver fully human OmniAb antibodies with high affinity, specificity, expression, solubility and stability. While transgenic mice expressing human antibodies date back to the 1990's, in recent years OMT and Crystal scientists were the first to create rats and chickens expressing diversified repertoires of antibodies with fully human idiotypes. OmniMouse® complements that to form the industry's only platform with three species.

12:50 Novel Method for Generation of Anti Idiotype Antibodies for PK Assay
Sponsored by Syngene
Saurabh Joshi, Senior Lead Investigator, Oncology, Syngene International Limited
Generation of anti idiotype (anti ID) antibodies is a must for any biotherapeutic

antibody program. This critical reagent generation is a strict time bound requirement. Identification of blocking as well as non-blocking anti IDs can become challenging task by simply immunizing biotherapeutic antibody molecule in the animals. This traditional approach is time consuming and laborious. Here, we have developed a novel immunization platform which provide increased chances of identifying anti IDs with less screening.

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

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

2:00 KEYNOTE PRESENTATION: Combining Local Immunotoxins Targeting Mesothelin with CTLA-4 Blockade Synergistically Eradicates Murine Cancer by Promoting Anti-Cancer Immunity
Ira H. Pastan, MD, Co-Chief, Laboratory of Molecular Biology; NIH Distinguished Investigator; Head, Molecular Biology Section
Immune check point blockade benefits a limited number of patients. SS1P and LMB-100 are immunotoxins used to treat mesothelin expressing cancers. To investigate synergy between check point inhibitors and immunotoxins, we developed a Balb/C mouse model using mouse breast cancer cells expressing human mesothelin. When immunotoxin was injected into the tumors and anti-CTLA-4 given I.P., anti-tumor immunity developed resulting in complete regressions of injected and distal un-injected tumors.

2:30 KEYNOTE PRESENTATION: Identifying Mechanisms of Resistance to Antibody-Targeted Cancer Immunotherapy
Louis Weiner, MD, Professor, Oncology and Lombardi Comprehensive Cancer Center, Georgetown University Medical Center
We developed an unbiased *in vivo* genome-wide RNAi screening platform that leverages host immune selection in strains of immunocompetent and immunodeficient mice to select for tumor cell-based genes that regulate *in vivo* sensitivity to immune attack. Utilizing this approach in a syngeneic Triple-Negative Breast Cancer (TNBC) model, we identified 709 genes that selectively regulated adaptive anti-tumor immunity, and validated the mechanisms that underlie the immune-related effects of expression of these genes in different TNBC lines, as well as tandem synergistic interactions. This approach has utility in identifying unknown tumor-specific regulators of immune recognition in multiple settings to reveal novel targets for future immunotherapies.

OVERCOMING MECHANISMS OF RESISTANCE TO IMMUNOTHERAPY FOR CHECKPOINT INHIBITORS

3:00 Chairperson's Remarks
Paul B. Chapman, MD, Physician & Scientist, Memorial Sloan Kettering Cancer Center

3:05 Loss of Peptide Presentation Apparatus as a Mechanism of Resistance to Checkpoint Inhibitor Therapy
Paul B. Chapman, MD, Melanoma Clinical Director, Attending Physician, Memorial Sloan Kettering Cancer Center; Professor, Medicine, Weill Cornell Medical College
Since melanoma cells frequently lose expression of HLA alleles, a potentially common mechanism of resistance to checkpoint inhibitors would be loss of antigen processing and presentation machinery. We are evaluating pre- and post-treatment tumor biopsies for defects in HLA class I antigen processing machinery as a mechanism for resistance to checkpoint inhibitors.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:25 Understanding Responses to Cancer Therapy: The Tissue is The Issue, but the Scoop is in the Poop
Jennifer Wargo, MD, Melanoma Research, MD Anderson Cancer Center
We have made major advances in cancer therapy through the use of targeted therapy and immunotherapy, however responses are not universal and are not always durable. A better understanding of mechanisms of response and resistance have been elucidated via analysis of longitudinal tumor and blood samples on therapy – providing potentially actionable strategies to overcome resistance. In addition to this, there is a growing appreciation of the role of the gut microbiome in modulating systemic and anti-tumor immune responses and insights into the role of the gut microbiome in response to immune checkpoint blockade will be discussed.

4:55 Personalized Cancer Vaccines as a Strategy to Overcome Resistance to Immunotherapy
Zhuting Hu, PhD, Research Fellow, Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School
Clonal evolution of cancer cells can lead to immune evasion, enabling tumors to avoid the attack by the immune response. Neoantigens, which arise from somatic tumor mutations, are highly immunogenic and therefore key targets of tumor cytolysis *in vivo*. Personalized cancer vaccines, by targeting a spectrum of different neoantigens expressed by a patient's tumor rather than a single antigen, can directly address the therapeutic challenge of tumor clonal heterogeneity and therefore potentially overcome resistance to immunotherapy.

5:25 End of Antibodies for Cancer Therapy

5:30 Registration for Dinner Short Courses*
**Separate registration required, please see page 6 for course details.*

Sixth Annual

ADVANCING BISPECIFIC ANTIBODIES AND COMBINATION THERAPY TO THE CLINIC

Creating the Killer Combo

RECOMMENDED SHORT COURSE(S)*

SC9: CAR T Cell Therapy for Solid Tumors

**Separate registration required, please see page 6 for course details.*

WEDNESDAY, MAY 2

7:30 am Registration and Morning Coffee

NEXT GENERATION OF BISPECIFIC CANCER BIOLOGICS: POTENTIAL OF GREATER CLINICAL BENEFITS OVER COMBINATIONS

8:30 Chairperson's Remarks
Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, MedImmune

8:40 Introduction and Overview of Bispecific Antibodies
Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, MedImmune

9:10 Using Oncolytic Viruses to Deploy Bispecific Antibodies for Targeted Cancer Therapy
Leonard Seymour, PhD, Professor, Gene Therapy, Oncology, University of Oxford

Oncolytic viruses replicate selectively within tumor cells and lyse them before spreading to infect other cells. We have 'armed' an oncolytic group B adenovirus to encode bispecific T cell engagers (BiTEs) and express them selectively within tumor cells, secreting them into the tumour microenvironment. In this way we can activate tumor-associated T cells to attack cancer cells (or cancer stromal cells) by judicious choice of BiTE specificity, whilst simultaneously avoiding any delivery-related systemic toxicities.

9:40 Bispecifics to the Rescue: Reviving Exhausted T Cells with Dual Costimulation
Raphael Clynes, MD, PhD, Vice President, Translational Biology, Xencor, Inc.

To improve therapeutic efficacy of single agent checkpoint blockade, engagement of multiple inhibitory receptors and/or agonist receptors offers the possibility to more robustly reinvigorate exhausted intratumoral T cells. Bispecific antibodies offer the potential to accomplish this with both enhanced selectivity and avidity for exhausted T cells, improving both on-target efficacy and limit off-target immunotoxicity. We will present the preclinical rationale for three bispecific antibodies anticipated to enter the clinic in 2018, including an anti-PD1/anti-CTLA4, an anti-CTLA-4/anti-LAG3, and an anti-PD1/anti-ICOS.

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

10:55 Target Expression, Generation, Preclinical Activity, and Pharmacokinetics of the BCMA-T Cell Bispecific Antibody EM801 for Multiple Myeloma Treatment
Dirk Hose, PhD, Priv.-Doz. Dr. med. Dr. biol. hom., Head, Multiple Myeloma Research Laboratory, Universitaetsklinikum Heidelberg, Medizinische Klinik V

B-cell-maturation antigen (BCMA) is a TCB-target expressed in all malignant plasma-cell samples at RNA (n=726) and protein (n=43) level, as on normal plasma-cells. The BCMA-TCB EM801 shows efficacy in 34/43 (79%) primary MM-patients' BM-samples, a H929-xenograft reconstituted NOG-mouse-model, and cynomolgus monkeys. EM801 kills malignant plasma-cells by coupling them with T-cells, inducing T-cell-activation, secretion of e.g. interferon-γ, granzyme B and perforin. The higher affinity derivative EM901 (CC-93269) is foreseen entering clinical phase I/II trials.

11:25 The Promise and Challenge of T-Cell-Redirecting Bispecific Antibodies Made by the DNL® Platform
Chien-Hsing Ken Chang, PhD, Vice President, Research & Development, Immunomedics, Inc.

Accumulating evidence has indicated the antitumor immunity of T cells induced upon ligation with a bsAb to target tumor cells also incurs a concurrent activation of various cell-bound as well as -secreted factors to promote tumor growth. Elucidating the relative contribution of each of these factors to the destruction and protection of tumor presents a challenge, and provides insights into selecting optimal combination therapy with T cells redirected by bsAbs.

11:55 Engineering High Affinity Tetravalent Bispecific Immune Cell Engagers to Destroy Malignant Cells with Low Target Expression
Michael Tesar, PhD, Research Program Head, Research and Development, Affimed GmbH
Affimed is a leader in NK cell directed therapies and its tetravalent bispecific immune cell engager platform utilizes a unique mode of action. Newest developments from our clinical and preclinical programs will be presented.

Sponsored by IGM Biosciences, Inc.

12:25 pm _A Potent, High Avidity IgM Bi-Specific Anti-CD20xCD3 Antibody with Longer Half-Life and Increased Safety
Ramesh Baliga, PhD, Vice President, Discovery Biology, IGM Biosciences, Inc.

12:55 LUNCHEON PRESENTATION I: A Novel Phenotypic Approach for Predicting Tumor Response

Sponsored by MITRA BIOTECH

Mark Paris, PhD, Associate Director, Translational Applications, Mitra Biotech

1:25 Developing First-In-Class Immune Cell Engagers for the Activation of Innate and Adaptive Immunity to Fight Cancer
Martin Treder, PhD, CSO, Affimed

1:55 Session Break

NEXT GENERATION OF BISPECIFIC CANCER BIOLOGICS: POTENTIAL OF GREATER CLINICAL BENEFITS OVER COMBINATIONS (CONT.)

2:10 Chairperson's Remarks
Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, MedImmune

2:15 PANEL DISCUSSION: Bispecific Oncology Biologics Efficacy and Safety: Do the Platforms of Bispecifics Matter?
Moderator: Rakesh Dixit, PhD, DABT, Vice President, R&D, Global Head, Biologics Safety Assessment, Translational Sciences, MedImmune
Panelists: Jacintha Shenton, PhD, Scientific Director, Biologics Toxicology, Janssen BioTherapeutics, Janssen R&D
Raphael Clynes, MD, PhD, Vice President, Translational Biology, Xencor, Inc.
Jennifer F. Nemeth, PhD, SCPM, Director, Biophysics, Structural Characterization, Biologics Discovery Sciences, Janssen Research & Development

- Challenges of more than 50 bispecific platforms
- Impact of effector function, half-life, bispecific targets (soluble vs. membrane bound antigens)
- Heme vs. non-heme tumors
- CMC, Manufacturing Considerations

Sponsored by applied biomath

3:15 Model Aided Drug Invention Case Studies in Research and Development
John Burke, PhD, Co-Founder, President and CEO, Applied BioMath, LLC
Two studies will be shown that highlight examples of Model Aided Drug Invention (MADI) efforts, which include mechanistic PK/PD and QSP approaches, that accelerated the discovery and development of best-in-class therapeutics and impacted critical decisions. Examples include: (1) predicting optimal drug properties and differentiation for bispecific biologics vs. fixed dose combinations (FDC) in targeting PD-1 and Tim-3; and (2) predicting optimal drug properties for a bispecific approach maximizing target coverage in the joint for Osteoarthritis.

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem-Solving Breakout Discussions

5:45 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

THURSDAY, MAY 3

8:00 am Morning Coffee

ENGINEERING THE NEXT WAVE OF BISPECIFICS: MORE THAN A SUM OF ITS PARTS

8:30 Chairperson's Remarks
Frank Comer, PhD, Scientist, MedImmune

8:35 KEYNOTE PRESENTATION: Bispecific Antibodies for the Treatment and Prevention of HIV/AIDS
David D. Ho, MD, Aaron Diamond AIDS Research Center, The Rockefeller University
The plasticity of HIV-1 demands additional improvements to these mAbs to better ensure their clinical utility. This talk will discuss engineered bispecific antibodies that are the most potent and broad HIV-neutralizing antibodies to date such as 10E8V2.0/iMab which reduced virus load substantially in HIV-1-infected humanized mice and also provided complete protection when administered prior to virus challenge. These bispecific antibodies hold promise as novel prophylactic and/or therapeutic agents in the fight against HIV-1.

9:05 Bispecific Antibodies and Antibody–Drug Conjugates (ADCs) Bridging HER2 and Prolactin Receptor Improve Efficacy of HER2 ADCs
Julian Andreev, PhD, Senior Staff Scientist, Oncology and Angiogenesis, Regeneron Pharmaceuticals
There is a need for HER2-directed ADCs effective in patients expressing low/moderate levels of HER2. Cross-linking HER2 to constitutively internalizing PRLR, using a HER2xPRLR bispecific ADC, dramatically enhances lysosomal degradation of HER2. Accordingly, bispecific ADCs improve upon T-DM1 efficacy in cells expressing intermediate levels of HER2. These results demonstrate that coupling a tumor-specific ADC target to a rapidly internalizing protein may be a useful approach to enhance efficacy of ADCs.

ADVANCING BISPECIFIC ANTIBODIES AND COMBINATION THERAPY TO THE CLINIC

Sponsored by AMUNIX

9:35 AMX-268 an EpCAM-Targeted T Cell Engager with Best in Class Therapeutic Index

Volker Schellenberger, CEO & President, Discovery, Amunix

AMX-268 is an EpCAM-targeted T cell engager engineered to reduce *in vivo* on-target but off-tumor toxicity by at least10 fold compared to other T cell engagers. AMX-268 is based on Amunix' proprietary ProTIA platform, which combines three targeting modalities: 1) tumor target binding, 2) local activation by tumor associated proteases, 3) Polymer exclusion form healthy tissues (EPR effect). Tumor specific antibodies can be rapidly converted into ProTIA and results for multiple targets will be shown.

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

11:05 Application of DART® Platform to Reverse Checkpoint Blockade and Enhance Immune Effector Function

Ross La Motte-Mohs, PhD, Scientist III, Cell Biology and Immunology, MacroGenics, Inc.

T cell exhaustion in cancer is associated with the expression of checkpoint molecules, including PD-1, CTLA-4 and LAG-3, that cooperate in inducing loss of immune cell effector function, leading to disease progression. Dual blockade of checkpoint molecules can overcome limitations associated with single molecule inhibition. Here we present an update on PD-1 x CTLA-4 (MGD019) and PD-1 x LAG-3 (MGD013) DART molecules as dual checkpoint inhibitors for restoring and/or enhancing T cell effector function.

11:35 PANEL DISCUSSION: Safety and Efficacy of Bispecific Antibodies vs. CAR T

Moderator: G. Jonah Rainey, PhD, Executive Director, Head of Antibody Research, MabVax Therapeutics Holdings, Inc.

Panelists: Carl Uli Bialucha, PhD, Oncology Biotherapeutics, Novartis Institutes for BioMedical Research, Inc.

Adrian Bot, MD, PhD, CSO, Kite Pharma, Inc.

Tara Arvedson, PhD, Director, Oncology Research, Amgen, Inc.

Bob Valamehr, PhD, Vice President, Cancer Immunotherapy, Fate Therapeutics

- Comparison of efficacy: approved and pipeline molecules. What is the best clinical endpoint?
- Costimulation: included as part of the CAR, but what about bispecifics?
- Toxicity: mechanisms of CRS/cytokine storm and ways to prevent and manage them
- On/off target activation: runaway CAR T proliferation, off-target effects, and antigen-independent T-cell activation

12:35 pm End of Advancing Bispecific Antibodies and Combination Therapy to the Clinic

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

Eighth Annual

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

Translating Preclinical Understanding to Clinical Success

THURSDAY, MAY 3

ADC-IO COMBINATIONS

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Gail Lewis Phillips, MSc, Senior Scientist, Translational Oncology, Genentech, Inc.

1:50 The Past, Present and Future of ADC-IO Combinations
Jay Harper, PhD, Senior Scientist, Oncology Research, MedImmune
Exciting preclinical data demonstrated immunomodulatory effects of antibody-drug conjugate (ADC) warheads and synergistic anti-tumor activity when ADCs are combined with immuno-oncology agents, leading to clinical development of such strategies. This presentation will highlight the key data supporting such ADC-IO combinations, provide an overview of the current ADC-IO clinical landscape, and will provide some insight into the next generation of these promising ADC-IO combinations.

2:20 Clinical Learnings from Mirvetuximab Soravtansine (IMGN853) and Pembrolizumab Combination Therapy
Eric Westin, PhD, VP & Head, Clinical Development, ImmunoGen

2:50 Combination of Antibody-Cytokine Fusions with Immunological Check-Point Inhibitors
Alessandra Micaela Villa, PhD, Head, Phage Display Technologies, Philochem AG
Antibody-cytokine fusion proteins ("immunocytokines") represent a novel class of antibody therapeutics that combine the disease-homing property of antibodies with the immunomodulatory activity of cytokine payloads. Immunocytokines are currently being developed for the treatment of cancer and other serious conditions. I will present preclinical and clinical data on the combination of immunocytokines with other therapeutic treatments, including immunological checkpoint inhibitors.

Sponsored by MabPlex

3:20 Regulatory Considerations in the IND Submission of Antibody and Related Prroducts
Audrey Jia, PhD, Former FDA CMC Senior Reviewer for Biological Products , Datarevive, Sponsored by MabPlex
This short presentation will discuss the general requirement for US IND applications, including the considerations in CMC, nonclinical and clinical perspective. Common questions regarding the IND application will be discussed for different clinical phases.

3:50 Networking Refreshment Break

CLINICAL ADVANCES

4:20 Antibody-Pyrrolobenzodiazepine Conjugates
Philip Howard, PhD, CSO, Spirogen; Senior Fellow, MedImmune
This talk will cover the development of Pyrrolobenzodiazepine (PBD) payloads for use in Antibody Conjugates. The presentation will also give an update on the clinical progress of Antibody PBD Conjugates.

4:50 Trop-2 as a Broad Solid Cancer Target for Antibody-Drug Conjugates
David Goldenberg, ScD, MD, Founder and Former CSO, Immunomedics, Inc.
Trop-2 is a transmembrane glycoprotein that transduce cytoplasmic calcium signal, activates MAPK/ERK pathway, and affects cell-cell adhesion. Using a proprietary linker technology to site-specifically conjugate an average of 7.6 molecules of SN-38 (the active metabolite of irinotecan, which inhibits nuclear topoisomerase I) per humanized IgG, my group demonstrated effective and selective tumor inhibition *in vitro* and in xenograft solid tumor models, as well as in phase 2 studies of ~500 patients with advanced, heavily-pretreated diverse solid cancers (e.g., breast, NSCLC, SCLC, urothelial).

5:20 End of Day

5:20 Registration for Dinner Short Courses

RECOMMENDED SHORT COURSE(S)*

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

SC10: Critical Considerations for the Design and Development of Antibody-Drug Conjugates

**Separate registration required, please see page 6 for course details.*

FRIDAY, MAY 4

8:00 am Morning Coffee

CLINICAL ADVANCES (CONT.)

8:30 Chairperson's Remarks
Philip Howard, PhD, CSO, Spirogen; Senior Fellow, MedImmune

8:35 KEYNOTE PRESENTATION: Early Clinical Development of Dolaflexin ADCs
Timothy B. Lowinger, PhD, CSO, Mersana Therapeutics
XMT-1522 is a HER2-targeting ADC that induces complete regressions in models of treatment-resistant HER2-positive breast and gastric tumors, as well as breast and non-small cell lung cancer (NSCLC) without HER2 gene amplification and lower levels of HER2 expression. XMT-1536 is a Dolaflexin ADC targeting NaPi2b that is highly active in models of NSCLC adenocarcinoma and epithelial ovarian cancer. Both XMT-1522 and XMT-1536 are in Phase 1 clinical development in patients with advanced solid tumors.

9:05 ABBV-399, a Clinical Antibody Drug Conjugate that Targets c-Met Overexpressing Solid Tumors
Ed Reilly, PhD, Senior Research Fellow, Project Director, Oncology Discovery, AbbVie
ABBV-399 (Teliso-V) is a novel first-in-class ADC comprised of the c-Met-targeting antibody ABT-700 conjugated to the cytotoxic MMAE. ABBV-399-mediated killing requires a threshold level of c-Met expressed by many tumors thereby reducing both the binding of ABBV-399 to normal tissues and the risk of on-target toxicity. ABBV-399 has progressed to a Phase 1 study where it has been well tolerated and has produced objective responses in c-Met-expressing non-small cell lung cancer (NSCLC) patients both as monotherapy and in combination. A summary of these clinical results will be presented.

9:35 Poster Highlight: The Journey of Mylotarg™ from Discovery to Regulatory Approval
Durgesh V Nadkarni, PhD, Senior Principal Scientist, Bioprocess R&D, Pfizer Inc.
Mylotarg™ (gemtuzumab ozogamicin) is an antibody-drug conjugate (ADC) indicated for the treatment of acute myeloid leukemia (AML). The ADC is composed of an anti-CD33 humanized IgG4 mAb that is covalently conjugated to a toxic small moleculr payload, N-acetyl-gamma-calicheamicin via a hydrazone linker. The linker-payload and ADC were first designed and synthesized in the early 1990s. This poster presents a historical account of the development of Mylotarg from early discovery through regulatory approval.

10:05 Networking Coffee Break

PRECLINICAL UPDATES

10:35 Novel Strategies for Developing 2nd Generation HER2-Directed Antibody-Drug Conjugates
Gail Lewis Phillips, MSc, Senior Scientist, Translational Oncology, Genentech, Inc.
Trastuzumab emtansine (T-DM1) is a HER2-directed ADC comprised of trastuzumab linked to the anti-mitotic agent, DM1, through a stable linker. We have designed a different HER2 ADC using a unique THIOMAB™ antibody with engineered cysteines for enhanced stability. To differentiate from T-DM1, we assessed numerous DNA-damaging drugs with cleavable and uncleavable linkers. Preclinical data will be presented for a 2nd generation HER2-ADC comprised of a disulfide-linked DNA damaging agent.

11:05 Preclinical Evaluation of a GCC-Targeted Antibody-Drug Conjugate (ADC) for the Treatment of Colorectal Cancers and Other GI Malignancies
Adnan Abu-Yousif, PhD, Senior Scientist II, Discovery, Takeda
Guanylyl cyclase C (GCC) is a transmembrane cell surface receptor that functions in the maintenance of intestinal fluid, electrolyte homeostasis, and restriction of cell proliferation. In normal human tissues, GCC expression is restricted to the mucosal cells lining the GI tract. Here we describe the activity of a GCC-targeted antibody drug conjugate in preclinical models of GCC-positive tumors. These promising preclinical data warrant advancement of this ADC to clinical evaluation.

11:35 Tackling Solid Tumours with Antibody Fragment Drug Conjugates (FDCs)
Mahendra Deonarain, PhD, CEO & CSO, Antikor Biopharma Ltd.
The significant majority of the ADC field are focusing on large, engineered IgG with low DAR but we believe that FDCs represent a major opportunity to treat solid tumours. We can engineer antibody fragments to carry a high quantity of cytotoxic payload, that will penetrate tumours rapidly, deliver the killer blow and clear from the circulation quickly resulting in lower adverse effects. We will present compelling efficacy and tolerability data to support the concept.

12:05 pm AbGn-107, an ADC for Gastrointestinal Tumors
David (Shih-Yao) Lin, MD, PhD, CMO, AbGenomics, Inc.

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

1:05 Networking Refreshment Break

PKPD ASSESSMENT AND MODELING

1:35 Chairperson's Remarks
Pamela Trail, Independent Consultant and Former Vice President, Oncology, Regeneron

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

1:40 Biomarkers of the Mononuclear Phagocytic System (MPS) for the Pharmacokinetics and Pharmacodynamics of the Antibodies and Antibody Drug Conjugates

William C. Zamboni, PharmD, PhD, Associate Professor and Director, Translational Oncology and Nanoparticle Drug Development Initiative (TOND2I) Laboratory, UNC Lineberger Comprehensive Cancer Center

The factors affecting the high pharmacokinetic (PK) and pharmacodynamic (PD) variability of antibodies (mAbs) and antibody drug conjugates (ADCs) are consistent with variability in the mononuclear phagocyte system (MPS). The high variability in MPS Fc-gamma-receptors (FcγRs) and function in blood are associated with the high PK and PD variability of mAbs and ADCs. The high PK variability of these agents is clinically important as they have a narrow therapeutic index.

2:10 Will Optimized Single Molecular ADC Species Set New Precedents for Clinical Performance?

Trevor J. Hallam, PhD, CSO, Sutro Biopharma

We demonstrate a cell-free antibody production system that enables the use of reactive non-natural amino acids to generate precisely positioned irreversible conjugates with high fidelity. We are able to rapidly generate many variants of full length IgG species with different conjugation sites within days at quantities and quality sufficient for pharmacodynamic and toxicological assessment allows iterative design to optimize ADC performance and reduces preclinical development times by 18 months. We'll provide updates on our lead clinical development candidates.

2:40 Translational Aspects of Auristatin-Based ADCs

Matthew Onsum, PhD, Director, Translational Sciences, Seattle Genetics

This presentation will assess the target expression and other patient characteristics vs. response; discuss dosing considerations and also explore pharmacodynamic and mechanism-of-action biomarkers supporting immuno-oncology combinations.

3:10 Harnessing Multiscale Modelling to Optimize Design of Antibody Drug Conjugates for Clinical Success

Renu Singh Dhanikula, PhD, Senior Research Investigator, MAP, Bristol-Myers Squibb Company

Mechanistic physiologically-based pharmacokinetic models (PBPK) can be used as a platform to study the impact of various ADC characteristics on their disposition in plasma, tissues and tumor, allowing us to build quantitative relationship between exposure and efficacy. The presentation will showcase how mathematical simulations can provide an efficient method for exploring the vast permutation and combinations of parameters influencing efficacy and toxicity of these complex molecules enabling selection of ADCs with an increased likelihood of success.

3:40 End of Conference

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Cambridge HEALTHTECH Institute
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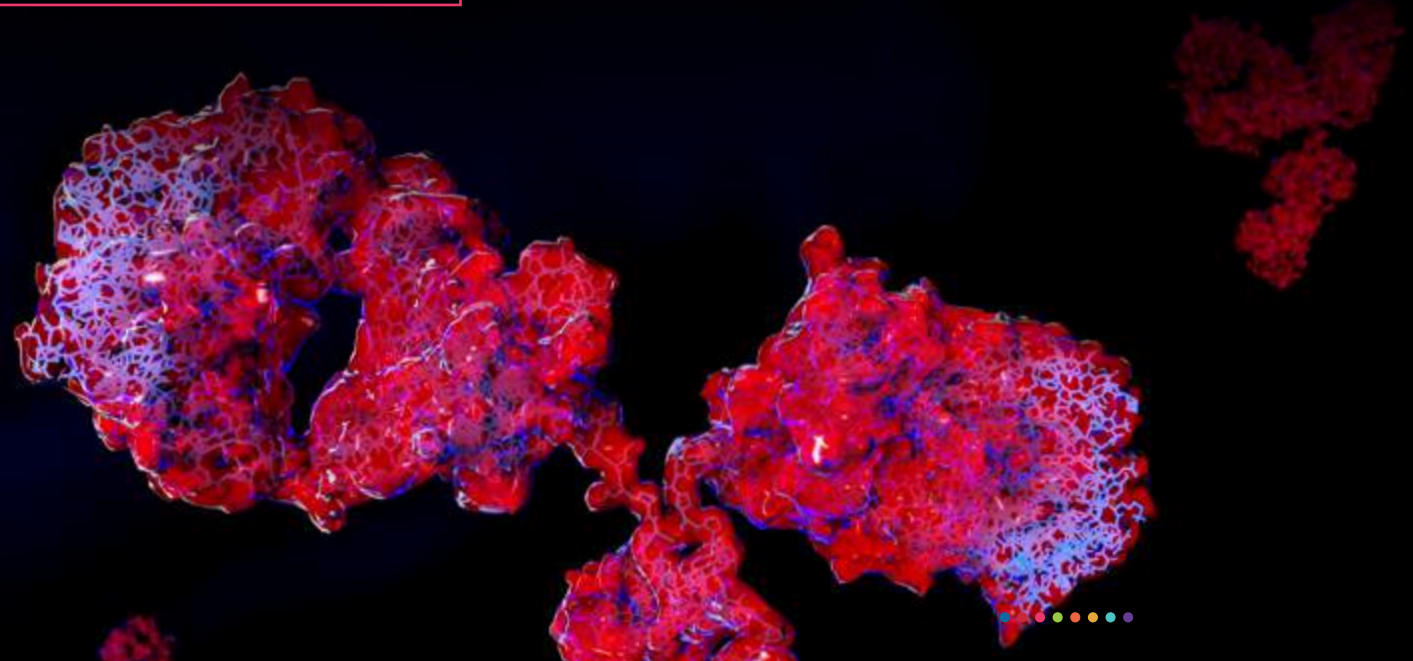
IMMUNOTHERAPY STREAM

- Improving Immunotherapy Efficacy and Safety
- CAR Ts, TCRs and TILs
- Agonist Immunotherapy Targets

Developing Next-Generation Targeted Cancer Immunotherapies

Immuno-oncology researchers are changing the way we treat cancer by unleashing the immune system and achieving functional cures in some cancers. At this year's PEGS summit, the immunotherapy stream has been designed to give attendees a complete picture of the field and its advances. Improving Immunotherapy Efficacy and Safety (April 30-May 1) will examine strategies for demonstrating T cell activity, preventing toxicology, dosing, and interactions with tumor microenvironment. The CARTs, TCRs and TILS (May 2-3) event will then focus on developing adoptive cell therapies, especially CARTs, for solid tumors as well as new targets of interest. Finally, Agonist Immunotherapy Targets (May 3-4) will examine new data as well as the biology and mechanisms of these emerging antibodies 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.



Third Annual

IMPROVING IMMUNOTHERAPY EFFICACY AND SAFETY

Predicting Outcome, Preventing Toxicity

SUNDAY, APRIL 29

RECOMMENDED SHORT COURSE(S)*

SC1: Preclinical and Clinical Assessment of Immunogenicity: Multidomain Therapeutics and New Modalities, Including Gene Therapy and CAR T

SC6: Practical Considerations for Biomarker Bioanalysis

**Separate registration required, please see page 6 for course details.*

MONDAY, APRIL 30

7:00 am **Registration and Morning Coffee**

NEW APPROACHES TO IMMUNOTHERAPY

8:30 **Chairperson's Remarks**
Daniel Christ, PhD, Associate Professor, Director Centre for Targeted Therapy, Garvan Institute of Medical Research

8:40 **KEYNOTE: Cancer Immunotherapy beyond PD-1/PD-L1**
Jessie M. English, PhD, Vice President, Head of Discovery, ImmunoOncology Translational Innovation Platform (TIP), EMD Serono
This talk will present the history and status of the emerging field of neo-antigen (mutanome) targeting in cancer immunotherapy. Current approaches used to identify cancer neo-antigen epitopes along with examples of how neo-antigens are being targeted in cancer immunotherapy clinical trials will be presented. How the mutanome is being used as a biomarker in immunotherapy will also be described. Finally, some of the current obstacles being faced in the field will be discussed along with a summary of the strategic position and future impact of neo-antigen targeting in the overall cancer immunotherapy landscape.

9:10 **Viral Vectors for Neoantigen Immunotherapy: Driving a Potent CD8 T Cell Response**
Andrew Allen, MD, PhD, President & CEO, Gritstone Oncology, Inc.

9:40 **Targeting Solid Tumors and Cancer Stem Cells with Prosthetic Antigen Receptor Modified T-Cells**
Carston R. Wagner, PhD, Professor, Department of Medicinal Chemistry, University of Minnesota, and CSO, Tychon Bioscience, LLC
Over the past decade, it has become increasingly clear that harnessing a cancer patient's T-cells to destroy tumor cells will be an important weapon in an oncologist's therapeutic arsenal. Nevertheless, although selective tumor cell killing and significant clinical success against B-cell malignancies has been demonstrated, the same level of success against solid tumors has remained elusive. To address this unmet need, our group has envisioned the potential of chemical biology and protein engineering to non-genetically modify T-cell membranes.

