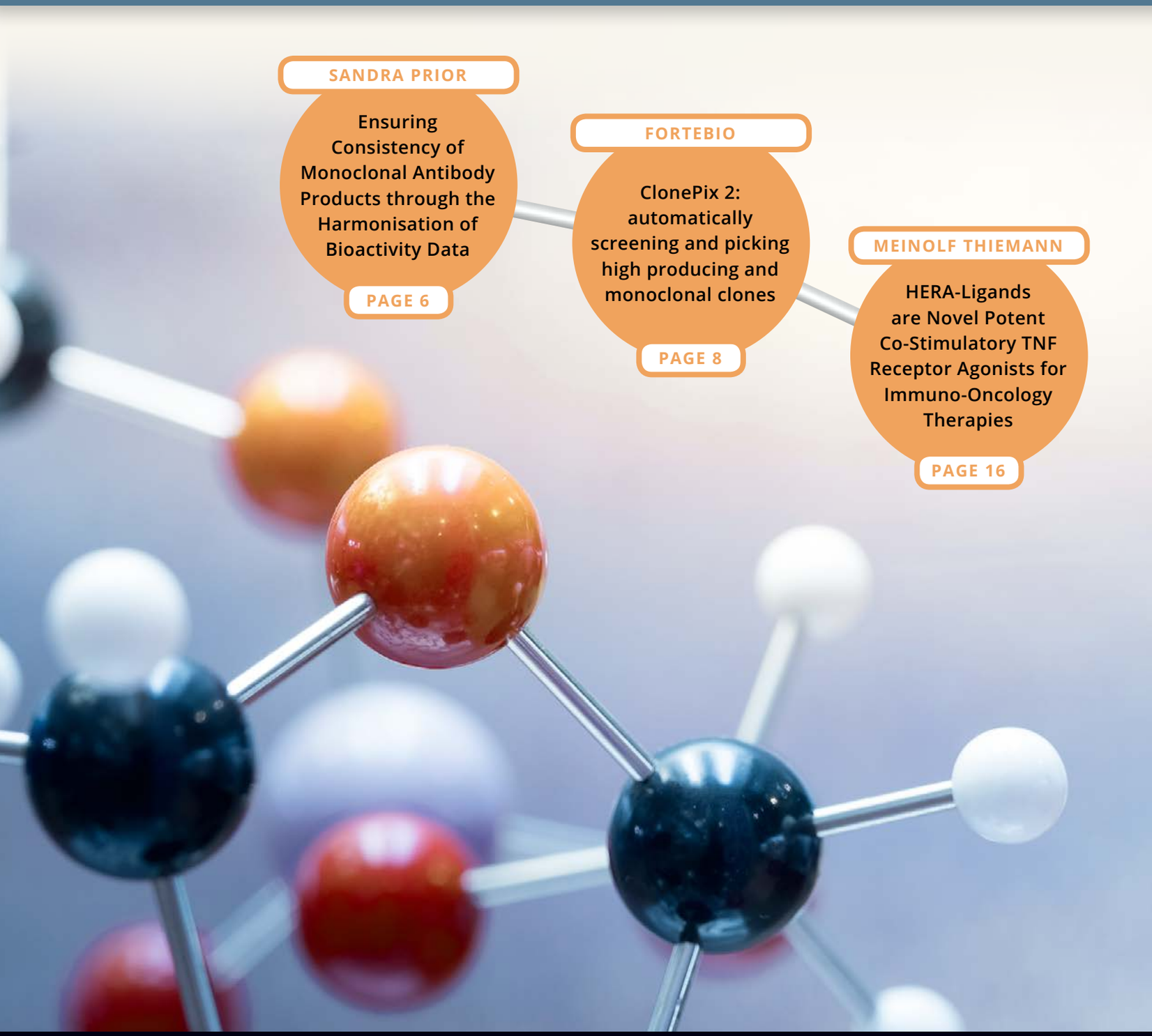
BIOLOGICS

12th Annual Proteins & Antibodies Congress | 6th Annual Peptides Congress | 6th Annual Biosimilars & Biobetters Congress

Pre-Event Newsletter



NOVOTEL LONDON WEST HOTEL

24 - 25 APRIL 2019 | LONDON, UK

OXFORD GLOBAL CONFERENCES

Contents

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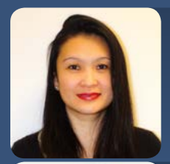
Meet the Team



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Director and Conference Producer (Proteins)

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General Manager & Biologics Portfolio Director

