HYBRID EVENT

Antibody Engineering & Therapeutics

December 12-16, 2021
Marriott Marquis San Diego
San Diego, CA
Delivered as a hybrid event

Annual Meeting of the ANTIBODY SOCIETY

THE ANTIBODY ENGINEERING COMMUNITY'S LEADING CONFERENCE FOR CUTTING-EDGE STRATEGIES TO ACCELERATE NEXT GENERATION ANTIBODIES & ACHIEVE COMMERCIAL SUCCESS

KEYNOTES SHARE PERSPECTIVES TO FAST-TRACK YOUR R&D

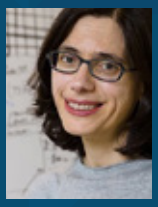
Untangling Pandemics in a Data-driven World

Kristian G. Andersen, Ph.D.
Professor, Department of Immunology and Microbiology,
Scripps Research Translational Institute

Discovering and Targeting Neo-epitopes in Cancer

James Wells, Ph.D.
Professor and Chair, Pharmaceutical Chemistry,
UCSF

Cell Atlases as Roadmaps in Health and Disease



Aviv Regev, Ph.D.
Executive Vice President,
Genentech Research and Early Development

NEW CONTENT AND SESSIONS FOR 2021

- "Engineered Cytokines for Cancer Immunotherapy" **New Half-Day Session**
- "Intratumoral Immunotherapy Administration" **New Half-Day Session**
- "When High Affinity Is Necessary in Antibody Therapeutics" **New Workshop**
- "Single Domain Antibodies: Repertoire, Engineering and Applications" **New Half-Day Session**
- "Progression of Innovative Antibody-based Therapeutics to Clinical Stage" **New Half-Day Session**
- "Vaccines and Antibodies to SARS-CoV-2: Dealing with Antigenic Variation" **New Half-Day Session**
- "HT Antibody Discovery/Engineering: Driving Innovation Towards 0-day Discovery" **New Half-Day Session**

CONNECT WITH THE ANTIBODY COMMUNITY THIS DECEMBER AT THE LARGEST ANTIBODY ENGINEERING CONFERENCE

600+

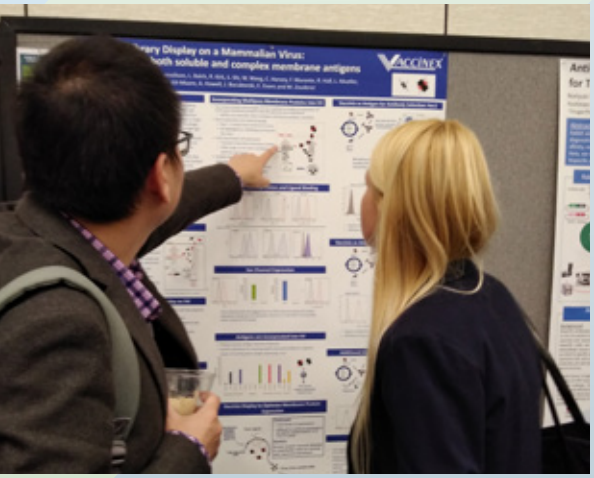
GLOBAL ANTIBODY SCIENTISTS AND EXECUTIVES

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

135+

GLOBAL SPEAKER PRESENTATIONS

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



125+

SCIENTIFIC 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.

PRE-CONFERENCE TRAINING COURSE

Sunday, December 12, 2021 9:00am-5:00pm

INTRODUCTION TO ANTIBODY ENGINEERING

Add-on 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.

INSTRUCTOR

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

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 effectively monitor 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.

COURSE TOPICS TO BE COVERED

- **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**

TRAINING COURSE SCHEDULE:

8:30am Registration

10:30-11:00 Morning Refreshment Break

12:30-1:30 Luncheon

3:00-3:30 Afternoon Refreshment Break

PRE-CONFERENCE WORKSHOPS
Sunday, December 12, 2021 1:00pm-5:00pm

Workshop A: MACHINE LEARNING FOR ANTIBODY AND PROTEIN ENGINEERING

1:15 **An Introduction to Machine Learning for Protein Engineering**

Machine learning (ML) is a rapidly emerging field that uses large data sets to extract features and patterns in order to make predictions on unseen data. Due to its adaptability, machine learning can be applied to fields ranging from self-driving cars to language processing. With experimental platforms capable of high-throughput expression and screening, protein engineering is yet another field in which machine learning is gaining popularity. Here, I will introduce some fundamentals of machine learning and how researchers are using ML to assist and guide protein engineering efforts.

Derek Mason, Ph.D., Director of Operations, deepCDR Biologics, Switzerland

1:45 **Exploring Protein Fitness Landscapes Using Machine Learning**

One of the biggest challenges in engineering protein therapeutics is co-optimization of multiple features at the same time. At LabGenius, we are using machine learning to explore protein fitness landscapes of the features of interest to design new drug candidates. In this talk, I will take you on a journey through our technology and show some results we have achieved so far.

Katya Putintseva, Ph.D., Data Scientist, LabGenius

2:15 **Accelerating Design of Antibodies with Neural Machines**

What can we do with billions of genomes and immune repertoire sequences? We now an amazing opportunity to develop machine learning methods that can exploit this enormous natural diversity and synthesized antibodies to accelerate the design of therapeutics. I will demonstrate how probabilistic generative modeling of antibody sequences can give surprisingly direct answers to developability and affinity design. I will end by introducing challenges for extending these methods to diverse applications to a broad range of biotechnology applications.

Debora Marks, Ph.D., Assistant Professor of Systems Biology, Harvard Medical School

2:45 **Networking Refreshment Break**

2:15 **Antibody Structure Prediction Using Interpretable Deep Learning**

I will present DeepAb, a deep learning method that outperforms existing grafting-based methods for predicting accurate antibody FV structures from sequence. By introducing a directly interpretable attention mechanism, we can show that the network attends to physically important residue pairs. I will also share a novel mutant scoring metric derived from network confidence and show that for a particular antibody, all ten of the top-ranked mutations improve binding affinity.

Jeffrey Gray, Ph.D., Professor, Chemical & Biochemical Engineering, Johns Hopkins University

1:45 **Epitope-specific Antibody Design Via Deep Learning based Structural Modeling**

The growing need for antibodies with customized specificity provides a rich environment for engineering efforts. Conventional protein design methods have offered a solid framework, and we recently launched new efforts in incorporating deep neural networks to the structural modeling tasks. By leveraging the unique properties of neural networks, we developed a generative model for immunoglobulin structures, with which diverse structures can be modeled with unprecedented speed. We will discuss the potential for designing epitope-specific antibodies by a novel flexible-backbone protein docking strategy.

Possu Huang, Ph.D., Assistant Professor of Bioengineering, Stanford University

4:15 **Antibody Knowledge Graph - Repurposing Publicly Available Antibody Data for Machine Learning Applications to Therapeutic Antibody Development**

Antibody data are distributed among heterogeneous public resources which hampers ad-hoc training/test set collection for machine learning purposes. To address this, we developed a framework that collects and links antibody sequence, structural and experimental information from major repositories into an antibody-specific knowledge graph. Such systematization of antibody information allows drawing novel conclusions about antibody biology, their therapeutic function and ultimately creation of sound datasets for machine learning.

Konrad Krawczyk, D.Phil., Chief Scientific Officer, NaturalAntibody, Germany

4:45 **Concluding Remarks and Discussion**

5:00 *Close of Workshop*

PRE-CONFERENCE WORKSHOPS
Sunday, December 12, 2021 1:00pm-5:00pm

Workshop B: WHEN HIGH AFFINITY IS NECESSARY IN ANTIBODY THERAPEUTICS

1:00 **Workshop Moderator's Remarks**

Stephen Parmley, Ph.D., Vice President, Molecular Biology & Protein Sciences, AnaptysBio

1:15 **Affinity Maturation of Surge-derived Antibodies by Combinatorial Codon Mutagenesis and Error-prone PCR**

In vitro affinity maturation was applied to four immuno-oncology scFvs isolated on the high-throughput Surge platform. Random mutagenesis was compared to a novel CDR-restricted technology. Despite distinct mutagenesis profiles, both methods improved scFv affinity with similar efficiency. Affinities for the corresponding full-length immunoglobulins were generally inferior to the scFvs and did not always translate into favorable immune checkpoint blockade, suggesting that screening with full-length antibody or Fab might be advantageous.

Jan Simons, Ph.D., Senior Director, Technology, GigaGen

1:45 **Engineering High Affinity SARS-CoV-2 Neutralizing Antibodies through Directed Evolution**

Here we describe the affinity maturation of several first-generation SARS-CoV-2 neutralizing antibodies (nAbs) to improve their binding affinity for RBD, creating a collection of second generation enhanced (e)nAbs. We then explore the relationship between binding affinity, in vitro neutralization potency and in vivo protection using the first generation nAbs and enAbs, with an emphasis on how viral mutations impact antibody function.

Joseph Jardine, Ph.D., Director of Product Discovery and Optimization, International AIDS Vaccine Initiative

2:15 **Practical Utility of Repertoire Data for Antibody Affinity Maturation**

Repertoire sequencing is frequently done in parallel with antibody discovery campaigns, but while informative, there is still need to expand its practical use. Clonal grouping of repertoire sequences with lead candidates can be used to understand likely maturation pathways. This information can be used to combine single SHM events from diverse branches of clonal expansion, and partially mature antibodies with minimal effort, complementing existing methods.

