Antibody Engineering & Therapeutics

December 11-15, 2017
Manchester Grand Hyatt
San Diego, CA

Annual Meeting of the ANTIBODY SOCIETY

THE LARGEST MEETING BRINGING YOU THE LATEST ANTIBODY SCIENCE, TECHNOLOGIES AND PARTNERS NEEDED TO ACCELERATE NEXT GENERATION ANTIBODIES TOWARDS COMMERCIAL SUCCESS

The Most Innovative Science Presented by Leading Industry and Academic Experts

The Largest Exhibition Devoted to Antibody Engineering

The Leading Forum to Partner with Global Antibody Innovators and Suppliers

Keynote Speakers Share Strategies to Accelerate Your Antibody Molecules

DECIPHERING THE HUMAN IMMUNOME

James E. Crowe, Jr., M.D.,
Director, Vanderbilt Vaccine Center,
Vanderbilt University Medical Center

PARACRINE DELIVERY

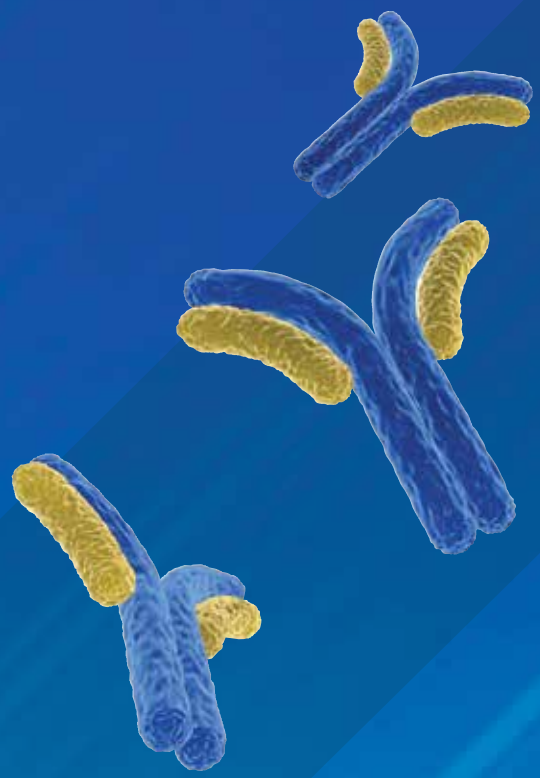
Andreas Plückthun, Ph.D.,
Professor and Director,
Department of Biochemistry,
University of Zürich, *Switzerland*

BIOLOGIC DRUG DELIVERY ACROSS THE BLOOD-BRAIN BARRIER WITH IgG FUSION PROTEINS

William M. Pardridge, M.D.,
Distinguished Professor Emeritus, UCLA and
Founder and Chief Scientific Officer, ArmaGen

OCRELIZUMAB IN RELAPSING AND PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS

Peter Chin, M.D.
Group Medical Director, Neuroscience,
SPECTRUM Medical Unit, US Medical Affairs,
Genentech



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#AntibodyEng

Register by October 6 and Save Up to $200 **www.antibodyeng.com**

THE GLOBAL MEETING PLACE FOR ANTIBODY SCIENCE, TECHNOLOGY AND NETWORKING

900+ ANTIBODY SCIENTISTS AND EXECUTIVES

Fast-track your antibody research to the clinic and beyond by collaborating with leading pharma, biotechs, academia and solution providers from North America, Asia and Europe.

125+ GLOBAL SPEAKER PRESENTATIONS

Expand your pipeline of antibody therapeutics by hearing case studies, new data and industry updates from experts working across the entire spectrum of antibody development and production.

100+ PEER-SUBMITTED POSTERS

Stay at the forefront of antibody innovation by accessing cutting-edge and unpublished data from fellow attendees.

75+ EXHIBITORS

Accelerate your promising therapeutic towards commercial success by connecting with leading technology and service providers.

New This Year!

- Session on Overcoming Delivery Challenges Including Brain & Intracellular Targets
- Full Day Track on Antibody-Based Innovations in the Tumor Microenvironment
- Workshop on Screening Against Cell-Surface Targets
- More Examples of Novel Therapeutic Indications and Non-Cancer Antibodies
- Expanded Focus on Immunotherapy, Immuno-oncology and Immune Mechanisms

WHAT YOU WILL LEARN BY ATTENDING

- ✔ **Find strategies** for novel antibody targets
- ✔ **Learn how to "engineer in"** improved drug-like properties for your antibodies
- ✔ **Prepare for the challenges** of complex and next-generation antibody therapeutics
- ✔ **Explore** immunotherapeutic mechanisms of antibodies
- ✔ **Hear the latest data** from multiple preclinical and clinical programs

OTHER EVENT HIGHLIGHTS

- ✔ Attendee Networking App to Help Facilitate Meetings
- ✔ Two Networking Cocktail Receptions and Two Networking Luncheons
- ✔ Evaluate Technologies to Help Your R&D via 20+ Scientific Briefings
- ✔ Antibodies to Watch in 2018 and Society Updates from the Antibody Society

PRESENT YOUR COMPANY'S CUTTING-EDGE ANTIBODY RESEARCH

Any registered attendee may submit a scientific poster for display in the exhibit & poster hall during the event. Presenting a poster is a great way to share your company's innovative research with 900+ global antibody scientists and executives. Visit the website to submit your poster abstract.

Poster submission deadline: **Friday, November 10, 2017**

ANTIBODY ENGINEERING & THERAPEUTICS SCIENTIFIC ADVISORY BOARD

Gregory Adams, Ph.D., Chief Development Officer, Chief Scientific Officer, **Eleven Biotherapeutics**

Mark Alfenito, Ph.D., President and CEO, **EnGen Bio, LLC**

Andrew Bradbury, M.D., Ph.D., Chief Scientific Officer, **Specifica**

Dennis R. Burton, Ph.D., Professor, Department of Immunology and Microbial Science, **The Scripps Research Institute**

Paul J. Carter, Ph.D., Senior Director and Staff Scientist, Antibody Engineering, **Genentech, Inc.**

Kerry A. Chester, Ph.D., Professor of Molecular Medicine, UCL Cancer Institute, **University College London,** *United Kingdom*

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Andreas Plückthun, Ph.D., Professor and Director, Department of Biochemistry**, University of Zürich,** *Switzerland*

Janice M. Reichert, Ph.D., Executive Director, The Antibody Society; Editor-in-Chief, mAbs; Managing Director**, Reichert Biotechnology Consulting LLC**

Jamie K. Scott, M.D., Ph.D., Professor and Canada Research Chair in Molecular Immunity, Department of Molecular Biology & Biochemistry and Faculty of Health Sciences, **Simon Fraser University,** *Canada*

Trudi Veldman, Ph.D., Senior Director, Biologics, **AbbVie Bioresearch Center**

Louis M. Weiner, M.D., Director, Lombardi Comprehensive Cancer Center, **Georgetown University Medical Center**

K. Dane Wittrup, Ph.D., C.P. Dubbs Professor of Chemical Engineering and Biological Engineering, Koch Institute for Integrative Cancer Research, **Massachusetts Institute of Technology**

AGENDA AT-A-GLANCE

	MONDAY, DECEMBER 11, 2017	
9:00 am - 5:00 pm	*Pre-Conference Training Course:* **Introduction to Antibody Engineering** *(Separate registration required)*	
1:00 pm - 5:00 pm	*Pre-Conference Workshop A:* **Selecting Antibodies against Cell-Surface Targets** *(Separate registration required)*	*Pre-Conference Workshop B:* **Antibody Developability** *(Separate registration required)*
	TUESDAY, DECEMBER 12, 2017	*Exhibit Hall & Poster Viewing Hours 4:00pm-7:15pm*
	KEYNOTE PRESENTATIONS	
8:15 am - 8:25 am	*Chairman's Opening Remarks:* James D. Marks, M.D., Ph.D., San Francisco General Hospital	
8:25 am - 9:15 am	**"Deciphering the Human Immunome"** James E. Crowe, Jr., M.D., Vanderbilt University Medical Center	
9:15 am - 10:05 am	**"Paracrine Delivery: Therapeutic Biomolecules Produced in situ"** Andreas Plückthun, Ph.D., University of Zürich, *Switzerland*	
10:35 am-11:25 am	**"Biologic Drug Delivery Across the Blood-Brain Barrier with IgG Fusion Proteins"** William M. Pardridge, M.D., UCLA and ArmaGen, Inc.	
11:25 am-12:15 am	**"Ocrelizumab in Relapsing and Primary Progressive Multiple Sclerosis"** Peter Chin, M.D., Genentech	
12:15 pm - 1:00 pm	*Scientific Luncheon Briefings:* **Carterra, Ligand, Berkeley Lights, Twist Bioscience, WSGR**	
1:15 pm - 1:45 pm	*Scientific Briefings:* **TTP Labtech, Isogenica, Innovative Targeting Solutions**	
1:45 pm - 2:15 pm	*Scientific Briefings:* **Trianni, ProImmune, Crystal Bioscience**	
2:25 pm - 6:15 pm	**OVERCOMING DELIVERY CHALLENGES INCLUDING BRAIN AND INTRACELLULAR TARGETS**	**NOVEL ANTIBODY DISPLAY, SELECTION AND SCREENING TECHNOLOGIES**
4:00 pm -4:45 pm	*Opening of Poster and Exhibit Hall*	
6:15 pm-7:15 pm	*Networking Cocktail Reception, Exhibit and Poster Viewing*	
	WEDNESDAY, DECEMBER 13, 2017	*Exhibit Hall & Poster Viewing Hours 9:45 am-7:15 pm*
7:30 am - 8:00 am	*Scientific Breakfast Briefing:* **Chemical Computing**	
8:10 am - 12:00 pm	**ENGINEERING AND APPLICATION OF THERAPEUTIC ANTIBODIES FOR NEURODEGENERATIVE DISEASES**	**ANTIBODY-DRUG CONJUGATES & FUSION PROTEINS**
12:00 pm - 12:30 pm	*Scientific Briefings:* **MaxCyte, Abzena, IntellCyt**	
1:45 pm - 2:15 pm	*Scientific Briefings:* **Aldevron, Geneious Biologics, ATUM**	
2:25 pm - 6:15 pm	**ROLE OF POST-TRANSLATIONAL MODIFICATION IN ANTIBODY FUNCTION**	**ANTI-TUMOR ANTIGEN ANTIBODIES IN CANCER IMMUNOTHERAPY**
6:15 pm - 7:15 pm	*Networking Cocktail Reception, Exhibit and Poster Viewing*	
	THURSDAY, DECEMBER 14, 2017	*Exhibit Hall & Poster Viewing Hours 9:45 am-2:10 pm*
8:10 am - 12:00 pm	**BIOLOGICAL IMPACT OF Fc RECEPTOR ENGAGEMENT**	**ANTIBODY BASED INNOVATIONS IN THE TUMOR MICROENVIRONMENT I**
12:00 pm - 12:30 pm	*Scientific Briefings:* **Applied Biomath, Morphotek,** SGI-DNA	
2:10 pm - 5:45 pm	**NOVEL THERAPEUTIC INDICATIONS FOR ANTIBODIES**	**ANTIBODY BASED INNOVATIONS IN THE TUMOR MICROENVIRONMENT II**
5:45 pm - 6:15 pm	**Special Session of the Antibody Society**	
	FRIDAY, DECEMBER 15, 2017	
8:25 am - 12:00 pm	**NOVEL ENGINEERING STRATEGIES TO ENHANCE ANTIBODY FUNCTIONS**	**IMMUNO-ONCOLOGY: CHECKPOINTS**
1:25 pm - 5:00 pm	**ROLE OF THE T-CELL REPERTOIRE IN CANCER, INFECTIOUS DISEASES AND AUTOIMMUNITY**	**INNOVATING ANTIBODY THERAPEUTICS**

PRE-CONFERENCE TRAINING COURSE 9:00 am - 5:00 pm

INTRODUCTION TO ANTIBODY ENGINEERING

Add this pre-conference training course to your main conference registration package for an additional fee and gain a comprehensive overview of antibody engineering in an easy-to-follow classroom setting to help you prepare for the main conference program. Training course registration begins at 8:30am.

TRAINING COURSE OVERVIEW

Today's wealth of knowledge of protein structures will be reviewed along with the genetics of diversity generation of antibodies, to give insights into the best strategies for improving protein function. There is particular emphasis on the choice of a functional assay to monitor effectively the changes in a desired property, and the use of functional enrichment steps where a library approach is employed. Not only is amino acid sequence amenable to engineering, but glycan structures and other modifications may also be engineered. The course will focus on the engineering and enhancement of antibodies and antibody-like scaffolds. Examples will include work on antibody fragment affinity improvement by 100-fold to low pM affinity. Also the engineering of bispecific antibodies by diverse approaches and the adaptation to generate Chimeric Antibody Receptor (CAR) constructs will be discussed. Expression platforms for producing antibodies for testing and for manufacture will also be covered. A background in biochemistry and molecular biology is useful, as the course is designed to progress rapidly from simple to advanced concepts.

