Science to Market 2016

“Leveraging Synergies”

The annual discussion and partnering conference for experts from academia, biotechnology and pharmaceutical industry.

March 7 - 8, 2016 | DECHEMA e.V. Frankfurt am Main | Germany

Organised by the **European Association of Pharma Biotechnology (EAPB)**
in cooperation with **TechnologieAllianz**

EAPB

European Association of
Pharma Biotechnology

Technologie Allianz

AIM & SCOPE

As a European event, the »Science to Market« EAPB Conference aims to promote partnership between academic settings and industry. The goal is to enhance the economical output of scientific research and direct them into marketable technologies and biopharmaceutical products. Recent biotechnological developments that may be of economic interest shall be identified and transfer of the academic know-how into product development shall be facilitated.

Therefore, European academic research scientists from universities and research institutions as well as representatives of the biotech and pharmaceutical industry are invited to exchange ideas that will lead to successful co-operations.

To achieve the conference goals, the congress offers plenary lectures on state-of-the art technologies and findings in biopharmaceutical developments as well as poster presentations on current projects and networking opportunities.

CONTENT

EAPB
European Association of Pharma Biotechnology

"LEVERAGING SYNERGIES"
March 7 – 8, 2016

Venue: DECHEMA e. V.
Theodor-Heuss-Allee 25, 60486 Frankfurt, Germany

WELCOME

Welcome to the 7th "Science to Market" conference of the European Association of Pharmaceutical Biotechnology (EAPB)

On behalf of the EAPB Board I cordially welcome the participants of the 7th "Science to Market" conference under this year's slogan "Leveraging Synergies".

Since our first Science-to-Market (S2M) conference in 2008, the efficacy of technology transfer from European academic and public research institutions has made big steps forward.

One of the driving forces was the insight that making scientific results available to industrial exploitation is not only advised from an economic standpoint in respect to re-financing research but is also of utmost importance for maintaining Europe's technological excellence. Consequently, many universities and research institutions have set-up own tech transfer units, others have joined together and created professional organizations, meeting industry on an equal footing now.

Today tech transfer has become much of a routine process, often efficiently supported by web-based technologies. But at the end it is always between people that contacts are made and contracts are closed. Therefore, EAPB continues the S2M conference series with its many opportunities for making new contacts between players from the scientific community and the industry, to make use of synergies in the field of pharmaceutical and medical biotechnology.

We are happy that in this year we have won the "Technologie Allianz" as an experienced partner for our conference supporting successful and efficient tech transfer processes.
We are grateful that this year's conference is generously supported by all our sponsors enabling us to organize this 7th "Science to Market" conference in Frankfurt.

We are confident that the mixture of a high quality scientific program, poster presentations, and open informal discussions will give plenty of opportunities for exchange and networking and thus we wish you an interesting and inspiring meeting.

Dr. Wieland W. Wolf
President of EAPB

WELCOME

The TechnologieAllianz, which is the German association of patent marketing and technology transfer agencies, welcome you to this years´ „Science-to-Market"-event.

The TechnologieAllianz represents German as well as Austrian universities and research institutes thus being a tremendous source of innovative technologies.

Thus, we are very glad in having teamed up with EAPB with regard to the "Science to Market".

At the "Science to Market" you will get access to the latest inventions from these sources. These comprise diagnostics, therapeutic approaches, platform technologies and research tools.

Equally important, the "Science to Market" provides an opportunity to meet the respective contact persons at the various technology transfer offices.

Helping you to get an easy and straightforward access to both the inventions and the "people behind the scenes" will be an important aim of the event!

We wish you an interesting and successful meeting and many new contacts!

Dipl.-Ing. Alfred Schillert
Chairman of TechnologieAllianz

ORGANISER / COMMITTEE / PARTNER

ORGANISER

European Association of Pharma Biotechnology

The European Association of Pharma Biotechnology – EAPB – is a non-profit association and the representative and central network to promote and develop Pharma Biotechnology in Europe, linking academia, industries and regulatory bodies. It is dedicated to the advancement of biotechnology in pharmaceutical sciences, specifically as applied to industrial materials, processes, products and their associated problems. Its members are scientists employed in industry, government and university laboratories, biotech companies and scientific organisations.

SCIENTIFIC AND PLANNING COMMITTEE

Dr. Holger Bengs	BCNP Consultants GmbH, Frankfurt, Germany
Michael Kahnert	BIO Deutschland e.V., Berlin, Germany
Dr. Jörg Knäblein	Bayer Pharma AG, Berlin, Germany
Prof. Dr. Willi Meier	DECHEMA e.V., Frankfurt, Germany
Dr. Sigrun Szepanski	Charité – Universitätsmedizin, Berlin, Germany
Dr. Jürgen Walkenhorst	PROvendis GmbH, Mülheim, Germany
Dr. Axel Wenzel	Pharma Scientific Services Team, Ltd., Munich, Germany
Dr. Wieland W. Wolf	ProBioGen AG, Berlin, Germany

COOPERATION PARTNER

TechnologieAllianz

TechnologieAllianz is the German association representing patent marketing agencies and technology transfer agencies – a nationwide association representing over 200 scientific institutes. TechnologieAllianz provides enterprises with access to the entire range of innovative research results from German universities and non-university research institutions. TechnologieAllianz offers a wide range of services for making inventions available to businesses, securing industrial property rights, and efficiently marketing R&D results.

