Antibody Engineering & Therapeutics Europe

05-07 June, 2018
Hilton Amsterdam
Amsterdam, The Netherlands

European Meeting of the ANTIBODY SOCIETY

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

Keynote Speakers to Help You Fast-Track Your Antibody Development

Frontiers of Immunotherapy

Clive Wood, Ph.D.
Corporate Senior Vice President, Global Head of Discovery Research, BOEHRINGER INGELHEIM, *Germany*

T cell Recognition in Human Cancer

Ton Schumacher, Ph.D.
Professor of Immunotechnology, LEIDEN UNIVERSITY and Principal Investigator, THE NETHERLANDS CANCER INSTITUTE, *The Netherlands*

How Antibodies Trigger Cytotoxicity?

Prof. Paul W.H.I. Parren, Ph.D.
Professor, Department of Immunohematology and Blood Transfusion, LEIDEN UNIVERSITY MEDICAL CENTER AND SPARRING BIOLOGICS B.V., *The Netherlands*

Microbiome and Checkpoint Inhibitors in Immuno-Oncology

Laurence Zitvogel, M.D., Ph.D.
Scientific Director, GUSTAVE ROUSSY CANCER CENTRE, *France*

Produced by the Organisers of the Antibody Engineering & Therapeutics San Diego Event

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THE INDUSTRY'S EUROPEAN MEETING FOR ANTIBODY AND PROTEIN THERAPEUTIC SCIENCE, TECHNOLOGY AND NETWORKING

SCIENCE

Accelerate your pipeline of antibody and protein therapeutics to market by applying best practices and lessons learned from case studies and new data presentations from global industry leaders working across the entire spectrum of antibody discovery and development.

TECHNOLOGY

Bring your product to market by meeting leading product and service providers showcasing exciting antibody technologies in our poster and exhibit hall.

NETWORKING

Connect with industry and academic scientists and executives from Europe and around the world focused on antibody and protein therapeutic discovery and development during lunches, cocktail receptions and networking breaks. Networking has never been easier with the included conference app that allows you to view the attendee list and schedule meetings before, during and after the event.

Tuesday, 05 June, 2018 • Pre-Conference Workshops*

*Additional registration fee applies. See the pricing page or visit the website for more details.

08:00 *Registration and Coffee*

Morning Half-Day Workshop • 08:40-12:15
Workshop A: The Nuts and Bolts of Antibodies

08:40 **Workshop Moderator's Remarks**
Mahendra Deonarain, Ph.D., Chief Executive and Science Officer, **Antikor Biopharma Ltd.,** *United Kingdom*

08:45 **Display Technology and Antibody Discovery**
John McCafferty, Ph.D., Founder and CEO, **IONTAS,** *United Kingdom*

09:15 **Antibody Fragments and How to Make Them Work as ADCs**
Antibody fragments like single-chain Fvs have long been thought of as a stepping stone to antibody-based therapeutics. ScFvs are often rebuilt into larger formats as they are viewed as being too small and are cleared from the body too quickly to make viable therapeutics. This presentation will show that scFvs, suitably engineered and conjugated to payloads can make effective drug candidates on their own and the clearance and penetration properties could be a better way to apply them in the field of antibody drug conjugates for solid tumours. Novel concepts in antibody discovery, structure, functions and bio-conjugation will be covered with a view to making effective FDCs (Fragment Drug Conjugates).
Mahendra Deonarain, Ph.D., Chief Executive and Science Officer, **Antikor Biopharma Ltd.,** *United Kingdom*

09:45 **Preclinical "Humanised" Tumor Models for the Characterisation of Functional Antibodies and Drug Conjugates**
To overcome the current constraints in preclinical evaluation of functional antibodies for cancer immune therapy we have developed PDX models on mice with a functional human immune system. At the time when the human immune system is developed, established patient-derived xenografts (PDX) were transplanted on these humanised mice, enabling appropriate preclinical studies on tumor immune biology, evaluation of new immune therapies and combinations, as well as the identification and validation of biomarkers for tumor immune therapy.
Jens Hoffmann, Ph.D., CEO, **EPO Experimental Pharmacology & Oncology Berlin-Buch GmbH,** *Germany*

10:15 *Networking Refreshment Break*

10:45 **Fundamentals of Mass Spectrometry in the Analysis of Protein Therapeutics**
Modern mass spectrometry (MS) has become a powerful technology in life sciences and provides unprecedented insights into the composition, structure and function of complex biopharmaceuticals. This workshop will describe the principles underlying MS-based strategies and the wide range of applications of MS to structurally and functionally assess proteins, and antibodies in particular.
Ewald Van den Bremer, Ph.D., Senior Scientist, **Genmab,** *The Netherlands*

11:15 **Fc-mediated Effector Functions and Engineering Strategies for Specific Modulation**
Monoclonal antibodies are able trigger various Fc-mediated effector functions such as antibody-dependent cell-mediated cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC) and phagocytosis. With a focus on cancer therapy the relative contribution of selected effector functions to therapeutic activity and engineering strategies to rationally design antibodies with tailor-made effector functions will be discussed.
Matthias Peipp, Ph.D., Professor and Head of Research, Division of Stem Cell Transplantation and Immunotherapy, **Christian-Albrechts-University Kiel,** *Germany*