INSTRUCTOR

David Bramhill, Ph.D., Founder, Bramhill Biological Consulting, **LLC** and **Research Corporation Technologies**

COURSE AGENDA

- **Functions amenable to engineering: affinity, specificity, stability, solubility, immunogenicity**
- **The measure of success: functional assays**
- **Engineering by design**
- **Engineering by random mutation**
- **Designed libraries**
- **Display technologies**
- **Improving manufacturing by protein engineering methods**
- **Glycosylation engineering – function and homogeneity**
- **Other protein modifications**
- **Immunogenicity engineering**
- **Bispecific antibodies**
- **Antibody-drug conjugates (ADCs)**
- **CAR-T strategies**
- **Expression of antibodies and fragments for discovery and testing**
- **Manufacturing platforms for antibodies and fragments**

PRE-CONFERENCE WORKSHOPS 1:00 pm - 5:00 pm

Workshop A:
SELECTING ANTIBODIES AGAINST CELL-SURFACE TARGETS

1:00 **Workshop Moderator's Remarks**
Andrew Bradbury, M.D., Ph.D., Chief Scientific Officer, **Specifica**

1:15 **Phage Display Selection of Conformation-sensitive Single Domain Antibodies against Intact Cells**
Single domain antibodies have a natural tendency to bind cavities and are often sensitive to conformational changes of their target. We are exploiting these properties and the power of phage display selection on intact cells to generate conformational sensors against difficult targets such as GPCRs of the mGluR family or RTKs of the EGFR family. Selection strategies and examples of applications will be discussed.
Patrick Chames, Ph.D., Principal Investigator, **Cancer Research Center of Marseille (CRCM), INSERM,** *France*

1:45 **Selection of Antibodies to Transiently Expressed Membrane Proteins Using Phage Display and Fluorescence-activated Cell Sorting**
Membrane proteins make difficult targets for phage display panning. Using whole cells for panning provides the native structure, but is complicated by a low receptor density against a high background of irrelevant antigens. Transient transfection of GFP-tagged membrane proteins, using alternating host cell lines, and combined with fluorescence-activated cell sorting, can be used to decrease these limitations while screening antibody phage libraries.
Martina Jones, Ph.D., Operations Manager, National Biologics Facility and Deputy Director, ARC Training Centre for Biopharm, AIBN,
The University of Queensland, *Australia*

2:15 **Antibodies to Challenging Receptor Targets through NGS and Cell-Based Antibody Phage Panning**
Several receptor targets cannot be made as soluble proteins and others are problematic for discovery of antibodies that bind to native protein conformations. Cell-based phage panning can identify antibodies to such targets, but is inefficient, often producing low antibody diversity. We utilized next generation sequencing to improve the robustness of cell-based selections.
John Wheeler, Ph.D., Principal Research Scientist, Janssen BioTherapeutics, **Janssen R&D**

2:45 *Networking Refreshment Break*

3:15 **Signal Amplification Methods in Immunoassays and Cell Biology**
Judicious use of antibody combinations can produce two-site ELISAs with great specificity. But even using high affinity antibodies, it may be difficult to detect very low levels of antigen in serum or tissue samples. In this case, some form of signal amplification can be used. A popular method exploits the use of peroxidase-labelled antibodies reacting with a tyramide-biotin derivative to generate a short-lived reactive product that biotinylates proteins in the immediate vicinity of the bound antibody. The biotin can then be detected using a suitable labelled streptavidin derivative. Since this is an enzyme-driven reaction, many biotin molecules can be deposited relative to the number of bound antibodies. Hence in principle, a major signal amplification is possible. However, these methods are no substitute for good high-affinity antibodies, and background signals can still be a problem. This talk will cover some of these issues and discuss other means of signal amplification. Finally, the use of tryamide-biotin in other applications such as proteomic proximity labelling will be discussed, to illustrate how these techniques, originally developed for immunoassays are beginning to receive much wider attention within the cell biology community.
Tony Jackson, Ph.D., Senior Lecturer, Biochemistry, **University of Cambridge,** *United Kingdom*

3:45 **Advances in Yeast Display Selections for Membrane Targets**
The presentation will discuss advances in yeast display technologies to select binders to membrane targets in their intact cellular context. The impacts of ligand and target accessibility and valency, and other elements of selection design, on enrichment, affinity stringency, and target specificity will be discussed in the context of alternative scaffold ligand discovery.
Benjamin Hackel, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, **University of Minnesota**

4:15 **Panel Discussion**

5:00 *Close of Workshop*

Workshop B:
ANTIBODY DEVELOPABILITY

MODERATOR

Mark Chiu, Associate Director of Development, **Janssen R&D**

OVERVIEW

This workshop will provide an overview of the nuts and bolts of antibody development and developability assessment to help you accelerate antibody drugs to the clinic. It will explore various strategies to discovering and designing antibodies with properties that are more likely to be successful in development. Building in "developability" and "manufacturability" assessments is crucial in any antibody discovery program, and this workshop will discuss case studies and lessons learned from a variety of antibody projects. Developability considerations to be discussed include: developability modeling and prediction, developability assessment methods, biophysical properties and PK, delivery, cell line development and more.

Confirmed Speakers *(as of July 19, 2017)*

Antibody-display Libraries in Mammalian Cells Created Using CRISPR/Cas9 and TALE Nucleases
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 populations of millions of monoclonal stable cell lines displaying antibodies on their surface from which novel binders including IgG formatted antibodies, have been isolated. This together with transcriptional "normalization" from a single locus and expression in cell lines used for production enable aspects of developability to be incorporated during antibody discovery.
John McCafferty, Ph.D., CEO, **IONTAS,** *United Kingdom*

Biophysical Properties of the Therapeutic Antibody Landscape
Max Vasquez, Ph.D., Vice President, Computational Biology, **Adimab LLC**

7:15 *Registration and Coffee*

8:15 **Chairman's Opening Remarks**

James D. Marks, M.D., Ph.D., Professor and Vice Chairman, Anesthesia and Perioperative Care, **University of California, San Francisco** and Chief of Anesthesia, **San Francisco General Hospital**

8:25 **Deciphering the Human Immunome**

We are sequencing the complete Human Immunome, defined as the repertoire of expressed B and T cell receptors. Deciphering the immunome, and associating the immune repertoire to antigen specificity, holds the transformative potential to usher in a new era of rational vaccine discovery and development of new and improved immunotherapies.

James E. Crowe, Jr., M.D., Director, Vanderbilt Vaccine Center, **Vanderbilt University Medical Center**

9:10 *Keynote Questions*

9:15 **Paracrine Delivery: Therapeutic Biomolecules Produced in situ**

Cancer will have to be fought with cocktails of therapeutics, which may have to include therapeutic antibodies against receptors, checkpoint inhibitors, as well as cytokines to modify the tumor microenvironment. We have recently developed a technology of using non-replicative adenovirus, engineered to target desired cells and also to be shielded from the immune response, as a vehicle for simultaneous delivery of multiple genes of therapeutic proteins, produced and secreted by the infected cells.

Andreas Plückthun, Ph.D., Professor and Director, Department of Biochemistry, **University of Zürich,** *Switzerland*

10:00 *Keynote Questions*

10:05 *Networking Refreshment Break*

10:35 **Biologic Drug Delivery Across the Blood-Brain Barrier with IgG Fusion Proteins**

Brain-penetrating biologic drugs are yet to be approved for brain disorders, owing to the lack of transport of these large molecule drugs across the blood-brain barrier (BBB). Any class of biologic drug (lysosomal enzyme, therapeutic antibody, decoy receptor, neurotrophin) has been re-engineered as BBB-penetrating IgG fusion proteins. The IgG domain is a peptidomimetic monoclonal antibody against the extracellular domain of an endogenous BBB peptide receptor/transporter, such as the insulin receptor or transferrin receptor. The receptor-specific IgG undergoes receptor-mediated transport across the BBB, and acts as a molecular Trojan horse to ferry into brain the fused biologic neurotherapeutic agent.

William M. Pardridge, M.D., Distinguished Professor Emeritus, **UCLA** and Founder and Chief Scientific Officer, **ArmaGen, Inc.**

11:20 *Keynote Questions*

11:25 **Ocrelizumab in Relapsing and Primary Progressive Multiple Sclerosis**

Ocrelizumab is a humanized monoclonal antibody that selectively targets CD20, a cell-surface antigen that is expressed on pre-B cells, mature B cells, and memory B cells but not on lymphoid stem cells and plasma cells. Clinical trial results of ocrelizumab in relapsing and primary progressive forms of multiple sclerosis will be discussed.

Peter Chin, M.D., Group Medical Director, Neuroscience, SPECTRUM Medical Unit, US Medical Affairs, **Genentech**

12:10 *Keynote Questions*

12:15 pm SCIENTIFIC LUNCHEON BRIEFINGS

carterra

See More, Do More: Accelerate Your Antibody Characterization with Carterra's State-of-the-art Array SPR Imaging Platform, the LSA

Carterra's new LSA platform enables high throughput mAb characterization, including kinetics, affinity, epitope binning, epitope mapping, and quantitation while using minimal sample volumes. We will present case studies highlighting the screening of multiple antigens at various concentrations over large mAb panels in a capture kinetics format; and a comprehensive epitope binning analysis on a 384-mAb array in a single run.

Yasmina Abdiche, Ph.D., Chief Scientific Officer, **Carterra**

Berkeley Lights

The Beacon™ Platform: Innovating Drug Discovery and Antibody Engineering

Berkeley Lights has developed the Beacon™ platform that transforms cell based biological processes to speed the discovery and development of therapeutics. Data will be presented on the workflows that incorporate massively parallel isolation, culture, analysis and selection of single cells in just one to two days for antibody engineering and discovery.

Keith Breinlinger, Ph.D., SVP Engineering and GM Biopharma, **Berkeley Lights, Inc.**

Ligand

OmniRat®, OmniMouse® and OmniFlic®: Transgenic Animals for the Generation of Fully Human Mono- and Bi-Specific Antibodies

Ligand's OmniAb® platforms (OmniRat®, OmniMouse® and OmniFlic®) are based on novel, transgenic rodents that produce highly diversified antibody repertoires. This platform offers accelerated discovery of fully human mono- and bi-specific antibodies that are naturally optimized in vivo for manufacturability, therapeutic efficacy and reduced immunogenicity.

Christel Iffland, Ph.D., Vice President, Antibody Technologies, **Ligand Pharmaceuticals**

TWIST BIOSCIENCE

Precisely Controlled, Highly Diverse Gene Mutant Libraries For Synthetic Biology and Bio-Therapeutic Drug Discovery

Emily Le Proust, Ph.D., CEO, **Twist Bioscience**

WSGR

1:15 pm SCIENTIFIC BRIEFINGS

INNOVATIVE TARGETING SOLUTIONS

How to Screen a Billion Drug Candidates? Single Cell Functional Assays: Ultra-sensitive, Ultra-fast, Ultra-high-throughput Next-Generation Drug Discovery

Improving the properties of antibody drug candidates targeting GPCRs is technically challenging since screens are optimally performed on the native functional receptor. We present data that using de novo mutagenesis coupled with single cell functional assays allows for the screening of billions of CDR optimized anti-GPCR variants for improved agonist or antagonist activities.

Michael Gallo, Ph.D., President, Research, **Innovative Targeting Solutions,** *Canada*

ttplabtech

High-Throughput Screening for Antibody Discovery Using Mirrorball

The antibody discovery industry has begun to set aside traditional assay formats such as ELISA or flow cytometry in favor of more sensitive, high-throughput technologies to screen for novel biologic candidates. This presentation will highlight a selection of multiplex assays for the screening of hybridoma supernatants enabling the discovery process.

Christyne Kane, Ph.D., Senior Scientist I, **AbbVie Global Biologics**

isogenica

Design, Build and Validation of Isogenica's Fully Synthetic Human Fab Library

We will present validation data on Isogenica's new fully synthetic human Fab library. Diverse heavy and light chain germlines, combined with the fully synthetic nature of the randomized CDR1, -2 and -3 regions ensure many issues with immune and naïve libraries can be overcome. Colibra™ DNA library technology minimizes the presence of CMC liability motifs.

Guy Hermans, Ph.D., Chief Scientific Officer, **Isogenica,** *United Kingdom*

1:45 pm SCIENTIFIC BRIEFINGS

TRIANNI

Exceptional Human Antibody Discovery with a Best-in-Class Transgenic Mouse

The Trianni Mouse is the only human transgenic antibody discovery platform offering a complete heavy, kappa and lambda repertoire in a single organism. Sequences of the variable domain exons are human while all genetic machinery including extensively optimized promoters and enhancers are of mouse origin. Titers and class switching are extremely robust making for highly efficient lead generation. This next-generation technology is seen as best-in-class by multiple Big Pharma and other licensees subsequent to extensive validation and benchmarking. Additional strains in development include Plasma Ig, Autoimmune/All Epitope and a "true" Bispecific.