10:10 **Networking Coffee Break**

ENGINEERING STRATEGIES FOR IMPROVED IMMUNOTHERAPY

10:45 **Chairperson's Remarks**
Daniel Christ, PhD, Associate Professor, Director Centre for Targeted Therapy, Garvan Institute of Medical Research

10:50 **Engineering Interleukin-2 for Cancer Immunotherapy**
Daniel Christ, PhD, Associate Professor, Director Centre for Targeted Therapy, Garvan Institute of Medical Research
Interleukin-2 is an established therapeutic agent used for cancer immunotherapy. It is generally believed that treatment efficacy is mediated by CD8+ and NK cell activity, and considerable efforts have focused on generating IL-2 variants that expand these subsets systemically. Here we describe a second and unexpected mechanism, namely the selective depletion of CD25+ CD4+ regulatory T-cells (Tregs), as a major determinant of antitumour activity. Our results outline mechanisms of action and provide important guidance for the development of next generation cytokine therapeutics.

11:20 Stem-to-T Cell, A New Approach to Immunotherapy
Steven J. Swanson, PhD, Senior Vice President, Research, ImmunoCellular Therapeutics, Ltd.
Our early stage Stem-to-T Cell program isolates hematopoietic stem cells from cancer patients, modifies them through genetic engineering, and after re-implantation, induces production of autologous cytotoxic T cells, which would recognize and kill tumor cells. This new approach to immunotherapy may have fewer safety issues such as cytokine release syndrome than current treatments, and could provide long term surveillance against tumor recurrence.

Mass spectrometry is the tool-of-choice to discover and validate the *in vivo* presence of HLA associated peptides on the tumor cell surface. Additionally, Proteomic strategies enable the copy number estimation of surface HLA-associated peptides antigens, to help in the decision-making of selecting the most effective and efficient therapeutic approach (bispecific vs CAR T cell). Current Proteomic methods complement immune-based and *in silico* (bioinformatics) approaches for aberrant peptide discovery.

11:50 The Use of Nanobodies to Improve Immune-Oncology Therapeutics
Carlo Boutton, PhD, Director Technology & Information Management, Ablynx
Small Nanobodies with their modular design make a perfect starting point for generating multispecific T-cell recruitment formats. The flexibility of our Nanobody platform allows the generation of T cell recruitment compounds simultaneously targeting different epitopes on one tumor anchor (biparatopics) or simultaneously targeting multiple tumor antigens (bispecifics). The benign safety profile of our TCRα/β reactive recruiter was evaluated extensively both *in vitro* and *in vivo* in non-human primates opening the opportunity for multi-specific Nanobody-based T cell recruitment therapies

12:20 pm Developing Next-Generation Targeted Cancer Therapies Requires Next Generation Immune Monitoring Tools to Guide Success
Sponsored by Precision for Medicine
Thomas Kleen, PhD, Vice President Immune Monitoring and Specialty Lab Services, Precision for Medicine
Success and failure of any immunotherapy is depended on engaging the immune system. Epiontis ID, a next generation tool based on qPCR-Assisted Cell Counting (qPACC), requires only 75ul-300ul of whole blood (or small amounts of tissue) to monitor up to 16 different human cell types. Precise and robust monitoring allows samples to be simply frozen on-site and easily shipped without any burden on clinical sites.

12:50 Luncheon Presentation I: Identifying Critical Immunotherapy Target Receptors and Assessing Target Specificity Using Cell Microarray Technology
Sponsored by RETROGENIX
Alex Kelly, US Business Development Manager, Retrogenix
Human cell microarray screening enables the discovery of primary cell surface receptors and off-targets for a variety of biotherapeutic molecules, including peptides, antibodies and proteins, as well as CAR T and other cell therapies. Case studies will demonstrate the utility of the technology in identifying novel immunotherapy targets as well as in specificity screening for biotherapeutics to aid safety assessment and provide key data to support IND submissions.

1:20 Luncheon Presentation II *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 Challenges and Opportunities in Engineering Protein Biopharmaceuticals
K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)
Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

4:55 The Next Generation of Cancer Immunotherapy: Targeting Myeloid Immune Checkpoints
Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital
Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

5:40 Welcome Reception in the Exhibit Hall with Poster Viewing
Sponsored by Precision for Medicine

7:15 End of Day

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

TUESDAY, MAY 1

8:00 am Registration and Morning Coffee

NOVEL APPROACHES TO IMMUNOTHERAPY

8:25 Chairperson's Remarks
Saad J. Kenderian, Assistant Professor of Medicine and Oncology, Mayo Clinic College of Medicine

8:30 Replicating Retroviruses for Manipulation of the Tumor Immune Ecosystem: Preclinical and Clinical Outcomes
Doug Jolly, PhD, Executive Vice President, Research & Pharmaceutical Development, Research & Pharmaceutical Development, Tocagen Inc.
Toca 511 is a replicating retroviral vector (RRV) encoding a modified yeast cytosine deaminase; Toca FC is an extended release formulation of flucytosine, metabolized to 5-FU by cytosine deaminase. RRV are tumor selective in animals and humans after intravenous or intralesional administration. Preclinical data shows direct tumor killing by 5-FU and depletion of 5-FU sensitive-immune suppressive myeloid cells leads to breaking of immune tolerance to the tumor, generation of anti-tumor immunity and long-term tumor regression.

9:00 Pexa-Vec: A Multi-Mechanistic Immunotherapeutic Modulator of the Tumor Microenvironment
Naomi De Silva, PhD, Associate Director, Preclinical and Translational Science, Clinical, Sillajen Biotherapeutics, Inc.
Pexa-Vec (pexastimogene devacirepvec, JX-594) is an oncolytic and immunotherapeutic vaccinia virus, engineered to preferentially infect tumor cells, disrupt vasculature, and stimulate anti-tumor immune responses. Clinical studies and preclinical modeling in a transgenic model of pancreatic neuroendocrine cancer demonstrates that Pexa-Vec rapidly alters the immune microenvironment, and this can be augmented with checkpoint inhibitors to improve efficacy. Combination studies and a Phase III trial evaluating Pexa-Vec in the treatment of advanced primary liver cancer is underway.

9:30 CART Cell Therapy: Beyond CD19
Saad J. Kenderian, Assistant Professor of Medicine and Oncology, Mayo Clinic College of Medicine

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

IMPROVING CAR T SAFETY AND EFFICACY

10:50 T Versus T: Optimizing CAR Function and Reshaping T Cell Response
Maksim Mamonkin, PhD, Instructor, Center for Cell and Gene Therapy, Baylor College of Medicine
Shared expression of most targetable antigens between normal and malignant T-cells complicates the development of CAR T therapies to T-cell tumors. I will review current challenges in the field and present solutions to increase therapeutic potential of CAR T cells by minimizing CAR-driven T-cell fratricide and excessive differentiation.

11:20 Universal Immune Receptor Based Therapy for "on Demand" Application of CAR-Like Therapies
Daniel J. Powell Jr., PhD, Associate Professor of Pathology and Laboratory Medicine, University of Pennsylvania

11:50 Exploring Optimization Parameters for Chimeric Receptors in T Cells
Kathleen McGinness, PhD, Director, Platform Technologies, Unum Therapeutics
T cells engineered to express chimeric receptors exert powerful cytotoxicity against tumors. Understanding optimization parameters for engineered T cells with respect to efficacy and safety is important for successful application to more challenging therapeutic environments. We have explored the composition of Antibody Coupled T-cell Receptors (ACTR) and the interplay between ACTR and targeting antibodies to identify design parameters to modulate and optimize engineered T cell activity.

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

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

2:00 Chairperson's Remarks
Kathleen McGinness, PhD, Director, Platform Technologies, Unum Therapeutics

2:05 A Novel T Cell Therapy Engaging the Whole T Cell Receptor
Alfonso Quintás Cardama, MD, CMO, Executive Leadership Team, TCR2 Therapeutics, Inc.
We report a novel way to engineer T cells that have to potential to overcome limitations of current T cell therapies. The initiation of a broader T cell signal cascade by the engagement of all T cell receptors subunits has the potential to overcome the hostile, immunosuppressive tumor microenvironment of solid tumors and MHC-independent antigen recognition makes TRuC-T cells less vulnerable to immune escape, such as loss of MHC.

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Cambridge HEALTHTECH Institute
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2:35 Enhancing Adoptive Cell Therapies through Exogenous Regulation

Steve Shamah, PhD, SVP,, Obsidian

The inability to control CAR T cells once administered presents considerable toxicity and efficacy challenges in many settings. Obsidian Therapeutics is using Destabilizing Domain (DD) technology providing pharmacological control of transgene protein levels through the dosing of safe, FDA-approved drugs. We will describe our DD discovery process and update on lead programs to develop CAR T cell products that are armed with regulated cytokines for enhanced efficacy and more favorable toxicity profiles.

3:05 Assessing the Safety of TCRs

Andrew Sewell, PhD, Professor, Division of Infection and Immunity, Cardiff University School of Medicine

The αβ TCR repertoire is dwarfed by the vast array of potential foreign peptide-MHC complexes. Comprehensive immunity requires that each T-cell recognizes numerous peptides and thus be extremely cross-reactive. Natural central tolerance culls T-cells that have a high affinity for self peptide-MHC. TCR engineering bypasses this process and can result in dangerous self-reactivity. These toxicities can be predicted and engineered out without loss of specificity for the target antigen.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

IMPROVING IMMUNOTHERAPY EFFICACY AND SAFETY

4:25 TCR-Based Cancer Immunotherapy – How to Find and Select the Right TCR Candidate

Claudia Wagner, PhD, Associate Director, TCR Discovery & Validation, Immatics

Tumor-specific T-cell receptors (TCRs) can serve as potent weapons for cellular-based therapies or bispecifics approaches. Ideal TCRs are selected through extensive efficacy testing and safety profiling, including a novel high-throughput approach using information from the large collection of healthy tissues and tumor biopsies to investigate on- and off-target specificity for selected TCR candidates.

4:55 End of Improving Immunotherapy Efficacy and Safety

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE(S)*

SC9: CAR T Cell Therapy for Solid Tumors

**Separate registration required, please see page 6 for course details.*

> The talks were all very high quality and **the networking opportunities and round-tables last night were very good too.**
>
> - Director, United States Pharmacopeial Convention

Fifth Annual

CAR Ts, TCRs AND TILs

Latest Innovations and Developments in Adoptive Cell Therapy

RECOMMENDED SHORT COURSE(S)*

SC8: Introduction to Biophysical Analysis for Biotherapeutics: Discovery & Development Applications

SC9: CAR T Cell Therapy for Solid Tumors

**Separate registration required, please see page 6 for course details.*

WEDNESDAY, MAY 2

7:30 am **Registration and Morning Coffee**

RECENT SUCCESS AND PROGRESS

8:30 **Chairperson's Remarks**
Mark Bonyhadi, PhD, Head, Research, Juno Therapeutics

8:40 **KEYNOTE: Future Challenges in Adoptive T-Cell Therapy**
Michel Sadelain, PhD, Director, Center for Cell Engineering, Memorial Sloan Kettering Cancer Center

9:10 **Development of Yescarta (Axicabtagene Ciloleucel), a First in Class CAR T Cell Product for Diffuse Large B Cell Lymphoma: A Translational Perspective**
Adrian Bot, MD, PhD., Vice President, Translational Sciences, Kite, a Gilead Company
Yescarta (Axicabtagene Ciloleucel) is an anti-CD19 CAR T cell therapy that received recently approval for treatment of relapsing or refractory DLBCL. Yescarta met its primary endpoint with 82% objective response rate, 54% complete response and 44% ongoing response at 6 months. This presentation will describe key elements of the translational program, correlates of toxicities and durable objective response, product characteristics, patient conditioning, and importance of tumor microenvironment.

9:40 **Development of an Anti-BCMA CAR T Cell Therapy That Delivers Durable Clinical Responses in Relapsed/Refractory Multiple Myeloma**
Molly Perkins, DPhil, Associate Director, Immunotherapy, bluebird bio
Our first anti-BCMA CAR T cell product candidate, bb2121, has demonstrated encouraging safety and efficacy in a Phase I trial for relapsed/refractory multiple myeloma. bb21217 is a second anti-BCMA clinical product candidate which is manufactured in the presence of a PI3k inhibitor, leading to a CAR T cell product enriched for potent, long-lived memory T cells. The preclinical and clinical data on bb2121 and bb21217 will be discussed, highlighting the key scientific lessons learned.

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

NOVEL PROTEIN ENGINEERING STRATEGIES IN CAR T

10:55 **CAR-Specific Activation and Kinetics of a BCMA-Directed CAR**
Collin Hauskins, Research Scientist, Protein Sciences, Juno Therapeutics
Reagents that specifically bind the CAR on genetically engineered cells may be used to detect and quantitate surface CAR expression, and can also be used to stimulate the CAR T cell directly through their engineered receptor. We describe the production of reagents that bind to CD19- and BCMA-directed CAR T cells. These reagents are capable of specifically activating and expanding CAR T cells, allowing us to interrogate the biology of CAR signaling. These reagents could have further applications in the manufacturing of CAR T cells.

11:25 **Dual-Switch CAR T Cells: Orthogonal Molecular Switches to Control Activation and Elimination of Cancer-Targeted CAR T Cells**
J. Henri Bayle, PhD, Director of Molecular Biology, Research and Development, Bellicum Pharmaceuticals
Chimeric Antigen Receptor (CAR) therapies are effective against disseminated cancers but often lack control over T cell efficacy and persistence against off-tumor reactivity and excessive cytokine release. Two platforms were engineered to separate tumor antigen-targeted first-generation CARs from an inducible costimulatory component, iMyD88/CD40, and a pro-apoptotic safety switch based on Caspase-9. These switches are orthogonally controlled by high-affinity, cell-permeable ligands, rimiducid and rapamycin analogs that direct targeted protein oligomerization.

11:55 **Carjacking CAR19 T Cells for Redirected Killing**
Paul Rennert, PhD, President & CSO, Aleta Biotherapeutics Inc
CAR19 cellular therapeutics benefit from interaction with bona fide antigen-presenting B cells (both normal and malignant). The integration of fusion protein modules into CAR19 lentiviral constructs endows CACR19s with

novel antigen recognition properties. These highly potent CARjacked CAR19s recognize both CD19 (directly) and novel antigens (redirected) enabling efficient cytotoxicity against diverse tumor types. The utility of this platform technology will be demonstrated for hematologic malignancies and solid tumors.

12:25 pm Convertible CAR-T Cells Provide Dose Control of Activity and Targeting Flexibility *Sponsored by* Xyphos

Kaman Kim, PhD, Vice President, Research, Xyphos

Current CAR cellular therapies have a number of limitations that impact their efficacy and perseverance in clinical settings including single antigenic targeting, utilization of non-human components, and lack of dose control. The Xyphos convertibleCARTM platform functions as a flexible and controllable system to address these limitations and maximize therapeutic versatility.

12:55 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:55 Session Break

TCR AND TILS

2:10 Chairperson's Remarks

Adrian Bot, MD, PhD., Vice President, Translational Sciences, Kite, a Gilead Company

2:15 Optimized Manufacturing SPEAR TCR T-Cell Therapy for Solid Tumors

Mark Dudley, PhD, Senior Vice President, Bioprocessing & Development CMC, Technical Operations, Adaptimmune

Specific peptide enhanced antigen receptor (SPEAR) T-cells that are genetically re-targeted to tumors can be part of an effective therapy regimen for some refractory solid cancers. SPEAR T-cells targeting NY-ESO show promise in synovial sarcoma and other indications. MAGE-A10, MAGE-A4, and AFP are currently being evaluated in early phase clinical trials. Opportunities and challenges for optimizing a single cGMP platform to manufacturing products for multiple indications will be discussed.

2:45 Learning What Works from Successful Tumor Infiltrating Lymphocyte Therapy

Andrew Sewell, PhD, Professor, Division of Infection and Immunity, Cardiff University School of Medicine

Over 20% of melanoma patients that have been refractory to other treatments undergo complete lasting remission after adoptive cell transfer of tumor-infiltrating lymphocytes (TILs). Dissection of these extraordinary successes by examining the dominant tumor-reactive T-cell clonotypes in the TIL infusion product and patient blood after 'cure' has revealed some surprising, exciting new HLA-restricted and non-HLA restricted targets that are expressed by many other tumour types.

3:15 Novel Phosphopeptide-Specific TCRs for Cancer Cell Therapy

Arthur A. Hurwitz, PhD, Vice President, Head of Preclinical Research, AgenTus Therapeutics

Agenus has developed two enabling platform technologies to identify PTT-specific T cell receptors (TCRs): 1) a primary T cell expansion protocol wherein PTT-specific cognate TCRαβ pairs are identified by functional screening and/or NGS-based sequencing; and 2) a TCR display platform comprising the generation of TCR α and β chain libraries from healthy donor PBMCs, followed by several rounds of TCR enrichment for PTT-specific binding. We have used these platforms to derive fully-human TCRs from central memory T cells of healthy individuals. Importantly, we demonstrate that these TCRs derived from the central memory compartment are highly potent at killing tumor cell lines displaying their cognate PTTs. Phosphopeptide recognition was sequence-specific and depended on the phosphoseryl moiety. The discovery of phosphopeptide-specific TCRs derived from the memory compartment of healthy donors implies prior immunological response to these phosphopeptides and also reveals TCRs that are expected to possess a preferential safety profile. Thus, these and other phosphopeptide-specific TCRs constitute prime candidates for clinical development.

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem-Solving Breakout Discussions

5:45 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

THURSDAY, MAY 3

8:00 am Morning Coffee

COMBINING INNATE AND ADAPTIVE IMMUNITY

8:30 Chairperson's Remarks

Bob Valamehr, PhD, Vice President, Cancer Immunotherapy, Fate Therapeutics

8:35 Adaptive NK Cells and Off-the-Shelf NK Cells to Treat Cancer

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

Cytomegalovirus exposure is uniquely associated with the expansion of natural killer (NK) cells that express NKG2C and the maturation marker CD57. Adaptive NK cells are epigenetically primed for enhanced anti-tumor activity alone and in combination with CD16 signaling. Clinically, adaptive NK cells should result in superior anti-cancer effectors from CMV+ donors or from off the shelf iPS derived NK cells genetically modified to mimic functional attributes of adaptive NK cells.

9:05 Combining Innate and Adaptive Immunity: NK Receptors for CAR T Cell Therapy

Peggy Sotiropoulou, PhD, Manager, Research and Development, Celyad

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Natural Killer cells possess innate capacity to target 'abnormal' cells through the recognition of a range of target ligands, many of which are present on tumor cells. Engineering NK receptors into a CAR format and expressing in T cells takes advantage of both NK specificity and T cell effector functionality. This approach will be discussed in the context in the pre-clinical setting and discussion of on-going clinical trials testing this approach.

9:35 Combinatorial IL13Rα2 Chimeric Antigen Receptor-T Cells Plus Checkpoint Blockade to Treat Solid Tumors in Murine and Canine Models

Yibo Yin, MD, Postdoc Fellow, DEPT of Neurosurgery, Perelman School of Medicine, University of Pennsylvania

We made two fully humanized IL13Ra2 targeting CAR-T cells for the treatment of human solid tumors. We also made canine IL13Ra2 targeting CAR-T cells binding the same epitope as human IL13Ra2 CAR for the treatment of canine solid tumor patients and translational research. The combination therapy of IL13Ra2 CAR-T cells were studies with systematically or locally delivered checkpoint blockades.

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

OFF-THE-SHELF CANCER IMMUNOTHERAPY

11:05 Pluripotent Cell Derived T and NK Cells: Cornerstone Approach for Off-the-Shelf Cancer Immunotherapy

Bob Valamehr, PhD, Vice President, Cancer Immunotherapy, Fate Therapeutics

Pluripotent cell technology represents a powerful approach to make cell-based immunotherapies available to a wide range of patients through the generation of a consistent and renewable "off-the-shelf" source of cellular therapeutics. I will discuss our progress towards developing unique and effective strategies to create a renewable source of genetically engineered "off-the-shelf" T and NK cells with augmented function. Updates on IND filings and FIH progress will also be given.

11:35 Continuously Growing NK Cell Line as a Source for an Off-the-Shelf, Engineered NK Cell Therapeutic in Cancer and Infections

Hans Klingemann, MD, PhD, Vice President, Research & Development, NantKwest, Inc.

NantKwest has developed the NK cell line NK-92 into an "off the shelf" activated NK (aNK) cell therapeutic. The safety of aNK as well as their activity against a broad range of cancers have been confirmed in several Phase I clinical trials. The aNK cells can be administered in the outpatient setting and serve as a universal cell-based therapy without need for individualized patient matching. The aNK cell platform has been bioengineered to incorporate a high-affinity antibody binding Fc-receptor (haNK). Both aNK and haNK cells can be equipped with chimeric antigen receptors (CARs) (called taNK) to further optimize targeting and potency.

12:05 pm Progress in Tumor Infiltrating Lymphocytes in Treatment of Solid Tumors

Maria Fardis, PhD, CEO, Iovance

Iovance Biotherapeutics is focused on the development and commercialization of novel cancer immunotherapies based on tumor infiltrating lymphocytes (TIL). In Phase 2 clinical trials conducted at the NCI, 56% and 24% of patients treated with this technology were reported by NCI to have achieved objective and complete response criteria, respectively. Our lead product candidate is an autologous, ready-to-infuse cell therapy, that has demonstrated distinctive efficacy in the treatment of metastatic melanoma.

12:35 End of CAR Ts, TCRs and TILs

Fourth Annual

AGONIST IMMUNOTHERAPY TARGETS

Stepping on the Gas with Costimulatory Agents

RECOMMENDED SHORT COURSE(S)*

SC10: Critical Considerations for the Design and Development of Antibody-Drug Conjugates

**Separate registration required, please see page 6 for course details.*

THURSDAY, MAY 3

LATEST UPDATES - OX40, 4-1BB

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Peter Ellmark, VP, Discovery, Alligator Bioscience AB

1:50 PD1-Fc-OX40L for Cancer Immunotherapy
Taylor Schreiber, PhD, CSO, Research & Development, Shattuck Labs, Inc.
We have developed a novel two-sided fusion protein that co-localizes costimulation via OX40 to the tumor microenvironment, while simultaneously providing competitive inhibition of PD-L1 and PD-L2. PD1-Fc-OX40L stimulates OX40 signaling, out-competes PD-1 in binding its ligands, stimulates T cell-mediated tumor cell killing, and leads to increased complete rejection of established tumors as compared to monotherapy or combinations of PD-1 and OX40 antibodies.

2:20 Combination Approaches with GITR and OX40 Agonists
Patrick Mayes, PhD, Executive Director, Head, IO Antibody Research, Incyte

2:50 A Novel FAP-Targeted 4-1BB Agonist and Its Combination with T Cell Bispecific Antibodies
Claudia Ferrara, PhD, Principal Scientist, Large Molecule Research, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Zurich
CD137 (4-1BB) is a promising agonistic target for cancer immune therapy. The clinical development of first generation 4-1BB agonistic antibodies has however been hampered by hepatic toxicity. Here we describe a novel FAP-targeted 4-1BB agonist, developed to be mainly retained at tumor site and as combination partner for T cell bispecific antibodies.

3:20 Poster Presentation: Multispecific and Multivalent Antibodies as OX40 Agonists
Francis Qufei Li, PhD, Invenra

3:35 Poster Presentation: Screening, Optimization and Characterization of a Novel 4-1BB x 5T4 ADAPTIR Bispecific Antibody
David Bienvenue, PhD, Senior Director, Protein Sciences, Aptevo Therapeutics

3:50 Networking Refreshment Break

4:20 Tumor Directed Targeting of Effector T cells and Regulatory T Cells
Peter Ellmark, VP, Discovery, Alligator Bioscience AB

4:50 Varlilumab, a Fully Human Agonist Anti-CD27 Antibody
Michael Yellin, MD, Vice President, Clinical Science, Celldex
The CD27 co-stimulation pathway for immune cells has shown potent activity in pre-clinical models to eliminate tumors both as single agent and in combination with checkpoint inhibitors. Clinical trials to date using varlilumab, an agonist anti-CD27 antibody, confirm this specific immune activation without significant immune toxicity. Durable single agent responses have been observed. Clinical studies of varlilumab in combination with other immune modulating agents will be discussed.

5:20 End of Day

5:20 Registration for Dinner Short Courses

FRIDAY, MAY 4

8:00 am Morning Coffee

TNFR AGONISTS

8:30 Chairperson's Remarks
Deborah H. Charych, PhD, Executive Director, Nektar Therapeutics

8:35 The Appeal of the TNFR2 Target for Immunotherapy: Tregs and Tumor Oncogenes
Denise L. Faustman, MD, PhD, Director of Immunobiology, Massachusetts General Hospital, Associate Professor of Medicine, Harvard Medical School

Immune checkpoint inhibitors have revolutionized cancer therapy but can exhibit variable efficacy. TNFR2 is a signaling molecule found on a subset of potent Treg cells that activates the proliferation of these cells. TNFR2 is also abundantly expressed on the surface of many human tumors as an oncogene. We propose blocking TNFR2 might target abundant TNFR2+ tumor-infiltrating Tregs and directly kill TNFR2-expressing tumors. TNFR2 inhibitors might also potentially constitute safer and more targeted immunotherapy.

9:05 HERA: Engineering Next Generation TNFR-SF Agonists for Cancer Immunotherapy

Oliver Hill, PhD, Vice President, Molecular Biology, Apogenix

The HERA technology platform developed by Apogenix is based on trivalent but single-chain molecular mimics of the TNF-SF Receptor binding domains (scTNFSF-RBDs) fused to a dimerization scaffold. Being hexavalent by design, the HERA fusion proteins are potent TNFR-SF agonists on their own and do not need secondary crosslinking events for their activity. The underlying engineering concept as well as selected *in vitro* and *in vivo* data obtained with HERA-CD40L, HERA-CD27L, HERA-GITRL, HERA-LIGHT and HERA-CD137L will be presented.

9:35 Bi-and Trifunctional Antibody-Cytokine Fusion Proteins for Cancer Immunotherapy

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

IL-15 and costimulatory members of the TNF-superfamily have shown great potential to support the generation and development of an antitumor immune response. In order to improve the efficacy of such molecules at the tumor site we designed bi- and trifunctional antibody-fusion proteins, focusing on targeted presentation and combined mode of action of diverse immunomodulatory molecules, demonstrating enhanced immune responsiveness *in vitro* and antitumor activity in a mouse model *in vivo*.

10:05 Networking Coffee Break

NOVEL AGONISTS - ICOS, TLR

10:35 KEYNOTE: Development of JTX-2011, A Novel ICOS Agonist Antibody

Debbie Law, DPhil, CSO, Jounce Therapeutics

JTX-2011 is an ICOS (Inducible T cell CO-Stimulator) agonist antibody currently in clinical development. It is designed to shift the balance in tumors from immunosuppressive towards anti-tumor activity by stimulating T effector cells and reducing intratumoral T regulatory cells. The preclinical data supporting the development of JTX-2011 as well as the safety evaluation of JTX-2011 from the Phase I portion of the biomarker-driven ICONIC trial will be described.

11:05 A Novel, Dual-Specific Antibody Conjugate Targeting CD134 and CD137 Costimulates T Cells and Elicits Antitumor Immunity

Adam J. Adler, PhD, Professor, Immunology, University of Connecticut

Combining agonists to different costimulatory receptors can be more effective in controlling tumors compared to individual agonists, but presents logistical challenges and increases the potential for adverse events. We developed a novel immunotherapeutic agent by fusing agonists to CD134 and CD137 into a single biologic, OrthomAb, that potentiates cytokine secretion from TCR-stimulated T cells more potently than non-conjugated CD134 + CD137 agonists *in vitro*, and reduces tumor growth *in vivo*.

11:35 Harnessing Potent Immunological Pathways for Better Medicine

Deborah H. Charych, PhD, Executive Director, Nektar Therapeutics

Many validated potent biological pathways do not translate well to therapy because of toxicities, poor pharmacokinetics or undesirable pharmacodynamics. We have engineered endogenous proteins and exogenous small molecules into accessible medicines using polymer conjugation technology. NKTR-214 is in Phase II clinical trials and is a key example of how polymer conjugation can bias the well-known IL2 receptor pathway to promote CD8 T cell tumor infiltration over Tregs. Other examples to be discussed are NKTR-255, an IL15 receptor agonist and NKTR-262, a small molecule conjugate that stimulates toll-like receptor (TLR). Each has been conjugated in unique ways to elicit desirable and controlled pharmacological and immunological outcomes.

12:05 pm Using Structural Insights for the Design of Improved TNFR Agonists

Eva Vanamee, PhD, Co-Founder and CSO, FusionBio, Inc.

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

1:05 Networking Refreshment Break

STING AGONISTS AND NEW TARGETS

1:35 Chairperson's Remarks

Harpreet Singh, President & CEO, Immatics US

1:40 Addressing Solid Cancers with Novel Targets and TCR-T Approaches

Harpreet Singh, President & CEO, Immatics US

Novel targets are required to address the unmet medical need particularly in solid cancers. The high-throughput mass spectometry-based XPRESIDENT® platform was applied to identify dozens of novel targets followed by generation of specific T-cell receptors (TCRs). Three adoptive cell therapy (ACT) approaches are being developed on this basis: (1) ACTolog using multiple endogenous T cells products, (2) ACTengine using gene-engineered

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T cells and (3) ACTallo using allogeneic gamma-delta T cells.

2:10 Intratumoral Delivery of Novel STING Agonists Synergizes with Checkpoint Modulation to Regress Multi-Focal Cancer

Casey Ager, Graduate Research Assistant, Department of Immunology, University of Texas MD Anderson Cancer Center

Therapeutic modulation of innate immune cells within the tumor microenvironment can complement checkpoint blockade regimens by ameliorating myeloid suppression and promoting T cell priming. We have developed novel high-affinity STING agonists and are investigating how intratumoral delivery of these agents can activate tumor myeloid populations and sensitize poorly immunogenic solid tumors to checkpoint blockade, and additionally whether this approach can effectively mobilize abscopal immunity against disseminated lesions.

2:40 *In vitro* Characterization and *in vivo* Anti-Tumor Efficacy of a Novel STING Agonist, MK-1454

Saso Cemerski, PhD, Principal Scientist, Merck Research Labs

MK-1454, a novel STING agonist, induces potent cytokine responses and activates several immune cell types *in vitro* including MDSCs and M2-macrophages, key suppressive myeloid cells in the TME. MK-1454 induces robust anti-tumor activity in mouse syngeneic tumor models and cytokine production and gene expression changes in *ex vivo*-stimulated human primary tumors. MK-1454 is currently being evaluated in cancer patients both as monotherapy and in combination with Keytruda.

3:10 Latest Progress and Learnings on Agenus's Agonist Portfolio

Robert B. Stein, MD, PhD, Senior Advisor, R&D, Agenus, Inc.