11:45 **IgA As a Novel Isotype for Treatment of Lymphoma and Neuroblastoma**
All therapeutic antibody in the clinic are of the IgG class. But IgA has great potential in vitro, it recruits neutrophils with a different mode of action. With a panel of new antibodies against CD20 for lymphoma and against GD2 for neuroblastoma we see clear advantages in preclinical models.
Jeanette Leusen, Ph.D., Associate Professor, Head Immunotherapy Group and UMAB Facility, Laboratory for Translational Immunology, **UMC Utrecht,** *The Netherlands*

12:15 *Close of Workshop A*

12:20 *Lunch Provided for Full-Day Workshop Attendees Only*
(Those registered for both workshop A and workshop B)

Afternoon Half-Day Workshop • 13:40-17:15
Workshop B: CAR-T & anti-CD3-based Bispecifics

13:40 **Workshop Moderators' Remarks**
Kerry A. Chester, Ph.D., Professor of Molecular Medicine, UCL Cancer Institute, **University College London,** *United Kingdom*
David Gilham, Ph.D., Vice President of Research and Development, **Celyad S.A.,** Belgium

13:45 **CAR-T Design Theory to Practice**
Martin Pule, Ph.D., Senior Lecturer in Haematology, UCL Cancer Institute, **University College London,** *United Kingdom*

14:15 **Engineering the NKG2D Receptor to Enable CAR T Cell Therapy of Cancer**
Natural Killer group 2D (NKG2D) is a NK activatory receptor that binds to 8 stress-inducible ligands which are known to be over-expressed in cancer. A CAR consisting of the fusion of the NKG2D protein with CD3z enables T cells to target these stress ligands and is currently being tested in phase I clinical trial. Our on-going work is seeking to understand how further engineering of the NKG2D CAR alters the functionality of receptor.
David Gilham, Ph.D., Vice President of Research and Development, **Celyad S.A.,** *Belgium*

14:45 **IL-18 Induces T-bet(High) FoxO1(Low) T cells with Improved Activity in the CAR T cell Therapy of Advanced Solid Tumors**
CAR T cells with inducible IL-18 release showed T-bet(high) FoxO1(low) signature, induced an overall change in the tumor immune cell landscape, showed superior activity against large established tumors of pancreatic and lung cancer.
Hinrich Abken, Ph.D., Professor, Genetics & Immunology, Center for Molecular Medicine Cologne, **University of Cologne,** *Germany*

15:15 *Networking Refreshment Break*

15:45 **ADAPTIR Platform: Rapid Development of Novel and Manufacturable Bispecific Therapeutics**
The presentation will highlight the activity, stability and manufacturability of ADAPTIR bispecifics and include recent data for a lead preclinical candidate, APVO436, which targets CD123 and CD3. APVO436 has shown potent biological activity in preclinical studies and is rapidly advancing towards first-in-human clinical trials. The presentation will also cover Aptevo's other pipeline candidates, including APVO414 (PSMA x CD3) and ALG.APV.527 (4-1BB x 5T4).
David Bienvenue, Ph.D., Senior Director, **Aptevo Therapeutics,** *USA*

16:15 **Late Breaking Presentation**

16:45 **Panel Discussion**

17:15 *Close of Workshop B*

Wednesday, 06 June, 2018 • Keynote Presentations

07:30 *Registration, Coffee and Exhibit/Poster Viewing*

08:25 **Chairperson's Remarks**

08:30 **Frontiers of Immunotherapy**

As our understanding of the molecular and cellular control of the immune system has grown, we have exploited this knowledge to bring about major advances in human health. Immunology has furnished both the tools, often in the form of monoclonal antibodies, as well as the insights in to disease mechanisms that have created breakthroughs in multiple therapeutic areas. The pace of this innovation continues to grow as exemplified by checkpoint inhibitors and engineered T-cell therapeutics. Examples of the next advances in immunotherapy will be discussed with an emphasis on treatments for autoimmune diseases and cancer.

Clive R. Wood, Ph.D., Corporate Senior Vice President, Global Head of Discovery Research, **Boehringer Ingelheim,** *Germany*

09:05 *Keynote Questions*

09:10 **T cell Recognition in Human Cancer**

The central ambition of our work is to determine which factors limit the ability of T cells to control human cancers, with the ultimate aim to overcome these barriers. Using assays of human tumour material we are determining how the differentiation state of intratumoral T cells can help predict therapy outcome. Furthermore, using genetic screening systems, we are identifying novel regulators of the immune checkpoints that control the activity of such intratumoral T cells. Collectively, this work is expected to yield novel therapeutic leads and improved biomarkers that may be used for patient stratification.