David Meininger, Ph.D., Chief Business Officer, **Trianni, Inc.**

PROIMMUNE www.proimmune.com

An Integrated Approach to Managing Immunogenicity Risk and Drug Immune Modulation

Immunogenicity is one of the most complex issues to address in drug design and development. Integrated platforms such as, Mass Spectrometry antigen presentation assays; DC-T and T cell proliferation assays for biologic lead selection/ optimization; HLA-peptide binding assays to characterize individual epitopes and undiluted whole blood cytokine storm assays, can be used to mitigate immunogenicity risk and characterize immune responses directed toward biologics.

Jeremy Fry, D.Phil, Director of Sales, **ProImmune Ltd.,** *United Kingdom*

CRYSTAL BIOSCIENCE

HuMab Chickens: The Next Generation Antibody Discovery Platform

Transgenic rodents producing human sequence antibodies are widely accepted as a reliable source of therapeutic candidates. However, their repertoires are limited by their evolutionary similarity to humans. Crystal Bioscience has expanded the repertoire of transgenic animals by engineering HuMab chickens producing fully human sequence, high affinity mAbs. In addition to revealing novel epitopes and, therefore novel IP, the Crystal Platform yields mAbs recognizing murine orthologs of human antigens that facilitate pre-clinical studies.

Bill Harriman, Ph.D., Chief Science Officer, **Crystal Bioscience**

Track 1: OVERCOMING DELIVERY CHALLENGES INCLUDING BRAIN AND INTRACELLULAR TARGETS

2:25 **Co-Chairs Remarks**

Paul J. Carter, Ph.D., Senior Director and Staff Scientist, Antibody Engineering, **Genentech, Inc.**

Andreas Plückthun, Ph.D., Professor and Director, Department of Biochemistry, **University of Zürich,** *Switzerland*

2:30 **Enhancing Therapeutic Antibody Delivery across the BBB with Bispecific Antibodies Targeting TfR or CD98hc**

The use of therapeutic antibodies for the treatment of neurological diseases is limited by poor penetration across the blood-brain barrier (BBB). One way to improve brain uptake of large molecules is to take advantage of endogenous receptors that mediate transcellular transport at the BBB. We used bispecific antibodies targeting TfR or CD98hc, receptors enriched at the BBB, as a means of improving antibody delivery to the brain.

Jasi Atwal, Ph.D., Scientific Manager, Department of Neuroscience, **Genentech**

3:00 **Tissue Specific Delivery of Antibodies Via a Caveolae Associated Protein to Improve Drug Efficacy**

Upon vascular administration, bio-therapeutics become broadly distributed throughout the body with only a fraction of dosed drug reaching the intended organ or tissue target. By targeting caveolae associated proteins, we improve both the delivery and efficacy of therapeutics that act within the lungs while concurrently reducing unintended interactions in tissues not being targeted.

M. Jack Borrok, Ph.D., Scientist II, **Medimmune**

Track 2: NOVEL ANTIBODY DISPLAY, SELECTION AND SCREENING TECHNOLOGIES

2:25 **Chairman's Remarks**

Andrew Bradbury, M.D., Ph.D., Chief Scientific Officer, **Specifica**

2:30 **How Big Are Antibody Libraries Really? How Do We Improve Them? Are We Accessing the Full Diversity?**

In vitro antibody libraries have been used to generate antibodies against many different therapeutic lead targets. Theoretical and experimental analyses indicate that one would expect to select 1-3 antibodies from a 1e7 library. However, this does not appear to scale to larger libraries with diversities estimated to be >1 billion, suggesting either that libraries are less diverse than thought, or selection methods do not tap the full diversity. This talk will discuss the use of NGS to explore these issues and the application of NGS to the creation of improved antibody libraries.

Andrew Bradbury, M.D., Ph.D., Chief Scientific Officer, **Specifica**

3:00 **Improved Methods for Discovering and Developing Antibodies with High Specificity and Favorable Biophysical Properties**

There are many challenges associated with antibody discovery and development that require key technical advances to improve the rational and reliable generation of potent antibody therapeutics. I will discuss our progress in understanding and overcoming fundamental challenges related to the design and selection of antibodies with high affinity, specificity, stability and solubility.

Peter M. Tessier, Ph.D., Albert M. Mattocks Professor of Pharmaceutical Sciences and Chemical Engineering, Biointerfaces Institute, **University of Michigan**

Track 1: OVERCOMING DELIVERY CHALLENGES INCLUDING BRAIN AND INTRACELLULAR TARGETS *(continued)*

3:30 **Nanobodies as Inhaled Biotherapeutics for Lung Diseases, with ALX-0171 As Case Study**

Local pulmonary delivery of biotherapeutics may offer advantages for the treatment of lung diseases. Delivery of the therapeutic entity directly to the lung has the potential for a rapid onset of action, reduced systemic exposure and the need for a lower dose, as well as needleless administration. Nanobodies are well suited for inhaled delivery to the lung which will be illustrated by the specific example of ALX-0171, a Nanobody in clinical development for the treatment of respiratory syncytial virus (RSV) infections.

Diane Van Hoorick, Ph.D., Senior Project Leader, **Ablynx,** *Belgium*

4:00 *Networking Refreshment Break and Opening of Exhibit and Poster Hall*

4:45 **Comparing the Cytosolic Delivery Efficiency of Protein Uptake Systems**

A variety of transporters are being investigated for their capacity to shuttle macromolecular cargoes, especially proteins, into the cytosol. We recently developed the biotin ligase assay that allows the objective comparison of relative delivery efficiencies of various transport systems. Employing this assay, we have obtained novel insights into the protein transport capabilities of cell-penetrating peptides, supercharged proteins and bacterial toxins.

Wouter Verdurmen, Ph.D., Research Associate, Department of Biochemistry, **Radboud University Medical Center,** *The Netherlands*

5:15 **Intracellular Protein Delivery – Towards Artificial Immunotoxins**

Learning from natural evolution of viruses and protein toxins, potent intracellular delivery carriers were generated by a chemical evolution process. Sequence-defined carriers by automated solid phase-assisted synthesis combine natural and artificial amino acids with other transport elements, providing receptor-targeting and endosomal release function. Screening in proper systems identified carriers for biomacromolecules including cytotoxic proteins or nanobodies.

Ernst Wagner, Ph.D., Chair, Pharmaceutical Biotechnology, Center for System-based Drug Research, Center for Nanoscience, **Ludwig Maximilians University,** *Germany*

5:45 **Bacterial Secretion Systems for Intracellular Protein Delivery**

Bacterial Type III Secretion Systems are essential for infection by many different pathogens. They are megadalton-sized syringe-like, membrane-embedded 'injectisomes' and transport bacterial proteins (toxins) across membranes directly into a eukaryotic host cell. Here we will discuss the requirements for substrate association with, transport through and exit from the injectisome. This guided the design of substrates that either become trapped or translocated as antibody-like molecules directly into eukaryotic cells.

Thomas Marlovits, Ph.D., Professor for Structural and Systems Biology, Institute of Molecular Biotechnology, **Austrian Academy of Sciences (IMBA),** *Austria*

Track 2: NOVEL ANTIBODY DISPLAY, SELECTION AND SCREENING TECHNOLOGIES *(continued)*

3:30 **Engineering Alternative Scaffolds via Yeast Display**

The presentation will discuss combinatorial design and yeast display selection of a set of ~20 small protein scaffolds including the Gp2 domain. The impacts of scaffold topology, library design, and selection strategies will be discussed.

Benjamin Hackel, Ph.D., Assistant Professor, Chemical Engineering and Materials Science, **University of Minnesota**

4:00 *Networking Refreshment Break and Opening of Exhibit and Poster Hall*

4:45 **Detecting and Attacking Cancer Surface-omes with Recombinant Antibodies**

The cell surface proteome (surface-ome) is the primary hub for cells to communicate with the outside world. Oncogenes cause huge changes in cells and we hypothesize many will lead to changes in the cancer surface-ome. Our lab uses new proteomic technologies to systematically understand how cancer cells remodel their membrane proteomes and generates recombinant antibodies to detect and attack them.

James Wells, Ph.D., Professor, Pharmaceutical Chemistry, Harry and Dianna Hind Professor of Pharmaceutical Sciences, **UCSF**

5:15 **Programming Antibodies and Antigens Using Deep Sequencing-Enabled Protein Engineering**

Next-generation sequencing has presented protein scientists with the ability to observe entire populations of molecules before, during, and after a high-throughput screen or selection for function. My group leverages this unprecedented wealth of sequence-function information to design and engineer antibody affinity, specificity, and function. My talk will present an overview of the above and detail ways to integrate these technologies into typical antibody discovery workflows.

Tim Whitehead, Ph.D., Associate Professor, Chemical Engineering and Materials Science, **Michigan State University**

5:45 **Functional Interrogation and Mining of Natively Paired Heavy:Light Human Antibody Repertoires**

Here we present a simple technology for analyzing antigen specificity and affinity of millions of human B cells, and for rapid human antibody discovery. Natively paired antibody VH:VL amplicons are generated en masse from single B cell emulsions, cloned into an optimized yeast display platform, and functionally interrogated by FACS. Here we show the development of this new display platform and its application isolate HIV-1 broadly neutralizing antibodies from the B cell repertoire of an HIV-1 slow progressor, and also to discover nM-affinity antibodies targeting Ebola virus (EboV) glycoprotein that were elicited by a Phase 1 EboV vaccine clinical trial.

Brandon DeKosky, Ph.D., Assistant Professor, Chemical & Petroleum Engineering, Department of Pharmaceutical Chemistry, **The University of Kansas**

6:15 **OPENING NIGHT RECEPTION** with Exhibits and Poster Viewing

Please join your fellow attendees in the exhibit hall for an evening of networking while enjoying beverages, and hors d'oeuvres!

7:30 am SCIENTIFIC BREAKFAST BRIEFING

Computational Approaches for Assessing Developability and Optimization of Biotherapeutics

Protein surface hydrophobic patches can lead to aggregation, poor solubility, and cross-reactivity. We present methods where homology models of sets of antibodies and related biologics with their calculated hydrophobic patches and charge properties may be used to perform solubility predictions. Liability reduction and solubility optimization while maintaining affinity are discussed.

Nels Thorsteinson, Scientific Services Manager, Biologics, **Chemical Computing Group**

CHEMICAL COMPUTING GROUP

Track 1: ENGINEERING AND APPLICATION OF THERAPEUTIC ANTIBODIES FOR NEURODEGENERATIVE DISEASES

8:10 **Co-Chairs Remarks**

Anne Messer, Ph.D., Professor of Biomedical Sciences, University at Albany and Principal Investigator, Neural Stem Cell Institute, **Regenerative Research Foundation**

Cynthia A. Lemere, Ph.D., Associate Professor of Neurology, Ann Romney Center for Neurologic Diseases, **Brigham and Women's Hospital and Harvard Medical School**

James S. Huston, Ph.D., Chairman, **The Antibody Society;** Managing Member, **Huston BioConsulting, LLC**

8:15 **Delivery of Antibodies Across the Blood-brain Barrier Using MRI-guided Focused Ultrasound**

Focused ultrasound (FUS), in presence of intravenously administered microbubbles, can be used to modulate the permeability of the blood-brain and blood-spinal cord barrier locally and transiently. In rodent models of neurodegenerative diseases, FUS increased the bioavailability of antibodies to the central nervous system and treatment efficacy, reducing pathology, promoting regeneration and improving cognitive functions. The delivery of therapeutics using MRI-guided FUS holds promises for the treatment of neurological disorders.

Isabelle Aubert, Ph.D., Senior Scientist, Sunnybrook Research Institute and Professor, Department of Laboratory Medicine and Pathobiology, **University of Toronto,** *Canada*

8:45 **Combinatorial Immunotherapeutic Approaches for Synucleinopathies of the Aging Population**

Synucleinopathies of the aging population includes PD, DLB and AD and affects over 5 million in the US, the main pathological feature is the abnormal accumulation of alpha-synuclein that also triggers inflammation, myelin loss and neurodegeneration. Active and passive immunotherapeutic approaches targeting alpha-synuclein have been developed and are moving into clinical trials. Although selective antibodies against alpha-synucleinare effective, additional treatments are needed that reduce inflammation and potentiate the effects of antibodies. Combinatorial approaches harnessing T Reg cells or targeting inflammatory pathways might be helpful toward this goal. Results supporting the synergistic effects of immunomodulatory and anti-inflammatory therapies with vaccination against alpha-synuclein shows promise in the treatment of synucleinopathies.