3:40 End of Conference

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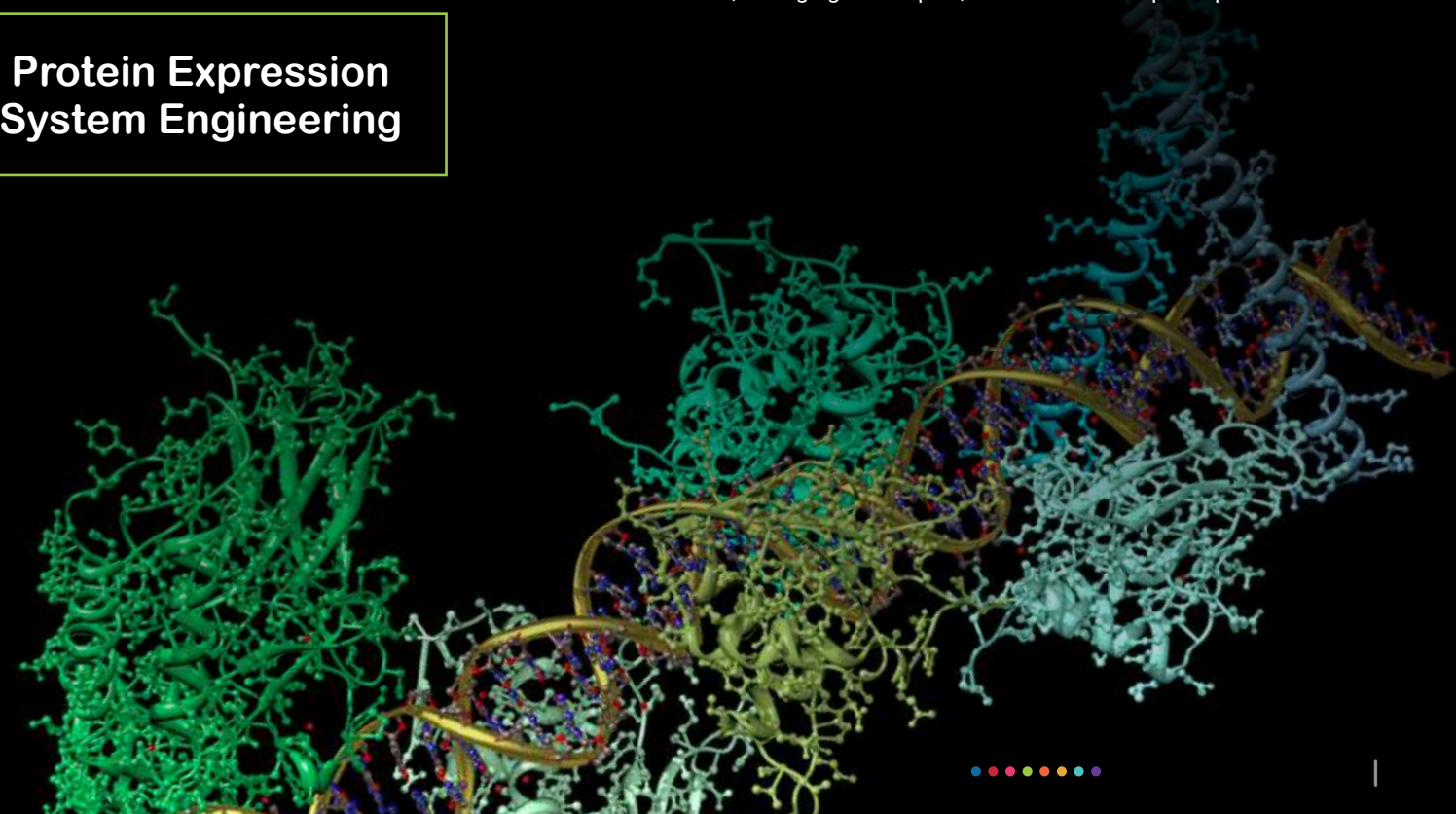
EXPRESSION STREAM

- Difficult to Express Protein
- Optimizing Protein Expression
- Protein Expression System Engineering

Engineering and Producing Quality Proteins for Expanding Demands

The ongoing production of proteins for the treatment and diagnosis of disease has always been a challenging pursuit. The continued success of immunotherapies along with other biologics, means that greater engineering finesse and streamlining technologies are needed to quickly produce higher volumes of quality, functional proteins. The 2018 PEGS Expression Stream provides insights into the best methods and strategies to engineer expression hosts and produce proteins in suitable quantity and stability to meet industry's ever-growing needs, and will include current trends, emerging techniques, and difficult-to-express proteins.



Thirteenth Annual

DIFFICULT TO EXPRESS PROTEINS

Strategies for Taming "Finicky" Proteins

SUNDAY, APRIL 29

RECOMMENDED SHORT COURSE(S)*

SC1: Preclinical and Clinical Assessment of Immunogenicity: Multidomain Therapeutics and New Modalities, Including Gene Therapy and CAR T

SC5: *In silico* Immunogenicity Predictions (Hands-On) Workshop

**Separate registration required, please see page 6 for course details.*

MONDAY, APRIL 30

7:00 am **Registration and Morning Coffee**

INNOVATIVE TOOLS FOR BOOSTING EXPRESSION QUALITY

8:30 **Chairperson's Remarks**
Hussain Dahodwala, PhD, Postdoctoral Researcher, Delaware Biotechnology Institute, University of Delaware

8:40 **Toolbox for Productivity Boost and Product Quality Improvements of Difficult-to-Express Proteins (DTE) in CHO Cells**
Martin Gamer, PhD, Early Stage Bioprocess Development, Boehringer Ingelheim Pharma GmbH & Co. KG
The increasing number of engineered, often antibody-derived molecule formats entering into biopharmaceutical development poses significant challenges on the generation of high-yielding CHO cell factories. This talk will highlight the most recent advances at Boehringer Ingelheim to improve cell line development of DTE proteins. Our toolbox comprises *in silico* methods to assess molecule developability leading to tailored development, a rationally designed novel host cell line ensuring high performances, robustness and scalability as well as innovative genetic elements and screening tools to select for outstanding CHO production cell lines.

9:10 **Novel Engineered CHO DG44 Host Cell Line Demonstrates Lowered UPR, Increased Titers & Superior Quality of Recombinant Vaccines**
Hussain Dahodwala, PhD, Postdoctoral Researcher, Delaware Biotechnology Institute, University of Delaware
In our workflow, high-producing clones share a common phenotype of increased viable cell density (VCD) and viability at later days in fed-batch culture. To address the production of viral antigens and therapeutic proteins a novel CHO DG44 host clone was engineered and selected for high VCD and viability in later days of fed-batch culture. Using this host, we achieved a 3 X increase in viral antigen titers and mAbs without changing the existing upstream process.

9:40 **Optimization for Heterologous Disulfide Bonded Protein Manufacture: Production of Antibody Fragments in the Periplasm and Cytoplasm of *E. coli***
Bhupal Ban, PhD, Research Assistant Professor, Antibody Engineering & Technology, University of Virginia
Our results show that the efficient production of soluble, biologically active scFv and VHH antibody fragments in the cytoplasm of engineered *E. coli* strain is cost effective and simplistic method. Further, free cysteine residues can be major bottleneck hampering the production of correctly folded soluble protein in both *E. coli* and mammalian cells.

10:10 **Networking Coffee Break**

OVERCOMING BOTTLENECKS

10:45 **Chairperson's Remarks**
Hussain Dahodwala, PhD, Visiting Scientist, Vaccine Production Program, Vaccine Research Center, NIH

10:50 **Identification of Intracellular Production Bottlenecks in Suspension-Adapted CHO Cells Producing Complex Biopharmaceuticals Using Fluorescence Microscopy**
Kerstin Otte, PhD, Professor, Pharmaceutical Biotechnology, Biberach University
With the advance of complex biological format therapeutics, mammalian expression systems often show low performance possibly due to accumulation or haltering of heterologous proteins within the different

cellular compartments disturbing transport or secretion. Since neither transcription nor translation processes satisfactorily explain low production capacity, we established a streamlined confocal microscopy-based methodology for CHO production cells which enables the identification of rate-limiting-steps and can also be used for automated detection of production bottlenecks during industrial cell line development processes.

11:20 Improving Transient Gene Expression in Insect Cells

Joop van den Heuvel, PhD, Department of Structure and Function of Proteins, Helmholtz Centre for Infection Research

Fast expression of recombinant protein is not limited to the use of *E. coli*. Plasmid based transient gene expression (TGE) in mammalian cell lines is an attractive method to screen for suitable expression constructs and to produce high quality recombinant mammalian proteins. Here we present which steps have been successful to reach high levels of expression in High Five insect cells. Additional miniaturization using an automated micro fermentation system allowed us to implement a high throughput splitGFP screen for expressible constructs. We show that TGE in High Five insect cells is a fast and cheap alternative to produce substantial amounts of high quality recombinant protein.

11:50 Breaking News in Expression Science: Suppression of the Immune Response as a Tool to Enhance the Expression of Recombinant Proteins in Plants

Fabio Cupri Rinaldi, PhD, Research Associate, Martin Lab, Cornell University

Many pathogens have evolved effector proteins that manipulate host defense mechanisms, including PCD. The plant pathogen Pseudomonas syringae includes in its immune suppression repertoire the effector AvrPtoB. Once inside the host cells, AvrPtoB binds to cellular kinases and inhibits the plant immune response. Extensive research has revealed that AvrPtoB is a general cell-death suppressor in plants. Here we demonstrate how we harnessed the ability of AvrPtoB to suppress PCD, and significantly enhance DTE protein accumulation up to five-fold. We envision developing this technology with the ultimate goal of boosting the production of commercially relevant proteins in plants.

12:20 pm Moving Beyond the Central Dogma: New Tools for the Industrial Production of Difficult to Express Proteins (DTEPs)

Sponsored by Lonza Pharma & Biotech

Colin Jaques, PhD, Senior Principal Scientist, Process Development, Research and Technology, Lonza

In recent years, mAbs were the primary protein therapeutic. Now heavily engineered DTEP next generation biologics dominate early phase pipelines. This shift requires tools developed to achieve economically viable concentrations and clinically relevant critical quality attributes. Tools for protein expression were traditionally based on the Central Dogma. For many DTEPs, expression problems occur outside the Central Dogma in post-translational processing. Two new approaches to increase production of DTEPs by targeting post-translational processing will be discussed.

12:50 Screening Challenging Clones at Light Speed *Sponsored by* BERKELEY LIGHTS

Keith Breinlinger, MS, PhD, CTO, Berkeley Lights, Inc.

Screening thousands of clones for production and function is critical for success when working with difficult to express proteins. The Beacon platform applies light and semiconductor technology in a nanofludic chip to isolate single cells, culture, assay, and export clones of interest. Now this can be done on thousands of clones in just a few days instead of months.

1:20 Approaches and HTP to Challenges for Recombinant Proteins Expressed in *E. coli*

Sponsored by FUJIFILM Diosynth biotechnologies

Nigel Shipston, PhD, Director, Program Design, FUJIFILM Diosynth Biotechnologies

From this talk you will learn to Avoid "re-inventing the wheel" for every product and to expedite the initial stages of process invention to enable rapid establishment of a process suitable for GMP manufacturing.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 Challenges and Opportunities in Engineering Protein Biopharmaceuticals

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)

Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

4:55 The Next Generation of Cancer Immunotherapy: Targeting Myeloid Immune Checkpoints

Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital

Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

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

Sponsored by PRECISION FOR MEDICINE THE FUTURE OF MEDICINE IS PRECISION

7:15 End of Day

Cambridge HEALTHTECH Institute
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TUESDAY, MAY 1

8:00 am Registration and Morning Coffee

EARLY ENGINEERING FOR EXPRESSION SUCCESS

8:25 Chairperson's Remarks
Matthew A. Coleman, PhD, Senior Scientist, Lawrence Livermore National Laboratory

8:30 Increasing Expression of an Antibody Fab Fragment in *Escherichia coli* with Unnatural Amino Acid (UAA) Incorporated by Strain Engineering & Process Development
Harunur Rashid, PhD, Principal Scientist, Ambrx, Inc.
Expression of a 'difficult-to-express' antibody Fab fragment with an UAA inserted at a selected site was systematically optimized by expression vector & strain engineering. Among the various genetic elements on expression vector tested, DNA coding sequence, periplasmic chaperone, Fab heavy chain (HC) carboxy-terminal extension and the presence of plasmid partition locus, parB, were beneficial. All of these four components were then put together into a single expression vector that resulted in several hundred-fold improvement in expression titer over the starting strain.

9:00 New Techniques in Heterologous Expression and Purification of Large Polytopic Integral Membrane Proteins
Paul Roepe, PhD, Professor, Chemistry, Biochemistry and Mol. Biology, Georgetown University
Optimized heterologous expression (codon optimization and other techniques) along with tandem chromatography and other analytical methods has been used to purify several very large malarial parasite membrane proteins. (All examples recently published in a series of "Biochemistry" papers, one additional currently in preparation for publication.)

9:30 A Novel Bicistronic Gene Design Couples Stable Cell Line Selection with a Fucose Switch in a Designer CHO Host to Produce Native and Afucosylated Glycoform Antibodies
Gargi Roy, MSc, Scientist I, Antibody Discovery and Protein Engineering/ Research, MedImmune LLC
Antibodies (mAbs) are complex glycosylated proteins important as therapeutic molecules. mAbs lacking the core fucose at Asn297 (afucosylated mAbs) show enhanced antibody-dependent cell-mediated cytotoxicity (ADCC) and increased efficacy. Following GlymaxX technology, a Chinese Hamster Ovary (CHO) host cell line was engineered to co-express a mAb with GDP-6-deoxy-D-lyxo-4-hexulose reductase (RMD), a prokaryotic enzyme that deflects an intermediate in the *de novo* synthesis of fucose to a dead-end product, resulting in stable expression of high titer, highly potent afucosylated mAb with enhanced ADCC activity suitable for manufacturing.

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

PROMISING TOOLS & TECHNIQUES

10:50 KEYNOTE PRESENTATION: Working through Difficult Proteins with Variants, Intensification and Automation
Randal Bass, PhD, Vice President, Just Biotech
Difficult to express proteins will inevitably enter the biotherapeutics development pipeline. As an industry, the better and faster we can adapt, optimize and streamline our response to these proteins, the greater extent to which we will lower costs and improve the chances these molecules will become safe and effective therapeutics. Here, I will discuss efforts that flow from molecular optimization through high-throughput process design, and even into the design of manufacturing facilities, to maximize the potential for molecules to successfully reach commercialization.

11:20 Cell-Free Production of a Functional Oligomeric Form of a Chlamydia Major Outer Membrane Protein for Vaccine Development
Matthew A. Coleman, PhD, Senior Scientist, Lawrence Livermore National Laboratory
Chlamydia is a prevalent sexually transmitted infection that infects over 100 million people worldwide. Chlamydia strains express a major outer membrane protein (MOMP) that is an effective vaccine antigen. However, approaches to produce a functional recombinant MOMP protein are limited due to poor solubility, low yield, and misfolding. We will present a cell-free co-translation method to make functional MOMP within a nanolipoprotein particle. Our approach solubilizes membrane-bound proteins for biochemical, biophysical characterization and antigen generation.

11:50 Applications of Modular Expression Toolboxes in High-Throughput Protein Expression
Ernest Weber, PhD, Senior Scientist, Antibody Lead Discovery, Biologics Research, Bayer AG
The presentation will focus on the setup of a modular expression toolbox, consisting of standardized elements influencing expression levels, which allow the rapid generation of multiple expression constructs and also the generation of complex expression optimization libraries. Advantages and implications of a modular cloning system including implementation into protein expression optimization workflows will be discussed and a number of successful case studies will be presented.

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12:20 pm Luncheon Presentation I: Talk Title to be Announced
Mike Keebler, PhD, Applications Scientist, Kuhner Shaker Inc

Sponsored By
GenScript

12:50 Luncheon Presentation II: New Ways to Boost Recombinant Protein and Antibody Yields in Transient Systems
Brady Wu, Associate Director, Protein Production, GenScript USA, Inc.
Transient expression is a fast and reliable way to generate recombinant

antibodies and proteins for all forms of research. However, there are several factors limiting the titer of the products in the system, thus the need for optimization at different steps of the process. At this talk, GenScript will demonstrate that one can improve the titer of transient products by tuning the systems in several ways including better anti-apoptosis effect, better cell growth, and more.

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

IMPROVING YIELD, STABILITY & FUNCTION

2:00 Chairperson's Remarks
Haruki Hasegawa, PhD, Department of Therapeutic Discovery, Amgen

2:05 Engineering a Patient-Derived Anti-MRSA rF1 Antibody to Develop an Antibody Antibiotic Conjugate (AAC) Therapeutic
Yi Xia, MD, Senior Scientific Researcher, Antibody Engineering, Genentech, Inc.
We have successfully cloned rF1 CDRs into pRK vector and repaired antibody light chain framework position 105-112 from patient's EIKR-AAA to germline EIKRTVAA (human Kappa 4), boosting antibody production yield from 0.5 mg/L to 75mg/L and solved more than 70% aggregation issues as well. We successfully molecular engineered and generated a promising anti-MRSA therapeutic antibody for antibody-antibiotic conjugate (AAC) clinic use.

2:35 Improving Yield and Stability of Cannabinoid Receptor
Alexei Yeliseev, PhD, Staff Scientist, Group Leader, LMBB, NIH, NIAAA
We expressed the recombinant cannabinoid receptor CB2 in *E. coli* cells as well as in expi CHO and expi HEK293 cells in milligram quantities. The yield of the functional target protein was enhanced by modifications of codon usage, testing multiple expression constructs and media compositions. Stabilization of the protein at high concentration in monomeric form was achieved by optimizing the N- and C-terminally truncated constructs of CB2, careful selection of stabilizing lipids and ligands, and controlling glycosylation. Examples of the 19F NMR and DEER measurements will be presented.

3:05 Artificial Protein Folding System to Enhance the Production of "Difficult-To-Express Proteins"
Sponsored By SOLA BIOSCIENCES
Akinori Hishiya, PhD, Principal Scientist, Biology, SOLA BioSciences
This presentation will discuss: 1) Protein folding is one of the major issues in protein production. Proteins with protein folding problems are so-called "difficult-to-express proteins" due to poor secretion and instability. 2) We have developed a novel technology exploiting protein folding machinery, in which the technology works only for the protein of interest. 3) The technology has successfully enhanced the production of many therapeutic proteins and the expression of some of GPCR proteins were significantly enhanced.

3:20 Development and Optimization of an Advanced Transient Expression System in CHO Cells
Sponsored By Polyplus transfection
Mathieu Porte, Project Leader Research & Development – Bioproduction, Research & Development, Polyplus-transfection
Transient expression in CHO cells is commonly used to rapidly produce antibodies but is often limited by transfection efficiency and inherent productivity. To overcome this issue, we developed an advanced transient expression system consisting in the synergistic association of a novel CHO chemically defined medium and a powerful transfection reagent.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

NEW SCIENCE OF IMPORT TO THE FIELD OF PROTEIN EXPRESSION

4:25 25 Effects of One Amino Acid Substitution on IgG Biosynthesis, Physicochemical Property, and Biologic Function
Haruki Hasegawa, PhD, Department of Therapeutic Discovery, Amgen
We investigated the biosynthetic process of two functional human IgG2κ mAbs that differ only by one amino acid in the LC-CDR1. Despite their near-identity, one mAb was secreted ~20-fold less than the other. We found that the poorly-secreted mAb induced Russell body in the ER during overexpression and triggered eIF2α phosphorylation. The observed poor IgG secretion was due to severe down-regulation of global protein synthesis as opposed to physical obstructions of secretory pathway trafficking.

4:55 PANEL DISCUSSION: Emerging Methods to Improve Expression of Difficult Proteins
Panelists: Haruki Hasegawa, PhD, Department of Therapeutic Discovery, Amgen
Ernest Weber, PhD, Senior Scientist, Antibody Lead Discovery, Biologics Research, Bayer AG
Yi Xia, MD, Senior Scientific Researcher, Antibody Engineering, Genentech, Inc.
Alexei Yeliseev, PhD, Staff Scientist, Group Leader, LMBB, NIH, NIAAA
Randal Bass, PhD, Vice President, Just Biotech
Matthew A. Coleman, PhD, Senior Scientist, Lawrence Livermore National Laboratory

5:25 End of Difficult to Express Proteins Conference

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE(S)*

SC8: Introduction to Biophysical Analysis for Biotherapeutics: Discovery & Development Applications

SC13: Sub Visible Protein Particles in Immunogenicity: Measurement, Characterization and Impact

**Separate registration required, please see page 6 for course details.*

Cambridge HEALTHTECH Institute
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Eighth Annual

OPTIMIZING PROTEIN EXPRESSION

Enhancing Expression Systems

RECOMMENDED SHORT COURSE(S)*

SC12: Transient Protein Production in Mammalian Cells

**Separate registration required, please see page 6 for course details.*

WEDNESDAY, MAY 2

7:30 am Registration and Morning Coffee

BREAKTHROUGH PROTEIN EXPRESSION STRATEGIES

8:30 Chairperson's Remarks

Jesse Rinehart, PhD, Associate Professor, Cellular & Molecular Physiology, Systems Biology Institute, Yale University School of Medicine

8:40 KEYNOTE PRESENTATION: Manufacturing as a Key Value Driver in Biopharmaceuticals

Jorg Thommes, PhD, Senior Vice President, Pharmaceutical Sciences & Technology, Visterra, Inc.

A robust manufacturing platform for recombinant protein and antibody manufacturing has emerged over the past decade, which has substantially increased productivity and operational reliability. Thus, manufacturing has matured from a "necessary evil" to a true value driver in biopharmaceutical operations. In this presentation, we will discuss the current state of protein drug manufacturing but also review new frontiers in this field, e.g., further industrialization of antibody manufacturing, accelerated manufacturing for early clinical testing, and manufacturing for new therapeutic modalities.

9:10 Implementation of New Strategies During Early Development of Innovative Therapeutic Molecules

Nicola Beaucamp, PhD, Head, Process Research, Roche Innovation Center Munich, Pharma Research and Early Development, Roche Diagnostics GmbH

More than 80% of large molecules developed in Roche pRED are novel and complex antibody formats. To minimize timelines and deliver requested quantity and quality, many innovative approaches with respect to throughput, automation and cell culture techniques were taken. These techniques were implemented to support delivery of differentiated molecules based on Roche's strategy on engineering technologies to patients. Technical challenges faced and how they were successfully solved will be presented by case studies.

9:40 Revolution or Evolution – Optimizing Protein Expression Platforms to Support Preclinical Research at AstraZenca

Robert Roth, PhD, Associate Principal Scientist, Innovative Medicines, Discovery Sciences, AstraZeneca

An overview of how AstraZeneca have refined and developed our protein expression platforms to supply reagents to support research across a diverse portfolio. Using specific examples to illustrate how challenges have been resolved through internal development efforts, collaborations with academic partners and technology providers. How do we approach a future where targets are increasingly complex and require bespoke solutions to identify and express proteins that are physiologically relevant?

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

CUTTING-EDGE TECHNOLOGIES TO ENHANCE PRODUCTIVITY

Sponsored By Syngene

10:55 Isolation of CHO Master Cell Lines and Targeted Cell Line Engineering using Recombination Mediated Cassette Exchange (RMCE) and Homology-Directed Repair (HDR)

Joop van den Heuvel, PhD, Research Group Leader, Recombinant Protein Expression, Helmholtz Centre for Infection Research

Chinese Hamster ovary (CHO) cells are one of the major providers of recombinant protein for biopharmaceutical industry and biomedical research. Long tradition in laboratory handling generated a wealth of experience in engineering CHO cell lines with a variety of genetic tools to achieve efficient production of recombinant proteins. Targeted manipulation of CHO cell lines based on recombinase-mediated cassette exchange (RMCE) and CRISPR-Cas-induced homology-directed repair (HDR) to generate high-expression CHO cell lines will be presented. High-expressing master cell lines have been isolated, which carry tagged expression cassettes. These cell lines are transferred with the help of a "selection trap" into producer cell lines by the exchange reaction. The efficiency of the isolation of clonal producer cell lines and quality of the protein production for challenging targets will be discussed.

11:25 A Versatile Platform for Biologics Research Protein Reagent Generation

Bernd Voedisch, PhD, Lab Head and Investigator III, NIBR Biologics Center, Novartis Institutes for Biomedical Research

During the early phases of Biologics research projects, it is necessary to produce a plethora of high quality protein reagents and recombinant cell lines in order to enable generation, screening, and in-depth characterization of therapeutic antibody candidates. The presentation will highlight various challenges in this context, and how these challenges were overcome by applying cutting-edge technologies (e.g., cell line engineering using CRISPR/Cas9 or transposases) in order to lay the foundation for successful Biologics discovery.

11:55 MultiBac: From Protein Complex Structures to Synthetic Viral Nanosystems

Imre Berger, PhD, Professor and Wellcome Trust Senior Investigator, Biochemistry, Biomedical Sciences and BrisSynBio Centre, University of Bristol

The MultiBac BEVS was conceived as a user-friendly tool-kit for producing multiprotein complexes for structural biology, and enabled structure determination of many molecular machines, including previously inaccessible high-value drug targets. More recently, MultiBac developments focus on customized baculoviral genomes tailored for specific applications, such as synthesizing artificial proteins by genetic code expansion, and DNA delivery in mammalian cells and tissues for CRISPR/Cas9-mediated gene editing. Some of these developments will be presented.

12:25 pm Accelerating Gene to Phase 1 Studies: Ultra-Rapid Multi-Dimension Screening Tools and Optimized Scale up Strategy to Deliver the Drug Substance from E coli

Sponsored By premas biotech partners in discovery

Prabuddha Kundu, PhD, Executive Director, CEO, Premas Biotech Pvt Ltd

With modern drug discovery, shortening to time to clinics is of utmost importance and a significant challenge. Premas has generated ultra-rapid methods, screening tools and scale up strategy to deliver a scalable process, validated drug substance for enabling a Phase 1 trial. Screens were established, optimized and operation excellence was implemented to determined the optimum conditions. This was accomplished within 22 weeks from the gene synthesis to deliver of drug substance.

12:55 Luncheon Presentation I to be Announced

Sponsored By THOMSON Solutions™ At Work INSTRUMENT COMPANY

Daniel Korostyshevsky, Tri-State Technical Sales Representative, Thomson Instrument Company

1:25 Accelerating Lead Magnetic Bead Purification Technology

Sponsored By GenScript Make Research Easy

Ray Low, PhD, Scientist, Amgen Inc.

High throughput purification is a critical step in antibody engineering and lead identification. Magnetic based technologies allow single step purification of targets by adding beads directly into bioreactors. This eliminates sample clearance through centrifugation - filtration and loading voluminous feedstocks to columns. Here, Amgen presents one of its latest innovations in the field of antibody screening and drug discovery using several parallel HTP platforms. Some of these systems are completed and licensed to GenScript.

1:55 Session Break

CHO CELL EXPRESSION

2:10 Chairperson's Remarks

Bernd Voedisch, PhD, Lab Head and Investigator III, NIBR Biologics Center, Novartis Institutes for Biomedical Research

2:15 The Application of Next-Generation Sequencing to Understand CHO Cell Biology

Colin Clarke, PhD, Principal Investigator, National Institute for Bioprocessing Research and Training (NIBRT)

The publication of genome sequences for CHO cell lines has facilitated study of these cell factories with unprecedented resolution. Our understanding of the CHO cell transcriptome, in particular, has rapidly advanced through the application of next-generation sequencing (NGS) technology to characterize RNA expression (RNA-Seq). In this talk, I will present examples of how RNASeq is being utilised to enhance the production of biopharmaceuticals in CHO cells.

2:45 Application of ^{13}C Flux Analysis to Identify High-Productivity CHO Metabolic Phenotypes

Jamey Young, PhD, Associate Professor, Chemical and Biomolecular Engineering, Vanderbilt University

Identifying metabolic phenotypes that promote high expression is a major goal of the biotech industry. We conducted a series of ^{13}C flux analysis studies to examine the metabolic response to IgG expression during early stationary phase of CHO cell cultures. Lactate consumption and citric acid cycle fluxes were most strongly associated with specific IgG productivity. These studies indicate that enhanced oxidative metabolism is a characteristic of high-producing CHO cell lines.

3:15 Implications of Choosing the Right Cell Engineering Technology on Early Stage Process Development

Sponsored By MaxCyte

James Brady, PhD, Vice President, Technical Applications and Customer Support, MaxCyte

Increasing productivity & maximizing data relevance during biotherapeutic development is possible when manufacturing the host cell early to produce sufficient quantities of candidates for extensive characterization and progression of promising candidates. Employing proper cell engineering, such as MaxCyte's high-performance cell engineering technology, drives rapid, scalable production of proteins in the manufacturing cell background while maintaining flexibility in downstream culture processes. This presentation discusses how a technology positively impacts productivity and fast-tracks biotherapeutic development.

3:45 **Refreshment Break in the Exhibit Hall with Poster Viewing**

4:45 **Problem-Solving Breakout Discussions**

5:45 **Networking Reception in the Exhibit Hall with Poster Viewing**

7:00 pm **End of Day**

THURSDAY, MAY 3

8:00 am **Morning Coffee**

ESCHERICHIA COLI

8:30 **Chairperson's Remarks**
Nicola Beaucamp, PhD, Head, Process Research, Roche Innovation Center Munich, Pharma Research and Early Development, Roche Diagnostics GmbH

8:35 **Massively Parallel Human Systems Biology in Synthetic Organisms**
Jesse Rinehart, PhD, Associate Professor, Cellular & Molecular Physiology, Systems Biology Institute, Yale University School of Medicine
Protein phosphorylation encompasses a central cellular language that determines every facet of normal cellular biology. We have recently created a technology that enables site-specific incorporation of phosphoserine 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 regarding the functional role of all human phosphorylation events.

9:05 **Evolving and Engineering *E. coli* Recombinant Protein Production Strains**
Jan-Willem de Gier, PhD, Professor, Biochemistry and Biophysics, Stockholm University
My laboratory has used both evolutionary and engineering approaches to create *E. coli* strains with improved properties for recombinant protein production. The evolutionary approaches will be illustrated by the isolation of BL21(DE3)-derived membrane protein production strains. The engineering approaches will be illustrated by the construction of an *E. coli* strain background with tighter regulation of rhamnose-induced protein production.

9:35 **Leveraging Modern Software to Organize, Optimize, and Measure Biologics R&D** *Sponsored By* Benchling
Sajith Wickramasekara, CEO and Co-Founder, Benchling
Scaling biologics infrastructure is an enormous challenge faced by R&D IT. Benchling is a biologics-native informatics platform used by over 100,000 scientists to configure biologics workflows and run day-to-day R&D. This presentation will highlight how Benchling has helped leading biopharma companies organize, optimize, and measure their biologics R&D.

9:50 **Myceliophthora Thermophila, "C1" a Recombinant Protein Production Platform** *Sponsored By* DYADIC
Mark Emalfarb, CEO, Dyadic International, Inc.
Dyadic has developed a novel eukaryotic gene expression platform with improved properties to speed up the development and lower the manufacturing cost of recombinant proteins. Intensive glycoengineering work is being done to develop cell lines to produce proteins at high yields, using low cost defined media with defined human glycoforms.

10:05 **Coffee Break in the Exhibit Hall with Poster Viewing**

INNOVATING PROTEIN EXPRESSION

11:05 **RAF1 Kinase: Everything but the Kitchen Sink**
William Gillette, PhD, Principal Scientist, Deputy Director, Protein Expression Laboratory, Leidos Biomedical Research, Inc.
RAF1 kinase is a critical protein in the regulation of cell proliferation in normal cells and is the focus of research due to its role in cancer. Obtaining highly purified, active RAF1 in quantities sufficient for HTP assays or structural biological research has not been reported in the literature. I will present a summary of our efforts to express and purify RAF1, and the impact of expression system, cell line, temperature, and length of expression.

11:35 **Development-Oriented Biologics Discovery**
Bingyuan Wu, PhD, Senior Research Scientist, Janssen, Pharmaceutical Companies of Johnson and Johnso
While the biologics market is expanding rapidly with novel and effective therapeutics, the challenges in discovery are steadily increasing. Discovery must be nimble and seamless with development. Recent examples will be discussed that demonstrate Janssen's robust and efficient expression systems to support and profile innovative protein therapeutics that make up the early portfolio.

12:05 pm **Optimisation of Transient Expression Platform to Increase Titre and Throughput**
David Humphreys, PhD, Director and Head, Protein Sciences, UCB Pharma

12:35 **End of Optimizing Protein Expression**

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

Fourth Annual

PROTEIN EXPRESSION SYSTEM ENGINEERING

Gene to Cell Line

RECOMMENDED SHORT COURSE(S)*

SC12: Transient Protein Production in Mammalian Cells

**Separate registration required, please see page 6 for course details.*

THURSDAY, MAY 3

THE NEXT GENERATION OF *ESCHERIA COLI*

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Shahram Misaghi, PhD, Senior Scientist, Early Stage Cell Culture, Genentech, Inc.

1:50 iML1515, A Computable Knowledge-Base of *Escherichia coli* Metabolism and its Structural Proteome
Colton Lloyd, PhD Candidate, Bioengineering, University of California, San Diego
This talk will introduce the latest genome-scale model of *E. coli* metabolism, iML1515, which models activity of 1,515 metabolic genes and provides a link to the 3D structure of each protein. In addition, it will expand on how the model can be applied to extract knowledge from emerging big data types in biology and to analyze differences in protein structural characteristics within the *E. coli* species.