Luke Burman, Senior Scientist, aTyr Pharma

2:45 **Networking Refreshment Break**

3:15 **One Size Does Not Fit All: Navigating the Multi dimensional Space to Optimize T-cell Engaging Bispecific Antibodies**

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

Javier Chaparro-Riggers, Ph.D., Executive Director, Pfizer

3:45 **Targeting Challenging Protein Targets Using Conformationally Selective Antibodies**

Identifying conformation- and composition-specific antibodies against proteins with high conformational entropy and large hetero-oligomeric complexes can help elucidate detailed structures and mechanisms using crystallography or single particle cryoEM. These Fabs also enable functional assays of particular states of the target protein by stabilizing otherwise transient intermediate states. Approaches that speed the identification of phage display selected antibody fragments to better understand dynamic proteins will be presented.

Charles S. Craik, Ph.D., Professor, Department of Pharmaceutical Chemistry, UCSF

4:15 **Panel Discussion with Workshop Speakers**

5:00 **Close of Workshop**

MAIN CONFERENCE KEYNOTE PRESENTATIONS

MONDAY, DECEMBER 13, 2021

7:15 *Registration and Coffee*

8:15 **Chair Opening Remarks**

8:25 **Cell Atlases as Roadmaps in Health and Disease**

In this talk, I will focus on how the recent advent of various methods has opened the way to develop atlases that help us to understand the relation between genotype to phenotype, especially in the context of human genetics and disease, from cells, to programs, to deciphering individual gene functions, using single cell genomics as a conceptual and technical framework, in complex disease, cancer, and even COVID-19.

Aviv Regev, Ph.D., Executive Vice President, **Genentech Research and Early Development**

9:10 **Keynote Questions**

9:15 **Untangling Pandemics in a Data-driven World**

Our group is using viral genomics, computational biology, and immunological approaches to gain insights into how viruses emerge, spread, and evolve in human populations. We have applied our approach of "genomic epidemiology" to the study of multiple severe human pathogens, including SARS-CoV-2, West Nile virus, Zika virus, Ebola virus, and Lassa virus.

Kristian G. Andersen, Ph.D., Professor, Department of Immunology and Microbiology, **Scripps Research**

10:00 **Keynote Questions**

10:05 *Networking Refreshment Break*

10:35 **Discovering and Targeting Neo-epitopes in Cancer**

Distinguishing cancer cells from normal cells remains a major challenge for cancer treatment. Proteolysis is a hallmark of cancer reflecting metastasis and tumor maintenance, yet we have little understanding of the proteolytic targets. Here, I'll present a platform for identifying and targeting proteolytic neo-epitopes in cancer beginning with the systematic identification of cell surface proteolytic events to the generation of antibodies to target them.

James Wells, Ph.D., Professor and Chair, **Pharmaceutical Chemistry, UCSF**

11:20 **Keynote Questions**

11:25 **Late Breaking Keynote Speaker**

12:10 **Keynote Questions**

MAIN CONFERENCE

MONDAY, DECEMBER 13, 2021

12:15 pm Scientific Luncheon Briefings

ABLEXIS
AlivaMab DISCOVERY SERVICES

Alloy Therapeutics

charles river | every step of the way.

Ligand

1:15 pm Scientific Briefings

abveris

ABZENA Enabling better biopharmaceuticals

ATUM

carterra

Sapidyne Instruments

MAIN CONFERENCE

MONDAY, DECEMBER 13, 2021

1:45 pm **Scientific Briefings**

AbCellera | charles river | Chemical Computing Group | fusionantibodies | PROIMMUNE www.proimmune.com

Track 1: ANTIBODY REPERTOIRES AND COVID-19

2:25 **Chairwoman's Remarks**

Nina Luning Prak, M.D., Ph.D., Professor of Pathology and Laboratory Medicine, **Hospital of the University of Pennsylvania**

2:30 **B Cell Clonal Networks: Mapping the Immune Response to SARS-CoV-2**

Some individuals who are exposed to SARS-CoV-2, COVID vaccines or both, generate large B cell clones. Here, we describe the analysis of large B cell clones to gain insights into how clones evolve and contribute to immune protection and potentially also to immunopathology.

Nina Luning Prak, M.D., Ph.D., Professor of Pathology and Laboratory Medicine, Perelman School of Medicine, **University of Pennsylvania**

3:00 **Autoantibodies in COVID-19 Infections and Vaccinations**

Some patients with COVID-19 produce autoantibodies against cytokines that are pathogenic and are strongly associated with adverse outcomes. New-onset autoantibodies have also been discovered, suggesting that SARS-CoV-2 may have the capacity to break tolerance to self. The speaker will describe recent studies of autoantibodies in COVID-19 infections and vaccinations.

PJ Utz, M.D., Professor of Medicine, Associate Dean for Medical Student Research, **Stanford University School of Medicine**

3:30 **Convergent Antibody Responses to the SARS-CoV-2 Spike Protein in Convalescent and Vaccinated Individuals**

Unrelated individuals can produce genetically similar clones of antibodies, known as public clonotypes, which have been seen in responses to different infectious diseases as well as healthy individuals. Here we identify 37 public clonotypes in memory B cells from convalescent survivors of SARS-CoV-2 infection or in plasmablasts from an individual after vaccination with mRNA-encoded spike protein. We identified 29 public clonotypes, including clones recognizing the receptor-binding domain (RBD) in the spike protein S1 subunit (including a neutralizing, ACE2-blocking clone that protects in vivo), and others recognizing non-RBD epitopes that bound the heptad repeat 1 region of the S2 domain. Germline-revertant forms of some public clonotypes bound efficiently to spike protein, suggesting these common germline-encoded antibodies are preconfigured for avid recognition. Identification of large numbers of public clonotypes provides insight into the molecular basis of efficacy of SARS-CoV-2 vaccines and sheds light on the immune pressures driving the selection of common viral escape mutants.

Elaine Chen, Graduate Student**, Vanderbilt University School of Medicine**

Track 2: NOVEL THERAPEUTIC TARGETS AND NON-CANCER INDICATIONS

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

Paul W.H.I. Parren, Ph.D., Professor, Department of Immunohematology and Blood Transfusion**, Leiden University Medical Center and EVP and** Head of R&D, **Lava Therapeutics,** *The Netherlands*

Katherine Harris, Ph.D., Vice President, Discovery, **TeneoBio**

2:30 **A Clinical Stage ROR1xCD3 Bispecific Antibody with Potential for Broad Cancer Specificity**

NVG-111 is a tandem scFv T-cell engager targeting Receptor tyrosine kinase-like Orphan Receptor 1 (ROR1); a transmembrane protein highly and widely expressed on both haematological and solid tumors. NVG-111, a potent killer of tumor cells, has entered Phase I trials in patients with chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL). Advances with NVG-111 will be presented.

Kerry A. Chester, Ph.D., Chief Scientific Officer**, Novalgen** and Professor of Molecular Medicine**, UCL Cancer Institute, University College London**

3:00 **Targeting Two Receptors Can Significantly Increase Cell Specificity**

Bispecific antibodies targeting two receptors expressed on a cell of interest can have much lower binding to healthy cells than mAbs. Success requires finding the right epitopes, then tuning affinities to optimize selectivity. We demonstrate this with bispecific antibodies targeting cancer cells and tumor-localized Tregs.

Jonathan Davis, Ph.D., Vice President of Innovation and Strategy, **Invenra, Inc.**

3:30 **Combination Immunotherapy with CAR T cells and Bispecific Antibodies**

This talk will discuss the current state-of-the-art for T-cell immunity as a therapeutic platform for cancer in the context of CAR T cells and bispecific antibodies. It will describe the pitfalls and opportunities for using these platforms in the treatment of brain tumors, highlighting the components of successful translation of these therapies into the clinic

Bryan Choi, M.D., Ph.D., Brain Tumor Surgeon, Department of Neurosurgery**, Massachusetts General Hospital/Harvard**

MAIN CONFERENCE

MONDAY, DECEMBER 13, 2021

Track 1: ANTIBODY REPERTOIRES AND COVID-19

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

4:45 **The T Cell Response to SARS-COV-2 Vaccines in a World of Variants**

Fortunately, the primary Covid vaccines on the market appear to maintain efficacy against variants of concern even though the Ab responses have vastly reduced neutralization. We map the T cell response of the vaccines and show their induced T cell response target epitopes that are conserved between the vaccine and the variants.

Harlan Robins, Ph.D., Chief Scientific Officer and Co-Founder**, Adaptive Biotechnologies**

5:15 **Sharing of AIRR-seq Data through the AIRR Data Commons: Standardization, Data Repositories and Data Mining**

Adaptive immune receptor repertoire sequencing (AIRR-seq) has profiled SARS-CoV-2 in the context of both natural infection and vaccination. The AIRR Data Commons (ADC), a set of geographically distributed repositories following data interoperability standards of the AIRR Community and FAIR principles, currently includes over 1 billion annotated sequences from 15 COVID-19 studies, with several researchers citing data re-use in novel studies. Here, we will discuss usage of the iReceptor Gateway to explore and analyze these data.