Tim Richters
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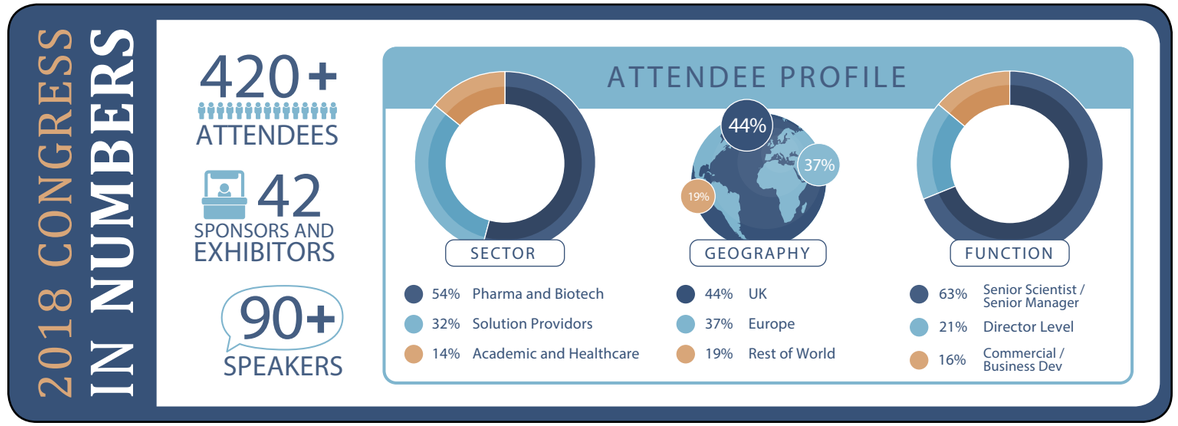
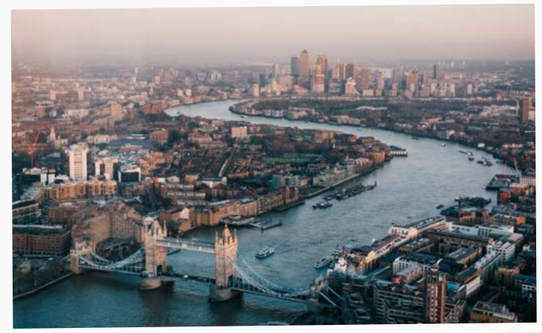


WELCOME TO THE SECOND EDITION OF OXFORD GLOBAL'S BIOLOGICS NEWSLETTER!



With the Biologics Series UK event returning to London in April, I am delighted to look back at some of the highlights of the 2018 congress and provide some details on a few of the key features & exciting additions in 2019.

The Series has grown year on year and 2018 was no different, bringing together over 400 attendees and 42 sponsors in London to discover collaborative solutions to biologics discovery & development challenges and discuss the latest developments in biotherapeutic applications. Alongside the exciting talks and extensive networking opportunities, last year's event saw the launch of the breakfast roundtables, with attendees advising the opportunity to discuss key challenges and knowledge share with their peers was invaluable.

In 2019, the series will again feature over 90 presentations across three programmes. Our Proteins & Antibodies programme will look at the key issues/updates in Protein and Antibody Engineering, Bioconjugates, Cloning, Expressions, Purification and Cell Engineering as well as the key successes in Biotherapeutics manufacturing and analytical development. Additionally, the event will feature two workshops, concentrating on Predicting Protein Stability and Analytics & CRISPS CAS 9 in Proteins and Antibodies.

With increasing number of Peptides heading to Clinical trials, our 2019 Peptides Congress will be focused on the application of peptides to key medical threats such as antimicrobial resistance, cancer and metabolic disorders as well as a shifting industry focus on biologics - covering the three key stages of peptide development from peptide research to therapeutics and manufacturing.

The Biosimilars & Biobetters programme returns in 2019, exploring the latest developments in the biosimilars field, including regulatory approval and the introduction of biosimilar medicines in clinical practice. We'll also review key challenges of interchangeability & CMC, Manufacturing and Analytics considerations.

Due to the popularity of the 2018 Breakfast Roundtables and Gala Dinner, these features will be returning in 2019, alongside our new & improved event app!

The Gala Dinner will be even bigger and better, offering attendees a chance to relax over a glass of wine and a sit-down dinner, enjoying the company of their peers. Read on for a range of interesting interviews and insights with some of 2019's industry-leading speakers and participating sponsors, and I look forward to welcoming you to the event in April!

- Chris Davies, General Manager

BIOLOGICS
SERIES UK 2019

NOVOTEL LONDON WEST HOTEL
24 - 25 APRIL 2019 | LONDON, UK

1. 12TH ANNUAL **PROTEINS AND ANTIBODIES** CONGRESS
2. 6TH ANNUAL **PEPTIDES** CONGRESS
3. 6TH ANNUAL **BIOSIMILARS AND BIOBETTERS** CONGRESS

WHO IS ATTENDING?

For the full attendee list please contact
marketing@oxfordglobal.co.uk

- **500+ antibodies, peptides and biosimilars & biobetters attendees** representing global pharmaceutical organizations, leading biotech companies and internationally renowned academic institutions.
- **VPs, Directors and Global Heads** working in protein and antibody engineering, peptide discovery and therapeutics, and biosimilar and biobetter development.