Ton N. Schumacher, Ph.D., Professor of Immunotechnology, Leiden University and Principal Investigator, **The Netherlands Cancer Institute,** *The Netherlands*

09:45 *Keynote Questions*

09:50 *Networking Refreshment Break and Exhibit/Poster Viewing*

10:30 **How Antibodies Trigger Cytotoxicity?**

Antibodies are the gatekeepers of our immune system. They latch on to cells or antigens recognised as foreign in a highly specific manner and mark them for killing and/or destruction. In immunotherapy, we have learned to exploit these unique qualities of antibodies for the generation of a myriad of successful drugs in a wide range of therapeutic indications. In this keynote lecture I will discuss how antibodies may induce cell killing, varying from recent insights into the mechanism of complement activation to the use of antibody-conjugates to deliver cytotoxic drugs.

Paul W.H.I. Parren, Ph.D., Professor, Department of Immunohematology and Blood Transfusion, **Leiden University Medical Center and Sparring Biologics B.V.,** *The Netherlands*

11:05 *Keynote Questions*

11:10 **The Microbiome in Cancer Immunotherapy: Diagnostic Tools and Therapeutic Strategies**

Over the last 5 years, the concept that the intestinal microbiota determines the efficacy of anticancer immunotherapies has been proven by epidemiological associations in clinical studies, as well as by experiments in mouse models. The microbiota offers new predicting diagnosis tools and promises to become the target for future antineoplastic therapies.

Laurence Zitvogel, M.D., Ph.D., Scientific Director, **Gustave Roussy Cancer Centre,** *France*

11:45 *Keynote Questions*

11:50 Scientific Briefing

Affinity Measurements: Ask the Right Question and Choose the Right Technology to Have an Unbiased Answer

Generation of high affinity antibodies is a design goal for many therapeutic programs. A number of technologies and instruments are available for measuring antibody affinities. Each one has its own merits and demerits, depending on the sensitivity and throughput requirements as well as whether the target is soluble or membrane expressed which will be discussed in the presentation.

Palaniswami Rathanaswami, Ph.D., Senior Scientist, Biologics Discovery, **Amgen, Inc.,** *Canada*

12:20 *Networking Lunch and Exhibit/Poster Viewing*

13:30 Scientific Briefings

Challenges and Opportunities in Early Stage Antibody Drug Discovery

LifeArc's BioTherapeutics group looks to collaborate in the translational drug discovery space between academia and industry. We aim to de-risk targets by developing biologics and validation studies to independently confirm published reports and develop therapeutics. We will discuss some case studies to show, together with our collaborative partners, we have helped develop novel targets to lead therapeutic candidates for indications such as osteoporosis, asthma and dementia.

David Matthews Ph.D., Head of BioTherapeutics, Associate Director, **LifeArc,** *United Kingdom*

Track 1: Intractable Targets/Antibody Discovery Technologies

14:00 **Chairman's Remarks**
John McCafferty, Ph.D., Founder and CEO, **IONTAS,** *United Kingdom*

14:05 **Immunomodulatory Target Discovery Using Antibody Technologies**
Antibodies able to modulate function of immune cells represent promising assets for prevention and treatment of disease, in particular, for autoimmune disorders and cancer. In this presentation, phenotypic screen approach that yielded antibodies able to restore function of impaired immune cells will be discussed.
Katarina Radošević, Ph.D., Global Head Biologics Research, **Sanofi R&D,** *France*

14:35 **Encapsulation of Single Cells for Antibody Discovery**
Andrew Griffiths, *Professor of Biochemistry,* **École Supérieure de Chimie Industrielles de Paris (ESPCI),** *France*

15:05 **Building a Single Donor Phage Antibody Library with NGS Validation?**
The traditional approach to generating natural phage antibody libraries has been to use as many donors as possible. However, given that naive B cells each have unique antibodies, it may be more important to use as many lymphocytes as possible, even if derived from a single donor. This talk will describe the creation of a highly functional antibody library from a single donor, in which all steps were quality controlled by next generation sequencing.
Andrew Bradbury, M.D., Ph.D., Chief Scientific Officer, **Specifica,** *USA*

15:35 *Networking Refreshment Break and Exhibit/Poster Viewing*

16:15 **Generation of Ion Channel Blocking Antibodies by Fusing Venom-derived "Knottins" into Antibody CDR Loops**
Cysteine-knot miniproteins (knottins) have potential as therapeutic agents to block ion channels and GPCRs in cancer, autoimmunity and chronic pain but suffer from manufacturing difficulties, short half-lives and a lack of specificity. Using X-ray crystallography and biochemical assays we have demonstrated that functional knottins can be inserted into peripheral antibody CDRs via short linkers This approach greatly increases the diversity of these peripheral CDR loops while allowing additional contribution of binding from the remaining CDRs. Thus, the resulting "knotbody" retains the advantage of blocking activity from the knottin while enjoying the extended half-life and additional specificity conferred by the antibody molecule.
Aneesh Karatt-Vellatt, Ph.D., Senior Research Scientist, **Iontas,** *United Kingdom*