2:20 Next-Gen Methods for Optimizing Biological Systems
Eric Kelsic, PhD, Staff Scientist, Wyss Institute, Harvard University
I will present work optimizing codon usage and protein function using high-throughput synthesis and DNA sequencing. To understand the determinants of codon choice in *E. coli*, we generated 12,726 *in situ* codon mutants in the *Escherichia coli* essential gene infA and measured their fitness with MAGE-seq. Our results shed light on natural codon distributions and should improve engineering of gene expression for synthetic biology applications. I will also share recent work optimizing AAV capsid variants for improved *in vivo* DNA delivery.

2:50 Multi-Omics Integration Accurately Predicts Cellular State in Unexplored Conditions for *Escherichia Coli*
Minseung Kim, MSc, Scientist, Computer Science, UC Davis Genome Center, University of California, Davis
We develop semi-supervised normalization pipelines and perform experimental characterization to create Ecomics, a multi-omics compendium for *Escherichia coli*. We then use this resource to train a multi-scale model that integrates four omics layers to predict genome-wide concentrations and growth dynamics. We demonstrate the predictive performance of the model for the various omics layers far exceeds various baselines. This work provides an integrative framework of omics-driven predictive modelling that is broadly applicable to guide biological discovery.

3:20 INTERACTIVE PANEL DISCUSSION: Next-Gen *Escherichia coli*
Moderator: William Gillette, PhD, Principal Scientist, Deputy Director, Protein Expression Laboratory, Leidos Biomedical Research, Inc.

3:50 Networking Refreshment Break

INNOVATING TECHNOLOGY

4:20 KEYNOTE PRESENTATION: Establishing Cell-Free Systems for Therapeutic Glycoprotein Synthesis
Michael Jewett, PhD, Charles Deering McCormick Professor of Teaching Excellence, and Associate Professor, Chemical and Biological Engineering, Northwestern University
Protein glycosylation is integrally involved in human biology and disease. Unfortunately, the study of glycans in native systems and the intentional manipulation of protein glycosylation patterns remain limited by the tools available for biochemical characterization of glycosylation enzyme activities and the synthesis of defined glycoforms. To address these limitations, we here describe a novel cell-free glycoprotein synthesis technology. This makes possible new application areas in the production of glycoprotein therapeutics.

4:50 Combining Metabolic and Process Engineering Strategies to Improve Recombinant Glycoprotein Production and Quality
Olivier Henry, PhD, Associate Professor, Chemical Engineering, École Polytechnique de Montréal

Cambridge HEALTHTECH Institute
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The accumulation of lactate and ammonia remains a major factor limiting the performance of fed-batch cell culture processes. These by-products have detrimental effects on production yields and can also negatively impact product quality. By combining process and cellular engineering strategies, we demonstrate that significant concomitant reductions in lactate and ammonia accumulation can be achieved in fed-batch cultures, leading to increased product titers without impacting product quality.

5:20 **End of Day**

5:20 **Registration for Dinner Short Courses**

RECOMMENDED DINNER SHORT COURSE(S)*

SC12: Transient Protein Production in Mammalian Cells

**Separate registration required, please see page 6 for course details.*

FRIDAY, MAY 4

8:00 am **Morning Coffee**

NEXT-GEN ENGINEERING

8:30 **Chairperson's Remarks**
Olivier Henry, PhD, Associate Professor, Chemical Engineering, École Polytechnique de Montréal

8:35 **Engineering an Expression System for the Production of Biotherapeutics Mimicking the Endogenous Counterpart**
Lars Stöckl, PhD, Senior Director, R&D, Glycotope GmbH
Some biopharmaceuticals, such as bispecific constructs or complex glycoproteins, remain very challenging in recombinant production. We present data from two case studies of host cell engineering, clone and upstream perfusion development for products that were produced in the human GlycoExpress cell line, which overcomes productivity and quality limitations compared to rodent cell lines.

9:05 **Mammalian Display: Antibody Discovery, Affinity Maturation and Developability Screening in IgG Format**
Michael Dyson, PhD, CTO, Antibody Engineering, IONTAS, Ltd.
Using directed integration of antibody genes by CRISPR/Cas9 and TALE nucleases, we have constructed large libraries in mammalian cells containing a single antibody gene/cell. This has permitted construction of millions of monoclonal stable cell lines displaying IgG antibodies on their surface from which antibodies have been selected by flow cytometry for specificity, binding affinity, species cross-reactivity and expression level. Expression in production cell lines also enables high-throughput developability screening.

9:35 **Protein Expression System Engineering**
Sponsored By horizon
Jamie Freeman, PhD, Product manager, Horizon Discovery Group
Aside from single gene knockouts to allow for metabolic selection systems, the CHO host remains largely unchanged. I will present how we have used a combination of techniques including genome engineering approaches such as CRISPR and rAAV to improve the biomanufacturing capacity of our GS knockout CHO K1 cell line.

10:05 **Networking Coffee Break**

HARNESSING CHO CELL ENGINEERING

10:35 **An Automated Metabolic Modeling and Analysis Pipeline for Chinese Hamster Ovary Clone Selection and Process Optimization**
Tobias Grosskopf, PhD, Scientist, Cell Culture Research, Roche Diagnostics GmbH
An increase in fermentation capacity and analytical capabilities has led to an ever growing amount of data to characterize antibody producing CHO cell lines. We have generated an automated pipeline to analyze all relevant process data by an integrated central model and generate a predictive score, which allows for selection of the lead clone among several candidate clones. The central model will get better over time and hence allow for the accumulation of biological and process knowledge.

11:05 **Engineering of Protein Secretion Using Systems Biology Models**
Nathan Lewis, Systems Biology & Cell Engineering, University of California, San Diego
The complexity of biotherapeutics and their host cells pose unique challenges to drug production. To address this, we are mapping out the complex cellular pathways controlling protein synthesis and secretion in CHO cells. Here, I demonstrate how this information provides insights into the protein-production capacity of CHO cells, and how metabolic needs differ across products. Furthermore, these resources allow us to control the production of toxic by-products and thereby improve bioprocess phenotypes.

11:35 **PKM1 Expression Appears to Drive Lactogenic Behavior in CHO Cell Lines, Triggering Lower Viability and Productivity; A Case Study**
Shahram Misaghi, PhD, Senior Scientist, Early Stage Cell Culture, Genentech, Inc.
Lactogenic behavior displayed by some CHO cell lines during manufacturing may result in a decline in viability, productivity, and alterations in product quality. We identified two lactogenic cell lines expressing different antibody molecules during the cell line development (CLD) process. These lactogenic behaviors were differentially mitigated through process development by optimizing either nutrient feeds or culture pH, depending on the cell line. CRISPR/Cas9 mediated knockout of the PKM-1 isoform abolished lactate

accumulation even under lactogenic conditions.

12:05 pm Mitochondrial-Derived Small RNAs as Powerful Tools to Boost CHO Cell Productivity

Lisa Alexandra Pieper, PhD, Postdoctoral Researcher, Early Stage Bioprocess Development, Boehringer Ingelheim Pharma GmbH & Co. KG

In an effort to improve the performance of a manufacturing clone expressing a complex therapeutic protein, we introduced the human mitochondrial genome-encoded small RNA-1978, resulting in a vastly increased specific productivity. Notably, by applying the respective small RNA in combination with directed modulations of the cell culture process we successfully maximized the final product titer, proving the superiority of integrated cell line engineering and process optimization.

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

1:05 Networking Refreshment Break

RE-WRITING THE GENETIC CODE FOR EXPRESSING PROTEIN

1:35 Chairperson's Remarks

Lars Stöckl, PhD, Senior Director, R&D, Glycotope GmbH

1:40 Development and Applications of Universal Platforms for Genetic Code Expansion

Abhishek Chatterjee, PhD, Assistant Professor, Chemistry, Boston College

The ability to site specifically incorporate unnatural amino acids (UAAs) into proteins in living cells has emerged as a powerful method to probe and manipulate protein structure and function. We are expanding the scope of this technology by establishing platforms that enable facile introduction of previously inaccessible chemical functionalities into the genetic code of both bacteria and eukaryotes.

2:10 Development of DNA-Encoded Chemical Libraries at Pfizer

Anokha S. Ratnayake, PhD, Principal Scientist, Pfizer Global R&D Groton Labs

The design and development of successful DNA-encoded libraries (DELs) require implementation of reliable analytical techniques and assays for on-DNA reaction monitoring, validation of on-DNA chemistries and assuring library quality (QC). This presentation will focus on the background on DNA-encoded library technology (DELT), elements of library design and the details of on-DNA chemistry validation, highlighting the associated analytical development processes.

2:40 Codon and Codon Pair Optimization in Synthetic Gene Design

Dimitris Papamichail, PhD, Assistant Professor, Computer Science, The College of New Jersey

Advances in *de novo* synthesis of DNA and computational gene design methods make possible the customization of genes and gene libraries by direct manipulation of features such as codon and codon context bias. In this talk, I will present computational methods to design genes with desired codon and codon context content, and tools that allow for the direct manipulation of protein-coding genes.

3:10 Quantity or Quality? Enhancing Co-Translational Protein Folding with Sub-"Optimal" Synonymous Codons

Patricia L. Clark, PhD, Rev. John Cardinal O'Hara C.S.C. Professor, Biochemistry, University of Notre Dame

Historically, "optimizing" a gene for heterologous expression consisted of substituting rare codons with synonymous common codons. This strategy can increase the amount of protein produced but may adversely affect the yield of native, active protein. This talk will focus on rare codon distribution in coding sequences and rational strategies for rare codon placement to enhance folding yield.

3:40 End of Conference

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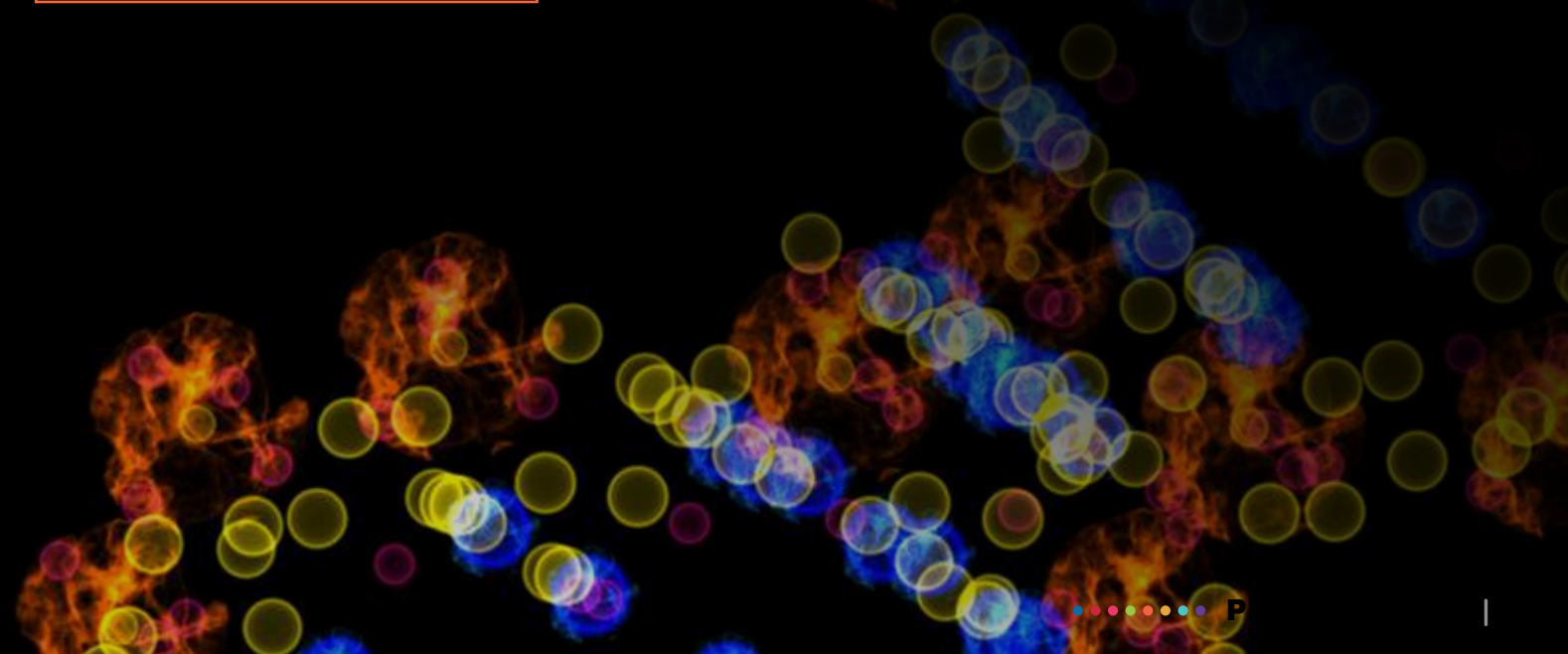
ANALYTICAL STREAM

- Characterization of Biotherapeutics
- Biophysical Analysis of Biotherapeutics
- Protein Aggregation and Stability in Biopharmaceuticals

Next-Generation Methods and Solutions for Analytical Characterization, Biophysical Analysis and Controlling Aggregation

The Analytical Stream focuses on the application of biochemical and biophysical characterization tools to gain detailed knowledge of proteins from discovery through all the stages of development, and presents the latest findings on the mechanisms and control of protein aggregation. This stream explores emerging analytical methods, addresses responses to regulatory requirements related to analytical characterization and presents best practice case studies from a wide range of industry and academic leaders. The three-part Analytical Stream at PEGS 2018 provides a comprehensive real-world perspective on this challenging and ever-changing arena.



Eighth Annual

CHARACTERIZATION OF BIOTHERAPEUTICS

New Methods, Instruments and Strategies for the Characterization of Next-Generation Product Formats

SUNDAY, APRIL 30

RECOMMENDED SHORT COURSE(S)*

SC2: Translational Considerations for Development of Monoclonal Antibodies and Emerging Constructs: Part I: Focus on Construct Design

SC7: Translational Considerations for Development of Monoclonal Antibodies and Emerging Constructs: Part 2: Focus on Preclinical Development

**Separate registration required, please see page 6 for course details.*

MONDAY, APRIL 30

7:00 am **Registration and Morning Coffee**

CHARACTERIZATION FOR NOVEL DRUG FORMATS

8:30 **Chairperson's Remarks**

Jennifer F. Nemeth, PhD, SCPM, Director, Biophysics, Structural Characterization, Biologics Discovery Sciences, Janssen Research & Development

8:40 **Development of a Cell-Based Assay Measuring Bispecific Antibody Binding to Predict PK-PD Responses**

Lynn Kamen, PhD, Scientist, Bioanalytical Sciences, Genentech

PK-PD modeling has traditionally relied upon drug concentration in serum along with affinity generated by SPR to predict efficacy and exposure. However, the advent of novel drug formats such as bispecific antibodies has heightened the need to develop biological characterization assays that are able to better predict PK-PD responses. This presentation will highlight a case study in which a novel cell-based binding assay was used to predict the PK-PD effects of a bispecific therapy.

9:10 **Characterization of CAR Ts and Cell Therapies**

Eric S. Alonzo, PhD, Scientist, Cellular Analytics, bluebird bio

Clinical-grade CAR T cell drug products contain a heterogenous mixture of phenotypically and functionally distinct cells. Such heterogeneity necessitates innovative strategies to define biomarkers that may predict responses to CAR T cell therapy. We improved biomarker characterization of our CAR T cell drug products by combining high dimensional mass cytometry with global gene expression analysis. These strategies identified multiple distinct memory T cell populations that may be associated with positive outcomes in CAR T cell therapy.

9:40 **Characterization of Gene Therapy Products**

Zhenhong Li, PhD, Senior Director, Analytics, RegenxBio

Thanks to the pioneers' perseverance and innovations, after greater than 20 years of development, the gene therapy industry is taking serious steps to advance therapeutics, leveraging knowledge and understanding from well-characterized biologics. The presentation will share our approach in selecting analytical methods to assess product characteristics with regard to product identity, content, purity/impurity, potency, and structural integrity in support of early phase clinical trials, including product release, stability and comparability.

10:10 **Networking Coffee Break**

10:50 **Top-Down Mass Spectrometry Strategy for Novel Drug Characterization**

Zhe Zhang, PhD, Senior Scientist, Integrated Biologics Profiling, Novartis

Mass spectrometry has shown to be a powerful tool to characterize different therapeutic protein formats. With peptide mapping, site-specific characterization can be achieved. Top-down mass spectrometry, however, can provide added value, for example avoiding digestion and artifact generation, sequence coverage on special regions, etc. Two case studies focusing on post-translation modification and clipping will be presented using top-down mass spectrometry. Integration of this technology can facilitate drug candidates developability-assessment.

11:20 **Analytical Characterization and Control of mAb Combination Products**

Michael Adamo, Senior Scientist, Bristol-Myers Squibb

Immuno-Oncology (I-O) may require targeting multiple pathways in the immune system leading to the emergence of combination I-O products and significant analytical challenges. This talk will discuss the analytical strategy that can be applied to control and characterize the individual mAb products in a combination I-O product. Several separation methods will be discussed for the control and characterization of key quality attributes of the combination mAb product including size and charge.

11:50 KEYNOTE PRESENTATION: Regulatory and Quality Considerations Associated with the Development of Novel Modalities

Anthony Mire-Sluis, PhD, Head, Global Quality, AstraZeneca

Novel modalities can challenge existing paradigms because they often require science and risk-based thinking that does not 'fit' familiar development pathways. Understanding the quality attributes of a new molecular entity can challenge standard analytical technology both physicochemical, and in particular, with biological assays. Creating robust manufacturing processes and control strategies can be challenging with even mature molecular platforms, so 'out of the box' thinking is necessary for novel modalities.

12:20 pm Comprehensive Workflow by Capillary Electrophoresis – Mass Spectrometry (CE-MS) for Biotherapeutics Drug Development

Mei Han, PhD, Senior Scientist, Pharmacokinetics & Drug Metabolism, Amgen, Inc.

Characterization of protein therapeutics by mass spectrometry is an essential part of all stages of drug discovery and development. Herein we discuss our CE-MS workflow for analysis protein therapeutics from pre-dose and post-dose samples. The discussion will include measuring intact mass, reduced samples, charge variants, and characterization of *in vivo* biotransformation.

12:50 Luncheon Presentation I: Next-Generation Capillary Electrophoresis Technology for Protein Analysis

Sponsored By proteinsimple

Karyssa Edwards, Assistant Scientist, Analytical Development, Celldex Therapeutics

Biotherapeutic proteins are complex molecules and challenging to analyze. Capillary electrophoresis (CE) is a highly efficient separation method which affords superior resolution, short separation time, and small sample volumes. The Maurice system innovates the conventional CE technology by combining both cIEF and CE-SDS detection schemes into a fully automated instrument, allowing your protein profiling either by size or charge. In this presentation, we demonstrate the application of Maurice system for analysis of biotherapeutic proteins.

1:20 Automated Data Processing and Analysis for Quality Monitoring of Biotherapeutics by Multi-Attribute Method (MAM)

Sponsored By Genedata

Joe Shambaugh, Head Genedata Expressionist, Genedata

Mass spectrometry (MS) enables simultaneously measurement of multiple biotherapeutic critical quality attributes (CQAs) at the molecular level. Applying a multi-attribute method (MAM) can increase product quality while reducing development and manufacturing costs. We present a MAM implementation using a single software platform for processing, analysis, and management of MS data. Dedicated workflows for a given biomolecule were tailored to measure CQAs, test for impurities, and check system suitability.

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 Challenges and Opportunities in Engineering Protein Biopharmaceuticals

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)

Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk, I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

4:55 The Next Generation of Cancer Immunotherapy: Targeting Myeloid Immune Checkpoints

Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital

Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

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

Sponsored by PRECISION FOR MEDICINE

7:15 End of Day

TUESDAY, MAY 1

8:00 am Registration and Morning Coffee

CHARACTERIZATION OF ANTIBODY-DRUG CONJUGATES

8:25 Chairperson's Remarks

Zhimei Du, PhD, Senior Principal Scientist, Merck & Company, Inc.

CHARACTERIZATION OF BIOTHERAPEUTICS

8:30 The Impact of Antibody Variants on the Quality Attributes of Immunoconjugates

Alex Lazar, PhD, Director, Analytical and Pharmaceutical Sciences, ImmunoGen, Inc.

One of the main components of immunoconjugates is the targeting antibody to which the payload molecules are attached. The antibody variants can have substantial impact on the consistency of the conjugation process and/or on the quality of the conjugated material. For monitoring the impact of antibody variants (e.g. tri-sulfides, incomplete masking) on the attributes of immunoconjugates, appropriate analytical methods were developed and results will be presented.

9:00 *In vitro* Biological Characterization of Kadcyla (Trastuzumab Emtansine)

Shan Chung, PhD, Principal Scientist and Group Leader, Genentech

Kadcyla (a.k.a. trastuzumab emtansine/ado-trastuzumab emtansine) is an antibody-drug conjugate composed of a humanized anti-HER2 antibody (trastuzumab) covalently conjugated to a cytotoxic drug (DM1). Kadcyla is indicated for the treatment of patients with HER2-positive metastatic breast cancer. This presentation will describe *in vitro* characterization of Kadcyla for biological activities pertinent to its mechanisms of actions, including DM1-induced apoptosis and trastuzumab-mediated inhibition of cell proliferation and induction of effector functions.

9:30 Size Exclusion Chromatography Mass Spectrometry (SEC-MS) – A Universal Approach for Quantitating DAR and Drug-Distribution of ADCs in a Research and Development Environment

Jay Jones, Senior Research Associate, Seattle Genetics

Native-intact mass analysis by SEC-MS can be used to quantitatively determine the drug-to-antibody ratio (DAR) of ADCs. To demonstrate suitability for use with a variety of ADC modalities, we successfully qualified this high-throughput DAR determination method using a variety of cysteinyl-linked ADC modalities. The SEC-MS method could be a universal approach for DAR determination to support process development in early phase, prior to the development of chromatographic assays used for release.

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

CHARACTERIZATION CHALLENGES

10:50 Linking Analytical Findings to Potency, Safety and Immunogenicity Risk Assessment

Vibha Jawa, PhD, Director, Biologics and Vaccine Development, Merck

Even with stringent control specifications, risk factors are often based on bioanalytical characterizations not necessarily related to biological thresholds and safety risks. It is difficult to evaluate clinical findings with lot to lot changes in product quality attributes. This talk reviews existing risk assessment tools and their applications as well as gaps in being able to perform a risk assessment related to changes in product quality attributes during different stages of biotherapeutic development.

11:20 Proteomics Identifies a CHO Host Cell Protein that May Impact Polysorbate Degradation

Kelvin Lee, PhD, Professor, Chemical & Biomolecular Engineering, University of Delaware

There is great interest in a better understanding of difficult to remove host cell proteins. We used proteomics approaches to identify different classes of difficult to remove CHO host cell proteins. One of the proteins that was identified may play a role in polysorbate degradation. We evaluated cell line development strategies to mitigate the expression of this protein and any resulting impact on polysorbate degradation.

11:50 Glycosylation Profile Characterization

Nathan Brown, PhD, Senior Scientist, AbbVie Bioresearch Center

Next to the amino acid sequence, protein oligosaccharide content can greatly influence function and disposition of a biologic. Complex therapeutic formats, such as fusion proteins, often contain multiple, surface-exposed sites of glycosylation which can significantly impact pharmacokinetics, tissue penetration, distribution and activity. Here, we present our strategy, utilizing multiple, orthogonal approaches, to characterize micro- and macro- glycan heterogeneity and guide early development.

Sponsored By
charles river

12:20 pm Luncheon Presentation I: Methods for Process Residuals in Biopharmaceutical Production Processes

Ian Parsons, PhD, Director, Analytical Development, Analytical Laboratory, Charles River

As companies develop manufacturing processes, they need to characterize them and show they consistently and reliably clear process residuals to acceptable levels in the drug substance. This presentation will describe the development, validation and application of a number of quantitative and limit test analytical methods for residuals, including complex analytes such as polyethylenimine, as well as traditional bioprocess residuals such as IPTG, antibiotics, antifoam, etc.

12:50 Luncheon Presentation II *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

MULTI ATTRIBUTE METHOD (MAM)

2:00 Chairperson's Remarks

Krishnan Sampath, PhD, Senior Director, Analytical and Drug Product Sciences, MacroGenics

2:05 Advancing Multi-Attribute Method in GMP Environment

Da Ren, PhD, Principal Scientist, Amgen

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As an emerging technology, Multi-Attribute Method (MAM) is a powerful assay that can monitor product quality attributes at the amino acid level. Recent technology advancement enables MAM to be implemented in GMP environment, which makes it possible to continuously monitor site-specific product quality attributes (PQAs) throughout the manufacturing process of biotherapeutics from product design to release testing. Considerations on implementing MAM in GMP environment will be discussed in this presentation.

2:35 MAM Consortium's New Peak Detection Round Robin

Rich Rogers, PhD, Scientist, Just Biotherapeutics

New peak detection, the purity component of the MAM, ensures novel modifications on biotherapeutics and process impurities are not overlooked. The MAM consortium has completed a New Peak Detection round robin study. The study had 34 participants from around the world. The NIST mAb was used for the study. The study included a reference sample, peptide spiked sample, stressed sample, and unknown sample. Multiple types of mass spectrometers and software packages were evaluated.

Sponsored By Waters THE SCIENCE OF WHAT'S POSSIBLE.

3:05 Lessons from the Development and Execution of an Automated Purification, Digestion, and Targeted LCMS Analysis (MAM) of Biotherapeutics

Anders Lund, PhD, Scientific Director, Bioanalytics Characterization Group, BioPharmaceutics Development, Sanofi

Multi Attribute Monitoring (MAM) can be used to track critical quality attributes (CQAs) all along the product lifecycle. To achieve aggressive TTC goals, a testing paradigm including automated protein A purification, enzymatic digestion and MAM analysis of biotherapeutic products was tested at three biopharmaceutical development sites (Framingham, Frankfurt, Vitry). The lessons learned, in addition to the challenges to design a proper testing paradigm across automation for sample purification digestion and LC-MAM will be presented.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

CHARACTERIZATION ISSUES IN LATE STAGE DEVELOPMENT

4:25 Development of Analytical Control Strategy for Late-Stage Biologics Programs

Krishnan Sampath, PhD, Senior Director, Analytical and Drug Product Sciences, MacroGenics

Monoclonal antibodies and bispecific DART® molecules are being developed for a variety of indications including immune-oncology. Stage-appropriate and risk-based analytical control strategy needs to be developed to ensure product quality as molecules progress from early to late stages of development. This presentation will discuss analytical control strategies developed based on evolving product understanding and process knowledge using the above molecules as case studies.

4:55 New Approaches for Characterization of Extractables and Leachables in Drug Product

Stacey Helming, PhD, Scientist, Analytical Sciences, Regeneron Pharmaceuticals

Single use components used in biomanufacturing processes require some degree of extractable and/or leachable (EL) risk assessment prior to use. How this assessment is performed, and what data are required, is largely left to the end user to determine. Improvements to efficiency in EL programs will be discussed, including what constitutes quality extractable data, guidance on leveraging existing data to risk-assess components, and conducting leachable studies at critical points during the process to ensure a comprehensive EL assessment.

5:25 End of Characterization of Biotherapeutics

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE(S)*

SC8: Introduction to Biophysical Analysis for Biotherapeutics: Discovery & Development Applications

**Separate registration required, please see page 6 for course details.*

Sixth Annual

BIOPHYSICAL ANALYSIS OF BIOTHERAPEUTICS

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

RECOMMENDED SHORT COURSE(S)*

SC8: Introduction to Biophysical Analysis for Biotherapeutics: Discovery & Development Applications

**Separate registration required, please see page 6 for course details.*

WEDNESDAY, MAY 2

7:30 am Registration and Morning Coffee

METHODS AND INSTRUMENTS

8:30 Chairperson's Remarks
George Bou-Assaf, PhD, Scientist, Technical Development, Biogen

8:40 Integrating Biophysical Analyses Earlier in the Discovery Process to Improve Final Lead Selection
Jennifer F. Nemeth, PhD, SCPM, Director, Biophysics, Structural Characterization, Biologics Discovery Sciences, Janssen Research & Development
Biophysical characterization has a critical role in drug discovery from target identification, to early hit lead screening, to intensive structural characterization at the pre-NME stage. Historically, biophysics has been applied heavily in the late discovery phases as a drug candidate approaches the NME declaration. I will examine what assays are having the greatest impact in our workflows across the discovery space, and where we are looking to make in-roads into new functional areas.

9:10 Alternatives to SEC for Measuring Aggregates and Fragments
David Hayes, PhD, Principal Scientist, Boehringer Ingelheim Pharmaceuticals, Inc.
It is known that some aggregates cause immunogenicity and therefore it is important for analytical scientists to use multiple techniques to robustly monitor and control aggregate levels. Analytical Ultracentrifugation (AUC) is the gold standard technique orthogonal to SEC for aggregate quantification. This talk will outline best practices for using AUC and also discuss limitations of AUC in terms of precision and repeatability illustrated with examples using synthetic data.

9:40 KEYNOTE PRESENTATION: Capturing, Identifying and Visualizing Preaggregate Transients Using Chaperonin-Based Biolayer Interferometry Platforms
Mark T. Fisher, PhD, Professor, Biochemistry and Molecular Biology, University of Kansas Medical Center
We can detect the presence of transient preaggregates within protein solutions using Chaperonin (GroEL) Biolayer interferometry (BLI) biosensors. ATP binding to GroEL Biosensors can specifically release captured proteins from the biosensor into microvolume aliquots. These released proteins are easily visualized by electron microscopy and evaluated using mass spectroscopy analysis. In some instances, we can even obtain low resolution 3D structures of released proteins released into these microvolumes using Electron Tomography.

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

10:55 AUC for the Biophysical Characterization of Gene Therapy Products
George Bou-Assaf, PhD, Scientist, Technical Development, Biogen
During production of AAV-based therapeutics, some viral particles remain empty while others incorporate a partial gene of interest. Both species constitute impurities. Hence, accurate separation and quantitation from the main product, the full particle, is indispensable for the characterization of AAV-based therapeutics. We developed two AUC-based methods for the quantitation of aggregates and empty versus full particle ratios in gene therapy products to enable process development and drug product characterization.

11:25 Screening and Miniaturization Approaches for Continuous Improvement in Biologics Development
Dana Filoti, PhD, Senior Scientist, Biologics Preformulation DPD, AbbVie Bioresearch Center

11:55 Evaluation of Factors Contributing to the Presence of Subvisible Particles in Dose Preparation and Administration Volumes for Biotherapeutics
Mark Pollo, Principal Scientist, Pfizer, Inc.
Particulate matter in drug products is a major concern in development of biopharmaceuticals and extensive work is performed in drug product

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development to minimize the level of particulates during manufacturing. Sources of particulates in dose preparation vary based on the formulation, manufacturing process and packaging. Studies were conducted to systematically investigate intrinsic and extraneous sources of particulate matter arising from materials and procedures associated with dose preparation and administration.

Sponsored By halo labs

12:25 pm High Throughput, Low Volume Subvisible Particle Screening
Robert Hart, CEO, Halo Labs
Halo labs will present a subvisible particle screening tool, the HORIZON, with detailed explanation of its Backgrounded Membrane Imaging (BMI) technology. A comparative analysis between HORIZON and flow imaging will be presented and key performance indicators including sample volume, throughput, dynamic range, instrument repeatability will be evaluated.

Sponsored By PEPSCAN

12:40 CLIPS-Based Protein Mimicry: Extending Epitope Mapping Technology with Paratope Mapping
Steffen van der Wal, PhD, Peptide Chemist, Pepscan
Most therapeutic antibodies recognize conformational epitopes. To address the 3D spatial conformation of complex epitopes, Pepscan has perfected its array technology through the addition of CLIPS chemistry resulting in CLIPS Precision Epitope Mapping. To comprehensively characterize Ab-Ag interactions also paratope mapping has been added to the platform technology.