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MONDAY, MARCH 7, 2016 PROGRAMME OVERVIEW

09:00 – 10:00	**Registration**
10:00 – 10:10	**Welcome, introduction & opening remarks** Wieland W. Wolf, President of the EAPB
10:10 – 12:10	**SESSION: MARKET TRENDS**
	Moderator Wieland Wolf
10:10 – 10:40	**Commercial Deal Structures and Recent Trends** Christi Mitchell, Highbury Ltd, Hitchin, UK
10:40 – 11:10	**Personalized medicine – are there also approaches outside Oncology?** Jochen Maas, Sanofi-Aventis Deutschland GmbH, Frankfurt
11:10 – 11:40	**Accelerating Innovation through collaboration** Cord Dohrmann, Evotec AG, Hamburg
11:40 – 12:10	**Panel discussion**
12:10 – 13:00	**TECHNOLOGY SLAM SESSION 1**
	Moderator: Marion Michaelis-Kronabel
12:10 – 12:25	**From Science to Market – legal obstacles to product success** Christian Lindemann, VOELKER & Partner Rechtsanwälte Wirtschaftsprüfer Steuerberater mbB, Reutlingen
12:25 – 12:40	**Patenting Biotech Inventions in the U.S. post Myriad and Mayo** Jörk Zwicker, Zwicker Schnappauf & Partner Patentanwälte | PartG mbB, München
12:40 – 13:00	**Poster Slam**
13:00 – 14:00	LUNCH BREAK
14:00 – 16:30	**SESSION: REGULATORY**
	Moderator: Jürgen Hess
14:00 – 14:30	**Medicines, medical devices and other healthcare products – differing regulatory systems** Jürgen Hess, Pharma Scientific Services Team (P.SS.T), München
14:30 – 15:00	**Challenges in the demarcation of material medical devices from medicinal products. Differences between legal and scientific assessment** Peter von Czettritz, Preu Bohlig & Partner, München
15:00 – 15:30	**Towards greater Data Transparency – Trends and Impact on Market Access in Europe** Alexander Natz, EUCOPE, Brussels, Belgium
15:30 – 16:00	**Current and upcoming regulatory requirements for In-vitro Diagnostics in EU** Dieter Schönwald, TÜV SÜD Product Service GmbH, München
16:00– 16:30	**Panel discussion**
16:30 – 17:00	COFFEE BREAK
17:00 – 18:30	**TECHNOLOGY SLAM SESSION 2**
	Moderator: Willi Meier
18:30 – 18:45	**Closing remarks** Wieland W. Wolf, President of the EAPB
	Come Together / Social Event at DECHEMA Haus

PROGRAMME OVERVIEW TUESDAY, MARCH 8, 2016

09:00 – 09:10	**Opening** Wieland W. Wolf, President of the EAPB
09:10 – 12:10	**SESSION: BIG DATA**
	Moderator: Holger Bengs
09:10 – 09:40	**Big Data in Human Genetics: Challenges and Chances for disruptive Business Models** Daniela Steinberger, bio.logis Group, Frankfurt am Main
09:40 – 10:10	**Digital Medicine: from the App to Big Data** Dr. Claus Kusnierz-Glaz, PricewaterhouseCoopers AG, Frankfurt
10:10 – 10:40	COFFEE BREAK
10:40 – 11:10	**Genetalk- an approach to end the diagnostic odyssey for patients with rare genetic disorders** Peter Krawitz, Institut für Medizinische Genetik der Charité – Universitätsmedizin Berlin
11:10 – 11:40	**Big Data: Big Business – Big Failures?** Martin Pöhlchen, Sinfonie Life Science Management GmbH, Planegg
11:40 – 12:10	**Panel discussion**
12:10 – 12:45	**TECHNOLOGY SLAM SESSION 3**
	Moderator: Holger Bengs
12:45 – 13:45	LUNCH BREAK
13:45 – 15:45	**SESSION: TECHNOLOGY TRANSFER**
	Moderator: Jürgen Walkenhorst
13:45 – 14:15	**Science-to-Commercialization – a Max Planck Model for Early Innovative Drug Discovery** Bert Klebl, Lead Discovery Center GmbH, Dortmund
14:15 – 14:45	**The Infinite Value-Inflection Point: Making the Untransactable Transactable** Iain Thomas, Cambridge Enterprise, Cambridge, UK
14:45 – 15:15	**Hands on Translation: From Infinity to Beyond** Michael Dalrymple, MRC Technology, London, UK
15:15 – 15:45	**Panel Discussion**
15:45 – 16:00	**EAPB Award**
16:00 – 16:15	**Closing remarks** Wieland W. Wolf, President of the EAPB

CVS AND ABSTRACTS OF PLENARY SPEAKERS

Commercial Deal Structures and Recent Trends

Christi Mitchell, Highbury Ltd, Hitchin, UK

Christi Mitchell, *Intellectual Property (IP) specialist; founded Highbury Ltd 17 years ago as an independent business development company, specialising in IP commercialisation. Christi's academic background includes Human Genetics, Molecular Biology and Business. She has over 25 year's of worldwide IP, technology and product collaboration and commercialisation experience specialising in the life sciences.*

Christi is a past President of the Licensing Executive Society Britain and Ireland and heads up their Healthcare IP group.

Pharmaceutical deal trends – values, structures, therapeutic areas and more; based on the Medius 2015 Annual Deal Watch analysis.

The presentation will focus on the current deal making environment in the pharmaceutical and biotechnology sectors. This will include a review of the types of deals being done, the deal valuations and their structures, and the key therapeutic and technology areas.

Over the last few years, the pharmaceutical industry has seen a huge increase in M&A activity. The drivers for M&A include the need to build and bolster product pipelines (especially with late stage products) and to improve market share and geographic coverage, as well as the desire to enter into new therapeutic areas.

The deals of 2015 encompassed both the traditional and some new trends. The era of the mega-merger is still with us, as seen by the Shire-Baxalta deal, at $32bn and the $160bn Pfizer-Allergan deal. 2015 saw a significant number of multi-billion dollar deals as the trend from licensing towards acquisition continued. The availability of financing also had an impact on early stage deals, as biotech companies (particularly in the US) raised money from shareholders in order to take products further in development.

Companies are also rationalising their businesses and divesting assets to streamline and focus their operations.

According to a new IMS Report- IMS Health, Global Medicines in Use in 2020 (Parsippany, NJ November 2015): by 2020, total patient spending on medicines will be $1.4 trillion (an increase of 20-32% from 2015).

Global spending on specialty medicines used to treat chronic, rare or genetic disease is expected to reach 28% of the total spending by 2020 (IMS). This report estimates that 225 new medicines will be introduced by 2020 with one third focused on treating cancer. In other words, the drug development market may be heading in a new direction. Early stage drug investment by the pharmaceutical companies is here seen as a higher investment priority than late stage drug development. Of those surveyed*, acquisition was a high – 94% priority. 50% of respondents said that they planned peer to peer research partnerships and 85% said that they planned to hire a CRO. Companies focusing on personalised meds and diagnostics are expected to rapidly increase.