Felix Breden, Ph.D., Professor, Biological Sciences**, Simon Fraser University,** *Canada*

5:45 **Epitope Profiling of Coronavirus-binding Antibodies Using Computational Structural Modelling**

Identifying the epitope of an antibody is a key step in understanding its function and its potential as a therapeutic. Sequence-based clonal clustering can identify antibodies with similar epitope complementarity, however, antibodies from markedly different lineages but with similar structures can engage the same epitope. We describe a novel computational method for epitope profiling based on structural modelling and clustering. The method identifies sequence-dissimilar but functionally-similar antibodies across the Coronavirus Antibody Database and achieves accuracy (92% of antibodies in multiple-occupancy structural clusters bind to consistent domains). Our approach functionally links antibodies with distinct genetic lineages, species origins, and coronavirus specificities. This indicates greater convergence exists in the immune responses to coronaviruses than is suggested by sequence-based approaches. Our results show that applying structural analytics to large class-specific antibody databases will enable high confidence structure-function relationships to be drawn, yielding new opportunities to identify functional convergence hitherto missed by sequence-only analysis.

Sarah Robinson, Ph.D. Student in Protein Informatics, **University of Oxford, United Kingdom**

Track 2: NOVEL THERAPEUTIC TARGETS AND NON-CANCER INDICATIONS

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

4:45 **Mitigating Cytokine Release with Novel Low Affinity Anti-CD3 based T-Cell Engagers**

Bispecific antibodies engineered using Teneobio's T cell redirection platform induce anti-tumor efficacy with reduced cytokine release in several pre-clinical models of oncology and in multiple myeloma patients in the clinic. The versatility of this platform enables rapid development of multi-specific antibodies targeting various solid tumors and hematological cancers.

Udaya S. Rangaswamy, Ph.D., Senior Scientist**, Teneobio**

5:15 **Novel DARPin® Approaches for the Development of T-cell Engagers with Improved Safety and Efficacy**

Highly potent T cell engagers (TCE) have entered clinical development, but are often accompanied by severe toxicity, elicited by on-target/off-tumor cytotoxicity and cytokine release syndrome. We generated several design strategies, based on our multi-specific TCE DARPin® platform, with potential to improve the benefit/risk profile. Targeting simultaneously two-to-three different tumor associated antigens (TAA) with an optimal affinity (e.g. CD33, CD123 and CD70) resulted in a substantial avidity gain through binding to at least two TAAs and likely improves the therapeutic window to help overcome dose limiting toxicities in acute myeloid leukemia therapy.

Christian Reichen, Ph.D., Associate Director Oncology Research**, Molecular Partners AG,** *Switzerland*

5:45 **The Conditionally Activated COBRA Demonstrates an Improved Therapeutic Window over Conventional T-cell Engagers in the Solid Tumor Space**

This presentation will discuss the pre-clinical characterization of initial COBRA clinical programs, TAK-186 (EGFR-targeted COBRA) and TAK-280 (B7H3-targeted COBRA). Including in the talk will be learnings related to 1) In Vitro potency 2) Depletion of established solid tumors in mice and 3) Establishing a therapeutic index in tumor-bearing mice, with murine target cross-reactive COBRA MVC-280 relative to an inherently active T-cell engager.

Danielle Dettling, Senior Director, Pre-Clinical Pharmacology**, Maverick Therapeutics**

6:15-7:15 **Opening Night Networking Reception, Exhibits and Poster Viewing**

Please join your fellow attendees in the exhibit hall for an evening of networking while enjoying beverages and appetizers.

MAIN CONFERENCE

TUESDAY, DECEMBER 14, 2021

7:30 am **Scientific Breakfast Briefings**

BIOCYTOGEN

BECKMAN COULTER Life Sciences

Track 1: HIGH-THROUGHPUT ANTIBODY DISCOVERY AND ENGINEERING: DRIVING INNOVATION TOWARDS 0-DAY DISCOVERY

8:10 **Chairman's Remarks**

Jean-Philippe Bürckert, Ph.D., Director, Bioinformatics, Large Molecule Discovery**, Charles River Laboratories**

8:15 **Massively Multiplexed Epitope Mapping and Specificity Cross-reactivity Characterization with Yeast Mating**

Funneling leads to a small number of strong binders results in the loss of antibodies with diverse epitopes, specificities, and cross reactivities – properties that cannot be recovered with later maturation. In his talk, David will describe how the AlphaSeq platform can be used to widen the antibody discovery funnel by quantitatively measuring millions of antibody-antigen interactions using yeast mating and next generation sequencing.

David Younger, Ph.D., Co-Founder & CEO**, A-Alpha Bio**

8:45 **Antibodies for the World: Engineering Antibodies for Ultra-high Concentration Injectable Delivery and Flexible Temperature Deployment outside of the Hospital Setting**

Antibody therapeutics are powerful but delicate, largely limiting their use to infusion settings in hospitals with cold storage controls. Here we demonstrate a combination of computational and wetlab bioengineering methods to adapt antibodies for austere environments - ultra-high concentration formulation (250-350mg/ml), aggregation resistance, agitation resistance, viscosity engineering, and extended stability outside of refrigeration constraints. A specific case study of Centi-B9 is presented: an injectable anti-SARS-CoV-2 therapeutic developed in partnership with the Medical Technology Enterprise Consortium and Naval Medical Research Center.

Jacob Glanville, CEO and President, **Centivax**

9:15 **Designing Therapeutic Antibodies with Synthetic Biology and Machine Learning**

We introduce BigHat Biosciences' platform for designing therapeutic antibodies. Machine learning guides the search for better molecules by directing and learning from each cycle of our synthetic-biology-based wet lab that synthesizes and characterizes hundreds of antibodies each week. We share several case studies of protein engineering using this novel platform.

Peyton G. Greenside, Chief Scientific Officer and Co-founder**, BigHat Biosciences**

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

Track 2: ENGINEERING THE FC REGION FOR THERAPEUTICS

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

Sally Ward, Ph.D., Professor and Director, **University of Southampton,** *United Kingdom*

Robert N. de Jong, Ph.D., Director Antibody Research & Technology**, Genmab,** *The Netherlands*

8:15 **Tafasitamab (MOR208): A Novel Fc-domain-engineered CD19-directed Monoclonal Antibody for the Treatment of B-cell Malignancies**

Tafasitamab is a humanized Fc-modified CD19 targeting monoclonal antibody, which mediates B-cell immune effector mechanism including ADCC and ADCP, as well as apoptosis. Monjuvi® (tafasitamab-cxix) was recently approved by the U.S. Food and Drug Administration in combination with lenalidomide for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). In this talk, we summarize the preclinical characterization and the clinical results of tafasitamab in the treatment of B-cell malignancies.

Martin Steegmaier, Ph.D., Senior Vice President and Head of Research**, MorphoSys,** *Germany*

8:45 **Afucosylated IgG Responses in Health and Disease: Friend or Foe?**

IgG contains a single functionally important N-linked biantennary glycan within the Fc tail. Unusual afucosylated IgG responses in humans occur to a varying degree to enveloped viruses, including SARS-CoV-2. In theory, this can lead to enhanced protection due to FcγRIII-mediated activities recruiting NK, monocytes, macrophages and neutrophils. However, in COVID-19 this leads to immune pathologies. Immune responses by current SARS-CoV-2 vaccines will be revealed and protective response in malaria.

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

9:15 **Clinical Development of FcRn Inhibitor Efgartigimod in IgG-driven Autoimmune Disorders**

Efgartigimod is human IgG1 Fc fragment and a first-in-class FcRn antagonist developed for IgG-driven autoimmune indications. Efgartigimod is clinically evaluated in phase 2/3 and 3 trials in generalized myasthenia gravis (gMG), chronic inflammatory demyelinating polyneuropathy (CIDP), immune thrombocytopenic purpura (ITP) and pemphigus. In this presentation an overview of the clinical development will be provided.

Sophie Steeland, Ph.D., Senior Clinical Scientist**, argenx,** *Belgium*

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

MAIN CONFERENCE

TUESDAY, DECEMBER 14, 2021

Track 1: HIGH-THROUGHPUT ANTIBODY DISCOVERY AND ENGINEERING: DRIVING INNOVATION TOWARDS 0-DAY DISCOVERY

10:30 **Taking Antibody Candidate Generation from the Lab to the Cloud with de novo Computational Design**

Antibodies are a therapeutic class of molecules with enormous potential, but the path to the clinic is beset by pitfalls related to developability and functionality. Display and immunization-based methods can often create high-affinity binders that struggle with aggregation, immunogenicity, and with limited mechanisms for targeting, these candidates often fail to have any functional impact on the target. Furthermore, large libraries of antibodies must be tested and filtered without clear information of whether they bind functionally relevant epitopes. Here we present a de novo computational design platform that integrates physics-based structural modeling algorithms with machine learning to create targeted candidate therapeutics that can be quickly validated in high-throughput systems in the lab.

Monica Berrondo, Ph.D., CEO**, Macromoltek**

11:00 **Late Breaking Presentation**

11:30 **Late Breaking Presentation**

Track 2: ENGINEERING THE FC REGION FOR THERAPEUTICS

10:30 **The 3rd Subclass is the Charm?**

Recent work profiling protective antibody responses across a diversity of disease states points to the potential importance of IgG3 antibodies. However, this subclass is conspicuously absent among approved antibodies and Fc fusion protein biologics. Here consistent evidence as to its importance to immunity learned from models of functionally potent and protective immune responses will be presented alongside antibody engineering strategies that recapitulate some of its special characteristics.