These companies and many more:

Lilly, Boehringer Ingelheim, Novartis, Pfizer, novo nordisk, Zealand Pharma, Takeda, teva, Shire, Johnson & Johnson, abbvie, Amgen, MSD, ucb, Ipsen, MedImmune

Sponsors 2019

PLATINUM

FORTÉBIO – Biologics by Molecular Devices

GOLD

MaxCyte, Lonza Pharma & Biotech, SCIEX

SILVER

Bio-Rad, Malvern Panalytical a spectris company

BRONZE

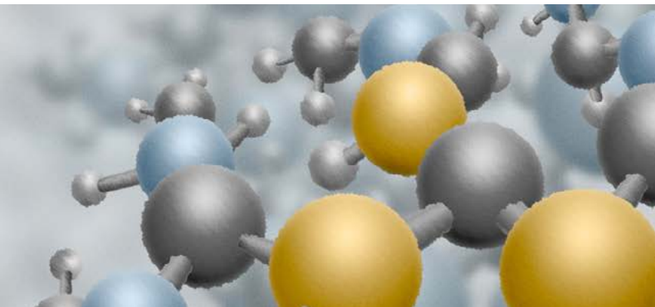
ATUM, Beckman Coulter, Pepscan shaping peptides to perfection, Fluidic Analytics, Bachem, carterra, Schrödinger, Provepharm Life Solutions UNLOCKING UNLIMITED POTENTIAL, BioAgilytix

NETWORK AND PROGRAMME

Iris Biotech GmbH, YUMAB, Chemical Computing Group, isogenica, ProteoGenex The Leader in Tissue Procurement, GL Biochem(Shanghai)Ltd., Sino Biological, Agilent Trusted Answers, FairJourney Biologics, Synthelis, MAbSilico, CEM, PolyPeptide Group, admescope, biotechne, Bio-Works, rssl science with service, ZEOCHEM, Promega, GTP From Gene to Protein, KBI Biopharma, GENOVIS, Luminex complexity simplified., PX Therapeutics, MOLTEMPER, SGIDNA, Belyntic, PEPSCAN Shaping peptides to perfection

It's not too late to join them!

REGISTER ONLINE



ENSURING CONSISTENCY OF MONOCLONAL ANTIBODY PRODUCTS THROUGH THE HARMONISATION OF BIOACTIVITY DATA: NEW INTERNATIONAL STANDARDS FOR THE NEW BIOSIMILARS LANDSCAPE

SANDRA PRIOR

The increasing complexity of the product landscape for biosimilar monoclonal antibodies emphasises the need for new International Standards for these important medicines. These public standards are intended for the calibration of bioassays and local standards. International Standards for monoclonal antibodies allow harmonisation and traceability of bioassay data across products. As a result, these preparations support a knowledge-based approach to addressing future challenges of potential drifts and divergence in the bioactivities over the lifecycle of these products and will contribute to long-term product consistency.

It is broadly understood that the complex nature of biological medicines is associated with the need for biological assays to assess bioactivity. Physicochemical tools, even when sophisticated methods are available, are insufficient to fully characterise these products. However, as bioassays are complex and variable, scientists soon came to the realisation that the bioactivity of a test sample can only be defined relative to a reference standard. The World Health Organization (WHO) International Standards (IS) for biologics have a long and successful history of supporting high quality, safe and efficacious biological medicines worldwide. Since the beginning of the 1900's, ISs have served to define units of biological activity (International Units) representing the so-called "gold reference standard" for many biological products and allowing the global harmonisation of bioassay potency data. Importantly, WHO ISs also contribute to the maintenance of a wide network of secondary and working standards that are routinely used during the development and manufacturing of biological products that patients receive, everyday, all over the world. Historically these reagents have derived from molecules found in nature through purification from tissues or fluids, but more recently, like the products they support, they are produced using biotechnology techniques.

Biotherapeutic monoclonal antibodies (mAbs) are one of the new and most successful additions to the repertoire of biological medicines with indications in the field of cancer and immunological disorders. The number of new mAb products approved is fast increasing and the end of market exclusivity of the first approved innovator products has permitted the growth of a mAb biosimilar market. A robust regulatory framework governs the definition and approval of these biosimilar mAbs products. This framework is set on both new and revised guidelines, and built upon the increased knowledge of manufacturers and regulators with a better understanding of the biosimilarity concept. However, the rapid change and prospects of the mAb biosimilar product landscape bring some new challenges. Post-approval process changes are common and bioactivity product drifts and evolution are therefore believed unavoidable for both innovator and biosimilars. In this complex multiproduct market, new questions arise. For example, - how can the current regulatory pathways ensure that these potential changes are not a cause of concern? How do the bioactivities of the different approved biosimilar products compare to each other or even, how will the bioactivities of the innovator and the biosimilar products compare to each other in several years' time, after post-approval process changes? These are questions that cannot be answered currently with either the manufacturers' proprietary in-house reference standards (used by the manufacturer to set product specifications and at different stages during product and bioassay characterisation) or the innovator's reference medicinal product (RMP), batches of which are used to define the target product profile during the biosimilar comparability studies.

> *"The World Health Organization (WHO) International Standards (IS) for biologics have a long and successful history of supporting high quality, safe and efficacious biological medicines worldwide."*

WHO ISs for mAbs can fill this knowledge gap, supporting consistency in the bioactivity of products across different jurisdictions and over extended periods of time. ISs for mAbs are publicly available reference standards that are lyophilised and formulated to ensure long term stability and allow the calibration of local reference standards and bioassays. The WHO ISs for mAbs are exclusively bioassay standards. They have no regulatory role, nor are they intended to change current dosing or labelling of approved products. They cannot define biosimilarity or specific activity, which are the unique and specific roles of the RMP and the competent regulatory authorities. However, by defining International units of bioactivity, they allow the harmonisation of reported data, through traceability to a common unitage. Therefore, the ISs for mAbs can be a useful tool to understand the potential differences in the bioactivity of various products through their evolution and product lifecycles. The benefits of using these reagents have already been demonstrated in the international collaborative studies for the 1st WHO IS for rituximab (NIBSC 14/210) and the 1st WHO IS for infliximab (NIBSC 16/170). These preparations are now readily available. Current standardisation programs include the development of candidate ISs for trastuzumab, cetuximab, adalimumab and bevacizumab ■

Sandra Prior will be expanding on this topic at our 6th Annual Biosimilars & Biobetters Congress with her presentation **'Long-Term Product Consistency Through Bioactivity Data Harmonisation'** on Day 2 of the event.