*ReedSmith, Life Lines; Life Sciences M&A and the Rise of Personalised Medicine (London 2015)

In January 2016 it was announced that a £50 million fund was launched by University College London and that a group of global pharmaceutical companies is teaming up with the tech transfer offices of three leading research universities in the UK to launch a £40 million (≈$57.3M) fund that will support commercialisation of key academic healthcare research.

AstraZeneca, GlaxoSmithKline and Johnson & Johnson Innovation will each contribute £10 million over six years to the Apollo Therapeutics Fund, which will support innovations from Imperial College London, University College London and the University of Cambridge. Each of the universities' tech transfer offices will contribute £3.3 million.

The aim of this innovative venture is that Apollo will advance preclinical research from these universities to a stage at which it can either be developed-on, by one of the industry partners or out-licensed. The three pharma partners will also offer their expertise in commercialisation and additional resources to help evaluate and develop the academic projects.

The presentation will review a range of recent deals to provide examples of the specific trends being discussed.

NOTES

CVS AND ABSTRACTS OF PLENARY SPEAKERS

Personalized medicine – are there also approaches outside Oncology?

Prof. Dr. Jochen Maas, Sanofi-Aventis Deutschland GmbH, Frankfurt, Germany

Jochen Maas *is appointed General Manager, Research & Development (R&D) at Sanofi-Aventis Deutschland GmbH, as of October 1st, 2010, based in Frankfurt. He is a member of the Global R&D Management Board and of the German Management Board. He was appointed as head of the German hub R&D organization in 2012.*

Jochen has huge experience in all phases of the R&D value chain. He started his career in PK, then he expanded his responsibilities to preclinical Development, preclinical and clinical Development and Research & Development. Afterwards, he was responsible for Global Research & Development in the Diabetes Division and acted as Vice President R&D Europe at sanofi-aventis.

Jochen also lectures in pharmacokinetics and administering medication as a professor at Gießen-Friedberg University of Applied Sciences.

He is a biologist and veterinarian. He has a doctorate in veterinary medicine including a specification in Radiology. He studied at the Universities of Zurich, Heidelberg and Munich. After joining the Group in 1992 as head of the pharmacokinetics laboratory, he held various R&D management positions in Germany and France.

Personalized or better stratified medicine is currently a hot topic in the scientific landscape and in the pharmaceutical industry. Background are significantly reduced costs of Genotyping from more than 1 Billion $ to approx.. 1000 $/genome resulting in much more genotyping activities and the availability of a huge amount of gene data. Those are particularly used in oncology where personalized medicine plays an increasingly important role since years. The majority of new compounds in this area reaches the market together with a companion-diagnostic kit allowing to identify the right patients for the respective medication.

But personalized medicine is much more than genotyping – and is significantly older. In the current discussion it is often forgotten that "personalized" approaches are state-of-the-art in medical treatment since decades. The classical antibiogramm – what is it other than personalized medicine? Dentistry, hip-replacements, other devices – what is it other than personalized medicine? Many approaches addressing a more individualized treatment of patients have nothing to do with genotyping but use phenotyping aspects.

This holds true also for the treatment of many actual disease burdens, Diabetes to be used as one example: On the one hand, there are already genes identified increasing the probability to get this disease slightly but phenotypic parameters are still the cornerstone to stratify diabetic patients: BMI, waist-circumference, HbA1c etc.. are the biomarkers used to define specific Diabetes populations. At least in the near future, an intelligent combination of several of those phenotypic biomarkers will control the stratification of Diabetes patient populations – and not genotyping activities. This might change mid- to long-term but at least today and in the near future there are more options to be used for personalized medicine than only genotyping – particularly in the indications outside of Oncology.

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CVS AND ABSTRACTS OF PLENARY SPEAKERS

Accelerating Innovation through collaboration

Dr. Cord Dohrmann, Evotec AG, Hamburg, Germany

Dr Cord Dohrmann *(born in 1964) joined Evotec AG as Chief Scientific Officer and Member of the Management Board on 01 September 2010. Dr Dohrmann has spent over 20 years in biomedical research at leading academic institutions and in the biotech industry. He started his academic career in 1983 studying Biology at Tübingen University in Germany and conducting research as a DAAD scholar at Duke University, Durham, USA. Dr. Dohrmann completed his MA thesis at the Max-Planck Institute in Tübingen and subsequently enrolled at the Harvard Medical School in Boston, USA, where he received his Ph.D. in Cell and Developmental Biology in 1996.*

Dr. Dohrmann continued his career as a Shiseido research fellow at the Massachusetts General Hospital in Boston before joining DeveloGen in 1999. He served the company in various management positions including CEO, leading DeveloGen from a start-up to an internationally recognised metabolic disease company with a pipeline of highly innovative preclinical and clinical products for the treatment of diabetes and related disorders. Dr. Dohrmann has been advising the European Commission, the Max-Planck-Institute as well as venture capital firms and authored and co-authored a number of publications and patents.

NOTES

CVS AND ABSTRACTS OF PLENARY SPEAKERS

From Science to Market – legal obstacles to product success

Dr. Christian Lindemann, VOELKER & Partner Rechtsanwälte Wirtschaftsprüfer Steuerberater mbB, Reutlingen, Germany

Christian Lindemann is attorney at law at the law firm VOELKER in Reutlingen Germany. He is a Certified Expert Attorney for International Business Law (Fachanwalt für internationales Wirtschaftsrecht) and also a Certified Expert Attorney for Intellectual Property Law (Fachanwalt für gewerblichen Rechtsschutz). He started working as a lawyer in 1998 and, since 2011, Christian serves as the Managing Partner of VOELKER.