16:45 **Opportunities for Therapeutic Antibodies Directed at G Protein-coupled Receptors and Ion Channels**
G protein-coupled receptors (GPCRs) and ion channels represent important target classes for therapeutic drug discovery across a wide range of diseases. Progress made with antibody-based therapeutics will be reviewed outlining the breadth and diversity of antibody molecules, target opportunities in the global R&D and the clinical pipeline, as well as the expansion of opportunities afforded by next-generation modalities.
Cath Hutchings, Ph.D., Independent Consultant, *United Kingdom*

17:15 **Targeting Challenging Antigens**
Antibody therapeutics have transformed the treatment of cancer and inflammatory conditions. However, many targets, including carbohydrates and structured nucleic acids, remain challenging. This is exemplified by a failure to develop broad and long-lasting antibodies against influenza and HIV, which are cloaked in self-carbohydrate. Here we describe strategies and mutational trajectories that overcome antibody affinity and specificity limitations.
Daniel Christ, Ph.D., Associate Professor, Director Centre for Targeted Therapy, **Garvan Institute of Medical Research**

Track 2: Antibody Effector Functions and Novel Formats

14:00 **Co-Chairs' Remarks**
Jeanette Leusen, Ph.D., Associate Professor, Head Immunotherapy Group and UMAB Facility, Laboratory for Translational Immunology, **UMC Utrecht,** *The Netherlands*
Matthias Peipp, Ph.D., Professor and Head of Research, Division of Stem Cell Transplantation and Immunotherapy, **Christian-Albrechts-University Kiel,** *Germany*

14:05 **Mechanisms Underlying Antibody-mediated Complement Activation**
To understand how antibodies activate the complement system, we studied C1-antibody complexes formed on liposomes and in solution by cryo-EM tomography and single-particle analysis, respectively. The data suggest that complement may be initiated both through proximity of multiple complexes, providing cross-activation of the C1 proteolytic enzymes, and by single isolated complexes through compaction of the C1q arms upon binding to antibody Fc-platforms.
Piet Gros, Ph.D., Professor, Chemistry and Biomolecular Sciences, Bijvoet Center for Biomolecular Research, **Utrecht University,** *The Netherlands*

14:35 **Improving Therapeutic Activity of DR5-specific Antibodies by Inducing Hexamer Formation upon Target Binding – A Role for C1q**
IgG antibodies organise via intermolecular Fc-Fc interactions into ordered hexamers upon cell surface target binding. We identified Fc mutations that enhance antigen-dependent hexamerisation resulting in enhanced complement activation and/or enhanced target clustering, while retaining solution-monomericity and developability characteristics of regular human IgG1 (HexaBody® technology). This technology was applied to two non-competing DR5-specific antibodies. The dual epitope targeting and enhanced antibody hexamerisation by the mixture of these two HexaBody molecules induces potent DR5 agonist activity and tumor cell death through hexamer-induced DR5 clustering, which was enhanced in the presence of C1q.
Marije Overdijk, Ph.D., Senior Scientist, **Genmab BV,** *The Netherlands*

15:05 **Inhibition of Complement by Antibodies**
Uncontrolled complement activation contributes to the pathology of several diseases. Therapeutic monoclonal antibody-mediated complement inhibition strategies will be discussed.
Peter Boross, Ph.D., Senior Scientist, **Prothix B.V.,** *The Netherlands*

15:35 *Networking Refreshment Break and Exhibit/Poster Viewing*

16:15 **A Novel FAP-targeted 4-1BB Agonist for Combination Immunotherapy**
Immune co-stimulation via 4-1BB agonism is an important element of next generation CAR-T cell therapy. The clinical development of first generation 4-1BB agonistic antibodies has been hampered by hepatic toxicity. Here we describe a novel tumor targeted 4-1BB agonist for combination with T cell bispecific antibodies which may represent an off-the-shelf alternative to CAR-T cell therapies.
Christian Klein, Head Oncology Programs & Department Head Cancer Immunotherapy Discovery, Roche Pharmaceutical Research & Early Development, **Roche Innovation Center Zurich,** *Switzerland*

16:45 **Fc Engineering to Enhance Immunostimulatory Antibodies for Cancer Therapy**
Clinical results with immunomodulatory mAb have revived the belief that the immune system holds the key to controlling cancer. Here we show that immunostimulatory mAb can deliver therapy through multiple mechanisms in pre-clinical tumour models, and that the mechanism used depends on antigen expression, mAb isotype and FcγR availability. Using this knowledge, we engineered novel agents that were able to more effectively harness these mechanisms and thereby enhance outcome. These data have broad implications for selecting new immune targets, designing combination therapies and engineering mAb.
Stephen A. Beers, Ph.D., Associate Professor in Cancer Immunology and Immunotherapy, Antibody and Vaccine Group, **Cancer Sciences Unit, University of Southampton,** *United Kingdom*