Sandra Prior, PhD

Senior Scientist, Department of Biotherapeutics
National Institute for Biological Standards and Control (NIBSC)

Sandra works at the National Institute for Biological Standards and Control (NIBSC) on the development of bioassay standards for therapeutic monoclonal antibodies (Prior et al., 2018, MABS 10(1) 129) and the investigation of structure-function in relation to the safety and efficacy of monoclonal antibody products. She is also currently a member of the European Directorate for the Quality of Medicines and HealthCare (EDQM) monoclonal antibody expert committee. She has over 15 years' experience in applied immunology and in vitro cell-based assay development acquired from the field of bacterial vaccines, investigating safety and protective mechanisms and the assessment of bioactivity and immunogenicity of Biotherapeutics.

Q&A SESSION WITH **JUTTA EICHLER**

FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG

Jutta Eichler, PhD
Professor of Medicinal Chemistry, University of Erlangen-Nuremberg

Upon receiving her Ph.D. in Bioorganic Chemistry from Humboldt-University in Berlin, Dr Eichler joined Torrey Pines Institute for Molecular Studies, San Diego, California, as a Postdoc and Assistant Member, respectively, and subsequently the Helmholtz Centre for Infection Research, Braunschweig, Germany, as a Group Leader. In 2008, Dr Eichler was appointed Professor of Medicinal Chemistry at the University of Erlangen-Nurnberg, Germany. Her research interests include the structure-based exploration of protein-protein interactions (PPIs) using synthetic peptides as protein binding site mimics, as well as the design and evaluation of inhibitors of PPIs involved in the pathogenesis of diseases, in particular the interactions of viral proteins with their target cell receptors.

Your work explores protein-protein interactions using assembled peptides as synthetic binding site mimics, could you give us a little background to your research and its critical applications?

The design and generation of molecules capable of mimicking the binding and/or functional sites of proteins, represents a promising strategy for the exploration and modulation of protein function through controlled interference with the underlying molecular interactions. Molecules that present the binding sites of proteins involved in a disease-associated protein-protein interaction (PPI), are promising candidates for therapeutic intervention. Such binding site mimetic molecules can be generated either through recombinant protein synthesis, or by means of chemical peptide synthesis. A specific advantage of synthetic peptides is that they can be generated as exact copies of protein fragments, as well as in diverse chemical modifications, which includes the incorporation of a large range of non-proteinogenic amino acids, as well as the modification of the peptide backbone. Apart from extending the chemical and structural diversity presented by peptides, such modifications also increase the proteolytic stability of the molecules, enhancing their potential as drug candidates.

Three conceptually different approaches are available for the design of protein binding site mimetic peptides. These approaches are based on one or more of the following information about the proteins of interest: structure, sequence and function. In random combinatorial methods based solely on protein function, such as phage display, and synthetic peptide combinatorial libraries, respectively, large populations of peptides are screened for binders to the respective partner protein, or for inhibitors of the PPI of interest. A strategy termed peptide scanning is based on the synthesis of the entire protein sequence – or large parts of it – in the shape of short, overlapping peptides, which are then individually tested for binding to the respective partner protein, enabling the identification of protein binding sites. The utility of this method, however, is largely limited to the identification of sequentially continuous binding sites, which are located in a protein sequence stretch of consecutive amino acids. Structure-based design, finally, involves the design and generation of protein binding site mimics based on the 3D structure of the protein-protein complexes. This structural information enables the design and generation of mimics of continuous, as well as of sequentially discontinuous protein binding sites, which are composed of two or more protein segments that are distant in protein sequence, but brought into spatial proximity through protein folding. Mimicking such discontinuous protein binding sites by synthetic peptides typically involves non-linear presentation of the respective protein fragments in assembled peptides.

Over the past 15 years, we have designed, generated and evaluated synthetic binding site mimics for a range of proteins, including the CD4 and coreceptor binding sites, respectively, of the HIV-1 envelope glycoprotein gp120, as well as paratope mimics for HIV-1 neutralizing antibodies. These mimetic peptides were shown to retain the binding specificities of the protein they were derived from, as well as function as inhibitors of the respective PPIs.

What are the key challenges in using assembled peptides as synthetic binding site mimics and how might these be overcome?