Christian has huge experience in all aspects of research and development collaborations and licensing agreements, including grant-financed research collaborations under government rules for the use and distribution of inventions. He advises in cross-border and multi-party agreements as well as in supply and contract manufacturing agreements for pharmaceutical products as well as for medical devices. He has expertise in pharmaceutical liability matters and advises manufacturers and pharmaceutical entrepreneurs in respect to incidents, accidents and product recalls.

Christian holds a doctorate in Law from the University of Tübingen, Germany and a Master of Laws (LLM) degree from the University of Leuven, Belgium.

The main factor that influences the success of a product is its medical benefit to patients. The health industry does invest remarkable amounts of money and scientists do dedicate brain and energy to develop drugs and medical devices that offer benefit to patients and that, at the same time, provide return on investment.

Everybody who is involved in the development is clearly aware of the scientific, biological, technical and clinical risks. For the rather small number of products which "survive" the entire development chain, it would turn out as a really sad story if they ultimately fail because of "side issues" that arise from the legal risks of research and development.

The list of potential legal obstacles includes situations in which it is uncertain who owns an invention that was the starting point of the development. Such uncertainties typically arise in grant-financed research and development co-operations under government rules for the distribution and use of inventions. Even high-level research and development agreements between companies do frequently neglect the requirements of anti-trust law, especially under the EU Group-Exemption Regulations No 1217/2010 and 316/2014.

In the medical devices industry, where the European regulatory framework is currently "on the move", market players tend to disregard legal issues that dramatically influence the product success. Important examples of problems that currently arise are the use of Apps for medical purposes and also the influence of Commission Recommendation No 2013/473/EU on contract manufacturing and supply agreements for medical devices.

Ultimately, the most sad result of product development is a product that really offers value for the patient but fails to qualify for re-imbursement under public health schemes and, therefore, at least in some(major) markets, will never be successful.

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CVS AND ABSTRACTS OF PLENARY SPEAKERS

Patenting Biotech Inventions in the U.S. post Myriad and Mayo

Jörk Zwicker, Zwicker Schnappauf & Partner Patentanwälte | PartG mbB, München, Germany

Jörk Zwicker is partner at Zwicker Schnappauf & Partner Patentanwälte PartG mbB (ZSP Patentanwälte). He started his carrer in Intellectula Property (IP) law in 1999. Since then he worked in several Germany IP boutiques and joined ZSP Patentanwälte – at that time named "Dr. Volker Vossius Patent- und Rechtsanwälte in 2006.

Jörk is admitted before the German Patent and Trademark Office, the German Federal Patent Court, the Office for Harmonization in the Internal Market, and the European Patent Office. He has actively managed the patent portfolios of clients as diverse as universities to large pharmaceutical companies, successfully handled oppositions and nullity actions and related litigations, and regularly conducts IP due diligences on behalf of investors or companies. Jörk's technical focus is in the fields of biochemistry, pharmacology, molecular biology, and chemistry. He represents well known European, US, and Japanese companies.

Jörk studied chemistry at the Technical University Berlin (TU) and biology at the Massachusetts Institute of Technology (MIT), U.S.A. He obtained a Master's of Chemistry (Dipl. Chem.) at the TU Berlin. He then started his Ph.D. work with Prof. Rolf Müller at the Institute of Molecular Biology and Tumor Research (IMT) at the Philipps-University Marburg. The Ph.D. was followed by postdoctoral research with Prof. Robert Tjian at the University of California, Berkeley, USA.

Jörk received fellowships of the "Studienstiftung des Deutschen Volkes", the German-American Fulbright Commission, the "Boehringer Ingelheim Fonds, Foundation for Basic Research in Medicine", the Howard Hughes Medical Institute, and an EMBO Postdoctoral fellowship.

Jörk is a member of several professional societies and participates in the working group "Life Sciences" of LES International.

The increasing wealth of information on the correlation of biological markers with diagnosis, patient stratification, treatment optimization and prognosis has spurred the fantasy of scientists, entrepreneurs and investors alike that we are on a shining way to personalized medicine. However, any endeavor to commercialize new concepts in the area of personalized medicine will depend on enforceable patent protection for such inventions.

It is, therefore important to consider the limits for patenting such inventions in the U.S. that were set out in recent U.S. Supreme Court decisions Mayo Collaborative Services v. Prometheus Laboratories, Inc., Association for Molecular Pathology v. Myriad Genetics, Inc., and Alice Corp. Pty. Ltd. v. CLS Bank Int'l. The U.S. Supreme Court signaled to patent applicants that process claims that purportedly implement laws of nature or natural phenomena without adding anything that was not already well-understood, routine, or conventional as well as natural products failed to establish patent-eligible subject matter, i.e. contravened the requirements of 35 U.S.C. 101.

The experiences of a European patent practitioner with pursuing patents for biotech inventions for European clients in front of the US-PTO post Myriad and Mayo will be presented and consequences for US patent filing strategies will be discussed.

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CVS AND ABSTRACTS OF PLENARY SPEAKERS

Medicines, medical devices and other healthcare products – differing regulatory systems

Dr. Jürgen Hess, Pharma Scientific Services Team (P.SS.T.), München, Germany

Jürgen Hess *(born in 1960) joined P.SS.T. as consultant in 2015 after spending more than 20 years in biomedical R&D at leading academic institutions and in the biotech industry. At TRION Pharma his research activities as Head of Scientific Affairs were focussed on bispecific antibody development towards cancer treatment (2007-2014).*

In his preceding leading R&D positions at november AG and responsif GmbH he was responsible for the development of autologous tumor cell vaccines (2000-2006). At the University Clinics in Ulm, Germany, and the Max-Planck-Institute for Infection Biology, Berlin (1992-2000), Jürgen worked on innovative recombinant BCG vaccine strains for tuberculosis prevention and on viable antigen delivery devices (e.g. attenuated Salmonella strains).

As biologist by training, Jürgen earned his PhD in Microbiology at the University of Würzburg, Germany. Furthermore, he gained his habilitation in Immunology at the University Clinics Ulm, Germany and did his post-doctoral work at the Sandoz Research Institute in Vienna, Austria. In the course of his research work he published more than 90 articles in peer-reviewed journals and is a co-inventor of more than 10 patents and patent applications.