Eliezer Masliah, M.D., Director, Division of Neurosciences, National Institutes of Aging, **NIH**

Track 2: ANTIBODY-DRUG CONJUGATES & FUSION PROTEINS

8:10 **Chairman's Remarks**

Gregory Adams, Ph.D., Chief Scientific Officer, **Eleven Biotherapeutics**

8:15 **Redox Selenium ADCs Improve Cancer Cell Monoclonal Antibody Cytotoxicity**

Currently there are ~ 30 FDA approved monoclonal antibodies (mAbs) for the treatment of various cancers. To improve the therapeutic efficacy of some mAbs; radioisotopes, drugs and other toxins have been attached to the mAbs, collectively called Antibody Drug Conjugates (ADCs). Most ADCs upon cell endocytosis require release of the drug from the mAb for the drug to be effective. With an understanding of endogenous redox oxidative stress inducing apoptosis in cancer cells, this laboratory has covalently attached redox selenium (Se) to targeting cancer mAbs. Such Se-labeled mAbs are shown to generate superoxide (O2.-) in vitro using a chemiluminescent assay and intracellularly using a dihydroethidium fluorescence assay. Toxicity of these Se-ADCs is time and dose dependent against cancer cells inducing oxidative stress within cells and apoptosis. Whereas some native mAbs may be relatively ineffective against cancer cell lines in vitro, Se-ADCs are often very cytotoxic against these same cancer cell lines. Triple Negative breast cancer (TNBC) cell lines are quite susceptible to Se-ADCs causing apoptosis. We believe this ADC redox Se approach to cancer therapy may be more beneficial over attempts to deliver toxic drugs as dead cancer cells from oxidative stress will not permit latter relapse from mAb or drug resistance.

Julian Spallholz, Ph.D., Professor, Nutritional Sciences, **Texas Tech University**

8:45 **Antibody-drug Conjugates for Treating Steroid-Resistant Malignancies and Autoimmune Diseases**

The occurrence of autoimmune reactions caused by immune checkpoint blockade in the treatment of cancer indicates the importance of the cross-disciplinary study of malignancy and autoimmune disease, which are two sides of the same coin. Although steroids have been commonly used for the treatment of malignancies and immune diseases, steroid resistance remains an unsolved problem, and therapeutic alternatives are clearly required. IL-7/IL-7R signaling, which physiologically regulates lymphocyte growth and survival, including antigen-responsive T lymphocyte selection, has been implicated in the development of malignancies and autoimmune diseases. However, the biological significance of IL-7/IL-7R signaling in steroid treatment is poorly understood. Here, we confirm the relationship between IL-7R signaling and steroid resistance in lymphoid malignancy and demonstrated the presence of steroid-resistant IL-7R-positive lymphocytes in mouse bone marrow and spleen following treatment with steroids. We further show that an anti-IL-7R antibody conjugated with SN-38 (A7R-ADC-SN-38) has strong anti-tumor effects against both parent and steroid-resistant cells. Although A7R-ADC-SN-38 efficiently eliminated IL-7R-positive cells, IL-7R-negative mature lymphocytes were preserved. Furthermore, an A7R-ADC conjugated to MMAE suppressed inflammation to a greater extent in a mouse autoimmune arthritis model than when it was conjugated to SN-38. This suggests that the cytotoxicity and immunosuppression of A7R-ADC could be modulated to address the individual types or activities of the malignancies or autoimmune diseases with an appropriate payload. Strong and specific elimination of enhanced IL-7R-positive cells, a common pathogenesis of both lymphoid malignancy and autoimmune disease, might prevent the development of malignancy or autoimmune disease in high-risk patients. Thus, A7R-ADC may be a promising strategy for treating malignancies and immune diseases, and may serve as a novel alternative to steroid therapy.

Masahiro Yasunaga, M.D., Ph.D., Unit Leader, Developmental Therapeutics, **National Cancer Center,** *Japan*

Track 1: ENGINEERING AND APPLICATION OF THERAPEUTIC ANTIBODIES FOR NEURODEGENERATIVE DISEASES *(continued)*

9:15 **Antibody Therapy for Alzheimer's Disease – Key Challenges**

Alzheimer's disease (AD) is characterized by the deposition of toxic protein aggregates in the brain, e.g. beta-amyloid peptides and tau proteins. Lowering such protein aggregates constitutes a major target for treatment and prevention of AD and related conditions. Enrolling subjects based on clinical criteria alone, however, may result in misclassification as evidenced by the relatively high percent of subjects negative on PET beta-amyloid scans in subgroups of two completed phase 3 studies. Consequently, novel study protocols were designed testing immunotherapy in subjects with proven beta-amyloid deposition in brain (Sevigny et al., Nature 2016). In addition, novel study protocols selected patients in earlier, even prodromal stages, e.g. PET beta-amyloid positive subjects with mild cognitive impairment (MCI) due to AD. Key challenges of immunotherapy include targeting the most relevant Aβ species, establishing a consistent dose-response, selecting the right timing and duration of the intervention, demonstrating a clinical / biomarker correlation and managing amyloid related imaging abnormalities (ARIA E/H). Novel imaging modalities using PET ligands allowing the assessment of amyloid and tau deposits along with advanced MRI measurements may help to identify the most suitable study population and to select appropriate biomarker and clinical endpoints for the monitoring of long-term outcome.

Christoph Hock, M.D., Professor and Director, Institute for Regenerative Medicine (IREM), **University of Zurich** and Co-Founder, **Neurimmune,** *Switzerland*

9:45 *Networking Refreshment Break, Exhibit and Poster Viewing*

10:30 **Treatment of Neuronal Pathology with Monoclonal Antibodies**

The notion that it is possible to treat pathology developing with neurons of the central nervous system by systemic administration of antibodies is quite new. One example of this approach is the attempt to prevent or reverse the development of neurofibrillary tangles in mouse models of Alzheimer's disease, and some successes have been reported. There are several ways in which this might work, although these are still all debatable.

Peter Davies, Ph.D., Scientific Director, Litwin-Zucker Center for Alzheimer's Disease and Memory Disorders, Feinstein Institute for Medical Research, **Northwell Health**

11:00 **Towards Development of Antibody Therapy for C9orf72 ALS/FTD**

We recently developed a BAC transgenic model of C9ORF72 ALS/FTD that develops key phenotypic and molecular features of the disease including decreased survival, paralysis, motor-neuron loss, anxiety-like behavior and cortical/hippocampal neurodegeneration. We will discuss preclinical immunotherapeutic approaches for this disease, including peripheral delivery of human antibodies that target the mutant RAN proteins in these mice.

Laura P.W. Ranum, Ph.D., Director, Center for NeuroGenetics, Kitzman Family Professor of Molecular Genetics and Microbiology, College of Medicine, **University of Florida**

11:30 **Altering APP Processing with a Proteolytic Diabody**

We engineered a bispecific tandem antibody fragment that has applications for treating AD and related neurodegenerative diseases by tailoring APP processing to promote neuroprotective processing while simultaneously inhibiting toxic amyloidogenic processing.

Michael Sierks, Ph.D., Professor, Chemical Engineering, **Arizona State University**

Track 2: ANTIBODY-DRUG CONJUGATES & FUSION PROTEINS *(continued)*

9:15 **Targeting Tumors and Their Vasculature with Antibody-drug Conjugates**

Targeting the tumor vasculature with antibody-drug conjugates (ADCs) is a promising anti-cancer strategy. We demonstrated an ADC-MMAE targeting CD276 destroyed CD276-positive cancer cells, but was ineffective against tumor vasculature. In contrast, pyrrolobenzodiazepine-conjugated CD276-ADC killed both cancer cells and tumor vasculature, eradicating large established tumors and metastases, and improving long-term overall survival. CD276 targeted dual-compartment ablation could aid in development of highly selective broad-acting anti-cancer therapies (Seaman S et al. Cancer Cell. 2017 Apr 10;31(4):501-515). Data for ADCs targeting other cancer-related molecules will be also discussed.

Dimiter Dimitrov, Ph.D., Senior Investigator, CCR, Cancer and Inflammation Program, NCI-Frederick, **NIH**

9:45 *Networking Refreshment Break, Exhibit and Poster Viewing*

10:30 **Novel Calicheamicin Antibody-Drug Conjugates**

Development and evaluation of the novel and stable calicheamicin antibody-drug conjugates will be presented. Emphasis will be made on the complexity of the correlation between in vitro cytotoxicity and in vivo efficacy. Impact of the linker structure and payload release mechanisms on the TI and overall toxicologic profile of ADCs will be discussed.

Julia Gavrilyuk, Ph.D., Principal Scientist, Discovery Chemistry, **Abbvie Stemcentrx**

11:00 **Small is Beautiful – Humabody® Drug Conjugates, HDCs a Real Alternative to ADCs**

Crescendo is developing a pipeline of novel multifunctional Humabody® therapeutics demonstrating excitingly differentiated efficacy compared with clinical mAbs. Optimally configured Humabody Drug Conjugates (HDCs) engage therapeutically valuable targets in a way that is different from whole antibodies, unlocking superior therapeutic index. Highly potent HDCs will play an important role in the next generation of targeted oncology therapeutics as a critical component of increasingly effective combination regimes.

Thomas Sandal, Vice President, R&D, **Crescendo Biologics Ltd.,** *United Kingdom*

11:30 **Late Breaking Presentation**

12:30 *Networking Luncheon, Exhibit and Poster Viewing*

12:00 pm SCIENTIFIC BRIEFINGS

intellicyt® A SARTORIUS COMPANY

A Novel High-Throughput Screening Platform for Identifying Optimal IgG Secreting Clones

Identification and selection of optimal clones that secrete high levels of antibody into the culture supernatant is critical to the cell line development process. This presentation, will highlight the use of the Cy-Clone PLUS System which is revolutionizing cell line development by enabling better decisions when ranking and selecting production clones by multiplexing critical productivity attributes in a single assay on a single platform.

Thomas Duensing, Ph.D., Chief Technology Officer, **IntelliCyt Corporation**

MaxCyte® FLOW TRANSFECTION

ABZENA Enabling better biopharmaceuticals

Optimization of Antibody Drug Conjugate in vivo Stability, Pharmacokinetics and Efficacy through Reagent Drug Design

By varying size, position and presence of a solubilising polymer and drug loading we have produced ADCs with different drug reagent architectures. Data highlighting reagent design, ADC production and systematic evaluation in vitro and in vivo using rodent pharmacokinetic and efficacy models will be presented to demonstrate critical impact of drug linker design on the in vivo properties of ADCs..

George Badescu, Ph.D., Vice President Scientific Affairs, **Abzena,** *United Kingdom*

1:45 pm SCIENTIFIC BRIEFINGS

geneious biologics

Scalable Sequence Data Analysis for Accelerated Precision Antibody Discovery

Next generation sequencing (NGS) technologies will, more than ever before, provide the ability to comprehensively characterize and evaluate the diversity and quality of antibody libraries, accelerating identification of potential drug candidates. However, NGS also necessitates software that can intelligently manage and process large volumes of sequence data together with masses of associated functional assay data.

Jannick Bendtsen, Ph.D., Vice President of Technology Services, **Geneious Biologics**

aldevron

ATUM

Build Better Biologics with Machine Learning and Synbio

ATUM (formerly DNA2.0) has pioneered the use of machine learning and synbio for wide ranging biotechnology applications. 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. 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.

Claes Gustafsson, Ph.D., Chief Commercial Officer, **ATUM**

Track 1: ROLE OF POST-TRANSLATIONAL MODIFICATION IN ANTIBODY FUNCTION

2:25 **Co-Chairs' Remarks**

Dennis R. Burton, Ph.D., Professor, Department of Immunology and Microbial Science, **The Scripps Research Institute**

Paul Parren, Ph.D., Professor, Department of Immunohematology and Blood Transfusion, **Leiden University Medical Center,** *The Netherlands*

2:30 **Integrative Mass Spectrometric Structural Analysis of Glycoprotein Therapeutics and Its Usage to Evaluate and Score Biosimilarity**

Biopharmaceutical products exhibit extensive structural micro-heterogeneity due to co-occurring post-translational modifications. These modifications affect their functionality and thus need to be characterized in detail. Here, we present an integrative approach, combining high-resolution native mass spectrometry and middle-down proteomics, to analyze this micro-heterogeneity. Taking mAbs and erythropoietin as model systems, we demonstrate an all-inclusive profiling of glycoproteins. We demonstrate the usage of a biosimilarity score to quantitatively assess structural similarities.

Albert J. R. Heck, Ph.D., Professor and Science Faculty, **Utrecht University,** *The Netherlands*

Track 2: ANTI-TUMOR ANTIGEN ANTIBODIES IN CANCER IMMUNOTHERAPY

2:25 **Chairman's Remarks**

K. Dane Wittrup, Ph.D., C.P. Dubbs Professor of Chemical Engineering and Biological Engineering, Koch Institute for Integrative Cancer Research, **Massachusetts Institute of Technology**

2:30 **Tumor Targeting Antibodies: Distinct Innate and Adaptive Immune Sensing**

Tumor cells express a panel of surface molecules to promote their growth and evade immune responses, such as oncogenic receptors. Tumor targeting antibodies have been designed to kill tumor cells. Several mechanisms have been proposed, including stress-induced apoptosis, antibody-dependent cytotoxicity, complement dependent cytotoxicity, and increased phagocytosis. We have now observed that anti-tumor antibodies-mediated tumor regression depends on distinct innate sensing pathway. Therefore, our studies have now revealed a distinct mechanism for antibody-mediated tumor regression that include different innate sensing and adaptive pathways and open new avenue for combinational therapies with other conventional drugs and immunotherapy.