17:15 **Targeting Immune Regulation at the Tumor Site: Defining the Interplay between Therapy and Tumor Microenvironment**
In recent years, several publications have demonstrated the essential role that the tumor microenvironment and Fc Receptors play for the vivo activity of checkpoint targeting antibodies. In this talk we will discuss novel development in this area relating the mechanism of action and the development of immune modulatory antibodies and combinations that promote intra-tumoural Treg with maximal modulatory activity.
Sergio A Quezada Ph.D., Professorial Research Fellow, Immune Regulation and Tumour Immunotherapy Group, **UCL Cancer Institute,** *United Kingdom*

17:45 *Networking Cocktail Reception and Exhibit/Poster Viewing*

07:30 Registration, Coffee and Exhibit/Poster Viewing

Track 1: Bioinformatics/Repertoires

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

Gunilla Karlsson Hedestam, Ph.D., Professor, Department of Microbiology, Tumor and Cell Biology, **Karolinska Institutet,** *Sweden*
Andrew Martin, D.Phil., Reader in Bioinformatics and Computational Biology, Institute of Structural and Molecular Biology, Division of Biosciences, **University aCollege London,** *United Kingdom*

8:30 **Patterns of Molecular Convergence in Antibody Repertoires Predict Antigen Exposure and Specificity**

Recent advances in high-throughput antibody repertoire sequencing are enabling highly quantitative analysis of adaptive immune responses. Here I will present, the computational and experimental methods my group has developed in antibody sequencing and their associated appliacations. For example, we are applying machine-learning approaches that enable prediction of the immune status of individual antibody clones. Finally, I will also highlight recent work in our group aimed towards applying genome editing technology in mammalian cells for directed evolution and antibody engineering.

Sai Reddy, Ph.D., Assistant Professor, Department of Biosystems Science and Engineering, **ETH Zurich/Swiss Federal Institute of Technology,** *Switzerland*

9:00 **Profiling Antibody Repertoires by Rep-Seq and RNA-Seq**

I will report our current approaches to antibody repertoire profiling starting from either RNA with unique molecular identifiers (UMI) introduced via 5'-RACE, or from RNA-Seq data. I will provide several examples from our current work, along with a basic explanation of technical parameters, limitations, and potential biases of the approaches.

Dmitriy Chudakov, Ph.D., Head of Genomics of Adaptive Immunity Department, **Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry,** *Russia*

9:30 **Repertoire Diversity and Maturation of Vaccine-Induced B Cell Responses**

Individualised/personalised antibody germline gene databases offer improved opportunities to study B cell responses in the context of vaccination, infection, autoimmunity, and cancer, providing a more comprehensive and accurate picture of antibody repertoires. I will describe our work on immunisation of non-human primates and show how HIV-1 vaccine-elicited antibody responses representing hundreds of unique HIV-1 envelope glycoprotein-specific monoclonal antibody lineages distribute in different immune compartments over different time points after immunisation.

Ganesh Phad, Ph.D. Student, Department of Microbiology, Tumour and Cell Biology, **Karolinska,** *Sweden*

10:00 *Networking Refreshment Break and Exhibit/Poster Viewing*

10:40 **Structurally Mapping Next-generation Sequencing Repertoires of Antibodies to Aid In-silico Therapeutic Design**

Provide an overview of the structural antibody database (SAbDab) and the computational antibody prediction toolset SAbPred developed by the Oxford Protein Informatics group. Tools include modelling and design pipelines. Discuss how predicted structural information can enrich data from next generation sequencing experiments.

Charlotte Deane, Ph.D., Professor of Structural Bioinformatics & Head of Department of Statistics, **University of Oxford,** *United Kingdom*

11:10 **Use of Antibody Sequence Analysis Tools to Discover anti-TIGIT Antagonists**

We conducted a proof-of-concept phage display study comparing and contrasting the performance of our currently available phage display libraries (XOMA, Distributed Bio, Mouse Immune). To analyze sequences from Sanger and NGS data, several antibody analysis tools (AbYsis, abgenesis, NetMHCIIpan, T20 Score Analyzer) were used to query our antibody leads. Some commonalities as well as some striking differences between the leads (generated from the three technologies) were discovered.

Aaron Sato, Ph.D., Chief Scientific Officer, **LakePharma,** *USA*

11:40 **Furthering our Understanding of Antibody Structure Space: The Pistoia Alliance Abvance Project**

The Pistoia Alliance Abvance Project is a pre-competitive initiative by pharma and academic partners to further our understanding of antibody structure space and enable faster and better decision-making in antibody drug discovery. Part of this is improving our ability to model antibody structure in situations where traditional experimental methods, such as X-ray crystallography, are not practical or too slow. We will outline our current efforts and how you can help.