It is a long way from bench to market. Currently, more than 10 years are finally required for medicinal products (i.e. drugs, biological, OTC products) from the patented idea to the market launch. The complete approval process for drugs/biologicals with CMC, preclinical and clinical evaluations costs about 1 billion EUR and at the end the European marketing authorisation application contains about 350.000 pages (and in the US still many more). Nevertheless, medicinal products are not the only therapeutic class of products on the markets, also medical devices have therapeutic function. However, these medical devices are subjects to a completely different regulatory concept. In addition, health-related products like biocides (eg. alcohol as disinfectant), insect repellent applied to skin (also commonly called „bug spray“) and food supplements as well as cosmetics belong to the group of “regulated products”, although the requirements for a marketing authorisation are less complex than those for medicines and medical devices. Thus, this presentation will sketch these different approval requirements.

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Challenges in the demarcation of material medical devices from medicinal products. Differences between legal and scientific assessment

Peter von Czettritz, Preu Bohlig & Partner, München, Germany

Peter von Czettritz *specialises on advising and representing national and international pharmaceutical enterprises and medical devices enterprises in all sectors of Drug Law (AMG), Law on Advertising in the Health Care System (HWG), Medical Devices Law (MPG), Patent Law and Competition Law. In addition, he focuses on handling marketing authorisation proceedings relating to the Drug Law and certification proceedings relating to the Medical Devices Law (Regulatory Affairs).*

Peter von Czettritz is the author of a variety of specialised publications and is a regular speaker on all topics of pharma law. He is a member of the legal committee of the Bundesverband der Arzneimittelhersteller (BAH) (Federal Association of Drug Makers) and of the „Medical Devices Law" network of the Bundesverbandes Medizintechnologie (BVMed) (Federal Association of Medical Technology). Peter von Czettritz is the publisher of the magazine PharmaRecht which appears in C.H.Beck and PMI-Verlag as well as the publisher of the magazine MedizinProdukteRecht appearing at Nomos Verlag. In 2001 he was awarded the PharmaRecht prize.

Medical devices are to be differentiated from other product classes according to their subjective and objective purpose. However the demarcation between substance-based medical devices and medici-nal products is highly complicated due to their essentially similar purpose. The definition for medical devices as well as for medicinal products as defined in Directive 93/42/EC and Directive 2001/83/EC are fully harmonized within the European Union. Accordingly a substance-based medical device means any material or other article, whether used alone or in combination, be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of: diagnosis, prevention, monitoring, treatment or alleviation of disease … and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

A medicinal product is (a) any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or (b) any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

The relevant difference is therefore a different effect of the product. While medicinal products achieve their principal intended action by pharmacological means medical devices must not achieve their prin-cipal intended action by pharmacological means but through a mechanical, physical or physico-chemical effect.

According to the demarcation guideline MEDDEV 2.1/3 ref. 3 a pharmacological effect is defined as "an interaction between the molecules of the substance in question and a cellular constituent, usually referred to as a receptor, which either results in a direct response, or which blocks the response to another agent. Although not a completely reliable criterion the presence of a dose-response correla-tion

is indicative of a pharmacological effect". With decision of 06th September 2012, case C-308/11, the ECJ declared the definition of the MEDDEV as legally binding.

Nevertheless the demarcation between material medical devices and medicinal products can be highly complicated in many individual cases, explicitly because the jurisdiction of the ECJ and the highest Civil German Court – the Federal Court of Justice (BGH) – are from the speakers' point of view not consistent.

The speaker will present recent jurisdiction of the ECJ, like the decision of 03. October 2013, case C-109/12 and decision of 06. September 2012, case C-308/11 and recent jurisdiction of the BGH – "Photodynamische Therapie" …; "Mundspüllösung" …. and "Darmreinigungspräparat" …. and will explain the differences.

In accordance with the definition of the ECJ also the BGH begins the demarcation between medicinal products and substance-based medical devices with the question whether the principal intended ac-tion is a pharmacological, an immunological or metabolic effect. However then the BGH is of the opinion that the principal intended action of a medical device is to be seen not only in the primary effect but also side- and follow-up effects need to be considered.

The speaker depicts that the actual problem in the demarcation between substance-based medical devices from medicinal products has been created by the BGH and is a mere result of the discrepancy between the point of view of scientists and the point of view of legal specialists.

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CVS AND ABSTRACTS OF PLENARY SPEAKERS

Towards greater Data Transparency – Trends and Impact on Market Access in Europe

Dr. Alexander Natz, EUCOPE, Brussels, Belgium

***Dr. Natz** is Secretary General of the European Confederation of Pharmaceutical Entrepreneurs (www.eucope.org). From 2008-2013 he has been heading the Brussels Office of Bundesverband der Pharmazeutischen Industrie e.V. (BPI). Before, he has been a lawyer with Sträter Law Firm in Germany and also worked in the pharmaceutical industry. Before, he has been working in the field of competition law with the European Commission. As a research assistant at Duke University (USA) he has dealt with international pharmaceutical law. His doctorate was supervised by former judge at the European Court of Justice, Prof. Dr. Dr. Ulrich Everling.*

The pharmaceutical and biotech industry is currently facing more and more calls for increased data transparency on one hand through the new Regulation of Clinical Trials (Regulation (EU) No. 536/2014) as well as the revised Transparency Policy of the European Medicines Agency (EMA) and on the other hand through the set-up of other mechanisms outside the scope of EU competences, namely the EURIPID database dealing with price transparency.

The so-called EMA Policy 0070 on the proactive publication of clinical trial data has become effective as of 1 January 2015. The finalisation of the implementation is foreseen for end of April 2016. This enables EMA to make clinical study reports submitted as of 1 January 2015 publicly available. With this crucial step, the Agency establishes its approach to an increased transparency of clinical trial data. One of the main concerns at EUCOPE is the protection of commercially confidential information (CCI) from marketing authorisation dossiers in Europe. Clear rules need to be established to protect commercially confidential data in order not to jeopardise the EU as an area for research in the field pharmaceuticals and weakening the incentives for investments in new developments.