Margaret Ackerman, Ph.D., Professor of Engineering**, Dartmouth College**

11:00 **Therapeutic IgG Antibody Combinations Designed to Collaborate**

The target space for therapeutic monoclonal antibodies is limited by expression in healthy tissues. Our HexElect® platform consists of Fc domain IgG antibody pairs engineered to show Boolean logic functionality: they are only activated after binding two different targets co-expressed at the same cell surface. We discuss different antibody engineering approaches to create strictly mutually dependent antibody pairs, as well as some potential applications. The HexElect platform may enable access to an untapped, combinatorial target space for the generation of antibody therapeutics that exhibit both selectivity and potency.

Robert N. de Jong, Ph.D., Director Antibody Research & Technology, **Genmab, The Netherlands**

11:30 **Engineered IgA to Activate Neutrophils and MDSC for Cancer Therapy**

All antibody drugs are based on IgG at the moment. IgG is a poor activator of neutrophils and MDSC. Data will be presented that IgA is a strong activator of neutrophils, but also the tumor-associated myeloid derived suppressor cells (MDSC). Also, the mode of action of IgA will be elucidated.

Jeanette Leusen, Ph.D., Associate Professor**,** Head Immunotherapy Group and UMAB Facility**, Laboratory for Translational Immunology, University Medical Center Utrecht**

12:05 pm **Scientific Briefings**

GENOVAC | LakePharma The Biologics Company | Ligand | SCHRÖDINGER.

12:35 **Networking Luncheon, Exhibit and Poster Viewing.**

MAIN CONFERENCE

TUESDAY, DECEMBER 14, 2021

1:45 pm **Scientific Briefings**

Antibody Solutions | aragen | AVID BIOSERVICES | Syngene

Track 1: VACCINES AND ANTIBODIES TO SARS-COV-2: DEALING WITH ANTIGENIC VARIATION

2:25 **Chairman's Remarks**

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

2:30 **Features of B Memory to SARS-CoV-2**

Michel Nussenzweig, M.D., Ph.D., Professor and Senior Physician**, The Rockefeller University**

3:00 **Adaptive Immunity and Immune Memory to SARS-CoV-2 and COVID-19**

Understanding immune memory to SARS-CoV-2 is critical for improving diagnostics and vaccines, and for assessing the likely future course of the COVID-19 pandemic. We analyzed multiple compartments of circulating immune memory to SARS-CoV-2 from 188 COVID-19 cases, including 43 samples at > 6 months post-infection. By studying antibody, memory B cell, CD4+ T cell, and CD8+ T cell memory to SARS-CoV-2 in an integrated manner, we observed that each component of SARS-CoV-2 immune memory exhibited distinct kinetics (Dan et al., Science 2021). I will also present a working model of the relationship between adaptive immune responses and COVID-19 disease.

Shane Crotty, Ph.D., Professor**, Center for Infectious Disease and Vaccine Research La Jolla Institute for Allergy and Immunology**

Track 2: INTRATUMORAL IMMUNOTHERAPY ADMINISTRATION

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 **Therapeutic In Situ Vaccination for Cancer**

We employ a bi-flank tumor model to screen immune stimulating agents for their ability to induce abscopal tumor responses. CpG (a TLR9 ligand) combined with an anti OX40 antibody or combined with Ibrutinib (a specific tyrosine kinase inhibitor) are particularly effective. Tumor specific, T cell -dependent, abscopal responses occur in a variety tumor models, including spontaneous breast cancer. We have extended this in situ vaccine maneuver to the neo-adjuvant setting, using the primary tumor as an immunization site prior to its surgical resection. Our clinical trials of in situ vaccination have yielded a high frequency and long durations of tumor responses in patients with lymphoma.

Ronald Levy, M.D., Professor of Medicine**, Stanford Medical School**

3:00 **Intratumoral Administration and Retention of IL-2 and IL-12 Bifunctional Fusion Proteins to Drive a Systemic Immune Response**

This presentation will discuss: 1) Intratumoral administration of cytokines without a retention strategy can trigger significant toxicity; 2) CLN-617 is a fusion protein that combines IL-2, IL-12, a collagen binder, and a spacer element to maximize bioavailability in the tumor and minimize systemic exposure and 3) Murine surrogates of CLN-617 drive robust systemic anti-tumor immunity without toxicity in checkpoint-resistant syngeneic tumor models

Naveen Mehta, Ph.D., Director of Preclinical Research and Development, Cullinan Oncology

MAIN CONFERENCE

TUESDAY, DECEMBER 14, 2021

Track 1: VACCINES AND ANTIBODIES TO SARS-COV-2: DEALING WITH ANTIGENIC VARIATION

3:30 **Deconstructing Polyclonal Antibody Responses at the Molecular Level Using cryoEM**

I will present a hybrid structural and bioinformatic approach to directly assign the heavy and light chains, identify complementarity-determining regions, and discover sequences from cryoEM density maps of serum-derived polyclonal antibodies bound to an antigen. When combined with next generation sequencing of immune repertoires we can specifically identify clonal family members, generate monoclonal antibodies, opening up new avenues for analysis of immune responses, iterative vaccine design, and immunotherapeutic discovery.

Andrew Ward, Ph.D., Professor, Department of Integrative Structural and Computational Biology**, The Scripps Research Institute**

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

4:45 **Structural Insights on Antigenic Variation of SARS-CoV-2 Spike for Antibody Recognition**

Many neutralizing monoclonal antibodies (nAbs) have now been isolated from COVID-19 convalescent patients and vaccinees. Most nAbs target the receptor binding domain (RBD) of the spike protein. We have determined many crystal structures of nAbs bound to the RBD to determine their binding sites (epitopes) and mechanisms of neutralization. We have also analyzed the structural effects of mutations in recent SARS-CoV-2 variants on antibody binding and neutralization to aid in design of next-generation-vaccine immunogens and therapeutics.

Ian Wilson, D.Phil, Hansen Professor of Structural Biology and Chair Department of Integrative Structural and Computational Biology California Campus**, Scripps Research**

5:15 **Tackling SARS-CoV-2 and Future Sarbecovirus Threats with Broadly Neutralizing Antibodies**

The continued spillover of coronaviruses from zoonotic reservoirs and the emergence of resistance SARS-CoV-2 variants in the human population highlights the need for broadly active counter measures. Here I will describe the identification of broadly neutralizing monoclonal antibodies (bnAbs) and cocktails thereof that potently neutralize SARS-CoV-2 variants of concern as well as pre-emergent SARS-like viruses and mitigate the emergence of resistance in vitro. The results support the development of bnAbs for the treatment and prevention of COVID-19 and future emerging sarbecovirus threats.

Laura Walker, Ph.D., Chief Scientific Officer**, Adagio Therapeutics and** Senior Director of Antibody Sciences**, Adimab LLC**

5:45 **Late Breaking Presentation**

Track 2: INTRATUMORAL IMMUNOTHERAPY ADMINISTRATION

3:30 **Blockade of Immune Checkpoints in Lymph Nodes through Locoregional Delivery Augments Cancer Immunotherapy**

Immune checkpoint blockade (ICB) was augmented through intratumoral and intradermal routes of administration that resulted in higher mAb accumulation within both the tumor and its draining lymph nodes (TdLNs) or TdLNs alone, respectively. Targeted delivery of mAb to TdLNs also enhanced antitumor immunity and improved therapeutic effects compared to systemic ICB, and these effects were sustained at reduced mAb doses and comparable to intratumoral administration. Locoregional routes of mAb administration thus augment ICB therapy by improving immunomodulation within TdLNs.

Susan N. Thomas, Ph.D., Woodruff Associate Professor**, Georgia Institute of Technology**

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

4:45 **Intratumoral Immunotherapy with Aluminum Hydroxide-tethered Cytokines**

Ankyra's platform enables stable tethering of cytokines and other immune agonists to the common vaccine adjuvant aluminum hydroxide. When administered intratumorally, these complexes form a stable depot in the tumor leading to prolonged immune activation and potent local and systemic anti-tumor efficacy with reduced toxicity after a single injection.

Michael Schmidt, Ph.D., Chief Scientific Officer, Ankyra Therapeutics

5:15 **In Situ Vaccination Induces Systemic Tumor Regressions and Potentiates PD1 Blockade**

In Situ Vaccination exploits adaptive immune cells ability to recognize tumor antigens optimally presented at the tumor site. Optimal presentation requires that key Dendritic Cell subsets be mobilized, loaded with tumor antigen, and activated, resulting in potent cross-priming of anti-tumor CD8 T cells. If they can be mobilized in an immunogenic way, the immune system can in turn recognize the cancer. By using the vaccine at 1 site to induce immune response, T cells will travel throughout the body to kill tumors throughout the body.

Joshua Brody, M.D., Director, Lymphoma Immunotherapy Program**, Mount Sinai School of Medicine**

5:45 **Intratumoral mRNA Immuno-oncology Therapies Induce Robust T-cell Responses Against Solid Tumors in Hard to Treat Solid Tumors**

Jacob Becraft, Ph.D., Co-Founder and CEO**, Strand Therapeutics**

6:15-7:15 **Networking Reception, Exhibit and Poster Viewing**

MAIN CONFERENCE

WEDNESDAY, DECEMBER 15, 2021

7:30 am **Scientific Breakfast Briefings**

PerkinElmer
For the Better

Track 1: ENGINEERED CYTOKINES FOR CANCER IMMUNOTHERAPY

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

Paul J. Carter, Ph.D., Genentech Fellow, Department of Antibody Engineering**, Genentech**

Jonathan Sockolosky, Ph.D., Scientist, Department of Antibody Engineering**, Genentech**

8:15 **Stromal Cell Evolution, Clinical Relevance and Therapeutic Targeting in Oncology and Fibrosis**

This talk will cover recent and emerging discoveries on the ontogeny, function and modulation of the stromal compartment and its interactions with lymphocytes and myeloid cells in inflammatory diseases including cancer and fibrosis. The application of new genetic and pharmacologic tools and approaches for finer mapping and selective and controlled manipulation of specific stromal cells will be discussed.