Yang-Xin Fu, M.D., Ph.D., Professor of Pathology, Mary Nell and Ralph B. Rogers Professorship in Immunology, **UT Southwestern**

Track 1: ROLE OF POST-TRANSLATIONAL MODIFICATION IN ANTIBODY FUNCTION *(continued)*

3:00 **Post-translational Modification of Antibodies in Rheumatoid Arthritis**

Rheumatoid Arthritis (RA) is an autoimmune disease characterized by inflammation of the joints. Sera of around 60% of the RA patients contain autoantibodies, such as rheumatoid factor and antibodies that target proteins that have been post-translationally modified by citrullination and carbamylation. Interestingly, antibodies can also be post-translationally modified. The presentation will focus on carbamylation and glycosylation of antibodies in RA.

Leendert A. Trouw Ph.D., Associate Professor, Department of Immunohematology and Bloodtransfusion, **Leiden University Medical Center,** *Leiden, The Netherlands*

3:30 **Regulation of Autoantibody Activity by the IL-23–TH17 Axis and Its Impact on Autoimmune Disease**

Our recent data show that the IL-23–TH17 axis controls the intrinsic inflammatory activity of autoantibodies and thereby triggers the clinical onset of autoimmune arthritis in mice and humans suffering from rheumatoid arthritis. TH17 cells regulate expression of sialyltransferases in newly differentiating antibody-producing cells and determine the glycosylation profile and activity of immunoglobulin G (IgG) that is produced by the consecutively emerging plasma cells.

Gerhard Krönke, M.D., Professor of Translational Immunology, Department of Internal Medicine 3, Institute of Rheumatology and Immunology, **University of Erlangen,** *Germany*

4:00 *Networking Refreshment Break, Exhibit and Poster Viewing*

4:45 **Diversification of Antibody Effector Function**

Antibodies produced in response to a foreign antigen are characterized by polyclonality, not only in the diverse epitopes to which their variable domains bind but also in the various effector molecules to which their constant regions (Fc domains) engage. Thus, while Fab-antigen interactions are crucial to the specificity of the antibody response, there is a crucial role for the Fc domain in mediating the diverse effector properties triggered by antigen recognition, even for processes traditionally attributed solely to recognition by the Fab, such as neutralization of toxins and viruses. Specific interactions of the IgG Fc domain with distinct receptors expressed by diverse immune cell types result in the pleiotropic effector functions for IgG, including the clearance of pathogens and toxins, lysis and removal of infected or malignant cells, modulation of the innate and adaptive branches of immunity to shape an immune response, and initiation of anti-inflammatory pathways that actively suppress immunity. The Fc domain mediates these diverse effector activities by engaging two distinct classes of Fc receptors (type I and type II) on the basis of the distinct conformational states that the Fc domain may adopt. These conformational states are regulated by the differences among antibody subclasses in their amino acid sequence and by the complex, biantennary Fc-associated N-linked glycan. I will discuss the diverse downstream proinflammatory, anti-inflammatory and immunomodulatory consequences of the engagement of type I and type II Fc receptors in the context of infectious, autoimmune, and neoplastic disorders.

Jeffrey Ravetch, Ph.D., Professor, Laboratory of Molecular Genetics and Immunology, **Rockefeller University**

5:15 **Biochemical Stability of the Clinical-stage Antibody Landscape**

Poor biophysical properties of antibodies can often lead to stability related issues during their development. Similarly, antibodies with chemically labile sites can present development challenges from degradation, loss of function to immunogenicity. Here we present data from characterization of ~140 clinical stage antibodies, by forced chemical degradation, for detection of chemically unstable sites, including Met oxidation, Asp isomerization and Asn deamidation.

Yingda Xu, Ph.D., Director, Protein Analytics, **Adimab**

5:45 **Sulfation of Broadly Neutralizing HIV Antibodies**

Tyrosine sulfation is a critical posttranslational modification in two of the human mAb classes targeting HIV Env co-receptor binding site and the V2 apex site. The sulfation pattern in co-receptor binding site mAbs allows them to interact with gp120 that mimic CCR5 chemokine receptor binding. The V2 apex bnAbs possess sulfated tyrosines in their CDRH3 loops that enable them to interact with Env V2 apex bnAb epitope in germline Ab configuration. The examples illustrate how tyrosine sulfation of human Abs contributes to antigen recognition on the surface of pathogens.

Raiees Andrabi, Ph.D., Research Associate, Burton Lab, **The Scripps Research Institute**

Track 2: ANTI-TUMOR ANTIGEN ANTIBODIES IN CANCER IMMUNOTHERAPY *(continued)*

3:00 **Innate and Adaptive Integrin-targeted Combination Immunotherapy**

We developed an engineered integrin-binding peptide-Fc fusion that recruits immune cell effector functions to tumors. The co-administration of the peptide-Fc fusion and an immune modulator, such as a checkpoint blockade inhibitor, results in significant control of tumor growth by invoking innate and adaptive arms of the immune system.

Jennifer R. Cochran, Ph.D., Co-Founder and Director, **Nodus Therapeutics**

3:30 **Cetuximab and Therapeutic T-cell Response**

Robert L. Ferris, M.D., Ph.D.., Hillman Professor of Oncology and Director, **UPMC Hillman Cancer Center**

4:00 *Networking Refreshment Break, Exhibit and Poster Viewing*

4:45 **NK Cell Engagement with TriNKETs™**

Ann Cheung, Ph.D., Director of Biology, **Dragonfly Therapeutics**

5:15 **Targeting Cell Surface Chaperone in Cancer Therapy**

Molecular chaperones are emerging as novel targets for immunotherapy. Under pathological conditions, Glucose Regulated Protein GRP78 (HSPA5/BiP) can relocalize to the cell surface where it exerts control over survival and invasiveness. The preferential expression of GRP78 on the surface of tumor cells but not normal organs in vivo enables antibody-based theranostics. This approach may be particularly relevant in targeting aggressive and resistant tumors which exhibit elevated levels of cell surface GRP78.

Amy S. Lee, Ph.D., Associate Director for Basic Research, **USC Norris** Comprehensive Norris Cancer Center and Professor of Biochemistry and Molecular Biology, Keck School of Medicine, **University of Southern California**

5:45 **Investigating the Basis for Efficacy and Resistance to Tumor Immunotherapy**

The reasons why some tumors respond to immunotherapy while others resist are incompletely understood. Applying mass cytometry and novel informatics tools to investigate these questions in mice, we discovered that effective immunotherapy requires a coordinated system-wide immune response involving multiple immune cell types. The results also reveal a critical role for CD4 T effector-memory cells and demonstrate how one mechanism of resistance can develop. The methods we developed for these studies can be used to analyze the effects of any disease or intervention on the immune system.

Edgar G. Engleman, M.D., Professor of Pathology and Medicine, **Stanford University School of Medicine,** Medical Director, **Stanford Blood Center**

6:15 **WEDNESDAY RECEPTION**
with Exhibits and Poster Viewing

The first half of the conference may have flown by, but the fun is just getting started! Enjoy another opportunity to interact with fellow industry professionals while enjoying cocktails and appetizers!

Track 1: BIOLOGICAL IMPACT OF Fc RECEPTOR ENGAGEMENT

8:10 **Co-Chairs' Remarks**

Trudi Veldman Ph.D., Senior Director Biologics, **AbbVie Bioresearch Center**

Chung-Ming Hsieh, Executive Director, Biologics Discovery Boston, **Merck Research Laboratories**

8:15 **SKY59: Novel Recycling Antibody against C5 with Improved Pharmacokinetics for the Treatment of Complement-mediated Diseases**

We generated a novel humanized antibody against C5, SKY59, which has long-lasting neutralization of C5. SKY59 has pH-dependent C5 binding for antibody recycling, and enhanced FcRn binding for PK prolongation without rheumatoid factor (RF) binding.

Kenta Haraya, Ph.D., Scientist, Research Division, Biologics Discovery, **Chugai Pharmaceutical Co Ltd.,** *Japan*

8:45 **Selective FcγR Engagement by Agonistic Anti-CD40 Abs**

The engagement of Fcγ Receptors (FcγRs) is required for the in vivo agonistic activity of anti-CD40 immunostimulatory Abs. I will describe the effect of different human FcγRs on the antitumor activity of anti-CD40 human antibodies and how we exploit this knowledge for selection of optimized next-generation Fc-engineered agonistic CD40 Ab.

Rony Dahan, Ph.D., Principal Investigator, Department of Immunology, **Weizmann Institute of Science,** *Israel*

9:15 **Potent Antitumor Activity of IL2-Fc Requires Fc-mediated Depletion of Tregs**

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 antitumor activity. Our results outline mechanisms of action and provide important guidance for the development of next generation cytokine therapeutics.

Daniel Christ, Ph.D., Associate Professor, Director Centre for Targeted Therapy, **Garvan Institute of Medical Research,** *Australia*

9:45 *Networking Refreshment Break, Exhibit and Poster Viewing*

Track 2: ANTIBODY BASED INNOVATIONS IN THE TUMOR MICROENVIRONMENT I

8:10 **Chairwoman's Remarks**

Kerry A. Chester, Ph.D., Professor of Molecular Medicine, UCL Cancer Institute, **University College London,** *United Kingdom*

8:15 **Strategies to Overcome Immune-inhibition in Childhood Solid Cancers**

Immune evasion is a hallmark of cancer, and the solid tumour microenvironment imposes a particularly hostile microenvironment to the immunotherapeutic function of effector cells. Whilst checkpoint inhibition has been a very successful strategy to overcome immune evasion in some cancers with high mutational load, solid cancers lacking strong adaptive immune responses are yet to be shown as sensitive to existing immune modulators. Paediatric cancers largely arise following acquisition of small numbers of mutations during development. Approaches to successful immunotherapy here are likely to require combination approaches of active immunity to target cell surface antigens, and agents to reverse immune evasion.

John Anderson, Ph.D., GOSHCC Professor of Experimental Paediatric Oncology and Honorary Consultant Oncologist, **UCL Great Ormond Street Institute of Child Health,** *United Kingdom*

8:45 **Co-stimulation of Immune Cells in the Tumor Microenvironment via Bispecific DART® and TRIDENT™ Molecules**

Agents that influence immune recognition and elimination of malignant tumor cells generally fall into two classes: those that antagonize immune inhibitory pathways (checkpoint inhibitors) and those that induce immune stimulatory pathways. A limitation of the either mechanism is unwanted immune effects on normal tissues. It is thus highly desirable to limit the immune modulatory activity to the tumor site, while sparing effects on normal cells. To accomplish this in the immune stimulatory context, we have generated bispecific molecules using our Fc-bearing DART and TRIDENT platforms that combine a tumor-specific recognition unit (anti-HER2, EphA2 or other tumor-associated antigen) with a T-cell costimulatory molecule binder (anti-CD137 or other) such that the agonistic activity of the latter is dependent on tumor recognition by the former. In this way not only the tissue localization, but also the agonistic activity, is rendered tumor-dependent, as triggering of the costimulatory molecule by the DART or TRIDENT proteins requires aggregation via tumor target engagement. An optimal level of tumor dependent T-cell agonistic activity was achieved by varying the relative position and valence of each binding site in the molecule. This was easily accomplished within the degrees of variation afforded by the DART/TRIDENT architecture. A case study on the data-driven process for one such molecule will be presented, on this process leading to both a clinical candidate as well as a "plug-and-play" format for facile integration with other tumor antigens. Aspects such as manufacturability, stability and PK will also be addressed.

Syd Johnson, Ph.D., Vice President, Antibody Engineering, **MacroGenics**

9:15 **Improved Cancer Immunotherapy by a CD25-mimobody Conferring Selectivity to Human Interleukin-2**

We addressed the most relevant shortcomings associated to IL-2 immunotherapy with the generation of a specific anti-hIL-2 antibody, termed NARA1. In vitro data showed that NARA1 efficiently blocks the CD25 binding site of hIL-2 acting as a high affinity CD25-mimobody. This resulted in selective stimulation of cytotoxic CD8+ T cells and natural killer cells while keeping low the levels of immunosuppressive Tregs leading to potent anti-tumor responses.

Natalia Arenas Ramirez, Ph.D., Post-doctoral Researcher, Department of Immunology, **University Hospital Zurich,** *Switzerland*

9:45 *Networking Refreshment Break, Exhibit and Poster Viewing*

10:30 **ProTIA – Bispecific T Cell Engagers Designed for**

Track 1: BIOLOGICAL IMPACT OF Fc RECEPTOR ENGAGEMENT *(continued)*

10:30 **Antibody Optimization for Treg Depletion in Cancer Therapy**

Modulation of the anti-tumor immune response with antibodies targeting co-inhibitory and co-stimulatory molecules is a promising strategy in cancer therapy. In some cases, the effectiveness of these antibodies is not limited to receptor activation or blockade and also relies on depletion of regulatory T cells (Treg). Characterizing the expression density of these targets in different T cell compartments and the myeloid cells involved in Treg depletion is therefore paramount for the design of the next generation of immune-modulatory antibodies.