On the other hand, the pan-European collaboration on the EURIPID database involving national agencies on a voluntary non-profit basis will increasingly affect industry in the years to come. The main goal of this initiative is to provide national pricing & reimbursement authorities with detailed information on prices for medicines in the participating EU Member States. The database, inter alia, provides for information on the manufacturer, wholesale, net retail and gross retail prices, as well as dosage form, ATC, route of administration and number of units, etc., particularly facilitating external reference pricing by creating a higher degree of price transparency. Therefore, it is to be expected that this database could become an important tool for the purposes of external reference pricing in Europe and beyond.

NOTES

Current and upcoming regulatory requirements for In-vitro Diagnostics in EU

Dr. Dieter Schönwald, TÜV SÜD Product Service GmbH, München, Germany

***Dieter Schönwald** is currently Manager of the IVD (In Vitro Diagnostics) Department of TÜV SÜD Product Service GmbH, Munich, Germany, Notified Body according to European Directive 98/79/EC on IVD Medical Devices and Head of TÜV SÜD's global IVD Service Line. He is familiar with the European Regulations on IVD and Medical Devices for more than 18 years due to his experience as an Auditor, Product Specialist and Technical Certifier for IVD as well as Head of the Certification Body respectively Deputy Head of the Certification Body at two different Notified Bodies for Medical Devices.*

Dieter Schönwald holds a Diploma in Nutrition and Dietetics, with emphasis on Biochemistry at University Bonn, Germany, and a PhD in the field of Immunology and Immunogenetics.

Before entering the regulatory field Dieter Schönwald gained experience as a research associate at university and as a research scientist in pharmaceutical industry with focus on biological products and diagnostics, as head of biological quality control / quality assurance in pharmaceutical industry and as a scientist in a biological test lab for medical devices and pharmaceuticals.

The current regulatory framework for the handling of in vitro diagnostic (IVD) Medical Devices in the EU is about to change.

Directive 98/79/EC on in-vitro diagnostic Medical Devices (IVDD), which the member states have transposed into national law through national legal acts, has been mandatory for more than fifteen years now. Throughout this period only a few amendments have been made.

A new In Vitro Diagnostic Regulation – directly applicable in all Member States without transposition into national law – is currently in preparation as part of the general revision of European medical device legislation. Some other regulatory changes have been already introduced by the Commission within the recent years to improve the existing regulatory system before the new IVD Regulation will come effective. These changes of the European legislation for IVD are closely linked to those currently ongoing for Medical Devices.

The EU IVD Regulation will bring a multitude of changes. The most important change will be the introduction of a new classification system which will result for many IVD products in a classification into a – in some cases reasonably – higher risk class compared to the existing legislation and increased efforts for the manufacturers to show compliance. The number of devices that must undergo conformity assessment with the involvement of a Notified Body will increase considerably.

Other important changes to come refer to the scope of the products affected by the IVD Regulation and products manufactured within a health institution. New obligations will be implemented for members of the supply chain. Introduction of a person responsible for regulatory compliance at the manufacturer or at the EU representative will become obligatory.

Measures for designation and monitoring of Notified Bodies will be tightened as well as surveillance of manufacturers by Notified Bodies. Reference laboratories will be designated to participate in assessment of high risk devices. For companion diagnostics a conformity assessment procedure including consultation of a competent authority in the field of medicinal products will be introduced.

Product-related requirements will be described in more detail directly in the IVD Regulation. A Unique Device Identification (UDI) system will be introduced to ensure the identification and traceability of products. Reasonably more details have to be disclosed to the public.

As the IVD Regulation is currently in the legislative procedure of the EU according to Article 294 of the Treaty on the functioning of the European Union, several items are not fixed in detail yet. We expect completion and publication mid of 2016. For a transition period it will be possible to place devices on the market under the IVDD or under the IVD Regulation.

The presentation will give an overview about key features of the current regulatory requirements and the most important changes to come with the IVD Regulation as well as on the status of the legislative process. Specific aspects of the upcoming requirements for companion diagnostics will be discussed.

NOTES

CVS AND ABSTRACTS OF PLENARY SPEAKERS

Big Data in Human Genetics: Challenges and Chances for disruptive Business Models

Prof. Dr. med. Daniela Steinberger, bio.logis Group, Frankfurt am Main, Germany

Daniela Steinberger *is a board certified physician for human genetics. She has more than 20 years experience in human genetic diagnostics and research, is a member of the medical faculty of the University Hospital Gießen-Marburg and holds an MBA from the European Business School (EBS) focusing on Health Care Management.*

Daniela Steinberger is founder and medical director of the diagnostic institution bio.logis Center for Human Genetics. In addition she is chief executive of bio.logis Genetic Information Management GmbH. bio.logis Genetic Information Management GmbH is a research and development company that focuses on IT and telemedical solutions for the management and communication of human genetic information.

During the last decades, the implementation of IT-infrastructures has changed all areas of life and consequently the global business landscapes respectively our personal daily routines. By the application of IT tools many business models or even complete professions vanished and were substituted by IT supported workflows and thus more economic processes. The increasing utilization of IT resulted in enormous streams of data which in turn harbor metadata with the opportunity to detect new associations and meta-knowledge. The latter could not be explored with traditional approaches of relational database architectures. New methods to enable the analyses of huge amounts of data structures to extract the herewith associated meta-information were designated as "Big Data" technologies.

In parallel to the advances in information technology, during the last two decades the amounts of genomic data have increased tremendously. This was and is still triggered by the increasingly rapid development of DNA analyses methods. To unfold the potential of DNA data for better decision finding in medicine, new methods and data infrastructures in the healthcare system are needed. Due to this situation, new opportunities and interesting business models are arising. For a successful integration of genomic data into medical routine, the specifics of the health care market that obviously are not following the principles of a conventional free market have to be considered.