Shannon Turley, Ph.D., Vice President, Cancer Immunology Discovery**, Genentech**

8:45 **Engineering Cis-Targeted Immunomodulators to Enhance Their Selectivity and Effectiveness as Therapeutics**

Cytokines are potent immune modulators. However, systemic administration of cytokines for therapeutic purposes can result in pleotropic effects, with heterogenous activity across different cell types, ultimately limiting efficacy. We are pioneering a new approach with our cis-targeted cytokine therapies to activate only the immune cell types that drive desired responses. Our cis-targeted immunotherapies offer a new level of selectivity, with optimized efficacy and minimized toxicity.

Andy Yeung, Ph.D., Chief Technology Officer**, Asher Biotherapeutics**

9:15 **Engineering Cytokines for Retention in the Tumor Microenvironment**

We are developing cytokines such as IL-12 as fusion proteins with domains that bind to the extracellular matrix in the tumor microenvironment. We have observed that intratumoral pharmacodynamics can be greatly extended by fusion of the A3 collagen-binding domain from von Willebrand Factor to IL-12, and this results in enhanced efficacy in multiple tumor models in mice.

Jeffrey Hubbell, Ph.D., Eugene Bell Professor in Tissue Engineering**, The University of Chicago**

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

10:30 **Tripokin: A Potency-matched Dual Cytokine Fusion for Cancer Therapy**

Tripokin is a novel fusion protein, capable of an exceptionally selective uptake at the tumor site. The product contains two highly synergistic cytokine moieties (interleukin-2 and tumor necrosis factor) fused to the L19 antibody, specific to the alternatively-spliced EDB domain of fibronectin. In the seminar, I will present the discovery and development of Tripokin towards clinical trials in patients with different types of cancer.

Dario Neri, Ph.D., CEO and CSO**, Philogen,** *Switzerland*

Track 2: SINGLE DOMAIN ANTIBODIES: REPERTOIRE, ENGINEERING AND APPLICATIONS

8:10 **Chairman's Remarks**

Mitchell Ho, Ph.D., Senior Investigator**, Laboratory of Molecular Biology, NIH NCI**

8:15 **The SHREAD Platform: SHielded, REtargeted ADenovirus for the Paracrine Delivery of Therapeutics**

In recent years we developed the SHielded REtargeted ADenovirus (SHREAD) system, which allows to produce a cocktail of therapeutics in the body at a defined location. It is based on DARPins as adapters to any cell-surface receptor desired and shielded from undesired interaction by a designed protein shield. The particles carry no viral genes. We will demonstrate a number of novel applications and analysis tools.

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

8:45 **Human Antibody Domains As Therapeutics Against Viruses and Cancer**

We designed and generated six large (1011 each) human VH and VL antibody domain libraries displayed on phage. Selected binders were with good developability and highly effective against HIV-1 as CARs (Anthony-Gonda K et al, Sci Transl Med 2019) and SARS-CoV-2 and related coronaviruses as Fc fusion proteins (Li W et al, Cell 2020; Sun Z et al mAbs 2020) including variants found in humans (Zhu X et al PLOS Biology, Sun Z et al bioRxiv, 2021) as well as against cancer as CARs (Schneider D et al, Frontiers in Oncology, 2018; unpublished). Some of the binders will be evaluated in human clinical trials this year.

Dimiter Dimitrov, Ph.D., Professor and Director, Center for Antibody Therapeutics (CAT)**, University of Pittsburgh Medical School and** Chief Scientific Officer**, Abound Bio**

9:15 **Camel and Shark Single Domain Antibodies Targeting Cancer and Viral Antigens**

We established large single domain antibody phage display libraries from camels (Camelus dromedarius) and sharks (Ginglymostoma cirratum). In my talk, I will discuss (i) construction and repertoire analysis of our libraries, (ii) screening of single domain antibodies targeting cancer antigens including GPC1, B7-H3 and PD-L1 and virus antigens including SARS-CoV-2 and Lassa virus, and (iii) therapeutic features of these single domain antibodies with a focus on CAR T cells.

Mitchell Ho, Ph.D., Senior Investigator, **Laboratory of Molecular Biology, NIH NCI**

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

10:30 **The NANOBODY Platform – From Discovery to Market**

A NANOBODY as variable domain of a heavy chain only antibody was first described in the early 90's. Since their initial discovery a lot of optimization was performed to turn these single domain antibody fragments into developable drugs. The presentation will highlight what parameters were fine-tuned and how a robust NANOBODY platform was built to generate a series of highly innovative drugs.

Carlo Boutton, Ph.D., Global Head Innovation**,** Large Molecule Research Platform**, Sanofi,** *Belgium*

MAIN CONFERENCE

WEDNESDAY, DECEMBER 15, 2021

Track 1: ENGINEERED CYTOKINES FOR CANCER IMMUNOTHERAPY

11:00 **Discovery of Tumor Targeting IL2Rb Agonist by mRNA Display Enabled Technology Platforms**

We have developed proprietary mRNA Display based mRNADisTM and mSCAFoldTM platforms for antibody discovery and protein engineering. Leveraging the technologies, we have discovered EPIM-001, a bifunctional IL2Rb agonist/Anti-PDL1 biologics for solid tumor treatment. It demonstrated selective immune cell activation and potent anti-tumor activity in mice.

Yan Chen, Ph.D., Founder & Chief Executive Officer, **Elpis Biopharmaceuticals**

11:30 **A Bispecific Antibody Agonist of The IL-2 Heterodimeric Receptor Promotes In Vivo Expansion Of CD8 And NK Cells**

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

Katherine Harris, Ph.D., Vice President, Discovery**, TeneoBio**

Track 2: SINGLE DOMAIN ANTIBODIES: REPERTOIRE, ENGINEERING AND APPLICATIONS

11:00 **Chicken Heavy Chain Antibodies to SARS-CoV-2 Spike Protein**

Single domain antibodies are found naturally in camelids and sharks, and humanized versions have been engineered. In chickens, heavy chain-only antibodies are readily expressed when the light chain is modified to remove the variable region. We have immunized these birds with target proteins and developed panels of diverse single domain antibodies of high affinity. We are currently engineering a humanized scaffold to produce human sdAbs in the OmniDabTM platform.

Phil Leighton, Ph.D., Senior Director of Molecular Biology, Ligand Pharmaceuticals

11:30 **Envafolimab: A Single Domain PD-L1 Antibody Given by Rapid Subcutaneous Injection That Is Being Studied in Pivotal Trials in the US and China**

Single domain antibodies have the advantages of being stable at high concentration and being administered subcutaneously by rapid small volume injection without the need for an adjuvant. Envafolimab (KN035), a novel, single-domain antibody against PD-L1, is the first subcutaneously injected PD-(L)1 inhibitor to be studied in pivotal trials. Envafolimab is currently being studied in the ENVASARC Phase 2 pivotal trial in the U.S. sponsored by TRACON, has been studied in a completed Phase 2 pivotal trial as a single agent in MSI-H/dMMR advanced solid tumor patients in China and is being studied in an ongoing Phase 3 pivotal trial in combination with gemcitabine and oxaliplatin in advanced biliary tract cancer patients in China. TRACON's partners Alphamab Oncology and 3D Medicines submitted an NDA to the NMPA in China for envafolimab in MSI-H/dMMR cancer that was accepted for review in December 2020 and granted priority review in January 2021. In the Phase 2 MSI-H/dMMR advanced solid tumor trial, the confirmed objective response rate (ORR) by blinded independent central review in MSI-H/dMMR colorectal cancer (CRC) patients treated with envafolimab who failed a fluoropyrimidine, oxaliplatin and irinotecan was 32%, which was similar to the 28% confirmed ORR reported in the Opdivo package insert in MSI-H/dMMR CRC patients who failed a fluoropyrimidine, oxaliplatin, and irinotecan and the 33% confirmed ORR reported for Keytruda in MSI-H/dMMR CRC patients who failed a fluoropyrimidine, oxaliplatin and irinotecan in cohort A of the KEYNOTE-164 clinical trial.

Charles Theuer, M.D., Ph.D., Director, President and CEO, Tracon Pharmaceuticals

12:00 pm Scientific Briefings

ABLEXIS / AlivaMab DISCOVERY SERVICES

BERKELEY LIGHTS

FUJIFILM Diosynth biotechnologies

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

MAIN CONFERENCE

WEDNESDAY, DECEMBER 15, 2021

Track 1: PROGRESSION OF INNOVATIVE ANTIBODY BASED THERAPEUTICS TO CLINICAL STAGE

2:10 **Co-Chairs' Remarks**

Janine Schuurman, Ph.D., Vice President, Research**, Genmab, The** *Netherlands*

James A. Ernst, Ph.D., Senior Director, Head of Development Sciences**, Xencor**

2:15 **Tumor-targeted CD28 Costimulatory Bispecific Antibodies Enhance T Cell Activation in Solid Tumors**

Solid tumors often lack expression of CD28 ligands, so we hypothesized that activation of CD28 signaling in the tumor micro-environment could be beneficial. We designed B7H3 x CD28 and PDL1 x CD28 bispecific antibodies that conditionally costimulate CD28 only in the presence of their respective targets and TCR engagement and show that they enhance activity of either anti-PD1 antibodies or TAA x CD3 T cell engagers.