Sebastian Kelm, D.Phil., Principal Scientist, CADD, **UCB,** *United Kingdom*

Track 2: Novel Antibody-based Therapeutics for Cancer & Immuno-oncology

08:25 **Co-Chairs' Remarks**

Agamemnon Epenetos, Ph.D., Consultant in Clinical Oncology, The Harley Street Clinic and Visiting Professor**, Imperial College London,** *United Kingdom*
Nicholas Wilson, Ph.D., Head of Immuno-Oncology, **Gilead Sciences**

08:30 **Targeting Intratumor Heterogeneity**

Expression of AXL earmarks melanoma cells resistant to BRAF and MEK inhibitors that either pre-exist in treatment-naive tumors or emerge in response to therapy. The combination of an AXL-MMAE antibody-drug conjugate with BRAF and MEK inhibitors eliminates heterogeneous melanoma cell populations and prolongs survival in experimental models at tolerable toxicity. This approach is currently being tested in clinical trials and provides insights into the therapeutic targeting of intra-tumor heterogeneity.

Daniel Peeper, Ph.D., Professor of Functional Oncogenomics, Head, Division of Molecular Oncology & Immunology, **The Netherlands Cancer Institute,** *The Netherlands*

09:00 **Antibody Targeted Radiotherapy (ATRT) for Side Effect Free Bone Marrow Conditioning**

The standard of care for bone marrow conditioning is HD-Melphalan followed by autologous or allogeneic HSCT. Conditioning with HD-Melphalan induces severe side effects such as diarrhea, mucositis and sepsis in the vast majority of patients, making HSCT a high risk and high cost therapy (18 days inpatient care). We have developed ATRT for side effect free bone marrow conditioning. We will report both about the preclinical development of ATRT as well as the clinical results generated in various diseases to be treated with bone marrow conditioning and HSCT.

Klaus Bosslet, Ph.D., Managing Director, **TheraPharm Deutschland GmbH,** *Germany*

09:30 **Cancer Immunotherapy beyond PD-1**

T cell checkpoint inhibitors set a clinical paradigm providing significant benefit to patients diagnosed with advanced cancer. Despite much success, a majority of patients do not respond to PD-1 or CTLA-4 blockade. Raising the number of patients benefiting from cancer immunotherapy requires novel therapeutic approaches aimed at these non-responders, for instance by modulating novel targets and pathways using antibodies and small molecules, as well as by rational combination therapy.

Andrea van Elsas, Ph.D., Chief Scientific Officer and Director, **Aduro Biotech Europe,** *The Netherlands*

10:00 *Networking Refreshment Break and Exhibit/Poster Viewing*

10:40 **CD38-specific Nanobody-based Heavy Chain Antibodies Show Potent Therapeutic Efficacy in a Systemic Human Lymphoma Xenograft Model**

The cell surface ecto-enzyme CD38 is a promising target antigen for the treatment of hematological malignancies. Llama-derived nanobodies have several advantages over conventional antibodies, including the capacity to bind and block the active site of enzymes, better tissue penetration in vivo, and the facile construction of bi- or multi-specific biologicals by genetic fusion (1). We have generated CD38-specific humanised heavy chain antibodies by fusion of CD38-specific nanobodies to the hinge and Fc-domains of wild type and engineered human IgG1. Some of these heavy chain antibodies mediate potent complement dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC) of CD38-expressing tumor cell lines in vitro. In vivo some of the heavy chain antibodies reduced the growth of systemic CA46 lymphomas in tumor-bearing SCID mice more effectively than Daratumuab, the benchmark conventional human IgG1 in the clinic.

Friedrich Koch-Nolte, Ph.D., Professor of Immunology, Institute of Immunology, **University Medical Center Hamburg-Eppendorf,** *Germany*

11:10 **Selective FcγR Co-engagement on APCs Modulates the Activity of Therapeutic Antibodies Targeting T Cell Antigens**

Therapeutic mAbs targeting co-inhibitory pathways, such as CTLA-4 and PD-1, have emerged as an important class of cancer therapies. Insights into the function of mAbs with different IgG isotypes have enabled modulation of the biological activity, providing opportunity to enhance their biological activity. We have discovered a previously unrecognized property of Fc-Fc gamma receptor co-engagement within the T cell-APC immune synapse that modulates the activity of mAbs targeting effector and regulatory T cell antigens.

Nicholas Wilson, Ph.D., Head of Immuno-Oncology, **Gilead Sciences**

11:40 **Click Chemistry-triggered Drug Release from a Tumor-bound ADC**

Current ADCs target internalizing receptors on cancer cells leading to intracellular drug release. Typically, only a subset of patients with solid tumors has sufficient expression of such a receptor, while there are suitable non-internalizing receptors. Here we report the development and in vivo validation of a non-internalizing ADC with the capacity to target cancer cells and release its therapeutic cargo extracellularly upon a click reaction with a chemical activator.

Marc Robillard, Ph.D., Chief Executive Officer and Founder, **Tagworks Pharmaceuticals,** *The Netherlands*

12:10 Scientific Briefing

chemcgenomix

12:40 *Networking Lunch and Exhibit/Poster Viewing*

13:50 Scientific Briefing

MaxCyte® FLOW TRANSFECTION

Track 1: Antibodies Alternative Delivery/Vaccines

14:20 **Co-Chairs' Remarks**

Özlem Türeci, M.D., Chair of CI3 (Cluster of Individualised Immune-Intervention) and Head of Clinical & Scientific Advisors Board, **BioNTech,** *Germany*

Ferry Ossendorp, Ph.D., Professor in Synthetic Vaccine Biology, Department of Immunohematology and Blood Transfusion, **Leiden University Medical Center,** *The Netherlands*

14:25 **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*

14:55 **A Tetanus-way of Boosting T cell Responses**

Immune complexes can greatly potentiate cross presentation and CD8 T cell activation. Herein a drug development project makes use of a drug design promoting antibody-drug complex formation in vivo to mediate improved T cell responses against a given antigen within the drug formulation.