Sponsored By NanoTemper

12:55 A Quick Protein Quality Ccheck That Will Improve Biotherapeutic Candidate Purification and Characterization Workflows
Peter Fung, PhD, Senior Manager, Product Marketing, NanoTemper Technologies
Starting with material of questionable quality for protein purification and characterization leads to irreproducible or ambiguous results. Transitioning between upstream and downstream workflows can be a challenge for bioprocessing researchers, particularly when the quality of the sample material is not known. We present a new platform that swiftly identifies sample quality and relative functionality in minutes complementing and guiding bioprocessing workflows—making go/no go decisions easy and quick—saving time, effort and producing more consistent results.

Sponsored By Chemical Computing Group

1:25 Luncheon Presentation II: Computational Approaches for Optimizing the Developability of Biotherapeutics
Nels Thorsteinson, Scientific Services Manager, Biologics, Chemical Computing Group
mAb candidates identified from high-throughput screening or binding affinity optimization often present liabilities for developability, such as aggregation-prone regions or poor solution behavior. In this work, we optimized an integrin α11 binding mAb for developability using homology modeling and rational design where reducing hydrophobic surface patches improved HIC behavior. A retrospective data analysis demonstrates that 3D descriptors and multi-parameter models can screen candidates and enrich libraries with favorable developability properties for a range of biotherapeutics.

1:55 Session Break

VISCOSITY MEASUREMENT

2:10 Chairperson's Remarks
Deniz B. Temel, PhD, Senior Research Investigator, Bristol-Myers Squibb

2:15 Predicting Viscosity of Therapeutic Antibodies: A Systematic Study Involving Small-Scale *in vitro* and *in silico* Methods
Hubert Kettenberger, PhD, Senior Principal Scientist, Protein Engineering, Roche Innovation Center Munich, Germany
Subcutaneous or intravitreal administration of antibodies often requires a high protein concentration as well as a low viscosity. Viscosity measurement is low-throughput, cumbersome and demands comparatively high sample amounts. Using a set of approximately 30 therapeutic antibodies, we aim at identifying small-scale *in vitro* and *in silico* methods to predict viscosity.

2:45 Emerging Automated Viscosity Measurements with Small Sample Size: An Evaluation of Multiple Methods and Technologies
Deniz B. Temel, PhD, Scientist, Amgen
It is crucial to optimize the usage of available samples and time for candidate differentiation, especially in terms of developability. There are many emerging methods and technologies with the promise to measure biophysical properties in a high throughput fashion with small sample consumption. In this talk, a number of instruments and methods, based on various physical principals, are evaluated and compared to measure (or predict) viscosity of biologics at high concentrations.

Sponsored By WYATT TECHNOLOGY

3:15 High-Throughput Biophysical Screening for Development and Formulation of Biologics
John Champagne, Northeast Regional Manager, Wyatt Technology
A smorgasbord of biophysical screening capabilities for development and formulation of biologics: light scattering does it in plates.

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem-Solving Breakout Discussions

5:45 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

THURSDAY, MAY 3

8:00 am Morning Coffee

ADVANCES IN SPECTROMETRIC METHODS

8:30 Chairperson's Remarks

Guodong Chen, PhD, Research Fellow, Bioanalytical and Discovery Analytical Sciences, Bristol-Myers Squibb

8:35 Development and Implementation of a Component-Based Hydrogen-Deuterium Exchange MS System

Kristopher Truncali, Scientist, Biophysics, Structural Characterization, Biologics Discovery Sciences, Janssen Research & Development

Hydrogen-Deuterium Exchange (HDX) mass spectrometry can provide critical insights into protein binding interactions. However, the technique's complexity has raised confusion around its routine utility and application. Here, we present an advanced HDX platform for early biophysical characterization of protein therapeutics. The workflow employs a LEAP H/D-X PAL, Thermo Orbitrap Fusion Lumos, Vanquish UHPLC, HDExaminer software, and in-house built automation software. The platform setup, applications, and limitations will be discussed.

9:05 Novel Mass Spectrometry-Based Strategies to Study Biomolecular Structure, Dynamics and Interactions in Complex Systems

Igor Kaltashov, PhD, Associate Professor, Chemistry, University of Massachusetts, Amherst

LC/MS is now routinely used in characterization of biopharmaceuticals, with reversed phase HPLC being the preferred separation method. In this presentation, we will discuss the advantages of using MS and MS/MS in combination with non-denaturing separation methods (ion exchange and size exclusion) to characterize complex therapeutic proteins. We will also present examples of using native LC/MS for characterization of other extremely heterogeneous macromolecular therapeutics, such as heparin and heparin-based medicines.

9:35 The QC Watchdog: Forensic ID of Any Particle

Sponsored By UNCHAINED LABS

Greg Manley, PhD, Product Manager, Unchained Labs

Particles muck up the quality of a drug and can shut down its production. Unchained Labs has the only tool out there that identifies particles by their shape and then forensically identifies them by their chemical and elemental fingerprints. In minutes, researchers know the culprit with-out a doubt, can track it back to the source, and fix their workflow or manufacturing process.

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

CHARACTERIZATION OF HIGHER ORDER STRUCTURE

11:05 Higher Order Structure Determination: Strategy and Case Study

Guodong Chen, PhD, Research Fellow, Bioanalytical and Discovery Analytical Sciences, Bristol-Myers Squibb

The higher order structure (HOS) of biologics plays an important role in stability, biophysical attributes, biological potency, and may have impact on safety and efficacy of biologics. Determining the HOS of biologics is a critical aspect of biologics discovery and development in the biopharmaceutical industry. This presentation will describe HOS determination strategy and methodology including case studies.

11:35 Novel Benchtop Method of Oxidative Footprinting for HOS Determination

Michael Brenowitz, PhD, Professor, Biochemistry and Molecular Pharmacology, Albert Einstein College of Medicine

Controlled oxidation is an insightful method of protein structure determination well-suited to mapping protein-protein interfaces such as those between antibodies and epitopes. We present a robust method of quantitative hydroxyl radical generation based on Fenton chemistry that is readily implemented on the benchtop using common laboratory tools and scalable to robotic sample handling. Example maps of protein surface accessibility and binding interfaces will be presented.

12:05 pm The Role of Biophysical Tools in Understanding Comparability and Biosimilarity

William Weiss, PhD, Principal Research Scientist and Group Leader, Biophysical Characterization, Eli Lilly and Company

Higher order structure (HOS) characterization is an important component of the broader analytical data package required to provide a comprehensive understanding of comparability/biosimilarity. This presentation will include an overview of established and emerging biophysical techniques for HOS characterization as well as discussion of important considerations for establishing comparability/biosimilarity of processes/products including selecting HOS techniques, developing and controlling methods based on these techniques, and comparing the resulting data.

12:35 End of Biophysical Analysis of Biotherapeutics

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Eleventh Annual

PROTEIN AGGREGATION AND STABILITY IN BIOPHARMACEUTICALS

Understanding and Controlling Protein Aggregation from Early Development through Scale-Up and Clinical Production

RECOMMENDED SHORT COURSE(S)*

SC8: Introduction to Biophysical Analysis for Biotherapeutics: Discovery & Development Applications

**Separate registration required, please see page 6 for course details.*

THURSDAY, MAY 3

AGGREGATION PRECURSORS

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
David Brockwell, PhD, Associate Professor, School of Molecular and Cellular Biology, University of Leeds, United Kingdom

1:50 Emerging Approaches for Understanding Early Aggregation Transients
Arun Alphonse Ignatius, PhD, Principal Scientist, Pfizer
Monoclonal antibodies could be susceptible to aggregation, especially at concentrations relevant to pharmaceutical formulations. (>100 mg/ml). Although conventional low resolution biophysical methods probe conformational stability of mAbs in relation to aggregation, molecular origins of aggregation are largely elusive. Nuclear magnetic resonance (NMR) studies on mAb and mAb fragments provide structural fingerprinting at an atomic resolution that can be potentially correlated to aggregation propensities of mAbs.

2:20 Protein Aggregation and Gelation – Insight from Combining Scattering, Rheology and Computer Simulations
Peter Schurtenberger, PhD, Professor, Physical Chemistry, Lund University, Sweden
Understanding and avoiding protein aggregation and gelation is essential in formulating biopharmaceuticals. We show how we can use a combination of advanced characterization techniques such as small-angle neutron (SANS) and X-ray scattering (SAXS), neutron spin echo measurements and microrheology experiments, combined with the theoretical toolbox from colloid physics and state-of-the-art computer simulations, to assess and predict aggregation and gel formation in concentrated solutions of biopharmaceuticals.

2:50 KEYNOTE PRESENTATION: Complement Activation in Human Serum by Protein Particles Is Influenced by Interactions with Containers
Theodore W. Randolph, PhD, Professor, Chemical & Biological Engineering, University of Colorado, Boulder
Acute immune responses to therapeutic proteins include anaphylactic shock, which may result from activation of the complement cascade. Container materials may affect the number of particles formed following freeze-thawing or agitation of protein formulations. Testing of these formulations in human serum shows that levels of activation of Bb, C3a and C5a, all critical intermediates on the complement activation cascade, are strongly correlated with levels of particles within antibody formulations.

3:20 Cruise Through Biologics Development with Uncle and Hunky
Sponsored By UNCHAINED LABS
Dina Finan, Product Manager, Marketing, Unchained Labs
Developing biologics requires picking the best candidates and assessing different formulations to ensure stability and minimize aggregation risk. Whether you're working with limited amounts of precious sample, or trying to understand even more about your molecules later on, Unchained Labs automates and simplifies these assessments. We'll discuss how you can use applications like thermal melting, sizing and polydispersity, and chemical denaturation to thoroughly characterize your samples.

3:50 Networking Refreshment Break

4:20 Assessing the Aggregation of Biopharmaceuticals *in vitro* and *in vivo*
David Brockwell, PhD, Associate Professor, School of Molecular and Cellular Biology, University of Leeds, United Kingdom
Protein-based biopharmaceuticals are susceptible to unfolding, mis-folding

and aggregation by environmental perturbations that include hydrodynamic flow. Aggregation thus poses an enormous challenge to biopharmaceutical development, production, formulation and storage. To address this problem, we describe an *in vivo* method to rapidly assess candidates for developability and an *in vitro* method to assess candidate manufacturability or process suitability for the manufacture of aggregation-prone biopharmaceuticals.

4:50 Combining Viral Particle Counting, Biological Characterization and Advanced Kinetics to Predict Vaccine Stability
Didier Clenet, PhD, Research Scientist, Formulation & Stability, Sanofi Pasteur, Canada
In-depth characterization of a purified rabies vaccine was performed in term of virus counted, aggregation state, and antigenic and genomic titer. Agreement between results from NTA (nanoparticle tracking analysis) and ELISA was assessed. Additionally, forced degradation study was combined with modern kinetic-based modeling approach to delimitate a time-temperature stability domain into which the vaccine would be kept antigenic. Based on a kinetic model, 3 years of vaccine stability was predicted at 5°C.

5:20 End of Day

5:20 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE(S)*

SC11: Strategic/Modular Bioassay Design and Analysis
**Separate registration required, please see page 6 for course details.*

FRIDAY, MAY 4

8:00 am Morning Coffee

DEVELOPABILITY EVALUATION

8:30 Chairperson's Remarks
Neal Whitaker, PhD, Associate Researcher, Macromolecule and Vaccine Stabilization Center, Pharmaceutical Chemistry, The University of Kansas School of Pharmacy

8:35 Chemical Stability Screening in Early Stage Discovery: New Isomerization and Deamidation Datasets
Yingda Xu, PhD, Director, Protein Analytics, Adimab
Isomerization and deamidation of therapeutic leads can often delay development timelines and provide challenge and risks for downstream process. Sequence-based prediction to scan for NG and DG can often lead to false positive results. Here we report the chemical liability analysis of ~140 clinical stage antibodies, under forced degradation conditions.

9:05 FEATURED PRESENTATION: Methods for Identifying Monoclonal Antibodies with Drug-Like Properties
Peter M. Tessier, PhD, Professor, Pharmaceutical Sciences and Chemical Engineering, University of Michigan
The success of antibody therapeutics is dependent not only on their specific bioactivities but also on their physiochemical properties. Here we report the development of methods for identifying antibodies with drug-like properties based on their chemical compositions and biophysical properties.

9:35 A Computational Framework for Predicting Protein Liabilities and Improvement of Antibody Developability
Sponsored By SCHRÖDINGER
Kannan Sankar, PhD, Postdoctoral Associate, Schrödinger
We present a novel algorithm to predict aggregation-prone regions based on 3D structures that uses the distribution of hydrophobic and electrostatic patches on the proteins' interaction surface. Machine learning techniques are applied to a large set of protein-specific descriptors to enable non-experts to produce statistically sound liability prediction models.

10:05 Networking Coffee Break

10:35 Developing a Screening Platform for Novel Biotherapeutics
Zhi (Jay) Guo, PhD, Senior Scientist, Global Protein Sciences, AbbVie Bioresearch Center
Novel bi-functional biologics with a variety of formats to choose from (scFv, Fab, mAb, etc.) and fused to different payloads (cytokines, growth factors, a different scFv, etc.) is of immense interest for targeted delivery and improved efficacy. Payloads can be fused at different positions and spacer lengths and it is now apparent that payloads dominate production and stability of biologics; thus, confounding drug-like properties (DLPs). To better understand structure-function relationship and rapidly advance candidates with good DLPs we will discuss our throughput screening process.

FORMULATION CONTROL OF PROTEIN AGGREGATION

11:05 Characterization of Aggregates That Are Concentration-Dependent
Neal Whitaker, PhD, Associate Researcher, Macromolecule and Vaccine Stabilization Center, Pharmaceutical Chemistry, The University of Kansas School of Pharmacy
High protein concentrations in biopharmaceutical drug products (>100 mg/ml) can lead to colloidal instability and elevated levels of aggregation. Numerous analytical techniques are required to characterize these aggregates, from small soluble aggregates, to submicron and subvisible particles to larger visible particles. This talk will present several case studies utilizing these methods with the aim of reducing the propensity of aggregate formation as part of the development of stable protein formulations.

PROTEIN AGGREGATION AND STABILITY IN BIOPHARMACEUTICALS

11:35 Optimizing Cryoprotectant to mAb Ratios to Mitigate Aggregation

Tom Crowley, PhD, Principal Scientist, Pharmaceutical R&D, Pfizer, Inc.

The use of disaccharides such as sucrose and trehalose as cryoprotectants in monoclonal antibody formulations is a well-established strategy in protecting against freeze thaw induced aggregation. This work explores the impact of varying the ratio of cryoprotectant to antibody to meet the challenges of ensuring protein stability, controlling viscosity, and maintaining isotonicity for high concentration dosage forms.

12:05 pm Controlled Nucleation During Lyophilization - Comparison of Nucleation Techniques and their Impact on Protein Aggregation

Andrea Allmendinger, PhD, Senior Scientist, Late-Stage Pharmaceutical and Processing Development, Biologics, F.Hoffmann-La Roche, Switzerland

Stabilizing proteins in liquid state can be challenging. Lyophilization offers a gentle way to increase storage stability, which is dependent on product attributes like residual moisture and cake structure directly impacted by the design of the lyophilization cycle. There is growing interest in controlling the ice nucleation event in order to reduce variability across samples. Roche/Genentech has evaluated the comparability of cakes produced with different technologies and findings are presented in this talk.

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

1:05 Networking Refreshment Break

PROCESS CONTROL OF PROTEIN AGGREGATION

1:35 Chairperson's Remarks

Zhi (Jay) Guo, PhD, Senior Scientist, Global Protein Sciences, AbbVie Bioresearch Center

1:40 Rapid, High-Resolution Analysis of Monoclonal Antibody Aggregates Using Chip LFMC

Raja Ghosh, PhD, Professor, Chemical Engineering, McMaster University, Canada

Laterally-fed membrane chromatography (LFMC) has been shown to be suitable for high-speed, high-resolution separation and analysis of biologicals such as monoclonal antibodies. A scaled-down Chip LFMC device suitable to rapid and high-resolution analysis of monoclonal antibody aggregates will be discussed. The typical separation time with Chip LFMC is of the order of a couple of minutes, which is significantly faster than UPLC. Also, the separation can be carried out using inexpensive low-pressure liquid chromatography systems.

2:10 Product Quality Control Strategy Development for Non-mAb Complex Modalities by Using Combinatorial Cell Engineering and OMICS Screening Tools

Zhimei Du, PhD, Head, Cell Line Development, Merck & Company, Inc.

New product-related impurities have been found to accompany non-mAb complex modalities, which usually don't exist in standard mAb production. Many of these PQAs are related to protein folding and assembly efficiency inside the cell, which impact post-translational modifications directly or indirectly. Our presentation will illustrate the importance of selecting appropriate cell/upstream conditions through screening and/or engineering, as part of quality control strategy to obtain the desired recombinant protein PQA profile.

2:40 Process Control Challenges in Controlling Aggregation

Jason Fernandez, Scientist, Protein Pharmaceutical Development, Biogen

Control of aggregation is a common goal across biopharmaceutical manufacturing processes, from the bioreactor through fill finish operations. As process controls vary along the manufacturing process, with each processing operation having unique challenges to aggregation control, an end-to-end process control strategy is important in minimizing the ultimate aggregate level in finished products. This talk will highlight the concept and challenges of end-to-end process control of aggregation.

3:10 Evaluation of Sub-Visible Particle Technologies Used to Characterize Particles from Packaging Components

John Rech, Technology Manager, Particle Testing, Analytical Laboratory, West Pharmaceutical Services

Measurement and control of sub-visible particles (SVP) in injectables is a growing concern in pharma because of potential to cause patient harm. Global compendia have specifications in the final drug product for particles >100µm and >10µm, but current methods can measure below 10µm and into the submicron range. To better understand SVP contribution, particularly from silicone-treated stoppers, a study was designed to determine optimal methods to measure and identify SVP.

3:40 End of Conference

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IMMUNOGENICITY & BIOASSAYS STREAM

- Immunogenicity Case Studies and Clinical Management
- Immunogenicity Assessment and Regulatory Approval of Biologics
- Optimizing Bioassays for Biologics

Ensuring the Safety and Efficacy of Biologics

This year's Immunogenicity & Bioassay Stream focuses on the latest science, technologies and strategies to ensure the safety and efficacy of novel biologics, with particular focus on immunogenicity clinical management and assay life cycles for bispecifics, ADCs, and CAR T cell therapies. Part One looks at new case studies and how to manage the clinical outcome of biologics; Part Two examines immunogenicity assay assessment, with the goal of meeting the regulatory requirements; 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.

Eleventh Annual

IMMUNOGENICITY CASE STUDIES AND CLINICAL MANAGEMENT

Improving Clinical Design and Tailoring Therapy Choices

SUNDAY, APRIL 30

RECOMMENDED SHORT COURSE(S)*

SC1: Preclinical and Clinical Assessment of Immunogenicity: Multidomain Therapeutics and New Modalities, Including Gene Therapy and CAR T

SC5: *In silico* Immunogenicity Predictions (Hands-On) Workshop

**Separate registration required, please see page 6 for course details.*

MONDAY, APRIL 30

7:00 am Registration and Morning Coffee

CLINICAL STUDIES AND MANAGEMENT

8:30 Chairperson's Remarks

Vibha Jawa, PhD, Director, Immunogenicity Strategy for Biologics and Vaccines, Pharmacokinetics, Pharmacodynamics & Drug Metabolism, Merck & Co., Inc.

8:40 FDA Perspective on Clinical Management

Amy S. Rosenberg, MD, Division Director, Office of Biotechnology Products, FDA/CDER

Immune responses to therapeutic proteins can be highly problematic if they neutralize life-saving therapeutics, cross react to endogenous proteins with non-redundant functions, or abrogate the efficacy of highly effective therapeutic proteins. Two strategies are increasingly being explored for mitigation: deimmunization of protein therapeutics and Immune tolerance induction (ITI). ITI is being increasingly explored in the context of autoimmune diseases, transplantation, and immune responses to life saving therapeutic proteins. Approaches that focus on antigen specificity, rather than global immune suppression are of greatest interest, but their utility may be limited by the clinical time frame for tolerance induction and clinical urgency. The development of "deimmunized" protein therapeutics has proven a daunting task but ultimately may have great utility. There is a clear need to better understand epitope spread and generation of subdominant T cell clones in this context.

9:10 Ten Years of Clinical Experience with Immunogenicity in Pompe Disease: Lessons Learned

Stephanie Austin, MS, MA, CGC, Genetic Counselor, Senior Research Program Leader, Duke University Medical Center

Cross reactive immunological material (CRIM)-negative infantile Pompe disease (IPD) usually develop high anti-drug antibodies (ADA) and a prophylactic immune tolerance induction (ITI) with rituximab, methotrexate, and/or IVIG is a standard of care. However, predicting the development of ADA is challenging in CRIM-positive infantile Pompe disease. We evaluated a scoring method for predicting individualized risk of ADA based on the sequence of their residual GAA and their HLA DR1 alleles. This and other clinical updates will be presented.

9:40 Clinical Relevance of Detecting Anti-Infliximab Antibodies with a Drug-Tolerant Assay: Post Hoc Analysis of the TAXIT Trial

Ann Gils, PhD, Professor, Pharmaceutical and Pharmacological Sciences, KU Leuven, Belgium

To evaluate the clinical relevance of anti-drug antibodies (ADA), ADA of 76 patients of the TAXIT trial who presented with an infliximab trough concentration (TC)<3µg/mL at screening were measured using both a drug-sensitive (DS) and drug-tolerant (DT) assay. The immunogenicity detection rate increased from 21% (DS) to 63% (DT). Q4 patients required a higher cumulative infliximab dose. All but one patient of Q4 were also ADA positive using DS.

10:10 Networking Coffee Break

10:45 Chairperson's Remarks

Vibha Jawa, PhD, Director, Immunogenicity Strategy for Biologics and Vaccines, Pharmacokinetics, Pharmacodynamics & Drug Metabolism, Merck & Co., Inc.

10:50 Clinical Immunogenicity Assessment: Decision-Enabling Immunogenicity Data and Analyses

M. Benjamin Hock, PhD, Director of Immunogenicity, BioMarin

Pharmaceutical Inc.

The commentary, "A Proposal to Redefine Clinical Immunogenicity Assessment" [Mytych et al., 2017, AAPS J; PMID: 28247192] described criteria whereby ADA bioanalysis might not take place by default for a low-risk protein therapeutic. One principle behind that argument is that ADA data should facilitate patient/physician- or product/program- decision-making.

11:20 Demystifying Immunogenicity Testing for Biotherapeutics

George R. Gunn, III, PhD, Head, Immunogenicity and Clinical Immunology, Bioanalysis, Immunogenicity and Biomarkers, In Vitro/In Vivo Translation Platform, GlaxoSmithKline

Immunogenicity assessment of biologic therapeutics is a scientific and regulatory expectation. Bioanalytical complexities, sampling strategies and interpretation approaches can contribute to differences observed for anti-drug antibody (ADA) incidences reported for biotherapeutics, even those with similar mode of action and patient population. Here we will put immunogenicity assessments into context regarding method limitations, capabilities and the interpretation of the clinical consequences of immunogenicity.

11:50 Rigorous Reagent Characterization and Life Cycle Management Is Critical for the Consistent Performance of Bioanalytical Assays: A Clinical Case Study

Kun Lu, PhD, Staff Scientist, Protein Biochemistry Group, Regeneron Pharmaceuticals, Inc.

Robust and reproducible bioanalytical assay performance depends on the quality of critical protein reagents (CPR). Data will be presented to demonstrate the quality of CPRs using a set of biochemical and biophysical characterization assays. Additionally, a clinical case study will be presented to demonstrate the importance of formulation conditions for CPRs when working with modified reagents, specifically ruthenium labeled reagents.

Sponsored by NDA

12:20 pm Early Development Strategy for Bacterial- or Viral-Vectored Gene Therapies: 2 Case Studies

Jennifer Sims, Non-Clinical Expert, NDA Advisory Board, NDA Group

Aligning product attributes & process variables with a preclinical program that enables translation into a risk management strategy for gene therapies is a challenge. We will present examples illustrating how an effective risk assessment may integrate a consideration of factors associated with transgene & vector components. This can be used to guide manufacture, product quality & preclinical study design decisions, while anticipating regulatory priorities for early clinical development, including mitigating the risks of undesirable immunogenicity.

12:50 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on your Own**

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 Challenges and Opportunities in Engineering Protein Biopharmaceuticals

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)

Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

4:55 The Next Generation of Cancer Immunotherapy: Targeting Myeloid Immune Checkpoints

Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital

Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

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

Sponsored by PRECISION FOR MEDICINE
THE FUTURE OF MEDICINE IS PRECISION

7:15 End of Day

TUESDAY, MAY 1

8:00 am Registration and Morning Coffee

MITIGATION STRATEGIES IN CLINICAL SETTINGS

8:25 Chairperson's Remarks

Sandra Garces, MD PhD, Senior Medical Advisor, Global Patient Safety, Eli Lilly

8:30 Proactive Therapeutic Drug Monitoring and Improved Outcomes over Standard of Care or Reactive Therapeutic Drug Monitoring

Adam Cheifetz, MD, Director, Center for Inflammatory Bowel Disease, Beth Israel Deaconess Medical Center; Associate Professor of Medicine, Harvard Medical School

Currently, empiric dose escalation or reactive TDM is standard of care in the treatment of inflammatory bowel disease (IBD). Reactive testing is cost-

effective and better directs care in IBD. However, there is some evidence that proactive testing of anti-TNF concentrations and antibodies to anti-TNF and optimization to a therapeutic window improves outcomes when compared to empiric dose escalation or reactive testing.

9:00 Immunogenicity of Therapeutic Antibodies: Monitoring Antidrug Antibodies in a Clinical Context

Theo Rispens, PhD, PI Antibody Structure and Function, Sanquin

Immunogenicity is one of the factors that may impact efficacy and safety of therapeutic antibodies in patients. Many immunogenicity assays are available for testing anti-drug antibodies (ADA), but the relationship between ADA and clinical outcome is often not clear. This presentation will address different types of immunogenicity assays and their clinical relevance in terms of drug tolerance, relation with PK, neutralizing antibodies, potential adverse events associated with ADA and prediction of future loss of response.

9:30 PANEL DISCUSSION

Moderator:
Sandra Garces, MD PhD, Senior Medical Advisor, Global Patient Safety, Eli Lilly

Panelists:

Amy S. Rosenberg, MD, Division Director, Office of Biotechnology Products, FDA/CDER

George R. Gunn, III, PhD, Head, Immunogenicity and Clinical Immunology, Bioanalysis, Immunogenicity and Biomarkers, In Vitro/In Vivo Translation Platform, GlaxoSmithKline

Theo Rispens, PhD, Immunopathology, Sanquin Research, Amsterdam, The Netherlands

Boris Gorovits PhD, Senior Director, Pharmacokinetics, Dynamics & Metabolism, Pfizer Inc

- What have we learned from using drug tolerant ADA assays in a clinical setting?
- Perspectives of FDA, sponsors and clinicians on the need of continuing to refine ADA assays (towards higher sensitivity and drug tolerance) and developing ADA tolerant PK assays
- What is the clinical usefulness of using ADA tolerant PK assays?
- How should clinicians use and interpret different types of PK and ADA assays?

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

PATIENT STRATIFICATION

10:50 Chairperson's Remarks

Darshana Jani, Senior Manager, Global Assay Lead, Drug Development, Pfizer

10:50 Use of Risk Assessment Information from Preclinical Stage to Drive Clinically Relevant Immunogenicity Strategy for Human Trials

Diana Montgomery, PhD, Principal Scientist, Predictive and Clinical Immunogenicity, Pharmacokinetics, Pharmacodynamics & Drug Metabolism, Merck & Co., Inc.

Unwanted immunogenicity to therapeutic proteins can impact the exposure (PK), response (PD) and drug safety, however the clinical manifestations can show a wide range of variation between different drugs. This presentation will cover both the *in silico* algorithm and *in vitro* based risk assessment strategy put in place for several drugs in discovery and how the strategy was refined for molecules with immunomodulatory targets. Examples will be used to illustrate possible relationships between predictive tools and clinical outcomes.

11:20 How Can Clinicians Use Immunogenicity Information to Better Understand Clinical Heterogeneity?

Sandra Garces, MD, PhD, Senior Medical Advisor for Immunogenicity, GPS Medical and Benefit-Risk Management, Eli Lilly and Company

Biologic therapies have significantly improved the prognosis of many patients with chronic inflammatory diseases. However, clinical responses to those therapies are very heterogeneous, varying from non-response to loss of response or to complete clinical remission. In cases of therapeutic failure, an empirical switch to any other approved biologic represents a common practice. In cases of clinical remission, no clear guidance exists to maintain, reduce or discontinue therapy. Therapeutic drug monitoring (drug levels and ADA) can work as a tool to help us understand clinical heterogeneity and adopt tailored therapeutic decisions that can improve the cost-effectiveness of biologic therapies.

11:50 Hemophilia A: A Case Study of Optimizing Patient Populations to Assess Immunogenicity

Steven Arkin, MD, Executive Director, Clinical Programs, Rare Disease Research Unit, Pfizer Worldwide R&D

Replacement biologics generated through recombinant DNA technology are used to treat many rare diseases but carry the risk of novel antigenic epitopes. Antibody immune responses observed in clinical studies may occur as a class effect or in response to the novel epitopes. By use of sub-populations at minimum risk for background antibody immune response, it is possible to characterize immunogenicity risk for the respective drug in the context of the small studies that are feasible in rare disease conditions.

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

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

CASE STUDIES OF NOVEL BIOLOGICS

2:00 Chairperson's Remarks

Darshana Jani, Senior Manager, Global Assay Lead, Drug Development, Pfizer

2:05 KEYNOTE PRESENTATION: Kymriah Case Study: First-Ever CAR T Cancer Drug and Its Journey to FDA Approval

Karen Thudium, PharmD, MSc, Head, Clinical Pharmacology Program, Cell and Gene Business Unit, Novartis

Kymriah is the first-ever gene therapy that was approved by the FDA in the US to treat pediatric acute lymphoblastic leukemia. It's a type of cancer immunotherapy, which harnesses the body's immune system to take on cancer cells. Kymriah did not have to go through a Phase III trial

IMMUNOGENICITY CASE STUDIES AND CLINICAL MANAGEMENT

because of the spectacular clinical responses in patients. Approximately, 83% of pediatric and adult patients with relapsed or refractory B-cell acute lymphoblastic leukemia (ALL) showed complete responses within just three months of treatment. This talk will focus on the development of Kymriah and its journey to FDA approval.

2:35 Immunogenicity Profile of an Enzyme-Substitution Therapy and Impact on Safety and Efficacy

Soumi Gupta, PhD, Director of Immunogenicity, Translational Sciences, BioMarin Pharmaceutical, Inc.

We have developed an extensive suite of assays to characterize the immunogenicity profile of an enzyme-substitution therapy in late-stage development. Here we will discuss the interpretation of that ADA data, and the impact of immunogenicity on safety and efficacy of a novel therapeutic.

3:05 Regulatory Expectations for Immunogenicity Assessment of Viral Vector-Based Gene Therapy Modality

Boris Gorovits, PhD, Senior Director, Pharmacokinetics, Dynamics & Metabolism, Pfizer Inc

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:25 Immunogenicity Screening for Designing Antibody Therapeutics, A Case of Emicizumab (Preclinical)

Chiyomi Kubo, PhD, DVM, Scientist, Research Division, Chugai Pharmaceutical Co., Ltd.

Immunogenicity of antibody therapeutics may reduce efficacy, safety and success rate of development. This talk will present a case study to screen anti-factors IXa/X bispecific humanized IgGs for a low immunogenic candidate on the basis of the activity observed in preclinical *in vitro* assay. In the Phase III-HAVEN1 trial where approximately 100 patients received the finally selected one, emicizumab, none tested positive for ADA (Oldenburg J et al. NEJM. 2017).