Frederick Arce Vargas, M.D. Ph.D., Research Associate, **University College London Cancer Institute,** *United Kingdom*

11:00 **Novel Effector Function Attenuating Mutations That Maintain Antibody Stability and Reduce Toxicity**

Successful pre-clinical antibody development requires that the molecular properties of therapeutic candidates translate from pre-clinical animal models to humans. For many therapeutic antibodies cytotoxic effector functions can be undesirable, creating safety liabilities by activating native host immune defenses against cells expressing the target antigens. Much research on the attenuation of effector function has focused on ADCC activities of human antibodies as mediated through modifications of the Fc region of the antibody, however, it remains largely unknown how such changes might translate in the context of a murine antibody in mouse models where most therapeutics are validated. We demonstrate that several commonly used variants, which are efficacious in attenuating effector function in primates, retain potent complement activation capacity in mice that can lead to safety liabilities. Here, we describe a novel combination of residue variants that eliminates complement binding and fixation as well as Fcγ dependent antibody-dependent cell-mediated cytotoxicity (ADCC) in both murine IgG2a and human IgG1 - in contrast to the results with aglycosylated antibodies - allowing more accurate translation between experiments in mice and primates. We further demonstrate that both human and murine antibodies containing these variants have typical pharmacokinetics in rodents and retain thermostability. This stability allows for efficient knobs-into-holes bispecific antibody production and a robust path to generating highly effector-attenuated bispecific antibodies for preclinical studies.

James A. Ernst, Ph.D., Senior Scientist & Group Leader, Department of Protein Sciences, **Genentech**

11:30 **Novel Engineered Fcs for Improved Half-life Extension and for Highly Selective Engagement of a Single Fcγ receptors or C1q**

This presentation will outline several recent advances from our lab on: (i) The engineering of novel Fc domains that impart very long antibody pharmacokinetics; (2) in vitro and in vivo function of antibodies that only activate complement without stimulating signaling via Fcγ receptors; (3) the biology and the therapeutic impact of FCRL receptors.

George Georgiou, Ph.D., Professor, Laura Jennings Turner Chair in Engineering, Department of Chemical Engineering, **The University of Texas at Austin**

Track 2: ANTIBODY BASED INNOVATIONS IN THE TUMOR MICROENVIRONMENT I *(continued)*

Local Activation in the Tumor Environment

Amunix is developing bispecific T cell engagers based on our proprietary ProTIA (Protease Triggered Immune Activator) platform. ProTIA therapeutics combine multiple mechanisms to widen the therapeutic window: 1) binding to a tumor antigen, 2) proteolytic activation in the tumor environment by tumor-associated proteases, 3) polymer targeting (EPR effect) due to an attached XTEN protein polymer. Most tumor-specific antibodies can be rapidly converted into ProTIA format that enables rapid microbial production as single protein chain. Amunix is currently developing ProTIA molecules against a variety of solid tumor targets. Our lead program AMX-168 is expected to enter clinical development in 2018.ProTIA molecules are based on Amunix' proprietary XTEN™ polymer technology which has been validated in hundreds of patients and through partnerships with companies such as Biogen, Lilly, Roche, Janssen, Genentech, and Versartis.

Volker Schellenberger, Ph.D., CEO and President, **Amunix**

11:00 **Combining Bi-specific Antibodies and Oncolytic Virus Therapy**

Bi-specific antibody has shown great promise in treatment of cancers. However, its efficacy for solid tumors is significantly limited by its short half-life and suboptimal tumor penetration. In addition, even low levels of tissue expression of tumor associated antigens (TAAs) on normal tissues can be recognized and targeted by bi-specific antibodies leading to deleterious toxicity. Here we described a new strategy to deliver bi-specific antibodies to solid tumors. Oncolytic vaccinia virus has been genetically modified to encode secretory bi-specific T-cell engagers (single chain variable fragment) that bind both to CD3 and to a tumor cell surface antigen. Bi-specific T-cell engager-armed oncolytic vaccinia virus (TEA-VV) exerts its activity through three mechanisms: i) VVs directly lyse tumor cells, ii) TE directs T cells to kill tumor cells that are not infected with VV (by-stander killing), and iii) TE promotes T-cell infiltration into tumors, and the cytokines released upon activation will create a pro-inflammatory microenvironment inhibiting tumor growth. In addition, TEA-VV's strategy provides a unique and effective approach with the ability of inducing local production of bi-specific antibodies that allows higher concentrations within the tumor tissue while reducing systemic side effects that are caused by BiTE.

Shautong Song, M.D., Ph.D., Chief Executive Officer, **Icell Kealex Therapeutics**

11:30 **Anti-tumor Antibodies Contribute to a Localized Cytokine Storm in the Tumor Microenvironment**

Classic monoclonal antibodies against anti-tumor associated antigens such as EGFR, CD20, and Her2 synergize with immune oncology therapies such as anti-PD-1 antibodies. One mechanism of action is the vaccinal effect by which anti-TAA antibodies deliver tumor debris to antigen presenting cells for cross presentation. A less well appreciated contribution is through the repolarization of the tumor microenvironment to a more inflammatory state, with significant increases in chemokines and cytokines.

K. Dane Wittrup, Ph.D., C.P. Dubbs Professor of Chemical Engineering and Biological Engineering, Koch Institute for Integrative Cancer Research, **Massachusetts Institute of Technology**

12:00 pm SCIENTIFIC BRIEFINGS

applied biomath
revolutionizing drug invention

Model Aided Drug Invention (MADI) Case Studies: Quantitative Modeling and Simulation Approaches Driving Critical Decisions from Research through Clinical Trials

MADI is a mathematical modeling and engineering approach to translational medicine leveraging mechanistic PKPD and Systems Pharmacology. It quantitatively integrates knowledge about therapeutics with an understanding of mechanism of action in the context of human disease mechanisms. We will show how MADI impacts biological understanding, new target proposals, lead generation, clinical candidate selection, IND support, and clinical go/no go decisions.

John Burke, Ph.D., Co-Founder, President, and CEO, **Applied BioMath, LLC**

morphotek

RESPECT™ (REsidue-SPEcific Conjugation Technology): Site-Specific Conjugation to Lysines in IgG by Microbial Transglutaminase

Morphotek's REsidue SPEcific Conjugation Technology (RESPECT™) is a transglutaminase-based conjugation technology that targets specific lysine residues in IgG. Whereas other enzymatic-based conjugation techniques require extensive antibody modification by either deglycosylation or addition of multiple-amino acid enzyme-recognition tags, RESPECT™ requires just a single amino acid addition or substitution to efficiently produce homogeneous site-specific antibody conjugates.

Jared Spidel, Ph.D., Principal Scientist, Antibody Core Development, **Morphotek**

SGI-DNA
A Synthetic Genomics, Inc. Company

Automated Antibody Library Construction Using the BioXp™ 3200 System

Building variant libraries continues to be a highly specialized process and is often outsourced to service labs, which are expensive, have long lead times, and vary in quality. Here, we describe the capability of the BioXp™ 3200 System, the world's first DNA printer, which allows hands-free, rapid antibody library construction, enabling researchers to engineer antibody segments and introduce mutations for functional studies.

Kurt Klimpel, Ph.D., Field Application Specialist, Product Development, **SGI-DNA**

12:30 *Networking Luncheon, Last Chance for Exhibit and Poster Viewing*

Track 1: NOVEL THERAPEUTIC INDICATIONS FOR ANTIBODIES

2:10 **Chairman's Remarks**
James Larrick, M.D., Ph.D., Managing Director and Chief Medical Officer, **Panorama Research Institute and Velocity Pharmaceutical Development**

2:15 **Therapeutic Antibodies That Silence B cells by Emulating Peripheral Immune Tolerance**

B cell-targeted therapies whose effects are mediated by B cell depletion have proven efficacious in a variety of autoimmune settings, but have substantial risks due to long-term compromise of adaptive immunity. Here we describe an alternative, non-B cell depleting approach, which employs emasculated antibodies directed against antigen receptor components to induce a reversible state of anergy. This approach has proven effecting in treatment of mouse models of type 1 diabetes, lupus and rheumatoid arthritis.

John Cambier Ph.D., Distinguished Professor and Chair, Department of Immunology and Microbiology, **University of Colorado SOM**

2:45 **PTPα Antibody for Fibrotic Diseases**

Idiopathic pulmonary fibrosis (IPF) is a chronic fatal lung disease with rapid, progressive loss of pulmonary function. TGF-β can induce fibroblast differentiation and is fundamental to the pathogenesis of pulmonary fibrosis. Protein tyrosine phosphatase α (PTP-α) has been shown to be a key regulator of the TGF-β-mediated fibrotic process in animal models of IPF. We have developed an antibody that binds to the extracellular domain of PTP-α to block pro-fibrotic signaling.

Bo Yu, Ph.D., Co-founder and Chief Scientific Officer, **Larix Bioscience LLC**

3:15 **Targeting APOC3 with a Therapeutic Antibody to Reduce Triglycerides and Risk of Coronary Artery Disease**

Despite aggressive LDL cholesterol reduction, substantial residual risk of coronary heart disease remains. APOC3 is a highly genetically validated therapeutic target for hypertriglyceridemia and cardiovascular disease. We generated a series of monoclonal antibodies, engineered them to extend their half-life, and showed that they markedly reduce triglycerides in a humanized mouse model. Targeting APOC3 with an antibody is an orthogonal approach to reducing LDL cholesterol in addressing residual risk of coronary disease.

Daniel J. Rader, M.D., Seymour Gray Professor of Molecular Medicine, Perelman School of Medicine, **University of Pennsylvania**

3:45 *Networking Refreshment Break*

Track 2: ANTIBODY BASED INNOVATIONS IN THE TUMOR MICROENVIRONMENT II

2:10 **Chairwoman's Remarks**
Janine Schuurman, Ph.D., Vice President, Research, **Genmab,** *The Netherlands*

2:15 **RNA Cancer Vaccination and Immunomodulatory Antibodies – Insights from Preclinical Research and Clinical Testing**

In vitro transcribed RNA technology is a tool for engineering cancer targeting antibodies as well as for inducing antibody responses by vaccination. In this presentation, I will focus on BioNTech's preclinical and clinical efforts to generate T- as well as B-cell responses. Moreover, I will discuss data on combination of cancer RNA vaccination with immunomodulatory antibodies.

Sebastian Kreiter, M.D., Vice President, Immunotherapy & Preclinical Research, **BioNTech RNA Pharmaceuticals,** *Germany*

2:45 **Imaging to Trace Immunogenic Cell Maturation: Understanding Tumor Microenvironment**
Edward Roberts, Ph.D., Scientist, **UCSF**

3:15 **Harnessing Fc Gamma Receptor Biology to Optimize Antibodies Targeting TNFR Superfamily Members**

Fc region choice can define the mechanism of action associated with many TNFR superfamily (SF) agonist antibodies. The presentation will cover our recent novel findings in the field of Fc receptor biology and its application to antibodies targeting TNFRSF members. Opportunities to translate lessons learnt into design strategies to more optimally modulate TNFRSF members will also be covered. Emerging data on the role of Fc biology to modulate non-TNFSF receptors will also be discussed.

Nick Wilson, Ph.D., Executive Director of Immuno-modulatory Drug Discovery, **Agenus**

3:45 *Networking Refreshment Break*

Track 1: NOVEL THERAPEUTIC INDICATIONS FOR ANTIBODIES *(continued)*

4:15 **Reversal of Acute Type 1 Diabetes with An Anti-TLR4/MD-2 Monoclonal Antibody**

We have reversed new onset type 1 diabetes (T1D) (hyperglycemia, polyuria and weight loss) in nonobese diabetic (NOD) mice by treatment with an agonistic TLR4/MD-2 specific monoclonal antibody ("TLR4-Ab"). 90% of mice treated with TLR4-Ab showed a clinical response (delay in progression to endstage T1D) and 70% have permanent reversal of T1D. Successfully treated mice demonstrate decreased islet inflammation and preserved insulin staining of islet beta cells. Although TLR4-Ab does not stimulate T cells directly, immune tolerance can be restored to the adaptive immune system by this treatment. The TLR4/MD-2 pathway is a promising new therapeutic approach for treating autoimmunity.

William Ridgway, M.D., Alice W. and Mark A. Brown Professor and Director, Division of Immunology, Allergy and Rheumatology, **University of Cincinnati College of Medicine**

4:45 **Action of Bispecific Anti-FGFR1/βKlotho Antibody in Obese Mice and Humans**

FGF21 analogs belong to an emerging class of therapeutic candidates for type 2 diabetes and fatty liver disease. We have engineered bispecific anti-FGFR1/βKlotho agonist antibody that acts as a long-acting FGF21-mimetic. I will present the mechanism of antibody action, together with the results from the first-in-human study performed with obese human subjects.