Sara Mangsbo, Ph.D., Senior Associate Lecturer, Department of Pharmaceutical Biosciences, **Uppsala University,** *Sweden*

15:25 **Antibody Engineering for Targeted Nanovaccines**

Dendritic cell (DC) vaccination uses autologous immune cells to evoke potent tumor responses in cancer patients. The therapy is currently used for treatment of melanoma, with no signs of adverse side effects. However, preparation of these vaccines ex vivo is difficult, laborious and costly. Therefore, we perform site-directed ligation of modular antibodies to deliver the necessary stimuli to DCs via nanoparticles in vivo.

Bas van der Schoot, Ph.D. Candidate, Department of Tumor Immunology, **Radboud Institute for Molecular Life Sciences,** *The Netherlands*

15:55 *Networking Refreshment Break and Exhibit/Poster Viewing*

Track 2: New Antibody Therapeutics in Inflammatory & Infectious Diseases

14:20 **Chairwoman's Remarks**

Marie Kosco-Vilbois, Ph.D., Chief Scientific Officer, **NovImmune SA,** *Switzerland*

14:25 **New Crystal Dissolving Antibodies for Treatment in Asthma**

Bart Lambrecht, M.D., Ph.D., Professor, **Ghent University,** *Belgium*

14:55 **Post-translational Modification of Antigens and Antibodies in Rheumatoid Arthritis**

Rheumatoid Arthritis is a common autoimmune disease. In a large proportion of the patients several types of autoantibodies are present that target post-translationally modified proteins. The use of these autoantibodies in the prediction, diagnosis and prognosis will be discussed. In addition, the findings that these antibodies themselves are also post-translationally modified and the functional consequences will be highlighted.

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

15:25 **The Neonatal Fc Receptor as Therapeutic Target: Results from a Double-blind Placebo-controlled Study in Generalized Myasthenia Gravis Using FcRn-antagonist ARGX-113**

Functional blockage of the neonatal Fc receptor results in a rapid and specific reduction of IgGs and therefore has been proposed as a novel therapeutic approach for the management of various IgG-driven autoimmune indications including myasthenia gravis (MG). This hypothesis formed the basis for a randomized double-blind placebo-controlled study evaluating the safety and efficacy of the FcRn antagonist ARGX-113 in generalized MG patients.

Peter Ulrichts, Ph.D., Research Fellow, Lead Scientist, **Argen-X N.V.,** *Belgium*

15:55 *Networking Refreshment Break and Exhibit/Poster Viewing*

Track 1: (continued) Antibodies Alternative Delivery/Vaccines

16:25 **Antibody-mediated Antigen Delivery to Antigen Presenting Cells via Fc Receptors**

Antibody-mediated antigen delivery is a technique that allows for the specific targeting of endocytic receptors on antigen presenting cells in vivo. Upon binding, this antigen-carrying antibody is internalised into the cell, followed by antigen degradation and MHC-presentation. The modified antibodies are unable to bind via their Fc region to Fc receptors. Beside our previous published results on targeting of murine C-type lectin receptors, solely expressed on dendritic cell subpopulations, we wanted to better understand, in which way an immune response might be changed, when antigens would be 1) disseminated to a variety of antigen presenting cells, and 2) delivered to activating or inhibitory receptors. We therefore have produced antigen targeting antibodies, which allow dissemination of antigens to a variety of antigen presenting cells by targeting broadly expressed activating and inhibitory Fcγ receptors (FcγRs). Beside a careful analysis of the Fc receptor expression profiles, our data indicate that dendritic cells play a pivotal role for the induction of primary CD4+ and CD8+ immune responses. Interestingly, we further found that the induced immune responses (tolerance versus immunity) were independent on the intracellular motifs of the Fc receptors. We consider antibody-mediated antigen delivery as a promising immunotherapeutic tool for future vaccine design.

Diana Dudziak, Ph.D., Professor of DC-Biology, Laboratory of Dendritic Cell Biology, **University Hospital of Erlangen,** *Germany*

16:55 **Developing Novel Antibodies against Cancer-associated Claudins**

Özlem Türeci, M.D., Chair of CI3 (Cluster of Individualised Immune-Intervention) and Head of Clinical & Scientific Advisors Board, **BioNTech,** *Germany*

17:25 **mRNA-Encoded Antibodies for Passive Immunization**

Delivery of mRNA represents a promising alternative to the use of recombinant proteins. A single injection of antibody-encoding mRNA rapidly leads to high titers of the encoded antibody and protects mice against lethal infection or intoxication. Furthermore, mRNA-encoded antibodies show also efficacy in preclinical models of malignant diseases.