Like peptides in general, assembled peptides are associated with some potential obstacles that need to be considered and, if necessary, addressed in the development of peptide drugs. The biggest challenge clearly is the limited metabolic stability of peptides, since they are rapidly degraded by proteolytic enzymes, precluding oral administration of peptide drugs. This challenge can be addressed by different means. First, unlike recombinant protein synthesis, chemical peptide synthesis is not limited to the proteinogenic amino acids as building blocks. A plethora of additional amino acids are currently available for chemical peptide synthesis. Apart from dramatically increasing the metabolic stability of peptides, incorporation of these amino acids also increases the chemical diversity presented by synthetic peptides, as these additional amino acids introduce chemical moieties that are not presented by the proteinogenic amino acids. Furthermore, conformational stabilization through cyclization, or through introduction of defined secondary structures, has been shown to shield peptides from proteolytic enzymes. Such shielding effects can also be achieved by coupling the peptide to larger inert molecules, such as polyethylene glycol.

Furthermore, due to their molecular size, with molecular weights ranging from three to seven kDa, assembled peptides are unlikely to passively pass cell membranes, hampering cellular uptake and limiting their potential therapeutic application to extracellular targets. This challange, however can be counteracted by fusing the assembled peptide to one of a large group of available cell-penetrating peptides, which are able to transport a variety of molecular cargo into cells.

In general, the chemical synthesis of peptides through solid phase synthesis is fairly straightforward, and has been optimized over the past decades, so that virtually all peptide sequences are accessible synthetically today. In our experience, however, the synthesis of highly complex peptides, such as assembled peptides, may require the use of specific protected amino acids and other building blocks, solid supports, linkers and other reagents, which significantly increases the cost of synthesis. These consideration may become relevant for the large-scale synthesis of peptide drugs, as well as peptide biomaterials.

Finally, the design of assembled peptides as synthetic binding site mimics, is typically based on the resolved 3D structure of the respective protein-protein complex. While such structures are increasingly becoming available through powerful x-ray crystallography technology, their generation is not trivial and contingent on the availability of suitable crystals of the protein complexes.

How do you see the field progressing over the next 5 years?

Protein-protein interactions have emerged as promising targets for therapeutic intervention. Several compounds have entered clinical trials, providing promising perspectives for novel therapies for highly prevalent and life-threatening conditions, including cancer and infectious diseases.

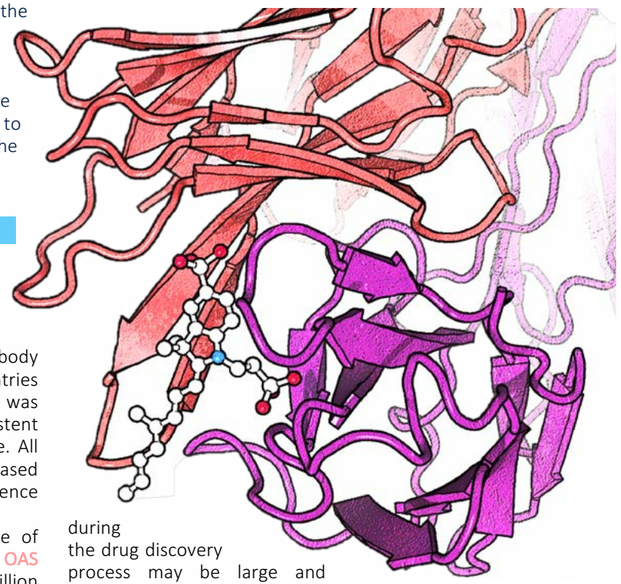
In general, PPIs are difficult targets for small molecule drugs, as they often cover a larger protein surface than classical protein targets, such as receptors and enzymes. Peptides, including synthetic protein binding site mimics may be a valid alternative, as they are able to form multiple intermolecular contacts with their target proteins, yet they are a lot smaller than monoclonal antibodies.

Overall, taking into account the tremendous technical and scientific progress in the field of using peptides as protein binding site mimics, I strongly believe that the significance of assembled peptides in biomedical research, as well as in biomaterial engineering, will continue to grow in the future ■

Jutta Eichler will be speaking at our 6th Annual Peptides Congress with her presentation **'Exploring Protein-Protein Interactions Using Assembled Peptides As Synthetic Binding Site Mimics'** on Day 1 of the event.

Computational Tools for Antibody Development from the Oxford Protein Informatics Group

As a result of their binding versatility, antibodies are one of the most prominent biotherapeutic classes of today. However, drug discovery remains a laborious and costly undertaking. In recent years, the Oxford Protein Informatics Group (OPIG), under the leadership of Professor Charlotte Deane, have developed a range of computational tools that can be used to complement existing experimental procedures and assist in the initial phases of the antibody development process.



DATA, DATA, AND MORE DATA

Many advances in antibody therapeutic development have arisen due to the increase in available data. It is therefore essential to be able to obtain pertinent subsets of this quickly and easily.

The Protein Data Bank currently contains over 3,350 antibody structures, but there is no simple way of isolating them and entries are often inconsistently handled. Our database, SAbDab, was designed to collect and curate these structures in a consistent fashion, and makes antibody structural data easily accessible. All structures are annotated and can therefore be searched for based on many properties, such as species, experimental details, presence of antigen, CDR lengths, and sequence similarity to a query.

We have also recently curated the first large database of antibody sequence data derived from Ig-seq experiments. OAS (Observed Antibody Space) is a collection of more than half a billion sequences from 53 different studies; all are sorted, cleaned, annotated, translated from the nucleotide sequence, and consistently numbered, and are therefore ready to facilitate large-scale investigations into antibody repertoires.