Junichiro Sonoda, Ph.D., Senior Scientist, Cancer Immunology, **Genentech, Inc.**

5:15 **Late Breaking Presentation**

Track 2: ANTIBODY BASED INNOVATIONS IN THE TUMOR MICROENVIRONMENT II *(continued)*

4:15 **Daratumumab, An IgG1 CD38 Antibody, Reduces Immune Suppressive Cells and Promotes An Adaptive Immune Response in Multiple Myeloma: Potential for Application in Solid Tumors**

Daratumumab (Darzalex™), a CD38 antibody approved for treatment of relapsed/refractory myeloma, demonstrated impressive clinical response rates and improved progression free and overall survival in patients treated with this therapy. Correlative studies revealed that along with rapid tumor cell reduction, Daratumumab is also able to significantly reduce CD38+ immune suppressive cells that are prevalent in the tumor microenvironment and contribute to progressive immune dysfunction. Regulatory B cells (Bregs) and myeloid derived suppressor cells (MDSC) express CD38 at high levels, as do a subpopulation of regulatory T cells (Tregs). These CD38+ immune suppressive cells were susceptible to Daratumumab in vitro, and patients treated with Daratumumab exhibited a marked reduction in theses cell types. In parallel, Daratumumab promoted an expansion of CD8+ cytotoxic T cells, and a significant increase in T cell repertoire (TCR) clonality. These data suggest that Daratumumab may have broad immune modulatory activity within the tumor microenvironment, through targeting of CD38+ immune suppressive cellular populations and increasing adaptive immune responses. This mechanism of action may expand the potential application of Daratumumab beyond myeloma therapy, and is currently being investigated in translational and clinical studies.

Kate Sasser, Ph.D., Vice President, Head of Oncology Translational Research**, Janssen**

4:45 **Target Expression, Generation, Mechanism of Action, Preclinical Activity and Pharmacokinetics of EM801, an IgG-based BCMA T-cell Bispecific Antibody for the Treatment of Multiple Myeloma**

We assessed BCMA as target for T-cell immunotherapy and generated/evaluated the BCMA-TCB EM801 for treatment of multiple myeloma, a malignant plasma cell disease. We identified BCMA as excellent target, including high-risk/refractory patients. EM801 shows high single agent activity, even in heavily-pretreated patients, without significant toxicity. Together with a weekly administration schedule, EM801 appears as attractive non-cross-resistant compound with high potential for single agent, combination, or long-term maintenance treatment in myeloma.

Dr. Dirk Hose, Head, Multiple Myeloma Research Laboratory, Department of Internal Medicine V, **Heidelberg University,** *Germany*

5:15 **An EGFR-targeting Probody™ T cell-engaging Bispecific Induces Tumor Regressions While Reducing On-target Toxicities in Preclinical Studies**

In the tumor microenvironment, protease activity is highly dysregulated, enabling tumor cell migration, invasion and metastasis, while in normal tissues, proteases are tightly controlled. By exploiting this differential, we have engineered a protease-activatable Probody T cell-engaging bispecific (Pb-TCB) targeting EGFR that effectively regresses tumors in mice and significantly reduces EGFR-dependent, and immune-mediated, toxicities in healthy tissues of cynomolgus monkeys. By localizing their activity to the tumor microenvironment, Probody TCBs have the potential to expand the target landscape for this potent modality in solid tumors.

Bryan Irving, Ph.D., Vice President, Cancer Immunology, **CytomX Therapeutics**

5:45 pm-6:45 pm SPECIAL SESSION OF THE ANTIBODY SOCIETY

Moderator: **Janice M. Reichert, Ph.D.,** Executive Director, **The Antibody Society;** Editor-in-Chief, **mAbs;** Managing Director, **Reichert Biotechnology Consulting LLC**

Antibodies to Watch in 2018 and Society Updates

Dr. Reichert will provide an overview of the antibody therapeutics granted first approvals in 2017, as well as antibodies likely to move to regulatory review in 2018 and those in late-stage clinical studies. New data on development metrics for antibodies, including clinical success rates, will be presented. Dr. Parren will discuss the Society's INN initiative, and other ongoing programs.

Janice M. Reichert, Ph.D., Executive Director, **The Antibody Society;** Editor-in-Chief, **mAbs;** Managing Director, **Reichert Biotechnology Consulting LLC**

Paul Parren, Ph.D., Professor, Department of Immunohematology and Blood Transfusion, **Leiden University Medical Center,** *The Netherlands*

The Antibody Society www.antibodysociety.org

The Antibody Society is an international, non-profit business association representing individuals and organizations involved in antibody research and development. We are an authoritative source of information about antibody therapeutics development, which we disseminate via our website, presentations and publications. The Society organizes and supports conferences on topics related to antibody research and development, and we engage with government and international agencies to discuss issues of importance to the antibody community.

Track 1: NOVEL ENGINEERING STRATEGIES TO ENHANCE ANTIBODY FUNCTIONS

8:25 **Chairman's Remarks**

Paul J. Carter, Ph.D., Senior Director and Staff Scientist, Antibody Engineering, **Genentech, Inc.**

8:30 **Agonizing the TNFR Superfamily for Cancer Immunotherapy**

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.

Greg Lazar, Ph.D., Director and Senior Scientist, Antibody Engineering Department, **Genentech**

9:00 **Isoelectric Point Engineering to Enhance the Potency of pH Dependent Antigen Binding Antibody**

Previously, isoelectric point engineering was used to improve pharmacokinetics and physicochemical property of antibody therapeutic. We found that isoelectric point engineering in variable region and constant region can applied to enhance the potency of pH dependent antigen binding antibody. Case study will be presented.

Taichi Kuramochi, Research Scientist, **Chugai Pharmabody Research Pte. Ltd.,** *Singapore*

9:30 **Adapted Fc-glycan Changes for Enhanced ADCC and/or CDC**

Glycosylation of the immunoglobulin G (IgG)-Fc tail is required for binding to Fc-gamma receptors (FcγRs) and complement-component C1q. Here we show that the not only afucosylated IgG1 antibodies, but more prominent combination of afucosylation and hypergalactosylation increases FcγRIIIa and FcγRIIIb by ~20-fold on top of the ~17-fold achieved by afucosylation alone. This increased binding is accompanied with similarly enhanced ADCC. On top of this, we convincingly show that elevated galactosylation also increased C1q-binding and downstream complement opsonization and CDC. In conclusion, antibodies can be tailored by natural glycan changes to have either enhanced CDC or ADCC, or both.

Gestur Vidarsson, Ph.D., Head of Immunoglobulin Research/PI, Experimental Immunohematology, **Sanquin Research,** *The Netherlands*

10:00 *Networking Refreshment Break*

10:30 **From Format to Function - Engineering Transformative Antibodies**

Bi- and multispecific antibodies enable the exploration of new biological concepts and treatment strategies. Within Roche such next generation biologics have found broad application prospects in onco-immunological and anti-inflammatory approaches. But their use goes far beyond these established applications to convey unique mode of actions. The CrossMAb technology has proven to be very versatile, allowing the generation of various bispecific antibody formats ranging from heterodimeric/asymmetric bivalent 1+1 CrossMAbs to more complex tri- (2+1), tetravalent (2+2) bispecific and multispecific antibody formats. Examples given will include new bispecific molecules for cancer immunotherapy and the use of novel targeting approaches to treat neurological disorders. The DutaFab technology platform brings forward a novel class of fully human monoclonal antibody drugs that bind any two antigens with high affinity and specificity. DutaFabs have a unique, proprietary CDR design with two independent paratopes within the natural human CDRs. DutaFabs have been found to be extremely stable and well behaved molecules and are therefore particularly well suited to be injected into the eye for treating burdensome diseases such as macular degeneration or diabetic retinopathy. The latest developments of the DutaFab -enabled antibody formats and applications will be reviewed.

Martin Steegmaier, Ph.D., Head of Discovery, Large Molecule Research, Roche pRED, **Roche Innovation Center Munich,** *Germany*

Track 2: IMMUNO-ONCOLOGY: CHECKPOINTS

8:25 **Chairman's Remarks**

James Larrick, M.D., Ph.D., Managing Director and Chief Medical Officer, **Panorama Research Institute and Velocity Pharmaceutical Development**

8:30 **Boosting Cancer Immunotherapy with Combined Immunomodulatory Drugs**

Effective therapy for difficult-to-treat cancers remains an unmet need. To improve the patient response rate to cancer immunotherapy, we have developed novel immunomodulatory drugs that suppress PD-L1 expression in tumor cells and inhibit the PD-L1/PD-1 checkpoint, resulting in the recruitment of NK cells into the tumor microenvironment that leads to tumor suppression. We propose to combine immunomodulatory drugs with checkpoint blockades to overcome difficult-to-treat cancers with tolerable side effects.

Mickey Hu, Ph.D., Principal Investigator and Director of Discovery Oncology, **Panorama Institute of Molecular Medicine**

9:00 **SIMPLE Antibody™ Platform Generates Unique Species Cross-reactive Antibodies against Immune Checkpoints**

Clinical lead candidate antibodies often lack species cross-reactivity, necessitating the development of substitute antibodies for pre-clinical development in mice or monkeys. Using argenx' SIMPLE Antibody™ platform we were able to generate functional human-mouse cross-reactive antibodies against several validated immune checkpoint proteins, including PD-1, VISTA and LAG-3. We will present in vitro and in vivo data of our antibodies to demonstrate their unique features.

Erik Hofman, Ph.D., Senior Scientist, Research Department, **Argenx,** *Belgium*

9:30 **Targeting Immunosuppressive Myeloid Cells to Enhance Cancer Immunotherapy**

Targeted therapy against myeloid-derived suppressor cells (MDSCs), using multikinase inhibitors such as cabozantinib and dactolisib, can synergize with immune checkpoint blockade antibodies (anti-CTLA4, anti-PD1) to eradicate metastatic castration-resistant prostate cancer.

Xin Lu, Ph.D., John M. and Mary Jo Boler Assistant Professor, Department of Biological Sciences, **University of Notre Dame**

10:00 *Networking Refreshment Break*

10:30 **A Novel Cytokine Receptor Agonistic Antibody by Design**

A key feature of effective cancer immunotherapy relies on enhanced anti-tumor immune response and reduced suppressive effects. As natural cytokines are made to maintain balance between activation and suppression, they are often unable to achieve desired therapeutic efficacy. Here we describe the design of a cytokine receptor agonist antibody that mimics IL-2's immune stimulatory effects on CD8 T cells with minimal Treg activation.

Cheng-I Wang, Ph.D., Senior Principal Investigator, Singapore Immunology Network, Biomedical Sciences Institutes, **ASTAR,** *Singapore*

11:00 **Cow Ultralong CDR3 Antibodies Targeting Exhausted T-cells**

Cow antibodies have unusually long CDR3 regions. We have characterized the genetic and structural properties of these antibodies, and have identified novel antibodies against HIV and exhausted T-cell targets.

Vaughn Smider M.D., Ph.D., Associate Professor, Molecular Medicine, **The Scripps Research Institute**

Track 1: NOVEL ENGINEERING STRATEGIES TO ENHANCE ANTIBODY FUNCTIONS *(continued)*

11:00 **Tumor Uptake of PEGylated Diabody: Balancing between Antibody Size and Systemic Clearance**

Antibody tumor targeting is a complex process involving many factors such as antibody size, distribution and clearance in the plasma. Antibody fragments with optimal profile balanced between size and systemic clearance hold potential for diagnostic and therapeutic applications of tumor malignancies. This talk focuses on the investigation of the correlation of hydrodynamic size, pharmacokinetic parameters and tumor uptake of PEGylated diabody.

Qing Li, Ph.D., Scientist I, **MedImmune**

11:30 **Late Breaking Presentation**

12:00 *Lunch on your own*

Track 1: ROLE OF THE T-CELL REPERTOIRE IN CANCER, INFECTIOUS DISEASES AND AUTOIMMUNITY

1:25 **Chairwoman's Remarks**

Jamie K. Scott, M.D., Ph.D., Professor and Canada Research Chair in Molecular Immunity, Department of Molecular Biology & Biochemistry and Faculty of Health Sciences, **Simon Fraser University,** *Canada*

1:30 **Mining Shared Neoantigen-Specific TCRs From Healthy Donors for Tailored Cancer Immunotherapy.**

There is a marked collapse of our TCR repertoire as we age resulting in a physiological immunodeficiency that compromises the immunosurveillance of infectious and malignant disease. As we enter an age of living drugs it becomes possible to mine TCRs from immunocompetent healthy donors for TCRs reactive against shared neoantigens. Using a proteomic approach, we identify shared surface HLA-bound neoantigens and characterize TCRs against these suitable for immunotherapeutic translation.

Mark Cobbold, M.D., Ph.D., Associate Professor of Medicine, Center for Cancer Immunology, **MGH Cancer Center**

2:00 **Dissecting the Tumor-specific T cell Response**

It is beyond doubt that immunotherapy can be highly successful in human cancer. In particular, the checkpoint targeting therapies have reach center stage of oncology treatment. At this point in time the clinical experience with these therapies is substantial, however the mechanisms of action are not fully unraveled. Using our pMHC multimer technology we are dissecting how checkpoint blockade is influencing the tumor-specific T cell response.