Johannes Lutz, Ph.D., Senior Scientist Immunotherapy, **CureVac AG,** *Germany*

17:55 *Close of Conference*

Track 2: (continued) New Antibody Therapeutics in Inflammatory & Infectious Diseases

16:25 **In Format Screening of Human Bispecific Antibodies with Factor VIII Mimetic Activity**

Bispecific antibodies can mimic factor VIII activity that is lacking in hemophilia A patients. However, such bispecific antibodies require a defined orientation of their two binding sites to functionally bridge Factor IXa and Factor X. Activity testing in the relevant bispecific format requires molecular biology, as well as expression and purification efforts, that significantly limit the number of combinations that can be evaluated. Taking advantage of the features of the bispecific κλ body platform, we have developed a high throughput combinatorial approach, by-passing the need for purification, thus enabling screening of thousands of native human bispecific IgGs. Streamlining discovery allowed the identification of multiple functional geometries driving pro-coagulant activity.

Nicolas Fischer, Ph.D., Head of Research, **Novimmune,** *Switzerland*

16:55 **ALX-0171 An Inhaled Anti-RSV Nanobody with Breakthrough Potential**

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. ALX-0171, a trivalent Nanobody is in phase2b clinical development for the treatment of respiratory syncytial virus (RSV) infections.

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

17:25 **TCR-mimic Bispecific Antibodies Targeting LMP2A Show Potent Activity against EBV Malignancies**

Epstein-Barr virus (EBV) infection is associated with a number of malignancies of clinical unmet need, including Hodgkin lymphoma, nasopharyngeal carcinoma, gastric cancer, and posttransplant lymphoproliferative disease (PTLD), all of which express the EBV protein latent membrane protein 2A (LMP2A), an antigen that is difficult to target by conventional antibody approaches. To overcome this, we utilised phage display technology and a structure-guided selection strategy to generate human T cell receptor (TCR)-like monoclonal antibodies with exquisite specificity for the LMP2A-derived nonamer peptide, C426LGGLLTMV434 (CLG), as presented on HLA-A*02:01. Our lead construct, clone 38, closely mimics the native binding mode of a TCR, recognising residues P3-P8 of the CLG peptide. To enhance anti-tumor potency, we constructed dimeric T cell engaging bispecific antibodies (DiBsAb) of clone 38 and an affinity-matured version clone 38-2. Both DiBsAb showed potent anti-tumor properties in vitro and in immunodeficient mice implanted with EBV transformed B lymphoblastoid cell lines and human T cell effectors. Clone 38 diBsAb showed a stronger safety profile compared to its affinity-matured variant, with no activity against EBV-negative tumor cell lines and a panel ofnormal tissues, and was less cross-reactive against HLA-A*02:01 cells pulsed with a panel CLG-like peptides predicted from a proteomic analysis. Clone 38 was also shown to recognise the CLG peptide on other HLA-A*02 suballeles, including HLA-A*02:02, HLA-A*02:04, and HLAA* 02:06, allowing for its potential use in additional populations. Clone 38 DiBsAb is a lead candidate to treat EBV malignancies with one of the strongest safety profiles documented for TCR-like monoclonal antibodies.

Mahiuddin Ahmed, Ph.D., Chief Scientific Officer, **Y-mAbs Therapeutics, Inc.,** *USA*

17:55 *Close of Conference*

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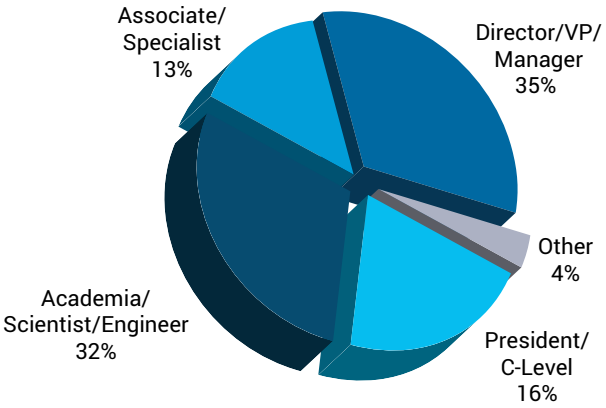

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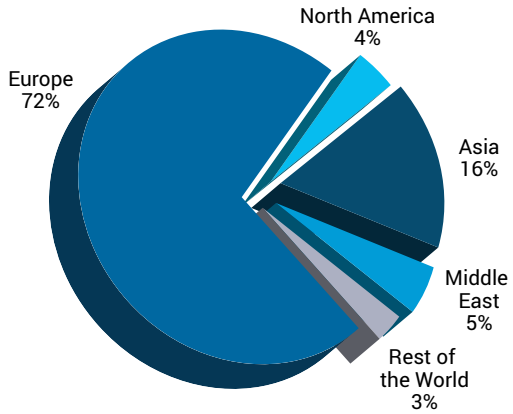

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