Gregory Moore, Ph.D., Director, Protein Engineering**, Xencor**

2:45 **DuoHexaBody-CD37: Translating Antibody Avidity Engineering into Therapeutic Applications**

Exploiting antibody avidity interactions through multi-targeting approaches and/or Fc engineering represents a promising strategy to boost antibody functional responses. Here, we present the preclinical development of DuoHexaBody-CD37, a novel CD37-targeting antibody for the treatment of B-cell malignancies. DuoHexaBody-CD37 molecules combine dual epitope targeting with Fc engineering in a bispecific (biparatopic) approach to enhance target-dependent antibody hexamerization and complement-mediated effector functions.

Simone Oostindie, Ph.D., Scientist, Early Stage Translational Research**, Genmab,** *The Netherlands*

3:15 **Overcoming Challenges in the Generation of Bispecific T Cell-Engaging Receptor (TCER®) Molecules Targeting Tumor Antigens**

Immunotherapy with TCR-based biologics targeting human leukocyte antigen (HLA)-presented peptides has emerged as a novel and promising treatment modality for malignant diseases. We have developed bispecific T cell-engaging receptors (TCER®) that are fusion proteins consisting of an affinity maturated TCR (generated via the XCEPTOR® technology) and a humanized T cell-recruiting antibody to redirect T cells towards the tumor target. The TCER® design confers antibody-like profiles for stability and manufacturability. In this talk we will focus on lessons learned while generating proof-of-concept data for a TCER® program.

Dominik Maurer, M.D., Vice President and Global Head of Immunology**, Immatics Biotechnologies GmbH,** *Germany*

3:45 **Networking Refreshment Break**

4:15 **Improved Brain Delivery of Antibodies with Enhanced Binding to FcRn at Neutral pH**

The blood-brain barrier (BBB) restricts brain penetration of therapeutic antibodies. FcRn is expressed abundantly at the BBB and may modulate the transport of IgG into the brain. We investigated how Fc mutations that improve IgG binding to FcRn at neutral pH impact cellular transcytosis in vitro and brain uptake in vivo and identified variants that enhanced partitioning of IgG to brain.

Jasi Atwal, Ph.D., Senior Scientist, Neuroscience**, Genentech**

Track 2: ANTIBODY LIBRARY DESIGN, SELECTION AND SCREENING

2:10 **Chairman's Remarks**

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

2:15 **The Greatest Competition in the History of Antibody Discovery**

Inadvertently, the Covid-19 pandemic resulted in an extraordinary worldwide unplanned experiment, in which numerous scientific groups generated antibodies against a single target: the CoV-2 spike protein. This provided a unique opportunity to compare the efficacy of different methods, and the specificities and qualities of antibodies generated by those methods. Generally, the most potent neutralizing antibodies come from convalescent patients and immunized animals, with non-immune phage libraries usually yielding significantly less potent antibodies. Here we show it is possible to generate ultra-potent (IC50 <2ng/ml) human neutralizing antibodies directly from a novel naïve antibody library format with affinities, developability properties and neutralization activities comparable to the best from hyperimmune sources, indicating that naïve antibody libraries can now effectively compete with immunization to provide therapeutic antibodies.

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

2:45 **Practical Application of a GAN-designed Antibody Library and Implications towards Rapid Pandemic Response**

We have successfully designed and implemented a generative adversarial network for the production of antibody sequences that bind to targets and exhibit functional activity. J.HAL, Just Humanoid Antibody Library, although moderately diverse, represents an important first step demonstrating the capability of GANs for therapeutic protein design. Moreover, the library can be biased towards many attributes such as developability increasing the likelihood of rapidly manufacturing efficacious therapeutics.

Rutilio Clark, Ph.D., Antibody Discovery and Molecular Design Scientific Director**, Just - Evotec Biologics**

3:15 **Parameters and Determinants of Responses to Selection in Antibody Libraries**

To gauge the impact of an antibody repertoire's scaffold on its potential to generate binders, we compare the response to selection of three different antibody libraries based on different scaffolds but sharing the same VH-CDR3 diversity, using phage display with a deep sequencing readout and statistical modeling. We find that libraries with maturated scaffolds have a lower response to selection against new targets than libraries with germline scaffolds.

Clément Nizak, Ph.D., CNRS Research Scientist**, Sorbonne Universite and College de France**

3:45 **Networking Refreshment Break**

4:15 **Towards Predicting Antibody-antigen at the Paratope-epitope Level Using Machine Learning**

Antibody-antigen binding relies on the specific interaction of amino acids at the paratope-epitope interface. The predictability of antibody-antigen binding is a prerequisite for de novo antibody and (neo-)epitope design. We will show recent work of ours that leverages combined structure- and sequence-based features of paratope-epitope binding and investigates conditions under which machine-learning-driven antibody design becomes feasible.

Victor Greiff, Ph.D., Associate Professor for Computational and Systems Immunology**, The University of Oslo,** *Norway*

MAIN CONFERENCE

WEDNESDAY, DECEMBER 15, 2021

Track 1: PROGRESSION OF INNOVATIVE ANTIBODY-BASED THERAPEUTICS TO CLINICAL STAGE

4:45 **Natural Killer Cell Engagers in Cancer Immunotherapy: Next Generation of Immuno-oncology Treatments**

In immuno-oncology, one innovative therapeutic approach is to stimulate the antitumor activity of innate immune cells, boosting not only their direct role in tumor elimination, but also their function in eliciting multicellular immune responses. This ultimately results in long-lasting tumor control by adaptive immunity. We will review the development of a new class of synthetic molecules, the Antibody-based Natural Killer cell Engager Therapeutics (ANKETTM), which are built from fragments of monoclonal antibodies and are designed to harness the immune functions of Natural Killer cells in cancer. As currently shown in preclinical studies, tri-specific and tetra-specific ANKETsTM are promising candidates for the next generation of tumor immunotherapies.

Eric Vivier, Ph.D., SVP and Chief Scientific Officer**, Innate Pharma,** *France*

5:15 **The Potential of NK Cell Based Therapies for Cancer Treatment**

T cells engineered with chimeric antigen receptors (CARs) have revolutionized the field of cell therapy and changed the paradigm of treatment for many patients with relapsed or refractory B-cell malignancies. Despite this progress, there are limitations to CAR-T cell therapy in both the autologous and allogeneic settings, including practical, logistical and toxicity issues. Given these concerns, there is a rapidly growing interest in NK cells as alternative vehicles for CAR engineering, given their unique biological features and their established safety profile in the allogeneic setting. Moreover advances in the development of bispecific (BiKes) and trispecific (TriKes) antibodies are proving very promising; these engineered receptors engage receptors on the surface of immune cells (e.g CD3 on T cells, CD16 on NK cells) from one end and from another end bind to antigens on the surface of tumor cells bringing effector and target cells closer together to enhance cytotoxicity. The pace of these developments will undoubtedly benefit from multiple innovative technologies, such as the CRISPR-Cas gene editing system, which offers great potential to enhance the natural ability of immune effector cells to eliminate refractory cancers.

Rafet Basar, M.D., Assistant Professor, Stem Cell Transplantation**, MD Anderson Cancer Center**

Track 2: ANTIBODY LIBRARY DESIGN, SELECTION AND SCREENING

4:45 **Deep Mutational Scanning Epitope Profiling to Inform the Development of Less Escapable Antiviral Antibodies**

The SARS-CoV-2 pandemic illustrates the importance of methods and strategies to evaluate the robustness of therapeutic antibodies to viral evolution. We developed a deep mutational scanning approach to comprehensively map antibody epitope, enabling prospective evaluation of the mutations that enable escape from antibody neutralization. These maps inform the administration of currently approved clinical antibodies, and aid in the development of future generations of antibodies with greater robustness to viral evolution.

Tyler Starr, Ph.D., Postdoctoral Fellow**, Fred Hutchinson Cancer Research Center**

5:15 **Function-first Antibody Discovery - Accelerating Target Deconvolution for Therapeutic Antibody Candidates Using Highly Parallelized Genome Editing**

Phenotypic (function-first) discovery promises to discover therapeutic antibodies towards novel targets, yet the target deconvolution remains a severe bottleneck. Here, we use pooled CRISPR/Cas9 screening to rapidly deconvolute the targets of 38 of 39 antibodies (97%), a success rate far higher than with existing deconvolution approaches. Our data establish CRISPR/Cas9 as an efficient target deconvolution approach, with immediate implications for the implementation of phenotypic discovery.

Jenny Mattsson, Senior Research Engineer**, BioInvent International AB,** *Sweden*

Annual Meeting of the ANTIBODY SOCIETY

Special Session of the Antibody Society

5:45-6:30 **Antibodies to Watch in 2022**

This "Antibodies to Watch" talk will summarize data for antibody therapeutics in regulatory review and recently approved in the US and EU, and project which may be approved in 2022. Trends in the development of antibody therapeutics for COVID-19 will also be discussed.