4:55 Cellular and Humoral Immune Responses in AAV-Mediated Gene Therapy

Katherine A. High, MD, Co-Founder, President and Head of R&D, Spark Therapeutics

Recombinant adeno-associated viral vectors (AAVs) are quickly becoming the preferred vector for gene delivery for the treatment of a wide variety of genetic disorders. However, since their use in a clinical trial targeting hemophilia B patients 10 years ago, immune responses to the AAV capsid have emerged as an issue that must be optimally managed to achieve therapeutic success. This talk will utilize data from clinical trials to illustrate optimal monitoring and management of human immune responses to the AAV vector, with a goal of achieving best outcomes in AAV-based gene transfer. A better understanding of both pre-treatment neutralizing antibodies, and cytotoxic T cell responses to recombinant AAV will lead to more efficacious gene transfer protocols in patients.

5:25 End of Immunogenicity Case Studies and Clinical Management

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE(S)*

SC13: Sub Visible Protein Particles in Immunogenicity: Measurement, Characterization and Impact

**Separate registration required, please see page 6 for course details.*

Eleventh Annual

IMMUNOGENICITY ASSESSMENT AND REGULATORY APPROVAL OF BIOLOGICS

Achieving Assay Quality and Clinical Success of Novel Biologics

RECOMMENDED SHORT COURSE(S)*

SC1: Preclinical and Clinical Assessment of Immunogenicity: Multidomain Therapeutics and New Modalities, Including Gene Therapy and CAR T

SC13: Sub Visible Protein Particles in Immunogenicity: Measurement, Characterization and Impact

**Separate registration required, please see page 6 for course details.*

WEDNESDAY, MAY 2

7:30 am Registration and Morning Coffee

DRUG TOLERANCE AND INTERFERENCES IN ASSAYS

8:30 Chairperson's Remarks
Shan Chung, PhD, Principal Scientist and Group Leader, Genentech, Inc.

8:40 Acid Treatment of Serum Samples in ADA Assays: To Treat or Not to Treat?
Uma Kavita, PhD, Senior Research Investigator, Analytical and Bioanalytical Operations, Bristol-Myers Squibb
Despite the common use of acid treatment to dissociate anti-drug antibody (ADA)-drug complexes, a systematic study of the impact of various acids at different pH levels on ADA of differing affinities and the resulting impact on assay drug tolerance and sensitivity has not been reported. Using a dimeric domain antibody therapeutic and several mouse monoclonal antibodies of well-defined association and dissociation rate constants and differing relative affinities as well as a rabbit pAb as ADA controls, we have addressed several important issues related to acid pre-treatment and impact on ADA assay sensitivity and drug tolerance.

9:10 Sample Pre-Treatment to Resolve Matrix Interference in a Neutralizing Antibody Assay
Lynn Kamen, PhD, Scientist, BioAnalytical Sciences, Genentech
Neutralizing antibody (NAb) assays detect the presence of anti-drug antibodies that neutralize the mechanism of action of a therapeutic. While interference from the drug is a common problem in development of NAb assays, interference from the sample matrix itself can also interfere. This presentation will highlight a case study in which matrix interference in a NAb assay was identified and resolved via sample pre-treatment, allowing the successful detection of NAbs.

9:40 Using ICP-MS to Measure Total Drug Levels and Differentiating between Free Drug and Bound Drug to Anti-Drug Antibodies
Julio Delgado, MD, MS, CMO, ARUP Laboratories; Division Chief, Clinical Pathology, University of Utah School of Medicine; Associate Professor, Pathology, University of Utah
Development of anti-drug antibodies (ADA) against biological agents contributes to therapeutic failure. An ICP-MS assay was developed for detection of free Infliximab and Infliximab bound to ADA. The difference in concentrations between free and bound Infliximab indicates presence of ADA. The ICP-MS assay showed high tolerance to residual infliximab, so testing can be performed right after infusion. Early detection of ADA is helpful to optimize treatment in the inpatient setting.

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

10:55 PANEL DISCUSSION
Moderator: Shan Chung, PhD, Principal Scientist and Group Leader, Genentech, Inc.
Panelists: Uma Kavita, PhD, Senior Research Investigator, Analytical and Bioanalytical Operations, Bristol-Myers Squibb
Julio Delgado, MD, MS, CMO, ARUP Laboratories; Division Chief, Clinical Pathology, University of Utah School of Medicine; Associate Professor, Pathology, University of Utah
Theo Rispens, PhD, Immunopathology, Sanquin Research, Amsterdam, Netherlands
Steven Bowen, PhD, Immunogenicity Reviewer, OBP/OPQ/CDER, FDA
Susan Richards, PhD, Presidential Scientific Fellow, Translational Medicine Early Development, Sanofi R&D
- Technical considerations for sample pre-treatment methods developed to reduce drug interference
- Epitope integrity during pre-treatment (e.g. non-denaturing)
- Subject, patient interfering factors: Cross-reactive antibodies (e.g.

rheumatoid factor, allo-antibodies)
- Applicability of these methods in the clinical laboratory setting
- Clinical significance/added value of ADA results generated from assays involving sample pre-treatment methods

IMMUNOGENICITY PREDICTION AND MITIGATION

11:25 The Use of Non-Clinical Assessments in Immunogenicity Risk-Assessment during Drug Development

Zuben E. Sauna, PhD, Research Biologist & Principal Investigator, Haemostasis Branch, Plasma Protein Therapeutics, Office of Tissues and Advanced Therapies, FDA/CBER

Immunogenicity (development of anti-drug antibodies) is an impediment to development and licensure of therapeutic-proteins. There has been significant progress in the development use of non-clinical assessments of immunogenicity-risk. The application of these tools will be illustrated using case studies and examples from our research. I will also present data evaluating different Factor-VIII products in a MHC-Associated-Peptide-Proteomics (MAPPs) assay. These results show that proteins with the identical primary sequence may present differently to the immune system.

11:55 T Cell Response to Biologics: From T Cell Epitope Mapping to Immunomonitoring

Bernard Maillere, PhD, Director, Research and Head of Immunochemistry Laboratory, Institute Frederic Joliot, SIMOPRO, CEA, University Paris-Saclay

As the T cell activation precedes and contributes to antibody response we evaluated the T cell response to biologics in heathy donors and in patients. With the perspective of immunogenicity prediction, we identified T cell epitopes from T cells collected in healthy donors of multiple biologics including infliximab, rituximab, adalimumab, natalizumab, FVIII en IFN-b. T cell epitopes identified from the healthy donors were shown to participate to the T cell response in the treated patients. Using a new triple-cytokine fluorospot assay we revealed a T cell response in multiple ADA- patients qualitatively different from that of ADA+ patients demonstrating that the lack of ADA did not imply an absence of immune response.

Sponsored by Lonza Pharma & Biotech

12:25 pm Immunogenicity Risk Assessment: Using Preclinical Tools during Lead Selection and Optimization

Noel Smith, PhD, Principal Group Leader, Applied Protein Services, Lonza Biologics

High attrition rates of preclinical candidates are primarily caused by lack of efficacy or safety issues. Immunogenicity leads to problems including dangerous cytokine response and/or generation of anti-drug antibodies that neutralize protein activity and/or alter PK/PD. Lonza has developed a comprehensive set of preclinical safety and immunogenicity risk assessment tools. This presentation will describe how these tools, used early in development, aid selection and optimization of candidates and help reduce the risk of failure.

Sponsored by ABZENA Enabling better biopharmaceuticals

12:55 Managing Unwanted Immune Responses to Antibodies including utilisation of MHC-Associated Peptide Proteomics (MAPPs)

Mark Fogg, PhD, Head, Immunology, Abzena

- Accurate and sensitive ways to assess the potential immunogenicity and development of anti-drug antibodies against proteins and antibodies *ex vivo* by measuring CD4+ T cell responses
- Methods for managing and reducing potential immunogenicity
- Introducing MHC-Associated Peptide Proteomics (MAPPs) to augment data sets to better inform immunogenicity risk

1:55 Session Break

2:10 Assessment, Observation and Mitigation of Immunogenicity: A European Perspective

Sophie Tourdot, PhD, BioMedicine Design, Pfizer

The talk will review emerging data and immunogenicity strategy from European investigators, including activities of the European Immunogenicity Platform (EIP), work from the Innovative Medicine Initiative - funded ABIRISK program (Anti-biopharmaceutical immunization: prediction and analysis of clinical relevance to minimize the risk), and the implications of the latest EMA guidelines.

RISK ASSESSMENT OF PRODUCT AND PROCESS-RELATED ATTRIBUTES

2:40 Chairperson's Remarks

Marisa K. Joubert, PhD, Principal Scientist, Process Development, Amgen, Inc.

2:45 Impact of Chemical Modifications on the Immunogenicity of IgG Subvisible Particles

Björn Boll, PhD, Head, Particle Lab and Higher Order Structure Protein Analytics, Physical Chemical Analytics, Novartis Pharma AG

The theoretical concerns regarding the potential immunogenicity of proteinaceous aggregates and subvisible particles in protein therapeutics have been widely debated. This talk will present the detailed mechanistic studies on the biological impact of aggregates and sub-visible proteinaceous particles in a hIgG1 transgenic mouse model. The results are discussed within the current status of related literature of *in vivo* and *in vitro* studies.3:15 Sponsored Presentation (Opportunity Available)

3:15 pm Immunomodulatory Effects of Host Cell Impurities in Biotherapeutic Monoclonal Antibodies

Shraddha Rane, PhD, Postdoctoral Research Associate, Infection Immunity and Respiratory Diseases, The University of Manchester

The ability of monoclonal antibodies to induce immune responses in patients, and the production of anti-drug antibodies (ADA), can reduce efficacy and provoke adverse health effects. There is increasing evidences that aggregation and presence of host cell impurities (even at very low levels) can enhance and

modify the immunogenic potential of monoclonal antibodies (mAb) and other protein therapeutics. Here we examined the ability of low levels of a common host cell impurity to modulate the immune responses to aggregates of two mAbs. The fact that HCP preferentially binds to mAb aggregates suggests that HCP impurities, although low, could be selectively concentrated by aggregate formation and thus contribute to an adjuvant-like stimulation of the immune responses.

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem-Solving Breakout Discussions

5:45 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

THURSDAY, MAY 3

8:00 am Morning Coffee

RISK ASSESSMENT OF PRODUCT AND PROCESS-RELATED ATTRIBUTES (CONT.)

8:30 Chairperson's Remarks
Marisa K. Joubert, PhD, Principal Scientist, Process Development, Amgen, Inc.

8:35 KEYNOTE PRESENTATION: Scientific Considerations for The Assessment of Immunogenicity Risk for Proteins, Peptides and Other Complex Drugs
Daniela Verthelyi, PhD, Chief, Laboratory of Immunology, Office of Biotechnology Products, Office of Pharmaceutical Quality, CDER
This talk will discuss the impact of innate immune response modulating impurities and aggregates on the immunogenicity risk assessment for therapeutic peptides and proteins with a particular focus on how they can modulate the local innate immune and inflammatory responses.

9:35 An Integrated Approach to Managing Immunogenicity Risk and Optimum Protein Design
Sponsored by ProImmune
Jeremy Fry, DPhil, Director, Sales, ProImmune
Integrated platforms can be used to mitigate immunogenicity risk and characterize immune responses during the drug design and development stages. ProImmune offers mutational activity mapping for optimal protein design, DC-T/T cell proliferation assays for biologic lead selection/ optimization, a Mass Spectrometry assay for characterization of antigen presentation; HLA-peptide binding assays to characterize individual epitopes & undiluted whole blood cytokine storm assays.

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

11:05 Case Studies Assessing the Impact of Key Product Quality Attributes on Safety of Biotherapeutics
Marisa K. Joubert, PhD, Principal Scientist, Process Development, Amgen, Inc.

11:35 Complexity of Phenomena and Factors that Influence the Aggregation of Biopharmaceuticals in Human Plasma Revealed by New Case Studies
Tudor Arvinte, PhD, Professor, Biopharmaceutics, School of Pharmacy Geneva-Lausanne, University of Geneva and Therapeomic, Inc.
Biopharmaceutical formulations, despite successful release for particulates according to regulatory requirements, may aggregate during *in vivo* administration. New *in vitro* studies of the aggregation of biopharmaceuticals in plasma show that: i) plasma aggregation occurs in many types of biopharmaceuticals, ii) can be different in plasma from patients and healthy donors, iii) there are donor-to-donor and patient-to-patient variations, iv) aggregation in animal model plasma can be different from human plasma, v) plasma aggregation may depend on the manufacturing clone, vi) stable formulations that do not aggregate in plasma can be developed.

12:05 Highlighted Poster Presentation: A Novel In-Vitro Human Skin Explant Test to Predict Adverse Immune Reactions to Biopharmaceuticals
Louis Bibby, BSc (Hons) MRes, PhD Student, Alcyomics/ Academic Haematology, Newcastle University, United Kingdom
To aid preclinical prediction of adverse effects of a hypersensitivity nature, we have developed a human in-vitro skin explant test, which uses human blood and non-artificial autologous skin to assess for histopathological damage indicative of adverse immune activation which could be used as a valuable preclinical tool. We have further extended this tool to a reconstituted human 3D skin equivalent for large scale assessment of adverse effects to biologics.

12:20 Highlighted Poster Presentation: A Novel In-Vitro Assay for Detection of Immunotoxicity of Aggregated Monoclonal Antibodies
Ana Patricia Ribeiro, Marie Curie PhD student, Institute Cellular Medicine, Medical School, Newcastle University, Newcastle upon Tyne, UK
We have developed a novel human *in vitro* skin test as a tool for the assessment of adverse immune reactions to aggregated mAbs. The output of this assay includes assessment of histopathological skin damage, T cell proliferation, cytokine release and cell death assays. In this study, aggregation of monoclonal antibodies was induced by a temperature stress protocol, followed by characterization of protein content by analytical ultra-centrifugation and transmission electron microscopy, revealing a 5% aggregation level of total protein content. Our results show that exposure to temperature can, in fact, cause conformational changes in the mAb structure that, ultimately, cause adverse immune reactions. Our novel *in vitro* assay showed that it was highly sensitive for determining an adverse reaction to mAb aggregation and demonstrates to be a promising tool to predict immunotoxicity caused by mAb aggregation.

12:35 End of Immunogenicity Assessment and Regulatory Approval of Biologics

Fourth Annual

OPTIMIZING BIOASSAYS FOR BIOLOGICS

Case Studies Demonstrating Successful Bioassay Development

THURSDAY, MAY 3

OPTIMIZING BIOASSAY DESIGN

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Jenny Hu, Scientist, PKDM, Amgen, Inc.

1:50 Identifying and Controlling Sources of Variation in Cell-Based Potency Assays
Emily Lowe, PhD, Senior Scientist, Analytical Sciences, Kite Pharma, a Gilead Company

Cell-based potency assays are essential for engineered cell therapy products to demonstrate that drug product activity is linked to biological critical quality attributes. One of the biggest challenges in designing and executing cell-based potency assays is identifying and controlling variability. A poorly controlled and highly variable potency assay can increase invalid and re-test rates, or worse, cause a manufacturing process to appear out of control or a drug product to appear unstable. Identifying and mitigating sources of variability begins during initial assay design, as part of QbD for method development, and should continue to be a focus through life cycle management. Here, we will discuss expected and unexpected sources of variability and control strategies through presentative case studies.

2:15 USP121: Insulin Bioassay Development to Replace *in vivo* Rabbit Test
Dirk Usener, PhD, Head, Analytical Development 2, Bioanalytics, Sanofi

Each insulin batch has to be released for marketed use in the USA with an *in vivo* Bio-ID test according to USP <121>. An *in vitro* cell-based assay (InCellWestern) was developed and validated to substitute the *in vivo* assay for all batch release and stability testings, which was approved by FDA for Insulin Glargine and Glulisine. Furthermore, this *in vitro* cell-based assay (ICW) is planned to be implemented in USP chapter <121> which has been pre-published in USP Pharmacopoeial Forum 43(4).

2:40 Bioassays for a Bispecific Antibody Drug Conjugate (ADC)
Ashley Mullan, Scientist, Development, Analytical Sciences, MedImmune

Antibody Drug Conjugates (ADCs) are a class of biotherapeutics in which a cytotoxic agent designed to induce target cell death is conjugated to a monoclonal antibody (mAb intermediate) specific for a tumor associated antigen. This presentation will be a case study for a bi-specific ADC targeting two distinct epitopes on the target antigen. In addition to the panel of lot release assays, characterization assays developed to monitor the two different target binding epitopes will also be discussed.

3:00 Development of Cell-Based Potency Assays for Multi-Specific Antibodies
Natalia Kozhemyakina, PhD, Head, Bioassay Laboratory, Analytical Development Department, BIOCAD

Multi-specific antibody formats provide a perspective platform for the development of novel generation of more effective biotherapeutics. However, the characterization of such antibody-based multi-specifics is often made complicated by the need assays which reflect MoA of antibody fragments of which they consist. The presentation highlights automated approach, which can be applied to conduct potency screening and full analysis of candidates. It allows choose the most potent of them in the shortest period of time and as a result reduce development time.

3:20 Near-Universal Equivalence Bounds for Similarity in Bioassay
David Lansky, PhD, President, Precision Bioassay, Inc.

3:50 Networking Refreshment Break

4:20 Development of a Reporter Gene Potency Assay for Bispecifics
Joseph Callahan, PhD, Technical Development Scientist, Genentech, Inc.

Bispecific antibodies bind two unique antigens. Here, we present a case study for a bispecific antibody reporter gene potency assay that uses two cell-types with a target cell-dependent luminescent readout. The assay was demonstrated to be MOA-reflective, robust, QC friendly, and sensitive to molecular changes in the drug. Strategies for optimization and qualification, stressed sample testing results, and efforts to enable future multi-product application will be discussed.

4:50 Adopting Multiplexing Technology for the Development of Anti-Bispecific Drug Neutralizing Antibody Bioassay
Jenny Hu, Scientist, PKDM, Amgen, Inc.

Bispecific therapeutic antibody (BsAb) recognizes two different antigen targets. BsAb usually requires separate assays to detect neutralizing antibody (NAb) response specific to each of the functional domain. Double efforts are needed for the development, optimization, and validation of two NAb assays. By utilizing multiplexing technology, we are able to develop one assay that

simultaneously detects NAbs against two functional domains of BsAb.

5:20 **End of Day**

5:20 **Registration for Dinner Short Courses**

RECOMMENDED DINNER SHORT COURSE(S)*

SC11: Strategic/Modular Bioassay Design and Analysis

**Separate registration required, please see page 6 for course details.*

FRIDAY, MAY 4

8:00 am **Morning Coffee**

COLLABORATING WITH YOUR STATISTICIANS

8:30 **Chairperson's Remarks**
Perceval Sondag, Senior Manager, Statistics, PharmaLex

8:35 **KEYNOTE PRESENTATION: Partnering with Statisticians throughout the Bioassay Lifecycle – From Clinical to Commercial**
Kenneth R. Miller, PhD, Principal Scientist, Global Technical Operations, Analytical, AstraZeneca
The bioassay lifecycle consists of three stages: (1) design and development, (2) performance qualification, and (3) continued performance verification. This presentation will show how bioassay scientists and statisticians work together during each of these stages of the bioassay lifecycle. Topics will include design and evaluation of screening and robustness, design of experiments (DoE) studies, transfer of methods from development to QC, and routine monitoring of bioassays in development and QC laboratories.

9:05 **The Total Error Approach Applied to Assay Validation and Transfer**
Perceval Sondag, Senior Manager, Statistics, PharmaLex

Sponsored by eurofins | Pharma Discovery Services

9:35 **Simplifying Implementation of Robust Bioassays in Development to QC Lot Release**
Jane Lamerdin, PhD, Director, Research & Development, Eurofins Pharma Discovery Services
Our quantitative and robust cell-based assay platform includes simple bioassays based on the native biology of the relevant receptors for potency determination & stability testing of biological drugs. These homogeneous assays employ convenient thaw-and-use cryopreserved cells to minimize assay variability and are highly scalable and suitable for automation. The talk will include bioassay qualification data for representative biosimilar and immune-oncology targets, and a bridging study to replace traditional bioassay for QC lot release.

10:05 **Networking Coffee Break**

10:35 **Review of Methods for Combining Estimates of Potency**
Areti Manola, Senior Principal Biostatistician, Non-Clinical Statistics, Manufacturing, Toxicology and Applied Statistical Sciences, Janssen, Pharmaceutical Companies of Johnson and Johnson
Biopharmaceutical products require as a condition for marketing a statement on the potency of the lot and its adherence to specifications, for example 80%LC <= potency estimate <= 125%LC. There may also be a specification on the confidence interval of the potency estimate. The potency estimate may arise from a bioassay procedure that yields multiple estimates of potency. Combining these individual estimates into a single pooled estimate is an important statistical practice. Combining potency estimates is also necessary during method validation and calibration of standards. Finney (1978) and Bliss (1952) have given extensive discussions on combining potency estimates. The USP and EP have also included a section on combining estimates. In this talk, we will review these methods and emphasize that none of these references have dealt with the question of correlated estimates. We will propose an approach within the framework of a hierarchical model and compare with standard and regulatory approaches.

11:05 **Everything You Always Wanted to Know about Relative Potency Bioassays… but Were Afraid to Ask**
Gaël Debauve, PhD, Associate Director, Bioassay Development, Analytical Sciences for Biologics, UCB
Biological activity is measured through appropriate relative potency methods. Because of the inherent variability of biological test systems, an absolute measure of potency is more variable than a measure of activity relative to a standard. This has led to the adoption of new statistical tools addressing bioassay specificities. Though case studies, we will illustrate how USP1033 validation requirements were tackled and even exceeded using, for example, total error and variance decomposition analysis. Finally, we will provide some insights to the question: "Is my bioassay stability indicating?"

11:35 **PANEL DISCUSSION: Challenges in Applying Statistics to Bioassay Design**
Moderator: Perceval Sondag, Senior Manager, Statistics, PharmaLex
Panelists: Kenneth R. Miller, PhD, Principal Scientist, Global Technical Operations, Analytical, AstraZeneca
Gaël Debauve, PhD, Associate Director, Bioassay Development, Analytical Sciences for Biologics, UCB
Areti Manola, Senior Principal Biostatistician, Non-Clinical Statistics, Manufacturing, Toxicology and Applied Statistical Sciences, Janssen, Pharmaceutical Companies of Johnson and Johnson
Steven Walfish, Principal Scientific Liaison, USP
- Applying design of experiments (DoE) approaches
- Optimizing bioassay design using statistics
- Fostering collaborations between statisticians and bioassay scientists

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- Application of the USP Bioassay Chapters

12:35 pm Luncheon Presentation *(Sponsorship Opportunity Available)*
or Enjoy Lunch on your Own

1:05 Networking Refreshment Break

BIOASSAY INNOVATIONS

1:35 Chairperson's Remarks
Steven Walfish, Principal Scientific Liaison, USP

1:40 The USP Bioassay Chapters: The Honeymoon's Over?
Steven Walfish, Principal Scientific Liaison, USP
USP Chapters <111>, <1030>, <1032>, <1033> and <1034> were last updated nearly ten years ago. The USP Statistics Expert Committee is performing a periodic review of the USP Chapters to determine if there is any new advancement that would make the bioassay chapters more valuable to their stakeholders. This presentation focuses on the USP suite of bioassay chapters. A discussion of the current state, and future plans will be shared with the participants. An open dialogue with participants is expected to gain valuable feedback on areas where the chapters can be improved to be more user-friendly. Do not miss your chance to be part of the change.

2:10 A New Class of International Standards to Support Biotherapeutic Monoclonal Antibody Products Quality and Consistency over Time
Sandra Prior, PhD, Senior Scientist, Biotherapeutics, National Institute for Biological Standards and Control (NIBSC)
The approval of biosimilar biotherapeutic monoclonal antibodies (mAbs) is controlled by robust regulatory processes. However, in an increasingly complex multi-product market place there is a need for public biological standards to support current controls. With this aim, we have developed the first World Health Organization (WHO) mAb potency international standard (IS) to support the performance and calibration of bioassays and local standards. These ISs are stable lyophilized preparations that define international units (IU) of bioactivity allowing data harmonization amongst stakeholders and promote product consistency overtime.

2:40 Thaw-and-Use Target Cells Pre-Labeled with Calcein AM for Antibody Dependent Cell-Mediated Cytotoxicity Assays
Shan Chung, PhD, Principal Scientist and Group Leader, Bioanalytical Sciences, Genenetech, Inc.
This presentation will describe the development and implementation of thaw-and-use pre-labeled target cells for *in vitro* antibody-dependent cell-mediated cytotoxicity (ADCC) assays. Cells were pre-labeled with the fluorescent dye calcein AM, cryopreserved in single-use aliquots, and used directly in assays after thawing. Compared to freshly labeled cells, these cells showed comparable viability, label retention, and reactivity to ADCC mediated by various effector cells, and provided favorable precision and accuracy, as well as improved consistency and robustness to ADCC assays.

3:10 The Ins and Outs of Automating Potency Assays
Adrienne Wildt, PhD, Associate Director, Bioanalytical Science, Immunogen
Routine assays with repetitive steps are major components of bioanalytical support. Automating these tasks increases throughput, reduces performance variations and decreases repetitive strain. Strategies for automating bioassays using various robotic liquid handling solutions used during CMC product development will be presented. Case studies on automating biochemical as well as cell-based assay that support drug substance release and characterization will be discussed.

3:40 End of Conference

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BIOCONJUGATES STREAM

- Fusion Protein Therapeutics
- Engineering Antibody-Drug Conjugates
- Clinical Progress of Antibody-Drug Conjugates

Bioconjugates as Therapeutics: from R&D to Clinical Development

The Bioconjugation Stream explores the exciting therapeutics created through linking a cytotoxic drug to a delivery vehicle to fight cancer and other diseases, and includes Fusion Proteins as well as Antibody-Drug Conjugates. The Stream investigates ongoing design and R&D efforts, along with the challenges of producing these complex molecules, while ensuring stability, specificity and efficacy. “Fusion Protein Therapeutics” examines the varying constructs achieved by combining modular building blocks to reach targets not accessible to antibodies; and possessing customizable functionality that translates into lower patient dosing, reduced production costs, and improved product homogeneity. The “Engineering Antibody-Drug Conjugates” conference reveals the next-gen efforts to improve target selection, find new cytotoxic drugs as warheads, increase half-life, and improve target specificity; while the “Clinical Progress of Antibody-Drug Conjugates” meeting addresses ADCs in the clinic at various stages of clinical trials, in light of recent approvals that have increased confidence in these promising molecules.

Fourth Annual

FUSION PROTEIN THERAPEUTICS

Engineering Next-Generation Biologics

SUNDAY, APRIL 30

RECOMMENDED SHORT COURSE(S)*

SC1: Preclinical and Clinical Assessment of Immunogenicity: Multidomain Therapeutics and New Modalities, Including Gene Therapy and CAR T

Separate registration required, please see page 6 for course details.

MONDAY, APRIL 30

7:00 am Registration and Morning Coffee

FIGHTING DISEASE WITH FUSION PROTEIN THERAPEUTICS

8:30 Chairperson's Remarks
Stefan Weigand, PhD, Global Head, Large Molecule Research, Roche Diagnostics GmbH

8:40 Sotatercept, a Ligand Trap Fusion Protein, Attenuates Vascular Remodeling in Two Animal Models of Pulmonary Arterial Hypertension
Ravindra Kumar, PhD, Senior Vice President & CSO, Acceleron Pharma, Inc.
Pulmonary arterial hypertension (PAH) is a progressive fatal disease characterized by remodeling of distal pulmonary arteries (more muscular), increased pulmonary vascular resistance, and right ventricular hypertrophy that ultimately lead to right heart failure. Mutations in BMP type II receptor (BMPR2) leading to reduced smad1/5/8 signaling have been implicated in familial PAH. Using *in vitro* and animal models of PAH, we show that sotatercept, a ligand trap based on soluble activin receptor type IIA, rebalances smad signaling and attenuates PAH.

9:10 A Novel Therapeutic Protein that Augments Tregs for the Treatment of Autoimmune and Inflammatory Diseases
Niranjana Nagarajan, PhD, Principal Scientist, Celgene-Delinia
Regulatory T cells (Treg) play a major role in maintaining immune system homeostasis by regulating effector T cells and other immune cells. This homeostatic balance is lost in many autoimmune and inflammatory diseases. The IL-2 pathway is central to maintaining Treg levels and functional activity, and early-stage clinical trials in multiple autoimmune and inflammatory diseases have highlighted the potential of augmenting Tregs with low dose IL-2 to provide clinical benefit. However, there are significant significant toxicity and tolerability issues which severely limits the therapeutic use of IL-2. We have developed a novel Fc fusion protein that combines an IL-2 moiety that is highly selective for the IL-2 receptor expressed on Tregs with an Fc moiety to optimize circulating half-life. The development and characterization of this protein will be discussed.

9:40 Safety and Clinical Efficacy of AGT-181, a Brain Penetrating Human IgG-Iduronidase Fusion Protein, in a Phase 2 Study with Pediatric Patients with Mucopolysaccharidosis Type I
Ruben Boado, PhD, Vice President, Research & Discovery, ArmaGen Technologies, Inc.
AGT-181 is an IgG-enzyme fusion protein comprised of iduronidase (IDUA) and a monoclonal antibody against the human insulin receptor, engineered to cross the blood-brain-barrier (BBB) and to address both the neurocognitive and peripheral burden in MPS I. Neurocognitive function, somatic effects and safety of a phase II proof-of-concept clinical trial in Hurler MPSI pediatric patients will be discussed. This represents the first in human clinical trial of a fusion protein engineered to cross the BBB.

10:10 Networking Coffee Break

FULFILLING THE PROMISE OF FUSION PROTEIN THERAPEUTICS

10:45 KEYNOTE PRESENTATION: Fc-Fusion Proteins: Past, Present and Future
Kenneth W. Walker, PhD, Director, Research, Therapeutic Discovery, Amgen, Inc.
While there are many options for enhancing the pharmacokinetics of therapeutic proteins and peptides, Fc-fusion proteins are by far the most widely used. When designing Fc-fusion proteins, there are many factors to consider, which can interact in unexpected ways and have a substantial impact on the success of the molecule. In addition, some unconventional formats can substantially improve the manufacturability and/or activity of these molecules.

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11:20 ELVERA - A Novel Fully Human Fusion Protein Platform to Improve Drug-Like Properties of Biopharmaceuticals

Patrik Strömberg, PhD, MBA, Senior Director, Head, Biomedical Science & Portfolio Innovation, Swedish Orphan Biovitrum AB (SOBI)

We are developing an innovative fusion protein technology that exploits the characteristics of a naturally occurring human protein sequence to protect and extend the circulatory half-life and target tissue exposure of active biological molecules. Using this technology, we were able to fine-tune the pharmacokinetic properties of therapeutic proteins, Affibody® molecules and antibody fragments. Also, we could show improved stability and reduced unspecific clearance of therapeutic enzymes. These results indicate that the ELVERA™ fusion protein technology could be used as a versatile platform to enhance the properties of a broad range of therapeutic proteins.

11:50 Novel Reversible Switch for Protein Bioconjugates

Sunny Zhou, PhD, Professor and Faculty Fellow, Chemistry and Barnett Institute, Northeastern University

We recently invented several site-specific methods to install novel switches that can be removed reversibly. One example is by light and native form can be restored – a process often referred to as photocaging. An additional advantage is that the payload, if any, can be released simultaneously. Our method and newly developed switches have broad applications such as biological probes, fusion protein, antibody drug conjugates (ADCs) and controlled drug release.

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on your Own**

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 Challenges and Opportunities in Engineering Protein Biopharmaceuticals

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)

Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

4:55 The Next Generation of Cancer Immunotherapy: Targeting Myeloid Immune Checkpoints

Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital

Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

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

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THE FUTURE OF MEDICINE IS PRECISION

7:15 End of Day

TUESDAY, MAY 1

8:00 am Registration and Morning Coffee

FUSION PROTEIN THERAPEUTICS FOR ONCOLOGY

8:25 Chairperson's Remarks

Patrik Strömberg, PhD, MBA, Senior Director, Head, Biomedical Science & Portfolio Innovation, Swedish Orphan Biovitrum AB (SOBI)

8:30 Modular Biologics: Roche's Approach to Tackle Cancer

Stefan Weigand, PhD, Global Head, Large Molecule Research - Therapeutic Modalities, Roche Pharma Research and Early Development, Roche Innovation Center Basel, F. Hoffmann-La Roche, Ltd.