NOTES

CVS AND ABSTRACTS OF PLENARY SPEAKERS

Digital Medicine: from the App to Big Data

Dr. med. Claus Kusnierz-Glaz, PricewaterhouseCoopers AG, Frankfurt, Germany

Dr. Kusnierz-Glaz *is heading the German Pharma- Biotech & Medtech- Industry Group at PwC. He started his career in 1974 studying human medicine in Hannover and Münster. He completed his doctoral thesis in Münster in 1983. He received clinical training in internal medicine and specialized in hematology, oncology and immunology. His postdoctoral, scientific training was taken place at the Stanford Universtity Hospital Center (Prof. KG Blume, 1990-1995). After a year at the university Düsseldorf, and concomitant further education in medical controlling and a MBA program in Ashridge (UK), he joined the consulting practice of Coopers & Lybrand. After merger of Coopers with Pricewaterhouse he specialized in commercial due diligence and valuation of pharma-/biotech & medtech development projects as well as companies. In 2012/3 he headed the HC-knowledge cluster EMEA, since than he also supporting pharma-, biotech- , medtech as well as HC clients in ehealth as well as mhealth solutions.*

After a short characteristic of Health IT, eHealth and mHealth Dr. Kusnierz-Glaz shows some IT characteristics of German physicians in private practice. Based on surveys as well as own interviews the basis for drivers of IT and IT tools like Apps is explained. A typical scenario for a successful launch of a new app with sponsor and Promoter is presented.

mHealth trends as well as drivers and hurdls from the PwC mHealth Study are presented as well as a few examples of possible applications. In addition to an overview of the functionality of current HC apps. Trends also allow to draw a picture of the near future in the HC system.

Data Analytics changes the ways Big Data can be handled and use to improve diagnostics and therapy by predictive analysis, but also have data analysis presented in (near-) real-time. Examples of improvement are presented. Especially in cancer diagnosis and treatment cost reduction of sequencing is driving high precision medicine in subtyping formerly homogenous looking cancer types, e.g. small cell carcinomas.

NOTES

CVS AND ABSTRACTS OF PLENARY SPEAKERS

Genetalk – an approach to end the diagnostic odyssey for patients with rare genetic disorders

Dr. med. Peter Krawitz, Institut für Medizinische Genetik der Charité – Universitätsmedizin Berlin, Germany

PD. Dr. med. Peter Krawitz, *Dipl. Phys. is cofounder of GeneTalk, one of the leading online platforms for the analysis and interpretation of high-throughput sequencing data. More than 1500 clinician scientists are using GeneTalk for their work on a daily basis to identify disease causing mutations in patients with rare genetic disorders. Peter and many professional users of GeneTalk were able to identify several novel disease genes via GeneTalk and are paving the way to personalised medicine.*

Peter studied medicine and physics in Munich and has worked at the Max Planck Institute for Molecular Genetics and the Department of Medical Genetics at Charité Universitätsklinikum Berlin for the last 7 years. Recently he obtained his professional teaching qualification for Genetics and he published more than 50 articles in peer-reviewed journals.

High-throughput sequencing technology enables us to detect mutations on a genomic scale.

The raw data generation for a whole genome has now become a routine procedure, that takes about 3 working days and costs currently about 1000 EUR.

In each individual, there are about three millions of variants, that is the differences compared to a reference sequence.

In a patient with a monogenic disorder, the disease causing mutation is hidden in this standard data set in two thirds of the cases.

The actual challenge is to identify the pathogenic mutation, whichis often referred to as finding a needle in a haystack.

We developed effective workflows for prioritizing candidates combining information from the molecular level as well as from deep-phenotyping.

With automated facial recognition for patients with dysmorphic features this approach is also applicable in a clinical setting without expert knowledge in syndromology.

By this disruptive technology we will be able to shorten the timespan from first contact of a patient with a medical professional to a definite molecular diagnosis.

NOTES

CVS AND ABSTRACTS OF PLENARY SPEAKERS

Big Data: Big Business – Big Failures?

Dr. Martin Pöhlchen, Sinfonie Life Science Management GmbH, Planegg, Germany

Over 20 years of experience in general management, R&D management, licensing, business & corporate development, sales & marketing, strategic transactions, mergers and acquisitions, intellectual property. Co-founder and Managing Director of Sinfonie LSM GmbH and previously CEO of Revotar AG and Pieris AG, VP Business Development at MediGene AG and European Commercial Director at Tripos (now Certara). He is a founding Board Member of the German Biotech trade association BIO Deutschland, Head of the new working group Bio-IT and Big Data since October 2014, Head of the working group intellectual property and technical licensing since 2006, nominated member of the BioPharm since 2009 and of the Innovation committee at BPI (Association of the Pharmaceutical Industry) since 2015. In 2004 he was honored as one of the finalists of the "Deutscher Zukunftspreis" by the German President. He studied chemistry at the Ruhr University of Bochum where he received a PhD in chemistry working on ab initio quantum chemistry calculations. Due to his professional background in the biotech and the IT industry he combines unique operational and technical knowledge at the intersection of biotech and information technology.

Big Data applications and analytics are transforming many different industries, including life sciences and healthcare. Whereas there are some near term economic and technical benefits expected in healthcare, e.g. related to improved claims processing and fraud detection it will be much more challenging to realize similar benefits for life sciences. More than a decade before scientists and investors hoped for the genomics revolution to result in innovative products too quickly. Scientists and investors need to carefully manage expectations and time lines in order to avoid big failures, both from a business and from a scientific point of view.

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Science-to-Commercialization – a Max Planck Model for Early Innovative Drug Discovery

Dr. Bert Klebl, Lead Discovery Center GmbH, Dortmund, Germany

Bert M. Klebl *has gathered more than 15 years of professional experience in drug discovery and early drug development from various positions in the life-science industry. Since its initiation in early 2008, he is managing director (CEO) and CSO of Lead Discovery Center GmbH (LDC) (Dortmund/Germany), a drug discovery enterprise, which was started by Max-Planck Innovation and the German Max-Planck Society (MPG). LDC leverages scientific excellence by incubating academic projects and turning them into products for commercialization. LDC considers itself as one of the few fully integrated "translational research centers". Today, LDC holds a broad portfolio of small molecule drug discovery projects at various stages and in different therapeutic fields along the value chain. Each individual project is a collaborative effort of LDC and an academic group (typically from the MPG). LDC also entertains early-type partnerships with biotech and pharmaceutical industries, e.g. license and option agreements as well as collaborations with Bayer, Qurient, Merck Serono, AstraZeneca and HMNC. LDC is a professionally managed drug discovery incubator connecting academic research and industrial application.*

Before joining LDC, Bert was the Head of Biology at GPC Biotech (Martinsried/Germany). Before that he was Axxima's (Martinsried/Germany) Vice President Research responsible for discovery and development of the company's portfolio of small molecule drug candidates for various therapeutic indications, which covered all stages of R&D, from target to the nomination of compounds for development. He was also strongly involved in business development aspects, such as deal making with pharma partners, and fund raising, both through grant applications but also venture capital funding.