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

MAIN CONFERENCE

THURSDAY, DECEMBER 16, 2021

Track 1: ADVANCES WITH CAR-EFFECTORS

8:25 **Co-Chairs' Remarks**

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

Shimobi Onuoha, Ph.D., Head, Protein Engineering**, Autolus Limited,** *United Kingdom*

8:30 **Rethinking Allogeneic CAR T Therapies**

Avoiding the induction of Graft versus Host disease is a key attribute required for developing allogeneic CAR T cell therapy. Strategies that utilize the co-expression of either an interfering peptide or shRNA alongside the CAR itself are now in the clinic and have delivered initial proof of principle that non-gene edited allogeneic CAR T therapy is feasible and suitable for further clinical development.

David Gilham, Ph.D., Chief Scientific Officer, **Celyad S.A., Belgium**

9:00 **Novel Engineered Tuneable CARs Using Single Domain Antibody Modalities**

CAR-T cells have demonstrated potent efficacy in several tumour settings. However, side effects such as CRS and on-target off-tumour activity still represent source of concern. We have developed a modular CAR architecture based on the interaction between a single domain antibody and a dedicated synthetic peptide which can be selectively displaced by a clinically safe small molecule. This format allows for a tuneable CAR activity with improved safety profile.

Mathieu Ferrari, Ph.D., Senior Director, Binder Discovery**, Autolus Ltd.,** *United Kingdom*

9:30 **Engineering Next-Generation CAR-T Cell Therapy for Cancer**

Chimeric antigen receptor (CAR) technology has provided a new category of cancer therapy, but the engineering of CAR molecules remains an imprecise art. Here, I will present recent work on tuning CAR signaling activities via rational protein design to achieve greater in vivo anti-tumor efficacy. This presentation will highlight the potential of synthetic biology in generating novel mammalian cell systems with robust therapeutic functions.

Yvonne Y. Chen, Ph.D., Associate Professor, Department of Microbiology, Immunology, and Molecular Genetics, Department of Chemical and Biomolecular Engineering**, University of California, Los Angeles**

10:00 **Networking Refreshment Break**

10:30 **Optimizing Costimulatory Antigen Receptors (CoStAR) to Enhance the Efficacy of TIL Therapy**

Tumor infiltrating lymphocyte (TIL) based therapy can be very effective against solid tumors. Instil Bio, Inc. has demonstrated the activity of its propriety TIL manufacturing process in melanoma patients including those with disease progression following checkpoint inhibitor therapy and targeted therapy. To potentially enhance the efficacy further we are optimizing our CoStAR approach whereby we engineer the TIL to provide tumor associated antigen specific costimulation. The activity of the optimized receptors will be described. This is a potentially general approach to the optimization of T-cell based therapy.

Robert Hawkins, M.D., Ph.D., Chief Strategy Advisor**, Instil Bio,** *United Kingdom*

11:00 **VivoVec, A Novel Gene Delivery Platform for Therapeutic CAR Production In Vivo**

VivoVec is a proprietary lentiviral vector-based platform to engineer immune effector cells in vivo, overcoming multiple issues associated with ex vivo immunotherapies, including long turnaround time, high manufacturing cost, and scalability. VivoVec particles are engineered to express surface proteins for enhanced binding and transduction of diverse immune effector cell populations. This novel approach to in vivo genetic engineering offers the potential to deliver advanced "off-the-shelf" immunotherapies at scale.

Byoung Ryu, Ph.D., SVP, Head of Discovery & Vector Biology**, Umoja Biopharma**

Track 2: TARGETED DRUG CONJUGATES

8:25 **Co-Chairs' Remarks**

Gregory Adams, Ph.D., Chief Scientific Officer**, Elucida Oncology**

Peter Senter, Ph.D., VP, Distinguished Research Fellow**, Seattle Genetics**

8:30 **ELU001, A Targeted Topoisomerase-1-C'Dot Conjugate for the Treatment of Folate Receptor Alpha Overexpressing Cancers**

C'Dot Drug Conjugates (CDCs) are ultra-small (6-7 nm) nanoparticle drug conjugates capable of efficient targeting and penetration of tumors including difficult to access tumors in the brain and pancreas. ELU001 is a potent CDC functionalized with ~20 molecules of exatecan and targeted to FRα overexpressing cancers with ~15 folic acids molecules. ELU001 exhibits potency in the low single digit nanomolar to sub-nanomolar range against cancer cells that express moderate to high levels of FRα outperforming anti-FRα ADC based on mirvetuximab soravtansine.

Gregory Adams, Ph.D., Chief Scientific Officer, Elucida Oncology

9:00 **Mechanisms of ADCs and Their Role in the Realm of Immune Oncology**

Antitumor activity of monoclonal antibodies conjugated to monomethyl auristatin E (MMAE), a microtubule-disrupting agent, results in mitotic arrest and apoptotic cell death. We have discovered that auristatin conjugated ADCs drive an immunogenic form of cell death, which results in direct engagement of the immune system. Preclinically, activation of the immune system with Auristatin ADCs is unique and associated with curative anti-tumor activity as monotherapy and potentiates the combinatorial activity of multiple Immune-oncology agents.

Shyra Gardai, Ph.D., Executive Director of Immunology**, Seattle Genetics**

9:30 **The Role of Bystander Killing in ADC Tissue Penetration and Design**

Antibody drug conjugates (ADCs) have made significant progress recently with 6 approvals in the past 2 years, included 3 ADCs for solid tumors. These ADCs are tailored to their specific target and include payloads capable of bystander killing, where the free payload diffuses out of a targeted cell and into nearby cells. Here, we quantify the penetration distance and cell killing efficiency of bystander payloads to facilitate next-generation drug design.

Greg Thurber, Ph.D., Associate Professor, Chemical Engineering and Biomedical Engineering**, University of Michigan**

10:00 **Networking Refreshment Break**

10:30 **XMT-2056: Targeted STING Agonism Via An Immunosynthen Antibody Drug Conjugate**

Although STING biology has been very well studied and plays a central role in innate immune activation, clinical approaches to enable this mechanism to date have been disappointing. The Immunosynthen platform has been developed specifically to harness the benefits of an antibody drug conjugate approach for tumor-targeted STING agonism to improve both efficacy and tolerability.

Timothy Lowinger, Ph.D., Chief Science and Technology Officer**, Mersana Therapeutics**

MAIN CONFERENCE

THURSDAY, DECEMBER 16, 2021

Track 1: ADVANCES WITH CAR-EFFECTORS

11:30 **Harnessing Immunogenic Chemotherapy to Enhance CAR-T Activity in Solid Tumors**

CAR-T cell therapy has proven transformative for hematological malignancies but has had limited success in solid tumors, where poor tumor infiltration and loss of T cell function are major barriers to efficacy. We show that immunogenic chemotherapies like oxaliplatin can remodel the tumor microenvironment to permit greater CAR-T cell entry. This regimen sensitized previously refractory tumors to checkpoint blockade, providing a strategy to improve CAR-T cell efficacy in the clinic.

Shivani Srivastava, Ph.D., Assistant Professor, Human Biology Division**, Fred Hutchinson Cancer Research Center**

12:00 **Networking Luncheon**

Track 1: NEXT WAVE OF IMMUNO-ONCOLOGY THERAPEUTIC ANTIBODIES

1:25 **Chairwoman's Remarks**

Jennifer Cochran, Ph.D., Professor and Department Chair of Bioengineering**, Stanford University**

1:30 **Anti-GD2 Antibodies Block GD2:Siglec-7 Interactions and Synergize with Anti-CD47 to Mediate Tumor Clearance in Neuroblastoma and Other GD2+ Malignancies**

Anti-GD2 antibody is part of the standard of care for patients with high-risk neuroblastoma. However, at least 40% of patients still relapse. CD47 is a macrophage checkpoint and CD47 blockade can enhance the efficacy of tumor targeting antibodies. We have demonstrated unique and profound synergy of anti-GD2 and anti-CD47 antibodies and our studies have uncovered new mechanistic insights into the role of GD2 as an immunomodulatory molecule.

Robbie Majzner, M.D., Assistant Professor, Pediatrics - Hematology & Oncology**, Stanford**

2:00 **Hard Targets in Cancer Therapeutics: Engineering a Next Generation Anti-VISTA Antibody**

Despite significant progress in cancer immunotherapy in recent years, resistance to existing immune checkpoint therapies is common. VISTA (V-domain immunoglobulin suppressor of T cell activation), a predominant myeloid immune receptor potently suppresses T cell activity in a variety of cancers and has been associated with a lack of response to checkpoint therapies clinically, making it a promising therapeutic target. However, with limited characterization of the VISTA pathway and uncertainty around the cognate VISTA ligand development of effective anti-VISTA antibodies has been challenging. Here, we will present how Hummingbird approaches challenging targets such as VISTA. HMBD-002 is a novel neutralizing anti-VISTA antibody, developed using Hummingbird Bioscience's AI-directed Rational Antibody Discovery Platform, that binds to a computationally predicted and species-conserved functional epitope, distinct from other anti-VISTA antibodies. HMBD-002 potently neutralizes VISTA activity and inhibits tumor growth by remodeling an immunosuppressive tumor microenvironment. Leveraging an IgG4 backbone, HMBD-002 is the only VISTA-targeting antibody that has been shown to block the inhibitory function of VISTA and induce an anti-tumor response, without depleting VISTA positive cells required for a robust immune response, thus manifesting favorable pharmacokinetic and safety profiles. In conclusion, HMBD-002 represents an effective therapeutic option for addressing VISTA mediated immunosuppression across a broad range of tumors.