A SEQUENCE TOOLBOX

OPIG has created several computational tools for annotating and cleaning sequence data.

ANARCI is an antibody numbering package – given a sequence or set of sequences, it quickly identifies the immunoglobulin domains, assigns species and germlines, and numbers the amino acids according to your chosen scheme. By using ANARCI, equivalent positions in the antibody can be easily identified and compared, for example when exploring possible mutations.

Although sequencing of the Ig gene repertoire produces large amounts of useful information, its high-throughput nature leads to high error rates. To combat this, we created ABOSS, a tool that filters sequences that are likely to be incorrect from an input dataset, including some that would be missed by other methods, by examining their structural viability. The user is left with only the most valuable data, which should lead to more informative analyses.

PREDICTIVE POWER

Antibody structures are invaluable to therapeutic development, however they are often unavailable and are difficult and expensive to acquire. Additionally, the number of potential designs conceived during the drug discovery process may be large and experimentally determining all of their structures would be intractable.

Computational structure prediction offers an alternative. Our antibody modelling pipeline, ABodyBuilder, predicts the 3D protein structure from sequence using templates from SAbDab. It produces high quality models, with comparable accuracy to other leading software, but in addition provides the estimated accuracy for each region, highlights potential developability issues, and can model nanobodies. It is also very fast, with each model taking approximately 30 seconds to complete, and can therefore be used in a more high-throughput manner that is not currently possible with experimental techniques. The ABodyBuilder pipeline includes tools formulated specially for antibody structure prediction, such as the only current antibody-specific sidechain predictor, PEARS, and a CDR-H3 prediction tool called SphinxH3. The models generated by our software can be exploited during therapeutic design to guide humanisation, suggest possible residues for mutation, and can be used as inputs to paratope and epitope prediction methods (such as our Antibody i-Patch and EpiPred software). Our antibody-related prediction tools are collectively known as SAbPred.

The most recent addition to SAbPred is TAP, the Therapeutic Antibody Profiler. Given the sequence of an antibody, TAP calculates a series of properties and highlights any potential developability issues, based on what has been observed in current post Phase-I therapeutics. TAP can hence be used to select the most promising antibodies from a list of possibilities, and thereby reduce the time and costs associated with failed therapeutic candidates.

The assortment of antibody-specific databases and tools developed in OPIG can be exploited during drug discovery, to complement current experimental approaches and inform the decisions that must be made by researchers during the design process.

The SAbDab/SAbPred platform is available as an easily-installed virtual machine image (SabBox), that can be purchased from process.innovation.ox.ac.uk/software. We also offer consultancy support to help with the installation and use of the SabBox software.

SAbDab
SAbPred

HERA-LIGANDS ARE NOVEL POTENT CO-STIMULATORY TNF RECEPTOR AGONISTS FOR IMMUNO-ONCOLOGY THERAPIES

DR. MEINOLF THIEMANN

Director Protein Analytics, Apogenix AG

Apogenix' TNFSF Receptor Agonists

The diverse functions of the immune system are orchestrated by a complex and delicately balanced interplay of stimulatory and inhibitory signals. Many key regulators of immune cell function belong to the so-called tumour necrosis factor superfamily (TNFSF) and their cognate receptors, the so-called TNF receptor superfamily. The TNFSF consists of 19 structurally related ligands, each binding to one or more of the 29 members of the TNF receptor superfamily. TNFSF receptors are of great importance in the anti-tumour immune process. They are expressed by a wide variety of immune cells including T cells and antigen-presenting cell populations, such as dendritic cells and macrophages, as well as by tumour cells themselves. This diverse expression pattern highlights the critical role that TNFSF receptors play in many parts of the body and in the various phases of the anti-tumour immune response.

TNFSF-mediated signaling induces a wide range of biological effects, including programmed cell death (i.e., apoptosis), proliferation, differentiation, and tumour growth. Therefore, TNFSF signaling is an attractive target for therapeutic intervention. TNFSF ligands naturally exist as homo-trimers with three receptor binding sites. The interaction of trimeric TNFSF ligands with their specific cell surface receptors leads to clustering of these receptors, followed by intracellular signal transduction. The trivalent structure of the TNFSF proteins and the resulting receptor clustering are prerequisites for the transmission of a signal delivered into the cell.

Apogenix is developing a novel class of TNFSF receptor agonists (HERA-ligands, see Figure) for the treatment of various types of cancer. Their unique molecular structure perfectly mimics the endogenous ligands and overcomes the known limitations of antibodies and other biologics targeting TNFSF receptors. Antibodies can only bind two TNFSF receptors in a spatially undefined manner and require secondary cross-linking via Fcγ receptors. In contrast, Apogenix' HERA-ligands lead to well-defined TNFSF receptor clustering without the need for further cross-linking. This results in a sufficient level of the appropriate signal being transmitted into the target cell, whereas agonistic antibodies transmit these signals at insufficient levels. Preclinical work at Apogenix has demonstrated the producibility and biological activity of these novel TNFSF receptor agonists as well as their superiority over agonistic antibodies.