Pia Kvistborg, Ph.D., Junior Group Leader, Department of Immunology, **The Netherlands Cancer Institute**

2:30 **CD39 and CD103 Identify Tumor-reactive CD8 T cells in Human Solid Tumors**

Identification of tumor-reactive CD8 T cells is key to better understand how antibody-mediated immunotherapies work in cancer patients and to improve success for adoptive T cell therapy. Here we identified a subset of tumor-infiltrating CD8 T cells (CD8 TIL) characterized by co-expression of CD103 and CD39 in human solid tumors. This cell population, which is specifically enriched at primary and metastatic tumor sites, appeared to be chronically stimulated and displayed characteristics of tissue-resident memory T cells. Importantly, these cells had a very distinct TCR repertoire as compared to other CD8 TIL subsets, and had the ability to kill autologous tumor cells in vitro. Finally, a higher frequency of those cells in human head and neck tumors correlated with a greater overall survival. Collectively, our findings are an important advance in the biology of tumor-reactive CD8 T cells and will help develop new therapeutics especially in patients with low frequencies of these cells.

Thomas Duhen, Ph.D., Senior Research Scientist, **AgonOx**

3:00 *Networking Refreshment Break*

Track 2: IMMUNO-ONCOLOGY: CHECKPOINTS *(continued)*

11:30 **ILC-mediated Regulation of Tumor-associated T cells: Implications for Immunotherapy**

We recently identified a unique innate lymphoid cell (ILC) population that suppresses the expansion and function of tumor-associated T cells, and is associated with early recurrence in high-grade serous cancer. This regulatory ILC population has properties that overlap with Natural Killer cells and other defined ILCs, yet can be differentiated by a distinct gene expression signature. Current studies are defining molecular interaction that control regulatory ILC function and identifying ways to target this population to enhance immunotherapies.

Sarah Crome, Ph.D., Banting Postdoctoral Fellow, Princess Margaret Cancer Centre, **University Health Network,** *Canada*

12:00 *Lunch on your own*

Track 2: INNOVATING ANTIBODY THERAPEUTICS

1:25 **Co-Chairs' Remarks**

Paul Parren, Ph.D., Professor, Department of Immunohematology and Blood Transfusion, **Leiden University Medical Center,** *The Netherlands*

William R. Strohl, Ph.D., Owner and President, **BiStro Biotech Consulting LLC**

1:30 **Computationally-driven Identification of Antibody Epitopes**

The identification of where and how antibodies recognize antigens can help define and distinguish mechanisms of action, provide insights into progression of immune responses, and facilitate targeted development of vaccines and therapeutic antibodies. An antibody's amino acid sequence implicitly encodes specific recognition of its antigen, and here we investigate the extent to which this information can be leveraged to localize epitopes. We have developed a method, EpiScope, which uses computational methods to hypothesize antibody-antigen binding modes and design targeted panels of antigenic variants to test these hypotheses via antibody binding assays. In prospective studies of two antibodies against tumor antigen B7H6, this integrated computational-experimental approach successfully localized epitopes with a designed panel of five or fewer antigenic variants for each antibody, or alternatively, a six-variant panel for both simultaneously. This use of antibody sequence to drive strikingly efficient epitope localization likely holds more generally; for 29 of 33 distinct antibody-antigen pairs in a retrospective analysis, designed panels required an average of only three antigenic variants to include one or more mutations likely to disrupt binding according to co-crystal structures. There is likewise general promise for design of antigen panels able to efficiently probe multiple antibody epitopes: an integrated four-variant panel designed to map twelve antibodies against vaccinia virus D8 revealed groups of specificities matching experimental binning studies, and contained mutations predicted to disrupt binding of members of each group. We conclude that computational modelling and antigen variant design reveal key determinants of antibody-antigen binding that enable effective epitope localization experiments.

Chris Bailey-Kellogg, Ph.D., Professor, Computer Science, **Dartmouth University**

2:00 **Evolution of Antibodies of Different Germline Gene Origins Proceed through Different Paths**

The variable domains of antibodies evolve in vivo, or are evolved in the laboratory, to achieve high-affinity interaction between its binding site and its epitope, thereby also in many cases achieving improved functional properties of the antibody. Affinity maturation of an antibody's variable domains is achieved by modification of key residues in the context of a framework that provide the stable basic fold of the domains. This process has to target the evolvable parts of the domains, mostly considered as the complementarity determining regions (CDR), but ought to leave other parts, the framework regions (FR) largely untouched. The outcomes in terms of positive selection of in vivo evolution is often interpreted in terms of patterns of silent and replacement-type mutations in these regions. Indeed, in vitro affinity maturation often implies evolution of sequences in complementarity determining regions. We hypothesized that preferred evolution patterns, in vivo and in vitro, may rather reflect the combined features of CDR and FR and that antibodies of different germline gene origins may have different possibilities in terms of paths forward in an evolution process.

Mats Ohlin, Ph.D., Professor, Department of Immunotechnology & SciLifeLab, **Lund University,** *Sweden*

Track 1: ROLE OF THE T-CELL REPERTOIRE IN CANCER, INFECTIOUS DISEASES AND AUTOIMMUNITY *(continued)*

3:30 **Using High-throughput TCR Sequencing to Read Immune Memory**

To examine the diagnostic potential of public T cell receptors (TCRs), we profiled the T cell repertoire of 666 subjects and developed a classification framework that could diagnose CMV status from the resulting catalog of public TCRβ sequences with high specificity and sensitivity in both the original and a validation cohort. We believe this is a proof-of-principle experiment for using public immune receptor sequences to read immune memory for the diagnosis of disease.

Ryan Emerson, Ph.D., Director, Computational Biology, **Adaptive Biotechnologies**

4:00 **Genetic Variation in MHC Proteins is Associated with T-cell Receptor Expression Biases**

In each individual, a highly diverse T cell receptor (TCR) repertoire interacts with peptides presented by major histocompatibility complex (MHC) molecules. Despite extensive research, it remains controversial whether germline-encoded TCR–MHC contacts promote TCR–MHC specificity and, if so, whether differences exist in TCR V gene compatibilities with different MHC alleles. We applied expression quantitative trait locus (eQTL) mapping to test for associations between genetic variation and TCR V gene usage in a large human cohort. We report strong trans associations between variation in the MHC locus and TCR V gene usage. Fine-mapping of the association signals identifies specific amino acids from MHC genes that bias V gene usage, many of which contact or are spatially proximal to the TCR or peptide in the TCR–peptide–MHC complex. Hence, these MHC variants, several of which are linked to autoimmune diseases, can directly affect TCR–MHC interaction. These results provide the first examples of trans-QTL effects mediated by protein–protein interactions and are consistent with intrinsic TCR–MHC specificity.

Eilon Sharon, Ph.D., Postdoctoral Research Fellow, Genetics, Howard Hughes Medical Institute, **Stanford University**

4:30 **Dynamics of the T cell Repertoire during Multiple Episodes of Hepatitis C Virus Infection**

The dynamics of the CD8 T cell receptor (TCR) repertoire and factors governing the selection of TCR clonotypes conferring protective immunity in real life settings are poorly understood. I will present our analysis of the dynamics and functionality of the hepatitis C virus (HCV)-specific CD8 TCR repertoire before, during and after primary infection and reinfection in relation to long-term protection against viral persistence.

Naglaa H. Shoukry, Ph.D., Professor, Department of Medicine, University of Montreal and Director, Viral Hepatitis Research Group, **CHUM Research Centre,** *Canada*

5:00 *Close of Conference*

Track 2: INNOVATING ANTIBODY THERAPEUTICS *(continued)*

2:30 **DNA-based Antibody Therapy via Antibody Gene Transfer**

Recombinant antibodies are one of today's most successful therapeutic classes in the field of inflammatory diseases and oncology. A wider accessibility and implementation, however, is hampered by high production costs, prolonged need for frequent administration, and adverse events. Moreover, the often limited therapeutic efficacy as a single agent has led to a surge in (antibody) combination therapies, which adds to the cost and risk of toxicity. The Antibody Gene Transfer Program, a young research branch within the Laboratory for Therapeutic and Diagnostic Antibodies, is dedicated to advancing DNA-based antibody therapy. This approach seeks to administer to patients the antibody-encoding DNA sequences, rather than the antibody proteins, thereby allowing the body to produce its own medicine. The current presentation provides a comprehensive overview of our Research Program, and illustrates how in vivo antibody expression can address several of the difficulties surrounding conventional antibody protein therapy. A selection of our pre-clinical work on the in vivo expression of tumor-targeting and immunomodulatory antibodies via gene electrotransfer is presented. Finally, opportunities and hurdles towards clinical application are discussed.

Kevin Hollevoet, Ph.D., Group Leader and Postdoc, Therapeutic and Diagnostic Antibodies, **University of Leuven,** *Belgium*

3:00 *Networking Refreshment Break*

3:30 **Structural Determinants for Modulating Antibody-Fc Receptor Interactions for Half-Life Enhancement and Effector Functions**

Engineering of antibodies for enhanced binding to neonatal Fc receptor (FcRn) and improved pharmacokinetics has been demonstrated in humans and other primates. The approaches used to identify the Fc variants have largely relied on random mutagenesis and display formats, which have often led to compromises in other critical attributes of the antibody, including effector functions and biophysical stability. We have developed a structure- and network-based framework to interrogate the engagement of IgG with multiple Fc receptors (FcRn, C1q, TRIM21, FcÎ³RI, FcÎ³RIIa/b, FcÎ³RIIIa). Using this framework, we identified structural features that govern Fc-FcRn interaction, thereby providing multiple distinct pathways to engineer enhanced antibody engagement with FcRn. We augmented our structural analysis with amino acid interaction networks, which provided insights into allosteric consequences of mutations that would have been overlooked by conventional structural analyses. Applying these principles, we have engineered a panel of novel Fc variants, including combinations of mutations, which enhance pH-dependent FcRn binding and retain robust biophysical properties and native binding to FcÎ³ receptors. Multiple antibodies harboring these Fc variants exhibit half-life improvement in various animal models (>9-fold in some instances) while maintaining robust effector functions, including ADCC, CDC and ADIN mediated by TRIM21.

Karthik Viswanathan, Ph.D., Director, Research, **Visterra, Inc.**

4:00 **Characterization of Circulating Antibodies Using Next Generation Sequencing and Mass Spectrometry**

Deep sequencing of peripheral blood mononuclear cells (PBMCs) has recently provided the ability to characterize a snapshot of the complex immunoglobulin repertoire. This sequenced antibody repertoire provides a wealth of information, but is a poor proxy for circulating antibodies. Direct interrogation of serum antibodies using mass spectrometry provides a complementary view of the immune response. We employ a proteogenomic approach integrating sequenced antibody transcripts from multiple tissue types with purified serum antibodies from a rabbit immunization experiment. We compare repertoires across time points and tissue origins. Furthermore, our proteogenomic platform enables us to perform antibody discovery and identify candidates directly from serum.

Natalie Castellana, Ph.D., Chief Executive Officer, **Digital Proteomics, LLC**

4:30 **Analysis of the Current Antibody Landscape and Meeting Highlights**

This presentation provides an overview of current publicly available clinical stage antibodies, Fc fusion proteins, and CAR constructs, of which there are currently over 800 examples. Different strategies and methods for addressing the 300-plus unique target antigens will be compared and contrasted. Additionally, the various strategies for using antibody-based constructs, including Fc engineered IgGs, bispecific approaches, ADCs, and CARs, will be covered on a target group basis. Finally, the presentation will cover significant highlights from the current meeting and integrate those highlights into the current and future state of antibody-based drugs.

William R. Strohl, Ph.D., Owner and President, **BiStro Biotech Consulting LLC**

5:00 *Close of Conference*

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For more information on how you can connect with these key buyers, contact:
Aimee L. Croke, Business Development Manager, Life Sciences
T: 857-504-6697 • E: aimee.croke@knect365.com

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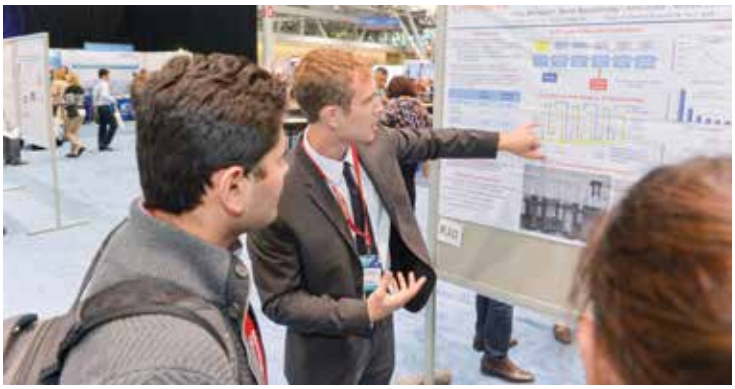

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Highlight your company's exciting research by presenting a scientific poster, which will be displayed in the exhibit & poster hall during the event. You must be a registered attendee to present a poster. Poster fee is $125 for industry attendees and free for academic/government attendees. **The deadline to submit your poster is November 10, 2017.**

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Venue Information:

Manchester Grand Hyatt San Diego

1 Market Place, San Diego, CA 92101
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Special Attendee Room Rate: $230/night + tax

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