This presentation will provide an overview on Roche's modular biologics approach in cancer therapy and provide examples from Roche's pipeline how to discover, design, develop and deliver differentiated, multi-functional therapeutics.

9:00 Cell-Penetrating Peptides and TLR Peptide Agonist: The Swiss Army Knife of Cancer Vaccines

Madiha Derouazi, PhD, CEO, Amal Therapeutics

Modulating the immune system to enhance immune responses has become a promising therapeutic approach in oncology. We have developed a protein based therapeutic cancer vaccine platform called KISIMA. The technology is based on the assembly within one chimeric fusion protein of the following three elements: a cell penetrating peptide for antigen delivery, a TLR-peptide agonist as adjuvant and a modulable multi-antigenic cargo that can be tailored for various indications.

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9:30 ImmTACs – Immuno-Oncology through TCR Targeted T Cell Redirection

Rachael Easton, MD, PhD, Executive Director, Clinical Development, Immunocore LLC

ImmTAC molecules are a new class of bi-specific biologic molecules that combine an affinity-enhanced T cell receptor (TCR)-based targeting system with an anti-CD3 (scFv) effector function to activate a highly potent and specific T cell response to recognize and destroy cancer cells. IMCgp100 is an ImmTAC therapeutic targeting the melanoma-associated antigen gp100 and is currently undergoing a pivotal clinical study as a monotherapy for the treatment of patients with metastatic uveal melanomas.

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

10:50 Ontak-Like Human IL-2 Fusion Toxin

Zhirui Wang, PhD, Assistant Professor, Surgery, Harvard Medical School; Senior Investigator/Head, Immunotoxin Laboratory, Center for Transplantation Sciences (CTS), Massachusetts General Hospital

Ontak® is an FDA approved diphtheria toxin-based fusion toxin for treatment of human CD25+ cutaneous T cell lymphoma (CTCL). However, it has been discontinued due to the production problem related to the bacterial expression system. Recently we have developed human IL-2 fusion toxin using advanced unique diphtheria toxin resistant yeast *Pichia pastoris* expression system. The *in vivo* efficacy was characterized using human CD25+ HUT102/6TG tumor-bearing immunodeficient NSG mouse model.

11:20 Development of a Novel Interleukin-2 Variant for Immunotherapy

Ekkehard Moessner, PhD, Group Leader and Scientist, Protein Engineering, Roche Innovation Center Zurich

The development of an interleukin-2 mutein throughout the preclinical development will be described, until entering phase 1 in the clinic.

11:50 Optimizing IL2 Immunocytokines for Different Therapeutic Approaches – Simple Cytokine Targeting or Combined Treatment Modalities

Stephen D. Gillies, PhD, Founder & CEO, Provenance Biopharmaceuticals

Immunocytokines target cytokines with anti-tumor activity to the tumor microenvironment. This can mean fusing a cytokine to a tumor-specific scFv or instead, to a whole antibody containing binding sites for Fc receptors and C1q of the complement cascade. New approaches where the antibody component of the IC is an antagonist make it necessary to lower the cytokine bioactivity to match the concentration needed for inhibition of the target and avoid cytokine-induced toxicity.

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

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

INNOVATING THERAPEUTIC FUSION PROTEINS

2:00 Chairperson's Remarks

Sunny Zhou, PhD, Professor and Faculty Fellow, Chemistry and Barnett Institute, Northeastern University

2:05 Multivalent Antibody-TRAIL Fusion Proteins for Cancer Therapy

Oliver Seifert, PhD, Scientist, Institute of Cell Biology and Immunology, University of Stuttgart

Engineering of multivalent antibody-scTRAIL (single-chain derivatives of TRAIL) by introducing different homodimerization modules leads to a novel platform of therapeutic molecules for cancer therapy. Our results show that both tumor targeting and enhancing the valency of scTRAIL fusion protein provides enforced apoptosis induction together with good anti-tumoral activity and tolerance *in vivo*. Due to the modular composition of this novel platform, exchanging the specificity of the antibody moiety facilitates the treatment of a broad spectrum of different cancer entities.

2:35 Nanofitin-Antibody Fusion as a Novel Multispecific Platform

Mathieu Cinier, PhD, CSO, Affilogic

Building on antibody expertise, many different bispecific formats have been engineered to allow the additional neutralization of an escaping pathway or the recruitment of effectors, but often at the expense of the overall physico-chemical properties of the biologic itself compared to the actual state of the art for monoclonal antibodies. Nanofitin-Antibody fusion is proposed as a novel multispecific platform, whereby additional targeting specificities are provided by the fusion of Nanofitins to existing antibodies without altering their initial physico-chemical properties.

3:05 Selected Poster Presentation: Allostery Communications in Fusion Two-Domain Proteins

Kristyna Bousova, PhD, PostDoc Fellow, Bioinformatics, Institute of Organic Chemistry & Biochemistry, Czech Academy of Sciences

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

4:25 Fusion Proteins as an Efficient Drug Delivery Platform in Coagulation Therapy

Nicola Pozzi, PhD, Assistant Professor, Biochemistry and Molecular Biology, Saint Louis University

Uncontrolled or inadequate delivery of current anticoagulant agents is the cause of bleeding diathesis and, in some cases, death. Engineering of fusion proteins is an attractive way to develop novel biotherapeutics with reduced side effects or enhanced pharmacokinetics. One such example is the rational design of anticoagulant fusion proteins obtained by fusing thrombin with the extracellular EGF456 domains of thrombomodulin through a peptide linker.

5:25 End of Fusion Protein Therapeutics

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE(S)*

SC13: Sub Visible Protein Particles in Immunogenicity: Measurement, Characterization and Impact

**Separate registration required, please see page 6 for course details.*

Eighth Annual

ENGINEERING ANTIBODY-DRUG CONJUGATES

Optimizing ADC Parameters for Next-Generation Design

RECOMMENDED SHORT COURSE(S)*

SC10: Critical Considerations for the Design and Development of Antibody-Drug Conjugates

**Separate registration required, please see page 6 for course details.*

WEDNESDAY, MAY 2

7:30 am Registration and Morning Coffee

ALTERNATIVE SCAFFOLDS AND NEW PAYLOADS

8:30 Chairperson's Remarks
Ravi Chari, PhD, Vice President, Chemistry & Biochemistry, ImmunoGen, Inc.

8:40 Abdurin-Drug Conjugates - Small Size and Long Half-Life to Improve Drug Concentration in the Target Tissue
Kurt Gehlsen, PhD, Vice President & CSO, Therapeutics, Research Corporation Technologies, Inc.

Abdurins are a novel antibody-like scaffold that can be engineered to bind to targets of interest and due to an FcRn binding motif, Abdurins have a circulating half-life longer than any other protein scaffold of similar size. Abdurins can be fused with protein toxins, other binding domains and engineered to carry payloads. Abdurin-drug conjugates retained high affinity binding and had *in vivo* half-life up to 70 hours for certain conjugates.

9:10 Antibody Targeted Amanitin Conjugates (ATACs) - Expanding the ADC Landscape with a New Payload Targeting RNA Polymerase II
Andreas Pahl, PhD, CSO, Heidelberg Pharma

Antigen-Targeted Amanitin-Conjugates (ATACs) represent a new class of ADCs using the payload Amanitin. This payload introduces a novel mode of action into oncology therapy, the inhibition of RNA polymerase II. The technology platform includes Amanitin supply, site-specific conjugation, demonstrated safety profile and biomarker. Improvements of the technology and an update of the development of HDP-101 will be presented. HDP-101 is the first ATAC directed against BCMA entering Phase I trials by the end of 2018.

9:40 Preclinical Validation of Site Specifically Conjugated ADCs with Potent Anthracycline Payloads
Roger Beerli, PhD, CSO, NBE-Therapeutics AG

We present a novel ADC format based on the site specific conjugation of a derivative of the anthracycline PNU-159682 using the transpeptidase Sortase A. The use of non-cleavable peptide linker provides exquisite stability *in vivo*, whereas the anthracycline payload endows the ADC with superior potency combined with attractive immune-oncology properties intrinsic to this class of compounds. Homogeneous PNU-ADCs directed against HER2 and ROR1 were generated and shown to have very high anti-tumor efficacy *in vivo*, both in PDX as well as in syngeneic solid tumor models. In case of HER2, the PNU-ADC exceeded the efficacy of T-DM1 used as a benchmark ADC. In syngeneic breast cancer models, both HER2, as well as ROR1 ADCs resulted in the induction of a long-lasting tumor-selective anti-tumor immunity involving activated CD8 T cells. Importantly, a repeated-dose non-GLP toxicology study in cynomolgus monkeys did not reveal significant toxin-related pathology of PNU-ADCs at any of the evaluated dose-levels, strongly supporting further preclinical and clinical development of this promising new ADC format.

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

10:55 Design of a Novel, Glycan Targeting Antimicrobial ADC as a New Therapeutic Strategy for the Treatment of *P. aeruginosa* Infection
Obadiah J. Plante, PhD, Director, Research, Visterra, Inc.

This presentation will describe Visterra's approach to the development of a novel antibody-based therapeutic for the treatment of established *P. aeruginosa* infections. The antibody targets a core region of lipopolysaccharide present at high density on *P. aeruginosa* and common across serotypes. To provide direct bactericidal activity, we have designed potent anti-microbial peptides that rapidly kill bacteria when directly conjugated to our antibody in the form of an ADC.

11:25 The Development of Antibody Conjugates for Targeted Delivery of siRNA
Chawita Netirojjanakul, PhD, Sr. Scientist, Therapeutic Discovery, Amgen

Advances in small interfering RNA (siRNA) technology result in numerous RNAi-based therapies being pursued in clinical trials. However, several challenges including targeted delivery of siRNA have limited the use of siRNAs as therapeutics. Here, we established a method to prepare and characterize

well-defined antibody-siRNA conjugates and demonstrated that using this platform, siRNA can be delivered into specific cells or tissues *in vitro* and *in vivo*.

11:55 Attachment Site Cysteine Thiol pKa is a Key Driver for Site-Dependent Stability of Disulfide & Maleimide-Linked THIOMAB(TM) Antibody-Drug Conjugates

Breanna S. Vollmar, PhD, Senior Scientific Researcher, Protein Chemistry, Genentech, Inc.

We set out to understand the underlying mechanisms of site-dependent stability for our THIOMAB™ antibody drug conjugate (TDC) platform utilizing engineered cysteines at specific sites on the antibody. Our observations suggest that cysteine thiol pKa is a significant driver of the circulation stability of TDCs utilizing disulfide or maleimide attachment chemistry and represents a new parameter for the optimization of next generation ADCs utilizing engineered cysteines.

Sponsored By Catalent BIOLOGICS

12:25 pm Latest Advances Developing Antibody Drug Conjugates (ADCs) and Other Bioconjugates Using SMARTag Technology

David Rabuka, Global Head, Research & Development, Chemical Biology, Catalent Biologics, Catalent Pharma Solutions

We have developed the SMARTagTM technology platform, which enables precise, programmable, site-selective chemical protein modification. We will present recent data on our novel protein modification platform and its application to generating novel bioconjugates, including ADCs, utilizing our new conjugation chemistries and linkers. Additionally, we will highlight progress in developing conjugates with a focus on preclinical studies as well as highlight our progress in cell line development and manufacturing of using this chemoenzymatic approach.

12:55 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on your Own**

1:55 Session Break

OPTIMIZATION OF LINKER-PAYLOAD CHEMISTRY

2:10 Chairperson's Remarks

Kurt Gehlsen, PhD, Vice President & CSO, Therapeutics, Research Corporation Technologies, Inc.

2:15 Chemical Fusion: A General Method for Equimolar Linking of Proteins and Payloads

Alain Wagner, PhD, Research Director, Biofunctional Chemistry, Faculty of Pharmacy, University of Strasbourg

We have designed a general conjugation methodology that involves native protein and leads to single DAR conjugates. Our method applies with virtually no limitations to all types of proteins and payloads. It enables preparation of conjugate bearing one, two or more payloads, with precise control for each of them. Noteworthy the simple mono-conjugated DAR 1 opened interesting prospects as a building block to engineer precise protein-oligonucleotide, protein-protein, protein-nanoparticle constructs.

2:45 Enzymatic (Dual) Site-Specific Conjugation of Engineered and Native Antibodies

Philipp Spycher, PhD, PSI Founder Fellow, Center for Radiopharmaceutical Sciences, Paul Scherrer Institut

We will show single and dual site-specific conjugation of engineered antibodies with various functional payloads as well as the controlled modification of antibody-fragments and other proteins using solid-phase immobilized microbial transglutaminase (MTG). Additionally, we will introduce a novel proprietary enzymatic conjugation technology that enables site-specific payload attachment to native antibodies, thus generating well-defined ADCs that have a native IgG antibody structure.

3:15 POSTER HIGHLIGHT I: A Novel Platform for Versatile Payload Conjugating to a Glyco-Engineering tri-Mannosyl Core Antibody

Chun-Chung Lee, PhD, Research Fellow, Institute of Biologics, Development Center for Biotechnology

In this study, we developed a novel site-specific tri-mannosyl core antibody-drug conjugate platform. The novelty of this platform is that we are able to control the antibody conjugating single payload (DAR=2 or 4) or dual payloads (DAR=2A&2B) by one step or stepwise of MGAT-1 and MGAT-2 treatments, respectively. Through this tri-mannosyl core ADC platform, we are able to control the different toxin dosages (DAR=2 or 4) conjugating to the same antibody. As a result, the correlation between conjugating dosages of toxin, safety and efficacy will be methodically evaluated. The platform will also be available for designing the therapeutic antibody conjugated with dual payloads, which will target the same molecule in cancer cells and induce different drug response. The platform is also available for use as companion diagnostics and therapy for cancers when the antibody conjugating both image dye and cancer drugs.

3:30 Poster Highlight II: Concisely Produced Homogeneous Antibody-Drug Conjugates by a Tryptophan-Selective Protein Bioconjugation

Kounosuke Oisaki, PhD, Lecturer, Graduate School of Pharmaceutical Sciences, University of Tokyo

In 2016, we reported a transition metal-free method for tryptophan (Trp)-selective bioconjugation of proteins. this method exhbits low levels of cross-reactivity and leaves higher-order structures of the protein and various functional groups therein unaffected. Recently, studies aiming at concise production of a homogeneous antibody-drug conjugate (ADC) using the Trp-selective bioconjugation are ongoing in our group. We would like to present recent progress.

3:45 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Problem-Solving Breakout Discussions

5:45 Networking Reception in the Exhibit Hall with Poster Viewing

7:00 End of Day

THURSDAY, MAY 3

8:00 am Morning Coffee

8:30 Chairperson's Remarks
Alain Wagner, PhD, Research Director, Biofunctional Chemistry, Faculty of Pharmacy, University of Strasbourg

8:35 KEYNOTE PRESENTATION: Clinical and Technological Advances in ADCs
Dennis Benjamin, PhD, Senior Vice President, Translational Research, Seattle Genetics
Clinical and preclinical studies of auristatin-based ADCS including brentuximab vedotin will be presented. Recent developments in ADC technology will also be discussed, including engineered antibodies for delivery and novel cytotoxic payloads.

NOVEL TARGETS

9:05 A Novel Cell Surface Target on Cancer Cells and Development of a Targeted ADC
Ginette Serrero, PhD, CEO, A&G Pharmaceutical, Inc.
The key to the ADC approach is the development of an antibody against a desired target preferentially expressed on cancer cells, that results in the internalization of the payload and eventual death of the cell, while limiting the off-target side effects. The presentation will cover antibody development and subsequent conjugation and payload selection for initial proof of concept studies prior to moving the antibody into linker and payload preclinical studies, using a real example of a mAb against a novel CSP target.

Sponsored by applied biomath

9:35 Computational Exploration of Mechanistic Determinants of ADC Pharmacokinetics Using QSP Modeling Strategies
John Burke, PhD, Co-Founder, President and CEO, Applied BioMath, LLC
The pharmacokinetics of ADC therapeutics typically show a discrepancy between PK of total antibody and of conjugated antibody, carrying one or more payload molecules. This discrepancy is often attributed to deconjugation, however recent evidence suggests that underlying mechanisms may be more complex. This presentation will demonstrate a computational approach to understand the impact of DAR and resulting changes in molecular properties on overall PK and relative payload disposition as observed in preclinical and clinical studies.

10:05 Coffee Break in the Exhibit Hall with Poster Viewing

EXPANDING THERAPEUTIC WINDOW AND IMPROVING STABILITY

11:05 Expanding Therapeutic Windows of Tubulysin Antibody-Drug Conjugates with Stable Hydrophilic Linkers
Robert Yongxin Zhao, PhD, CEO, Hangzhou DAC Biotech Co., Ltd.
To address the liver toxicity issue in our original anti-Her2-tubulysin ADC, we developed a novel stable hydrophilic linker which, while maintaining better efficacy than T-DM1 in xenograft mouse models, proved significantly less toxic than T-DM1 in mice and cynomolgus monkeys. The overall therapeutic window was 4-6 times wider than that of T-DM1. The most percentage of metabolite of tubulysin analog was found in urine of animals demonstrating a clear correlation between its much reduced side effect and the metabolic pathway.

11:35 IMGN632, A Novel ADC with Uniquely Wide Therapeutic Window in Preclinical Models of AML
Yelena Kovtun, Associate Director, Pipeline R&D, ImmunoGen, Inc.
IMGN632 is a novel conjugate of anti-CD123 antibody with mono-imine containing Indolinobenzodiazepine payload. Unlike other conjugates (including ADCs with proven clinical success), only IMGN632 demonstrated potent anti-leukemic activity at the concentrations 100-fold lower the levels that impact normal human cells. The strategy to select an optimal antibody, payload, linker and conjugation method to achieve this uniquely wide therapeutic window will be covered in the presentation.

12:05 pm ADC Pumping into Solid Tumors Boosts Drug Potency and Efficacy
Jan E. Schnitzer, MD, Director, Professor, Cellular & Molecular Biology, Proteogenomics Research Institute for Systems Medicine (PRISM)
Current ADC can't deliver drugs inside solid tumors specifically, rapidly or robustly. Near MTD doses required to drive ADC across endothelial barriers are inadequate to unleash drug potency solely inside tumors. Off-target toxicities minimize therapeutic indices. We circumvent this passive transvascular delivery paradigm by utilizing caveolae pumping and the first antibody to actively penetrate tumors. Immunoconjugates concentrate imaging and therapeutic agents inside resistant and metastatic tumors, enabling precise imaging within 1 hr and boosting therapeutic indices >100-fold (<<<MTD eradication).

12:35 End of Engineering Antibody-Drug Conjugates

Register Online!
PEGSummit.com

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

Eighth Annual

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

Translating Preclinical Understanding to Clinical Success

THURSDAY, MAY 3

ADC-IO COMBINATIONS

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks
Gail Lewis Phillips, MSc, Senior Scientist, Translational Oncology, Genentech, Inc.

1:50 The Past, Present and Future of ADC-IO Combinations
Jay Harper, PhD, Senior Scientist, Oncology Research, MedImmune
Exciting preclinical data demonstrated immunomodulatory effects of antibody-drug conjugate (ADC) warheads and synergistic anti-tumor activity when ADCs are combined with immuno-oncology agents, leading to clinical development of such strategies. This presentation will highlight the key data supporting such ADC-IO combinations, provide an overview of the current ADC-IO clinical landscape, and will provide some insight into the next generation of these promising ADC-IO combinations.

2:20 Clinical Learnings from Mirvetuximab Soravtansine (IMGN853) and Pembrolizumab Combination Therapy
Anna Berkenblit, MD, MMSc, Vice President, CMO, ImmunoGen

2:50 Combination of Antibody-Cytokine Fusions with Immunological Check-Point Inhibitors
Alessandra Micaela Villa, PhD, Head, Phage Display Technologies, Philochem AG
Antibody-cytokine fusion proteins ("immunocytokines") represent a novel class of antibody therapeutics that combine the disease-homing property of antibodies with the immunomodulatory activity of cytokine payloads. Immunocytokines are currently being developed for the treatment of cancer and other serious conditions. I will present preclinical and clinical data on the combination of immunocytokines with other therapeutic treatments, including immunological checkpoint inhibitors.

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Networking Refreshment Break

CLINICAL ADVANCES

4:20 Antibody-Pyrrolobenzodiazepine Conjugates
Philip Howard, PhD, CSO, Spirogen; Senior Fellow, MedImmune
This talk will cover the development of Pyrrolobenzodiazepine (PBD) payloads for use in Antibody Conjugates. The presentation will also give an update on the clinical progress of Antibody PBD Conjugates.

4:50 AbGn-107, an ADC for Gastrointestinal Tumors
David (Shih-Yao) Lin, MD, PhD, CMO, AbGenomics, Inc.

5:20 End of Day

5:20 Registration for Dinner Short Courses

RECOMMENDED SHORT COURSE(S)*

SC10: Critical Considerations for the Design and Development of Antibody-Drug Conjugates

**Separate registration required, please see page 6 for course details.*

FRIDAY, MAY 4

8:00 am Morning Coffee

CLINICAL ADVANCES (CONT.)

8:30 Chairperson's Remarks
Philip Howard, PhD, CSO, Spirogen; Senior Fellow, MedImmune

CLINICAL PROGRESS OF ANTIBODY-DRUG CONJUGATES

8:35 KEYNOTE PRESENTATION: Early Clinical Development of Dolaflexin ADCs
Donald A. Bergstrom, MD, PhD, CMO, Mersana Therapeutics
XMT-1522 is a HER2-targeting ADC that induces complete regressions in models of treatment-resistant HER2-positive breast and gastric tumors, as well as breast and non-small cell lung cancer (NSCLC) without HER2 gene amplification and lower levels of HER2 expression. XMT-1536 is a Dolaflexin ADC targeting NaPi2b that is highly active in models of NSCLC adenocarcinoma and epithelial ovarian cancer. Both XMT-1522 and XMT-1536 are in Phase 1 clinical development in patients with advanced solid tumors.

9:05 ABBV-399, a Clinical Antibody Drug Conjugate that Targets c-Met Overexpressing Solid Tumors
Ed Reilly, PhD, Senior Research Fellow, Project Director, Oncology Discovery, AbbVie
ABBV-399 (Teliso-V) is a novel first-in-class ADC comprised of the c-Met-targeting antibody ABT-700 conjugated to the cytotoxic MMAE. ABBV-399-mediated killing requires a threshold level of c-Met expressed by many tumors thereby reducing both the binding of ABBV-399 to normal tissues and the risk of on-target toxicity. ABBV-399 has progressed to a Phase 1 study where it has been well tolerated and has produced objective responses in c-Met-expressing non-small cell lung cancer (NSCLC) patients both as monotherapy and in combination. A summary of these clinical results will be presented.

9:35 Sponsored Presentation *(Opportunity Available)*

10:05 Networking Coffee Break

PRECLINICAL UPDATES

10:35 Novel Strategies for Developing 2nd Generation HER2-Directed Antibody-Drug Conjugates
Gail Lewis Phillips, MSc, Senior Scientist, Translational Oncology, Genentech, Inc.
Trastuzumab emtansine (T-DM1) is a HER2-directed ADC comprised of trastuzumab linked to the anti-mitotic agent, DM1, through a stable linker. We have designed a different HER2 ADC using a unique THIOMAB™ antibody with engineered cysteines for enhanced stability. To differentiate from T-DM1, we assessed numerous DNA-damaging drugs with cleavable and uncleavable linkers. Preclinical data will be presented for a 2nd generation HER2-ADC comprised of a disulfide-linked DNA damaging agent.

11:05 Preclinical Evaluation of a GCC-Targeted Antibody-Drug Conjugate (ADC) for the Treatment of Colorectal Cancers and Other GI Malignancies
Adnan Abu-Yousif, PhD, Senior Scientist II, Discovery, Takeda
Guanylyl cyclase C (GCC) is a transmembrane cell surface receptor that functions in the maintenance of intestinal fluid, electrolyte homeostasis, and restriction of cell proliferation. In normal human tissues, GCC expression is restricted to the mucosal cells lining the GI tract. Here we describe the activity of a GCC-targeted antibody drug conjugate in preclinical models of GCC-positive tumors. These promising preclinical data warrant advancement of this ADC to clinical evaluation.

11:35 Tackling Solid Tumours with Antibody Fragment Drug Conjugates (FDCs)
Mahendra Deonarain, PhD, CEO & CSO, Antikor Biopharma Ltd.
The significant majority of the ADC field are focusing on large, engineered IgG with low DAR but we believe that FDCs represent a major opportunity to treat solid tumours. We can engineer antibody fragments to carry a high quantity of cytotoxic payload, that will penetrate tumours rapidly, deliver the killer blow and clear from the circulation quickly resulting in lower adverse effects. We will present compelling efficacy and tolerability data to support the concept.

12:05 pm Trop-2 as a Broad Solid Cancer Target for Antibody-Drug Conjugates
David Goldenberg, ScD, MD, Founder and Former CSO, Immunomedics, Inc.
Trop-2 is a transmembrane glycoprotein that transduce cytoplasmic calcium signal, activates MAPK/ERK pathway, and affects cell-cell adhesion. Using a proprietary linker technology to site-specifically conjugate an average of 7.6 molecules of SN-38 (the active metabolite of irinotecan, which inhibits nuclear topoisomerase I) per humanized IgG, my group demonstrated effective and selective tumor inhibition *in vitro* and in xenograft solid tumor models, as well as in phase 2 studies of ~500 patients with advanced, heavily-pretreated diverse solid cancers (e.g., breast, NSCLC, SCLC, urothelial).

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

1:05 Networking Refreshment Break

PKPD ASSESSMENT AND MODELING

1:35 Chairperson's Remarks
Pamela Trail, Independent Consultant and Former Vice President, Oncology, Regeneron

1:40 Biomarkers of the Mononuclear Phagocytic System (MPS) for the Pharmacokinetics and Pharmacodynamics of the Antibodies and Antibody Drug Conjugates
William C. Zamboni, PharmD, PhD, Associate Professor and Director, Translational Oncology and Nanoparticle Drug Development Initiative (TOND2I) Laboratory, UNC Lineberger Comprehensive Cancer Center
The factors affecting the high pharmacokinetic (PK) and pharmacodynamic (PD) variability of antibodies (mAbs) and antibody drug conjugates (ADCs) are consistent with variability in the mononuclear phagocyte system (MPS). The high variability in MPS Fc-gamma-receptors (FcγRs) and function in blood are associated with the high PK and PD variability of mAbs and ADCs. The high PK variability of these agents is clinically important as they have a narrow therapeutic index.

Cambridge HEALTHTECH Institute
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2:10 Will Optimized Single Molecular ADC Species Set New Precedents for Clinical Performance?

Trevor J. Hallam, PhD, CSO, Sutro Biopharma

We demonstrate a cell-free antibody production system that enables the use of reactive non-natural amino acids to generate precisely positioned irreversible conjugates with high fidelity. We are able to rapidly generate many variants of full length IgG species with different conjugation sites within days at quantities and quality sufficient for pharmacodynamic and toxicological assessment allows iterative design to optimize ADC performance and reduces preclinical development times by 18 months. We'll provide updates on our lead clinical development candidates.

2:40 Translational Aspects of Auristatin-Based ADCs

Jeff Wallin, PhD, Senior Director and Head, Biomarkers & Diagnostics, Seattle Genetics

This presentation will assess the target expression and other patient characteristics vs. response; discuss dosing considerations and also explore pharmacodynamic and mechanism-of-action biomarkers supporting immuno-oncology combinations.

3:10 Harnessing Multiscale Modelling to Optimize Design of Antibody Drug Conjugates for Clinical Success

Renu Singh Dhanikula, PhD, Senior Research Investigator, MAP, Bristol-Myers Squibb Company

Mechanistic physiologically-based pharmacokinetic models (PBPK) can be used as a platform to study the impact of various ADC characteristics on their disposition in plasma, tissues and tumor, allowing us to build quantitative relationship between exposure and efficacy. The presentation will showcase how mathematical simulations can provide an efficient method for exploring the vast permutation and combinations of parameters influencing efficacy and toxicity of these complex molecules enabling selection of ADCs with an increased likelihood of success.

3:40 End of Conference

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

EMERGING THERAPEUTICS & TECHNOLOGIES STREAM

- Emerging Indications for Therapeutic Antibodies
- CRISPR for Genome Engineering
- Nanotechnology in Medicine

Cutting-Edge Science and Technology to Deliver New Approaches in Therapeutics, Delivery and Diagnostics

NEW at PEGS this year is the Emerging Therapeutics & Technologies stream. This stream, comprising of 3 new and unique topics, will offer an interdisciplinary approach for scientists from discovery, genomics, biology, chemistry, engineering and nanotechnology, to come together to uncover new therapeutic applications and cutting-edge technologies. Emerging Indications for Therapeutic Antibodies will reveal new targets and novel mechanisms of actions for development of next-generation therapeutics beyond oncology. CRISPR for Genome Engineering will dive into CRISPR's capabilities and applications in drug discover from screening to genome editing; while outlining the technology limitations. Nanotechnology in Medicine will appraise the latest developments in nanomaterials and nanoparticles, and their promising applications in delivery, diagnostics and therapeutics.

Inaugural

EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES

R&D Advances in Non-Cancer Indications for Antibodies and Other Biotherapeutics

SUNDAY, APRIL 30

RECOMMENDED SHORT COURSE(S)*

SC2: Translational Considerations for Development of Monoclonal Antibodies and Emerging Constructs: Part I: Focus on Construct Design

SC7: Translational Considerations for Development of Monoclonal Antibodies and Emerging Constructs: Part 2: Focus on Preclinical Development

**Separate registration required, please see page 6 for course details.*

MONDAY, APRIL 30

7:00 am **Registration and Morning Coffee**

THERAPEUTIC ANTIBODIES FOR CNS INDICATIONS

8:30 **Chairperson's Remarks**

Joachim Feldwisch, PhD, Director, Preclinical Development, Affibody AB, Sweden

8:40 **New Approaches in CNS Drug Discovery; Challenges and Opportunities for Biologic Drugs**

Leonard Kaczmarek, PhD, Professor, Pharmacology, Cellular and Molecular Physiology, Yale University School of Medicine

Basic research on all aspects of cellular physiology, including nervous system function, has always relied on small molecule inhibitors or activators of biochemical pathways linked to membrane receptors, second messengers and protein kinases. Typically, however, major breakthroughs have occurred with the development of specific biologic agents that perturb these pathways. This talk will give an account of such developments in basic research and potential applications to disease treatment.

9:10 **Discovery and Development of PRX002 (Targeting α-synuclein) for Parkinson's Disease**

Robin Barbour, Head, Antibody and Assay Development, Research, Prothena Biosciences

Millions of patients suffer from Parkinson's Disease (PD) and currently no disease-modifying therapy is approved for this neurodegenerative disorder. PD brains contain neuronal inclusions (Lewy Bodies) composed mainly of α-synuclein, a protein also genetically linked to the disease. We will discuss the discovery and development of PRX002, an antibody that decreases α-synuclein pathology, protects synapses, and improves behavior in transgenic PD mouse models. We will also review the current findings from our Phase I studies.

9:40 **Targets in the Complement Pathway**

Gabriela Dos Santos Cruz De Matos, PhD, Senior Scientific Investigator, Biopharm Molecular Discovery, GlaxoSmithKline, United Kingdom

Complement plays a key role in the immunopathology of immune-mediated inflammatory diseases. Existing therapies only target a small proportion of known family members in the complement pathway. This talk will focus on trying to define the role in disease of these large families of molecules and how this knowledge may lead to the identification of tractable targets for the development of future transformational medicines.

10:10 **Networking Coffee Break**

THERAPEUTIC ANTIBODIES FOR MIGRAINE AND PAIN

10:50 **Development and Clinical Update for an Anti-CGRP Antibody for Migraine**

Dan Allison, PhD, Senior Director, Antibody Technologies, Alder Biopharmaceuticals

Approximately 1% of the world's population suffers from debilitating migraine headaches. A link between migraines and calcitonin gene-related peptide (CGRP) is clearly established, and we have developed the monoclonal antibody Eptinezumab to antagonize the peptide. In this presentation, I will discuss some highlights of the discovery, development and pharmacology of this highly potent antibody, and provide an update on its clinical development.

EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES

11:20 Structure-Based Epitope Targeting for Engineering Functional Antibodies against Nav1.7 for Pain

Luke Robinson, PhD, Associate Director, Research, Visterra, Inc.

Ion channels remain a challenging class of targets to generate functional antibodies. Using our Heirotope® and AbMatch platforms for protein design, we have incorporated a structure-based approach to the discovery of antibodies against Nav1.7. We have engineered proteins to represent conformational and functionally relevant target epitopes of this channel. We will present how our approach facilitates engineering of antibodies to target epitopes that are obscured from conventional discovery methods.

11:50 KEYNOTE PRESENTATION: Trends and Challenges in the Development of Therapeutic Antibodies for Non-Oncology Indications

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

Although antibodies for cancer garner substantial attention, those for non-cancer indications comprise nearly half of the 560 commercially sponsored antibody therapeutics currently in clinical studies. Antibody therapeutics in development are designed to prevent or treat a wide variety of diseases, including headaches, infections, diabetes and hemophilia, as well as immune-meditated disorders. In this presentation, the clinical pipeline and approval success rates of antibodies for non-cancer indications will be discussed.

12:20 pm Sponsored Presentation *(Opportunity Available)*

12:50 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:50 Session Break

2:20 Problem-Solving Breakout Discussions

3:20 Networking Refreshment Break

PLENARY KEYNOTE SESSION

4:00 Chairperson's Remarks

4:10 Challenges and Opportunities in Engineering Protein Biopharmaceuticals

K. Dane Wittrup, PhD, C.P. Dubbs Professor, Chemical Engineering and Biological Engineering; Associate Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology (MIT)

Arthur C. Clarke's First Law posits that "When a distinguished but elderly scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong." Bearing this in mind, in this talk, I will highlight areas of protein drug development that appear poised for breakthroughs in the coming decade or so.

4:55 The Next Generation of Cancer Immunotherapy: Targeting Myeloid Immune Checkpoints

Kipp Weiskopf, MD, PhD, Resident Physician, Internal Medicine, Brigham and Women's Hospital

Immune cells of the myeloid lineage hold tremendous potential as effectors of cancer immunotherapy. The CD47/SIRPα axis is a key molecular pathway that governs the interaction between myeloid cells and tumors. Therapies that target the interaction are effective across multiple preclinical models of cancer and are now under investigation in clinical trials. Further studies have revealed additional regulators of myeloid cell activation that can be exploited as myeloid immune checkpoints.

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

Sponsored by PRECISION FOR MEDICINE — THE FUTURE OF MEDICINE IS PRECISION

7:15 End of Day

TUESDAY, MAY 1

8:00 am Registration and Morning Coffee

THERAPEUTIC ANTIBODIES FOR AUTOIMMUNITY AND INFLAMMATION

8:25 Chairperson's Remarks

Gregory C. Ippolito, PhD, Research Assistant Professor, Molecular Biosciences, Georgiou Lab, The University of Texas at Austin

8:30 Selection and Differentiation of High Affinity Antigen Specific B Cells *in vivo*

Ali Zarrin, PhD, Senior Scientist, Immunology and Antibody Engineering, Genentech

B cells diversify their immunoglobulin light chain or heavy chain genes to produce high affinity antibodies. Antigen specific B cells are selectively differentiated in the germinal centers to seed short- or long-lived plasma cells, a process known as affinity maturation. It is not clear how B cells commit to short or long-lived plasma cell fate. Our study provides insights on how this decision might be made during normal immune response as well as autoimmune disease.

9:00 Discovery of PAD3/PAD4 Cross-Reactive mAbs, Potential Therapeutics for RA

Gregory C. Ippolito, PhD, Research Assistant Professor, Molecular Biosciences, Georgiou Lab, The University of Texas at Austin

PAD4 enzyme contributes to RA pathogenesis by providing a continual source of citrullinated autoantigens that induce autoimmune responses. Autoantibodies to PAD4 (and cross-reactive with PAD3) are associated with disease severity and severe erosive joint damage. We will present insights into the polyclonal anti-PAD serum immune response in RA (using a synergistic combination of IgG protein mass spectrometry and B-cell VH:VL NGS) which may facilitate improved patient stratification of RA patients and development

EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES

of targeted therapeutics.

9:30 Treatment of Psoriasis Using the Engineered IL-17 Blocking Affibody Ligand Trap ABY-035: Interim Safety and Efficacy Results from Phase I/II

Joachim Feldwisch, PhD, Director, Preclinical Development, Affibody AB, Sweden

ABY-035 consists of two small Affibody® domains for IL-17A inhibition and an albumin binding domain for half-life extension. In a Phase I/II study, dose escalation safety was assessed in 46 healthy volunteers (2-40mg) and safety and preliminary efficacy in 26 psoriasis patients (single IV or multiple SC administrations). ABY-035 was safe and well tolerated at all dose levels. Even low single doses of ABY-035 (0.03mg/kg) resulted in an early onset of effect and lower disease burden.

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

ANTI-INFECTIVES

10:50 Antibacterial Monoclonal Antibodies: A Strategy to Prevent Serious Bacterial Infections

Christine Tkaczyk, PhD, Senior Scientist, Infectious Diseases/Vaccines, MedImmune

We have developed two human mAbs, MEDI4893 and SAR114, respectively against *Staphylococcus aureus* virulence factors alpha toxin and ClfA. mAb combination showed broad strain coverage in multiple animal models through complementary mechanism of action. MEDI4893 prophylaxis also demonstrated efficacy in a *S. aureus* + Gram-negative mixed lung infection model. Together our data hold some promise as an alternative therapy for the prevention of *S. aureus* diseases.

11:20 B-Cell Cloning and Screening to Improve the Potency of Antibodies against Infectious Diseases

Devin Sok, PhD, Director, Antibody Discovery and Development, International AIDS Vaccine Initiative (IAVI)

Over 200 HIV broadly neutralizing antibodies (bnAbs) have been isolated and the most potent of these are being developed and evaluated for use as prophylaxis. The discovery of highly potent HIV bnAbs can be attributed to 1) the availability of donor samples that have been screened and selected for activity and 2) new technologies to isolate antibodies from memory B cells. These approaches are being explored with other infectious diseases.

11:50 Development of Next-Generation Antibody Therapeutics against Infectious Diseases

Tianlei Ying, PhD, Head, Antibody Engineering and Drug Discovery Group, School of Basic Medical Science, Fudan University, China

Therapeutic antibodies have shown clinical success in the treatment of many diseases. By using extraordinarily large human antibody libraries, we have identified a number of potent mAbs against emerging and chronic infectious diseases, including MERS, H7N9 influenza, Zika, HBV, HIV, etc. We have also been working on the development of novel antibody constructs (from 14 kDa to 180 kDa) as the next-generation safer, cheaper, and more potent antibody-based therapeutics.

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

1:20 Ice Cream Break in the Exhibit Hall with Poster Viewing

THERAPEUTIC ANTIBODIES FOR OTHER EMERGING INDICATIONS

2:00 Chairperson's Remarks

Thomas Mikita, PhD, Director, Centers for Therapeutic Innovation, Pfizer, Inc.

2:05 Clinical Update: PCSK9 Monoclonal Antibodies for Cholesterol Lowering

Robert P. Giugliano, MD, Senior Investigator, TIMI Study Group, Staff Physician, Cardiovascular Medicine, Brigham and Women's Hospital; Associate Professor, Medicine, Harvard Medical School

Monoclonal antibodies inhibiting circulating PCSK9 result in profound (50-70%) reduction in LDL-cholesterol. When added to standard therapy with a statin, PCSK9 inhibitors permit the majority of patients to achieve LDL-cholesterol levels that are below even the most stringent guideline recommendations, and significantly reduced myocardial infarction and stroke in randomized clinical trials. PCSK9 inhibitors have been added to recent practice cholesterol guideline updates, thereby solidifying their role in clinical practice.

2:35 High Affinity Factor XIa-specific IgGs and Reversal Agent as Potential Treatment for Thrombotic Disease

Thomas Mikita, PhD, Director, Centers for Therapeutic Innovation, Pfizer, Inc.

We generated a high-affinity anti-FXIa mAb that does not bind the FXI zymogen or inhibit other coagulation proteases or plasma kallikrein and prevents thrombosis in two *in vivo* models at clinically relevant doses without detectable increases in spontaneous or induced bleeding. The co-crystal structure of this mAb bound to FXIa accounts for its high selectivity. We have also developed two reversal agents that quickly counter the effect of this mAb.

3:05 Engineering Cells at the Protein Level with Intracellular Antibodies

Andrea Marschall, PhD, Postdoctoral Researcher, Biochemistry, Brandeis University

Intracellular antibodies (intrabodies) can knock down functions by acting at the protein level and allows gradual quantitative tuning of membrane-receptors. We demonstrated gradual reductions of vascular adhesion molecule 1 (VCAM1) *in vitro*. In the world's first transgenic intrabody mouse that we generated, ablation of VCAM1 by an intracellular antibody resulted in aberrant localization of B cells in adult animals. Intrabody mice were viable although genetic knockouts of VCAM1 are lethal.

3:35 Refreshment Break in the Exhibit Hall with Poster Viewing

Cambridge HEALTHTECH Institute
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EMERGING INDICATIONS FOR THERAPEUTIC ANTIBODIES

4:25 Humanized Anti-FIXa/FX Bispecific Antibody for the Treatment of Hemophilia A

Hikaru Koga, Researcher, Biologics Discovery Department, Chugai Pharmaceutical Co., Ltd., Japan

Emicizumab is humanized anti-FIXa/FX bispecific antibody for the treatment of hemophilia A, which was filed for regulatory approval. In this presentation, I will introduce how emicizumab was created, its preclinical data, kinetics understanding of FVIII mimetic activity, and Phase III study data. In addition, novel antibody engineering to further improve the property of emicizumab will be presented.

4:55 Antibodies as Protease Inhibitors: Lanadelumab Inhibition of Plasma Kallikrein for Hereditary Angioedema Prophylaxis

Dan Sexton, PhD, Director, Pharmacology, Shire

While there are several small molecule protease inhibitor therapies for hereditary angioedema, their off-target selectivity could be associated with associated side effects. Monoclonal antibody inhibitors of proteases can exhibit high potency and specificity combined with a long therapeutic half-life. Lanadelumab is one such antibody inhibitor of plasma kallikrein, discovered using phage display that is in clinical development for the prophylactic treatment of hereditary angioedema due to C1 inhibitor deficiency.

5:25 End of Emerging Indications for Therapeutic Antibodies

5:30 Registration for Dinner Short Courses

RECOMMENDED DINNER SHORT COURSE(S)*

SC8: Introduction to Biophysical Analysis for Biotherapeutics: Discovery & Development Applications

**Separate registration required, please see page 6 for course details.*

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

Inaugural

CRISPR FOR GENOME ENGINEERING

Transforming Drug Discovery and Therapeutics Development

WEDNESDAY, MAY 2

7:30 am Registration and Morning Coffee

DRUG DISCOVERY AND IDENTIFICATION OF NEW GENES

8:30 Chairperson's Remarks
John Feder, PhD, Associate Director, Genome Biology, Bristol-Myers Squibb

8:40 Cellular Engineering for Drug Discovery
Aaron T. Cheng, PhD, Head, PTS Discovery Genome Editing, Protein Cellular and Structural Sciences, R&D Platform Technology & Science, GlaxoSmithKline
This talk will highlight our application and learnings from use of CRISPR genome editing in building cellular systems for drug discovery.

9:10 Genome-Wide CRISPR Screens Identify New Genes and Pathways Driving Breast Cancer Development and Progression
Gus Frangou, PhD, Fellow, Molecular and Integrative Physiological Sciences, Harvard TH Chan School of Public Health
Identifying genetic drivers of metastatic breast cancer and the timing during which these lesions occur is critical to developing effective therapeutics. In this talk, novel modifications of CRISPR/Cas9 genome-editing technology we have developed, including high-efficiency *in vivo* phenotypic screens and inducible gene targeting, to interrogate the functions of cancer-driver mutations will be discussed. Significantly, these CRISPR/Cas9-based genetic screens provide a systematic phenotypic measurement of loss-of-function lesions in disease progression and provide novel insights into the molecular underpinnings of metastasis.

9:40 Dissecting Complex Biological Processes with Pooled CRISPR-Cas9 Screens
Patrick Collins, PhD, Senior Scientist, Genome Analysis Unit, Amgen
Pooled CRISPR screens have been shown by multiple groups to significantly outperform shRNA technology for identifying fitness genes. While every pooled screen inherently measures fitness over time, we can also apply selection(s) to study nearly any cell autonomous phenotype of interest. We will discuss the application of pooled CRISPR screens to study complex biological processes such as mechanisms of resistance and host factors modulating viral vector infection.

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

10:55 KEYNOTE PRESENTATION: Bringing CRISPR to the Clinic
Tony Ho, MD, Executive Vice President, Head of R&D, CRISPR Therapeutics
I will be discussing the data that supports the first CRISPR-based cell therapy clinical trial for b-thalassemia, including selection of gRNA and evaluation of target events, efficacy of editing and pharmacodynamics effects. In addition, I will also discuss the use of CRISPR/Cas 9 in generating potent allogenic multi-edited CAR T therapeutics across variety of tumors.

11:25 Antibody-Display Libraries in Mammalian Cells Created Using CRISPR/Cas9 and TALE Nucleases
John McCafferty, PhD, CEO, Antibody Engineering, IONTAS Ltd.
Using directed integration of antibody genes by CRISPR/Cas9 and TALE nucleases, we have constructed large libraries in mammalian cells containing a single antibody gene/cell. This has permitted construction of millions of monoclonal stable cell lines displaying IgG antibodies on their surface from which antibodies have been selected by flow cytometry for specificity, binding affinity, species cross-reactivity and expression level. Expression in production cell lines also enables high-throughput developability screening.

11:55 Genome-Scale Activation Screen Identifies a lncRNA Locus Regulating a Gene Neighborhood
Julia Joung, Graduate Student. Biological Engineering, MIT
Mammalian genomes contain thousands of loci that transcribe long non-coding RNAs (lncRNAs). Despite their potentially important roles, it remains challenging to identify functional lncRNA loci. Here, we developed a CRISPR–Cas9 activation screen targeting >10,000 lncRNA loci and found 11 that mediate melanoma drug resistance. Detailed analysis of one candidate revealed that its transcriptional activation resulted in dosage-dependent activation of four neighboring genes, one of which confers the resistance phenotype.

12:25 pm Poster Highlight: SMART Libraries and Phage-Induced Directed Evolution of Cas9 to Engineer Off-Target Activity
Barrett Steinberg, PhD, Scientist II, Protein Engineering, Editas Medicine
RNA-guided endonucleases such as Cas9 often show efficient editing in cells but can cleave at off-target loci in the genome. Engineered variants of

S.pyogenes Cas9 (Sp.Cas9) have been developed to globally reduce off-target activity, but individual off-targets may remain or on-target activity may be compromised. In order to engineer decreased editing at specific off-targets and maintain on-target activity, we created a phage-based selection system in which we can negatively select for cleavage of specific sequence sin a competitive pool and positively select for cleavage at our desired on-target. Directed evolution using our system demonstrates a structure-independent methodology to effectively engineer nuclease activity.

12:55 **Luncheon Presentation I: Build Better Biologics with Machine Learning and Synbio**

Sponsored by ATUM

Claes Gustafsson, Chief Commercial Officer, ATUM (formerly DNA2.0)

This presentation will showcase how ATUM combines recent developments in genome engineering, automation, big data and product analytics to increase efficiency of engineering and developability of biologics and cell lines. Cell lines generated using the LeapIn® transposase combined with optimized vector constructs, proprietary codon optimization and QSAR-based protein engineering allow for an information rich and efficient optimization of mAbs, bispecifics, CAR-T molecules, and the increasingly complex biologics approaching the market place.

1:25 **Luncheon Presentation II** *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

1:55 **Session Break**

2:10 **Chairperson's Remarks**

Aaron T. Cheng, PhD, Head, PTS Discovery Genome Editing, Protein Cellular and Structural Sciences, R&D Platform Technology & Science, GlaxoSmithKline

2:15 **Development and Optimization of CRISPR Gene Editing for Drug Discovery Applications**

John Feder, PhD, Associate Director, Genome Biology, Bristol-Myers Squibb

NEXT-GENERATION SEQUENCING FOR GENE EDITING

2:45 **Development of a Qualifiable NGS Assay for Precise and Accurate Quantitation of Small Insertions and Deletions (Indels) That Are Introduced in the Human Genome by Gene Editing**

Marina Falaleeva, PhD, Scientist I, Development, Sangamo Therapeutics

Gene editing by targeted engineered nucleases in living cells is tracked by the detection of introduced indels (small insertions and deletions) at specific nucleotide sequences using Next-Generation Sequencing. Comparisons of nuclease efficiency and monitoring of results in patient samples requires the development of quantitative assays. The purpose of this talk is to discuss application of these established principles to the challenge of indel quantitation.

3:15 **Sponsored Presentation** *(Opportunity Available)*

3:45 **Refreshment Break in the Exhibit Hall with Poster Viewing**

4:45 **Problem-Solving Breakout Discussions**

5:45 **Networking Reception in the Exhibit Hall with Poster Viewing**

7:00 **End of Day**

THURSDAY, MAY 3

8:00 am **Morning Coffee**

DISEASE MODELING

8:30 **Chairperson's Remarks**

Patrick Collins, PhD, Senior Scientist, Genome Analysis Unit, Amgen

8:35 **Genome Editing to Model and Treat Cardiac and Neuromuscular Diseases**

Chengzu Long, PhD, Asst Professor, Department of Medicine, New York University

Our projects focus on advancing the novel genome editing technology to model and treat cardiac and neuromuscular diseases. Duchenne muscular dystrophy (DMD) is a fatal muscle disease affecting 1 in 3,500 boys. Dilated cardiomyopathy (DCM) and heart failure are common and lethal consequences of DMD. We have advanced genome editing to cells from DMD patients by engineering the permanent skipping of mutant exons in the genomes of DMD patient-derived induced pluripotent stem cells (iPSCs).

9:05 **Modelling the Pathogenic Effect of Mutations in Rare Mendelian Conditions**

Colin A. Johnson, PhD, Professor of Medical & Molecular Genetics, Section of Ophthalmology and Neurosciences, Leeds Institute of Molecular Medicine

To gain novel unbiased insights into essential biological processes and to identify roles for unanticipated pathways in human genetic disease, we have developed our existing gene discovery research to include cellular disease modelling using CRISPR-Cas9 genome and base editing approaches. We will discuss recent advances in modelling ciliopathies, neuromuscular and neurodevelopmental conditions, and inherited retinal dystrophies.

9:35 **Poster Highlight: Directed Evolution of CRISPR-Cas9 to Increase Its Specificity**

Joonsun Lee, PhD, Researcher, Platform R&D, ToolGen, Inc.

We have developed a directed evolution approach to improve the specificity of SpCas9. By screening a library of random mutants of SpCas9 generated by error-prone PCR, a mutant named Sniper-Cas9 was identified, and it shows high specificities without sacrificing on-target activities in human cells. Sniper-Cas9 is fully compatible with extended or truncated sgRNAs and functions well in a preassembled ribonucleoprotein (RNP) form which facilitates DNA-free genome editing.

10:05 **Coffee Break in the Exhibit Hall with Poster Viewing**

ALTERNATIVE DELIVERY AND ANTI-CRISPR MECHANISMS

11:05 pm **CRISPR-Cas9 Inactivation by Bacteriophage Proteins**

Bettie Osuna, PhD, Graduate Student, Bondy-Denomy Lab, University of California, San Francisco

CRISPR-Cas adaptive immune systems defend prokaryotes from invasion by foreign genetic elements, including viruses (bacteriophages/phages). Phages have coevolved counter-attack strategies, including inactivation of CRISPR-Cas with "anti-CRISPR" proteins. We have discovered proteins encoded by *Listeria monocytogenes* phages, AcrIIA1-4, that suppress CRISPR-Cas9 activity. Our work aims to characterize anti-CRISPR-Cas9 mechanisms in this natural context to gain insight into CRISPR-Cas9 evolution and allow the use of anti-CRISPRs as "off-switches" in gene editing applications.

11:35 **Structural Basis of CRISPR/Cas9 and Anti-CRISPR Mechanisms for Precise Genome Editing**

Fuguo Jiang, PhD, Postdoc Fellow, Molecular and Cell Biology, University of California, Berkeley

CRISPR/Cas9 technology shows great promise in treating cancer diseases at a genetic level. The recently discovered natural Cas9-specific "anti-CRISPRs" present important tools that can be used to regulate CRISPR/Cas9-mediated genome editing specificity. I will talk about our structural studies on CRISPR/Cas9 and anti-CRISPR mechanisms, with the hope to support CRISPR/Cas9 site-specific genetic control and therapeutic applications.

12:05 pm **Closing Q&A**

12:35 **End of CRISPR for Genome Engineering**

Inaugural

NANOTECHNOLOGY IN MEDICINE

Engineering Nanoparticles for Delivery, Therapeutics and Diagnostics

THURSDAY, MAY 3

NANOSENSING AND IMAGING

12:00 pm Registration

12:35 Luncheon in the Exhibit Hall with Poster Viewing

1:40 Chairperson's Remarks

Christopher Hartshorn, PhD, Program Director, National Cancer Institute, National Institutes of Health

1:50 KEYNOTE PRESENTATION: Development of Uniform-Sized Inorganic Nanoparticles for Clinical Applications

Taeghwan Hyeon, PhD, SNU Distinguished Professor, School of Chemical and Biological Engineering, Seoul National University

Since 1997, our laboratory has focused on large-scale synthesis and medical applications of uniform-sized nanoparticles. We reported on high-resolution MR imaging using uniform 2 nm-sized iron oxide nanoparticles in non-human primate models. We demonstrated that intravenously administered ceria nanoparticles could substantially reduce the damage from ischemic strokes, and 2 nm-sized ceria–zirconia nanoparticles can effectively reduce mortality and systemic inflammation in sepsis models.

2:20 Targeted Nanoparticles for Imaging, Drug Delivery and Biosensing

Paul Millner, PhD, Professor of Bionanotechnology, School of Biomedical Sciences, University of Leeds

Functionalising nanoparticles with antibodies or "synthetic antibodies" (Affimers) brings a range of potential biomedical applications. mAb addressed fluorescent silica nanoparticles locate efficiently to colorectal cancer xenographs. The same functionalisation of lanthanide doped nanoscrystals allows fluorescence up-conversion base quantification of medical analytes with nM to pM sensitivity. Finally, functionalization of lipidic nanoparticles should allow targeting of low cost anti-cancer agents. In all cases, correct design of surface chemistry minimizes non-specific interactions.

2:50 Assemble Nanoparticles *in vivo* for Cancer Imaging and Treatment

Jianghong Rao, PhD, Professor, Radiology and Chemistry (courtesy), Molecular Imaging Program, Cancer Biology and Biophysics Programs, Stanford University

3:20 Sponsored Presentation *(Opportunity Available)*

3:50 Networking Refreshment Break

4:20 Biomimetic Nanotechnology Enhances Surface Detection of Circulating Tumor Cells in Peripheral Blood from Head and Neck Cancer Patients

Seungpyo Hong, PhD, Professor, Pharmaceutics, Pharmaceutical Sciences Division, School of Pharmacy, University of Wisconsin-Madison

We report the development of a biomimetic CTC capture chip that utilizes multi-antibody, multivalent binding, and biomimetic cell rolling concepts to significantly improve overall CTC capture sensitivity and specificity. We demonstrated that the combination of multi-antibody and multivalent binding improves CTC capture sensitivity, and the cell rolling effect improves CTC capture specificity (up to 38%). Our data also suggest CTC can be an important biomarker for head and neck cancer disease monitoring and surveillance.

4:50 Digital Resolution Biomolecule Sensing by Photonic Resonator Absorption Microscopy (PRAM) with Plasmonic Nanoparticle Tags

Brian T. Cunningham, PhD, Willett Professor of Engineering, Director, Micro and Nanotech Lab, Electrical and Computer Engineering, University of Illinois at Urbana -Champaign

Using gold nanoparticles that are engineered to match the resonant wavelength of a photonic crystal biosensor surface, we have developed a new form of microscopy called Photonic Crystal Absorption Spectroscopy (PRAM) that enables individual adsorbed nanoparticles to be dynamically counted with high signal-to-noise ratio. We utilize PRAM for counting virus particles, miRNA, and proteins for application in simple, rapid, and ultrasensitive diagnostics with digital analyte resolution that does not require enzymatic amplification.

5:20 End of Day

5:20 Registration for Dinner Short Courses

Cambridge HEALTHTECH Institute
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FRIDAY, MAY 4

8:00 am Morning Coffee

NANOTHERAPEUTICS

8:30 Chairperson's Remarks
Paul Millner, PhD, Professor of Bionanotechnology, School of Biomedical Sciences, University of Leeds

8:35 Development of Novel Antibody Directed Nanotherapeutics for the Treatment of Solid Tumors
Daryl Drummond, PhD, Head of Research, Merrimack Pharmaceuticals
Antibody targeted nanotherapeutics offer the promise of multiple levels of targeting due to the combination of size-related delivery to solid tumors via the EPR effect when combined with antibody-specific penetration in solid tumors. Engineered lipid based delivery systems have been clinically validated, and next generation nanotherapeutics with antibody targeting are currently being explored in early Phase clinical trials.

9:05 Enabling and Expanding the Use of Microbial-Derived Biologics through the Use of Tolerogenic Nanoparticles
Kei Kishimoto, PhD, CSO, Selecta Biosciences
The pharmaceutical industry has exploited the microbiome to create small molecule drugs to a wide variety of diseases. However broad use of microbial-derived biologics or 'xenobiologics' is limited by immunogenicity. Here we describe the use of tolerogenic nanoparticles to create improved and novel xenobiologic drugs. I will present case examples of applying tolerogenic nanoparticles to a fungal-derived uricase enzyme, in Phase 2 clinical trials for the treatment of gout, a bacterial-derived immunotoxin for cancer therapy, and adeno-associated virus for gene therapy.

9:35 Panel Discussion : Targeted Nanoparticle-Mediated Drug Delivery
Moderator: Paul Millner, PhD, Professor, Bionanotechnology, School of Biomedical Sciences, University of Leeds
- Potential for minimizing off-target drug dose
- Potential for delivering generic cytotoxins in a targeted manner (affordable medicine for the developing world)
- Possibility of multifunctional particles (delivery and imaging)
- Range of nanoparticle material ranging from hydrophilic to hydrophobic

10:05 Networking Coffee Break

10:35 Safe and Effective Nanomedicines for Cancer and Inflammatory Diseases
Hayat Onyuksel, PhD, Professor, Biopharmaceutical Sciences, University of Illinois
Application of nanotechnology to drug delivery provides targeted therapy, which results in higher efficacy at the site of action, and significantly lower drug toxicity to the healthy tissues for a given dose. Using phospholipid micelles as nanocarriers (15nm) our laboratory has developed several nanomedicines that were effective and safe on animal models of cancer and inflammatory diseases. In this talk the parameters required to develop successful nanomedicines will be presented.

11:05 A Modular Platform for Targeted RNAi Therapeutics Using Biologically-Lipidated Antibodies
Itai Benhar, PhD, Professor, Molecular Microbiology and Biotechnology, The George S. Wise Faculty of Life Sciences, Tel Aviv University
We present a modular platform to target specific cell types using siRNA loaded lipid nanoparticles (LNP) coated with oriented, targeting antibodies. The antibodies are non-covalently bound to a membrane-anchored lipoprotein that recognizes their Fc domain. In one example, intravenously injected anti-Ly6C-coated LNP encapsulating TNF siRNAs were taken up selectively by Ly6C+ monocytes and activated tissue macrophages, suppressed TNF-alpha expression in the colon and ameliorated inflammatory bowel disease symptoms in a DSS-induced colitis mouse model.

11:35 Smart, Multifunctional Liposomal Nanoformulation for Treating Fabry and Other Rare Diseases
Jose Luis Corchero Nieto, PhD, Senior Scientist, Nanobiotechnology Group, CIBER-BBN, Institute of Biotechnology and Biomedicine, Universitat Autonoma de Barcelona
Preparation of new liposomal formulations by DELOS-SUSP, based on the depressurization of CO2-expanded liquid organic solutions, has shown the great potential of this methodology to prepare nanomaterials with therapeutic interest. Here, we will discuss the preparation and characterization of nanovesicles containing therapeutic proteins for treatment of rare diseases, and their development, up to the end of the regulatory preclinical phase, under the frame of the European "Smart-4-Fabry" project.

12:05 pm Targeted Ultrasmall Silica Nanoparticles as Next-Generation Treatment Tools for Drug Delivery
Michelle Bradbury, MD, PhD, Co-Director, MSK-Cornell Center for Translation of Cancer Nanomedicines; Prof, Radiology, Memorial-Sloan Kettering Cancer Center
Advances in nanotechnology have fueled a paradigm shift in targeting and safely delivering drugs in conjunction with image-directed approaches. The ability to flexibly adapt the formulation of clinically-promising drugs to improve their physicochemical and/or biological properties, in combination with particle probes and metabolic imaging tools, will be important to quantify and establish suitable clinical trial endpoints. The future success of molecular medicine rests upon improved clinical trial designs addressing these issues.

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

1:05 Networking Refreshment Break

Cambridge HEALTHTECH Institute
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NANOCARRIERS FOR DELIVERY

1:35 Chairperson's Remarks

Brian T. Cunningham, PhD, Willett Professor of Engineering, Director, Micro and Nanotech Lab, Electrical and Computer Engineering, University of Illinois at Urbana -Champaign

1:40 Talk Cancelled - Please attend alternative talks in other concurrent conference sessions

2:10 Designing Nanoparticles to Actively and Specifically Penetrate Solid Tumors

Jan E. Schnitzer, MD, Director, Professor of Cellular & Molecular Biology, Proteogenomics Research Institute for Systems Medicine (PRISM)

Nanocarrier utility in drug delivery has been questioned. Current nanoparticles can only move across endothelial cell barriers passively. Their size and RES uptake limit solid tumor penetration and targeting. We have discovered an active transvascular delivery system and applied it to pump nanoparticles carrying imaging and therapeutic cargo across endothelium and specifically into solid tumors within one hour of intravenous injection. Tumor-specific imaging, size constraints and therapeutic impact will be addressed.

2:40 Synthetic Nanocarriers for the *in situ* Programming of Disease-Specific T Cells

Matthias Stephan, MD, PhD, Associate Member, Fred Hutchinson Cancer Research Center, Associate Professor, University of Washington

Despite the obvious advantages afforded by targeted T cell therapies, the complexity and costs involved in producing genetically-modified lymphocytes remain major obstacles to their implementation as standard-of-care. In this talk, I will introduce a new injectable nanoreagent our group developed that that can quickly program tumor- or pathogen-recognizing capabilities into circulating T cells without the need for laboratory manipulations.

3:10 Bioresponsive Nanotechnologies for Systemic RNA Delivery to Tumors

Jinjun Shi, PhD, Assistant Professor, Center for Nanomedicine, Brigham and Women's Hospital, Harvard Medical School

Biologically responsive nanotechnologies have attracted tremendous attentions for controlled delivery of therapeutic molecules and the development of precision medicines. Dr. Shi and his laboratory have developed various bioresponsive nanoparticle platforms to tackle the challenges associated with systemic siRNA delivery to tumor cells, such as enzymatic degradation, poor pharmacokinetics, and insufficient tumor penetration, cellular uptake and endosomal escape. In a recent effort, nanoparticle-mediated systemic delivery of therapeutic mRNA has also been demonstrated in various tumor models.

3:40 End of Conference

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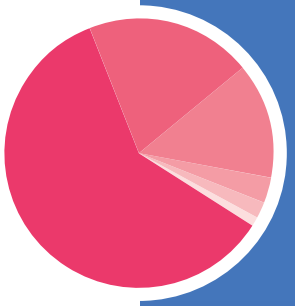

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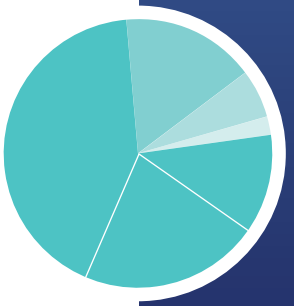

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