HERA-CD40L Induces T-Cell–Mediated Anti-Tumour Immune Response through Activation of Antigen-Presenting Cells

Exemplarily, efficacy data for one HERA-ligand family member are presented here. CD40 - the receptor for HERA-CD40L - is expressed on the surface of antigen presenting cells (APCs) as well as some tumour cell types. Binding of CD40 to its natural ligand leads to increased APC activation and an enhanced immune response. CD40 agonist therapy plays an important role in APC maturation and their migration from the tumour to the lymph nodes, resulting in elevated antigen presentation and T cell activation.

HERA-CD40L provides efficient receptor agonism on CD40-expressing cells and, importantly, does not require FcγR-mediated cross-linking. Strong activation of NFκB signaling was observed upon treatment of B cells with HERA-CD40L. Monocyte treatment with HERA-CD40L promoted differentiation towards the M1 spectrum and repolarization of M2 spectrum macrophages towards the M1 spectrum phenotype. Treatment of in vitro co-cultures of T and B cells with HERA-CD40L triggered robust anti-tumour activation of T cells, which depended upon direct interaction with B cells. In contrast, bivalent anti-CD40 antibodies and trivalent soluble CD40L displayed weak activity which critically depended on cross-linking.

In vivo, a murine surrogate of HERA-CD40L stimulated clonal expansion of OT-I specific murine CD8+ T cells without affecting non-specific immune cells. In the syngeneic CT26wt mouse model mHERA-CD40L treatment converts cold into hot tumours by increasing infiltration of CD8+ and CD4+ T cells. In addition, mHERA-CD40L showed single-agent anti-tumour activity in the CD40-negative syngeneic MC38-CEA mouse model, suggesting an involvement of the immune system in controlling tumour growth.

In summary, HERA-CD40L is a potent agonist that is able to establish single-agent anti-tumour immune responses. In comparison to bivalent benchmark antibodies, HERA-CD40L showed superior biological activity which qualifies this molecule as an ideal candidate for combinatorial cancer treatments.

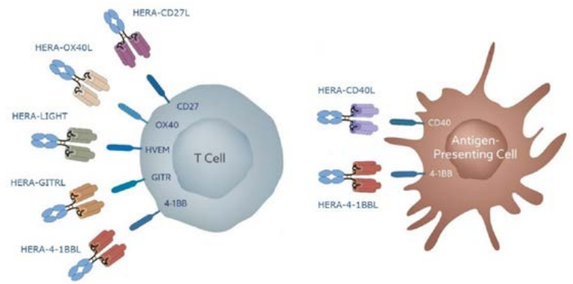


Fig: Apogenix' HERA-ligands in preclinical development

WEBINAR EXCERPT: Q&A SESSION WITH **PHILIPP SPYCHER**

Dr Philipp Spycher
PSI Founder Fellow,
Radiopharmaceutical Sciences,
Paul Scherrer Institute

Dr. Spycher is a PSI Founder Fellow at the Paul Scherrer Institute (PSI) Villigen (Switzerland) since end of 2017 working on the site-specific modification of native antibodies. He studied at the University of Basel (Switzerland) Nanoscience and at ETH Zurich (Switzerland) Biomedical Engineering with a focus on drug delivery and targeting. During his doctoral studies at ETH Zurich, he worked on protein and materials engineering for the site-specific immobilization of proteins onto micro-patterned surfaces using enzymes. He then performed a post-doc at PSI Villigen on chemical and site-specific modification of antibodies and fragments for diagnostic and therapeutic applications. Dr. Spycher has over 8 years of experience with ADCs and materials engineering, he is particularly interested in the development of improved drug delivery and targeting systems.

Does the enzyme need a recognition motif for conjugation or how does the enzyme work?

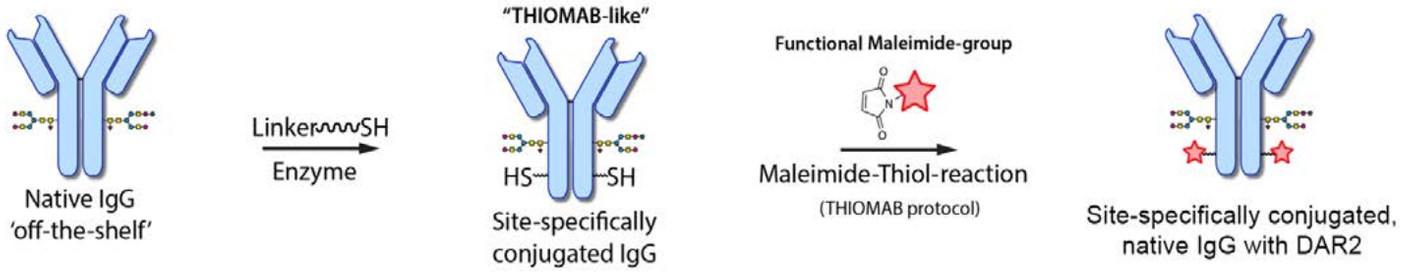
There are two parameters that govern whether the rest will be conjugated or not, the more important parameter is whether it's accessible for the enzyme. The additional parameter is sequence that is around the residue, both parameters need to be given otherwise the enzyme will not conjugate. In principle, the enzyme doesn't need a sequence, in the instance of a sequence not matching, it will not conjugate. In this case, the residue is accessible enough for the enzyme and it is embedded within a favourable sequence.