Jerome Boyd-Kirkup, Ph.D., Chief Scientific Officer and Co-Founder**, Hummingbird Bioscience**

Track 2: TARGETED DRUG CONJUGATES

11:00 **ImmunoPET with 89Zr-Df-crefmirlimab for Imaging CD8 T Cell Responses to Immunotherapy**

Non-invasive imaging of immune responses could provide key information to select patients for immunotherapy, monitor responses, and accelerate the development of new therapies. Engineered antibody fragments (cys-diabodies and minibodies) recognizing murine or human CD8 have been radiolabeled for preclinical/clinical PET imaging. A Phase I and ongoing Phase II clinical trial confirm the ability to image CD8+ cells in patients using 89Zr-Df-crefmirlimab and demonstrate the potential of directly imaging immune responses.

Anna Wu, Ph.D., Chair and Professor, Department of Immunology & Theranostics**, City of Hope**

11:30 **Late Breaking Presentation**

12:00 **Networking Luncheon**

Track 2: INNOVATIVE TARGETS FOR ANTIBODY-BASED THERAPIES

1:25 **Chairman's Remarks**

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

1:30 **Targeting NEDD9 to Inhibit Platelet-endothelial Adhesion and Pulmonary Thrombosis**

In human pulmonary artery endothelial cells, hypoxia upregulates the Cas protein NEDD9 including increased expression of a pro-thrombotic peptide on the extracellular plasma membrane surface (N9-p). In turn, N9-p functions as a ligand for activated platelets and modulates thrombotic pulmonary vascular remodeling. Inhibiting N9-p through antibody technology has important therapeutic implications for patients with chronic thromboembolic pulmonary hypertension and other clinical disorders characterized by increased platelet-endothelial adhesion.

Bradley Maron, M.D., Associate Professor of Medicine**, Harvard Medical School**

2:00 **Engineering Targeted Antibody Therapeutics Against Multi-drug Resistant Bacterial Infections**

One of the most salient infectious disease threats at present stems from multi-drug resistant bacteria (MDR). Despite the urgent and unmet need for new therapies against MDR pathogens, there are only 6 monoclonal antibody drugs in the clinical pipeline targeted toward MDR infections. Our project harnesses molecular discovery platforms to isolate novel antibodies against MDR Klebsiella pneumonaie surface proteins in order to design novel therapeutics that mediate MDR bacterial clearance.

Jamie Spangler, Ph.D., Assistant Professor, Biomedical Engineering and Chemical & Biomolecular Engineering**, Johns Hopkins University**

2:30 **Therapeutic Antibody Against GDF-15 for Cancer-associated Cachexia and Cancer Immunotherapy**

Growth differentiation factor 15 (GDF15) is a member of the TGF superfamily. GDF15 induces cachexia and prevents excessive immune cell infiltration during tissue damage. GDF15 is over-expressed in many tumor types, and the elevated GDF15 levels correlate with poor prognosis and reduced overall survival. We have developed a humanized antibody targeting GDF15 for cancer-associated cachexia and cancer immunotherapy.

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

MAIN CONFERENCE

THURSDAY, DECEMBER 16, 2021

Track 1: NEXT WAVE OF IMMUNO-ONCOLOGY THERAPEUTIC ANTIBODIES

2:30 **Improved Therapeutic Index to CTLA4 with An Acidic pH-selective Antibody**

Although therapeutically efficacious, Ipilimumab exhibits dose-limiting toxicity that prevents maximal efficacious clinical outcomes. We hypothesized that an acidic pH-selective Ipilimumab (pH Ipi), which preferentially and reversibly targets the acidic tumor microenvironment over the neutral periphery, will have a more favorable therapeutic index. While Ipilimumab has pH-independent CTLA4 affinity, pH Ipi variants have been engineered to have up to 100-fold enhanced affinity to CTLA4 at pH 6.0 compared to pH 7.4. In hCTLA4-knock-in mice, these variants have maintained anti-tumor activity and reduced peripheral activation, a surrogate marker for toxicity. pH-sensitive therapeutic antibodies may be a differentiating paradigm and a novel modality for enhanced tumor targeting and improved safety profiles.

Peter Lee, Ph.D., Principal Scientist**, Bristol Myers Squibb**

3:00 **Networking Refreshment Break**

3:30 **High Avidity, Bispecific IgM Antibodies as T Cell Engagers for Treatment of Hematologic Malignancies**

Bruce Keyt, Ph.D., Chief Scientific Officer**, IGM Biosciences**

4:00 **A Novel Platform for Next-generation T-cell Bispecific Antibody**

We have developed a next-generation T-cell bispecific antibody with superior anti-tumor efficacy to conventional ones. Our novel platform enables the antibody to improve T-cell status and tumor microenvironment by adding an extra MoA on current one. Details of the lead antibody generation, protein engineering, and preclinical results will be presented.

Shun Shimizu, Researcher, **Chugai Pharmaceutical co., ltd.,** *Japan*

4:30 **Advancement of MATCH Antibodies to Clinical-stage: Novel Therapeutics with Tumor Targeted Immunomodulatory Functions and the Potential for Favorable Benefit-risk Profiles**

Several therapeutic approaches based on Numab's MATCHTM platform are presented which aim at multispecific designs with superior efficacy and favorable safety. NM21-1480 is a trispecific scMATCH-3 currently in phase 1 clinical testing. NM21-1480 potently stimulates anti-cancer immune responses by tumor-localized activation of the immune stimulatory receptor 4-1BB and concomitant blockade of the immune suppressive PD-L1 pathway. We discuss the relevance of molecular formats, 4-1BB epitopes and relative affinities to each target protein to exploit the full synergistic potential of dual pathway modulation and at the same time to avoid systemic activity/toxicity. Preliminary data from the ongoing, first-in-human, open-label, phase I/IIa trial of NM21-1480 in advanced solid tumors are presented. Furthermore, design and key preclinical data of therapeutic concepts based on our MATCH-CD3 platform, targeting MSLN and other TAAs are discussed.

Tea Gunde Ph.D., Vice President, Discovery**, Numab Therapeutics AG,** *Switzerland*

5:00 **Close of Conference**

Track 2: INNOVATIVE TARGETS FOR ANTIBODY-BASED THERAPIES

3:00 **Networking Refreshment Break**

3:30 **Poly-GA antibodies for the therapy of C9orf72 ALS and FTD**

A hexanucleotide-repeat expansion in an intron of C9orf72 is the most common cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). We discovered that the expanded repeat is translated in all reading frames into aggregating dipeptide repeat proteins, most abundantly poly-GA. Anti-GA antibodies inhibit the cell-to-cell transmission of poly-GA and downstream pathology. We are exploring the mode of action to develop anti-GA antibodies for the therapy of C9orf72 ALS/FTD.

Dieter Edbauer, M.D., Professor of Translational Neurobiochemistry**, DZNE, Germany**

4:00 **Antibody Targeting of APOE-HSPG Interactions to Promote Resistance to Alzheimer's Disease**

We reported on the association of the APOE3 Christchurch variant to resistance to autosomal dominant Alzheimer's disease. APOE3 Christchurch is severely deficient in its ability to bind heparin sulphate proteoglycans (HSPG), a defect that we hypothesize is critical for its robust protective effects. We developed monoclonal antibodies that bind to APOE isoforms and inhibit binding to HSPG.

Joseph Arboleda-Velasquez, M.D., Ph.D., Assistant Professor of Ophthalmology**, Harvard Medical School**

4:30 **Pathogenesis to Therapeutic: Paradoxical Actions of IgG on Insulin Sensitivity**

Systemic low-grade inflammation is a hallmark of insulin resistance; however, the mechanisms by which the immune system can propagate systemic insulin resistance remains poorly understood. IgG antibodies can display paradoxical properties both propagating inflammation, and conversely suppress inflammation when given at sufficiently high doses. Here, we demonstrate that IgG can exert this paradigm on insulin sensitivity. Engineering the Fc region of IgG, we further demonstrate its ability to function as a novel insulin sensitizer. These results demonstrate new insights into the systemic nature of insulin resistance, a novel mechanism of the disease, and an innovative therapeutic strategy for treating type 2 diabetes.

Andrew Lipchik, Ph.D., Assistant Professor of Pharmaceutical Sciences**, Wayne State University**

5:00 **Close of Conference**

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Guest Session Chairs

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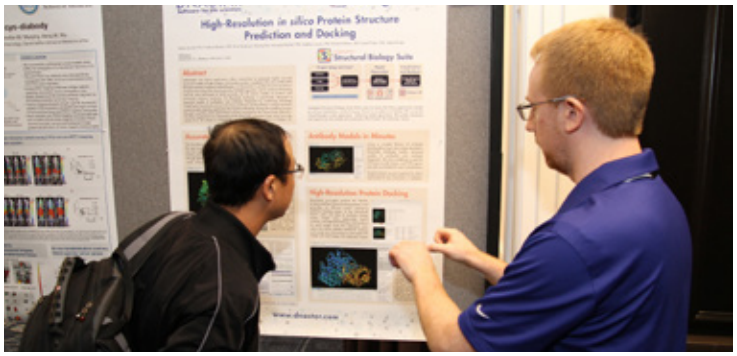

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