Does it also work for other IgG-subclasses and animal IgGs?

We tested for other human IgG antibodies and found that it works well for humans and especially well on a mouse. It works well for most mouse or IgG antibodies but there are some mouse antibodies where the conjugation didn't work as well as for humans and IgG one antibodies. We are trying to optimize the protocol to work for IgG antibodies. In general, if there's an FC part-present that is from a human origin, it will work very well because the conjugation takes place at the FC part of the protein or the antibody.

Is the enzyme available?

Yes, it is available and in large scale, I was informed by the manufacturer that the enzyme is likely to enter for trials as the enzyme's purity is adequate for commercial use.



This Q&A was an excerpt from the webinar ***New ADC Platform, Modifying Antibodies without Engineering***

The full recording is available at: www.oxfordglobal.co.uk/biologics-series/resources/

WEBINAR HIGHLIGHTS

- Advances in maximizing TI of ADCs
- Next generation of cytotoxic warheads
- Advances in bispecific ADCs
- Translational approaches to ADC Development

OXFORD GLOBAL CONFERENCES

FORTHCOMING EVENTS

OXFORD GLOBAL CONFERENCES

Biologics Series

UK

12th Annual Proteins & Antibodies Congress
24 - 25 April 2019 | London, UK

6th Annual Peptides Congress
24 - 25 April 2019 | London, UK

6th Annual Biosimilars & Biobetters Congress
24 - 25 April 2019 | London, UK

Co-located Events

Biomanufacturing Congress
17 - 18 September 2019 | London, UK

US

Proteins & Antibodies USA Congress
18 - 19 November 2019 | Boston, USA

Biomarkers Series

UK

14th Annual Biomarkers Congress
21 - 22 February 2019 | Manchester, UK

US

4th Annual Biomarkers & Precision Medicine USA Congress
08 - 09 October 2019 | San Diego, USA

Cell Series

UK

8th Annual Cell Culture & Bioprocessing Congress
24 - 25 October 2019 | London, UK

6th Annual Stem Cell & Regenerative Medicine Congress
24 - 25 October 2019 | London, UK

5th Annual Cell & Gene Therapy Congress
24 - 25 October 2019 | London, UK

Co-located Events

US

Cell Culture & Bioprocessing USA Congress
14 - 15 May 2019 | Boston, USA

Cell & Gene Therapy USA Congress
14 - 15 May 2019 | Boston, USA

Co-located Events

Formulation & Delivery Series

UK

5th Annual Formulation & Drug Delivery Congress
29 - 30 April 2019 | London, UK

4th Annual Inhalation & Respiratory Drug Delivery Congress
29 - 30 April 2019 | London, UK

Co-located Events

US

2nd Annual Formulation & Drug Delivery USA Congress
18 - 19 March 2019 | San Diego, USA

2nd Annual Inhalation & Respiratory Drug Delivery USA Congress
18 - 19 March 2019 | San Diego, USA

Co-located Events

Immuno-Oncology Series

UK

4th Annual Advances in Immuno-Oncology Congress
20 - 21 May 2019 | London, UK

US

2nd Annual Advances in Immuno-Oncology USA Congress
08 - 09 October 2019 | San Diego, USA

PharmaTec Series

UK

17th Annual Pharmaceutical IT & Data Congress
25 - 26 September 2019 | London, UK

3rd Annual Artificial Intelligence in Drug Development Congress
25 - 26 September 2019 | London, UK

Cyber Security & Data Protection in Pharma & Healthcare Congress
25 - 26 September 2019 | London, UK

SmartLabs & Laboratory Informatics Congress
25 - 26 September 2019 | London, UK

Co-located Events

R&D Series

EU

20th Annual Drug Discovery Summit
11 - 12 June 2019 | Berlin, Germany

7th Annual Discovery Chemistry & Drug Design Congress
11 - 12 June 2019 | Berlin, Germany

Neuroscience in Discovery & Development Congress
11 - 12 June 2019 | Berlin, Germany

Bispecifics in Discovery & Development Congress
11 - 12 June 2019 | Berlin, Germany

Co-located Events

SynGen Series

UK

11th Annual Next Generation Sequencing & Clinical Diagnostics Congress
07 - 08 November 2019 | London, UK

7th Annual Single Cell Analysis Congress
07 - 08 November 2019 | London, UK

5th Annual Genome Editing Congress
07 - 08 November 2019 | London, UK

2nd Annual Synthetic Biology Congress
07 - 08 November 2019 | London, UK

Digital PCR Congress
07 - 08 November 2019 | London, UK

Co-located Events

US

5th Annual Next Generation Sequencing & Clinical Diagnostics USA Congress
14 - 15 May 2019 | Boston, USA

5th Annual Single Cell Analysis USA Congress
14 - 15 May 2019 | Boston, USA

3rd Annual Genome Editing USA Congress
14 - 15 May 2019 | Boston, USA

2nd Annual Synthetic Biology USA Congress
14 - 15 May 2019 | Boston, USA

Co-located Events

Register your interest, e-mail us:
info@oxfordglobal.co.uk