In a previous position at Hoechst Marion Roussel and Aventis, he led a global kinase drug discovery platform and worked as project team leader and lab head. A biologist by training, he earned his PhD in Biochemistry at the University of Konstanz, Germany and did post-doctoral work at the Biotechnology Research Institute of the NRC Canada in Montréal, Canada.

In the course of his research work he published more than 40 articles in peer-reviewed journals and is a co-inventor of more than 20 patents and patent applications.

Connecting Academia and Pharmaceutical Industry

The Lead Discovery Center GmbH (LDC), founded in 2008 by Max Planck Innovation GmbH transforms results from basic research into novel drug candidates. LDC closely interacts with basic researchers, in particular with the scientists of the Max Planck Society to leverage excellent biomedical basic research from approximately 40 Max Planck institutes, representing a research pipeline of several thousand people and ideas. LDC is considered a translational incubator for academic project ideas. Max-Planck's initiative of creating such a drug discovery incubator has come from insufficient commercialization of basic research results. Today, LDC hosts an industry-style drug discovery infrastructure, focusing on small molecule pharmaceuticals, covering all needs of drug discovery to the stage of preclinical development. LDC's infrastructure has not been exclusively built for Max-Planck projects only. It is open for collaborations with other academic institutions, biotech companies and pharmaceutical industry as well. Typical LDC products are high quality lead compounds with proof-of-concept in vivo or development candidates. Currently, LDC entertains a portfolio of ~20 highly innovative drug discovery projects, which are conducted in a collaborative fashion. Project entry criteria are the level of innovation and medical need. The entry stage for projects is flexible, either at the target or assay or compound (hit) stage. LDC tries to transform these innovative early-stage projects into attractive licensing opportunities.

Meanwhile, LDC has partnered 14 drug discovery projects and has another ~20 unencumbered projects at different stages of development, which may be partnered at any time. Usually they are licensed at lead stage with proof-of-concept. Partnered projects include exclusive and commercially rewarding licensing deals, such as with Bayer AG in 2011 and Qurient (2013 and 2015). Potential revenues are being shared with the collaboration partner(s) and LDC's shares are re-invested into novel drug discovery approaches.

NOTES

CVS AND ABSTRACTS OF PLENARY SPEAKERS

The Infinite Value-Inflection Point: Making the Untransactable Transactable

Dr. Iain Thomas, Cambridge Enterprise, Cambridge, UK

Dr. Iain Thomas *is Head of Life Sciences at Cambridge Enterprise.*

Cambridge Enterprise's Life Sciences product portfolio includes alemtuzumab (Sanofi), breast cancer markers (Brevagen) and mouse touch screen chambers (Campden Instruments). Recent spin-outs include Mission Therapeutics, Cambridge Epigenetix, XO1 Therapeutics, Z-factor and Phoremost. Recent transactions include licences in fields as diverse as therapeutics, diagnostics, biofuels, IVF and epigenetics and the sale of XO1 to Johnson & Johnson. Iain led discussions with GSK in respect of the University of Cambridge–GSK open innovation drug discovery initiative based at the SBC.

Great advances in biological and medical science from research institutions are where very many great treatments for patients originally came from and there is no doubt there will be many more such opportunities. That said, we who work at that interface between new academic and technology and the commercial world of biotech, pharma and investors are all too frequently told that what we have is too early: **Untransactable** of, at that time zero value, no less.

It is our task to dream, create and work with our academics colleagues to generate opportunities in which our industrial and investor partners have belief and see value and thus are **Transactable** and of non-zero value. How do we make this transition effectively? If we do that job well how much value have we added? We started with zero so the relative added-value is infinite. Isn't that the most exciting value inflection point of all?

NOTES

CVS AND ABSTRACTS OF PLENARY SPEAKERS

Hands on Translation: From Infinity to Beyond

Dr. Michael Dalrymple, MRC Technology, London, UK

After a career in academic research, Mike's first job in the commercial sector was at Inveresk Research, a CRO. In 1990, Mike joined PPL Therapeutics where he rose from molecular biology team leader to Head of New Product Discovery. After 8 years at PPL, through a period of rapid company growth, an IPO on the LSE and the creation of several famous sheep, Mike left to become CEO of the MRC Collaborative Centre in Edinburgh, an organisation that was subsumed into MRC Technology in 2000.

Mike has taken a number of senior roles within MRC Technology: Director of Applied Research, Director of Intellectual Property and, most recently, Director of Business Development. He was directly involved in creating the MRC's Development Gap Fund (a proof of concept seed fund for MRC Units), the Centre for Therapeutics Discovery (MRC Technology's early stage drug discovery facility), the Centre for Diagnostics Development (MRC Technology's new translational facility for diagnostic tests) and leading a number of major licensing deals. Mike has also been the MRC nominee director on the boards of several companies including Domantis, Aptuscan, Anacrine and Virogen (the latter as Chairman).

The majority of IP flowing from academic sources is deemed by industry to be too 'early stage' and a high risk investment prospect. For several years now governments and organisations operating to commercialise academic research have been funding activities to push early stage IP towards the market. I will describe some initiatives that MRC Technology has invested in, alone and with partners, to 'translate' such research to a point where it is more attractive to commercial organisations. These include: Proof of Concept funding, early stage drug discovery and (most recently) diagnostics development.

NOTES

POSTER OVERVIEW

Session 1a: Therapeutics

1a-1 **S- Oxprenolol for treating amyotrophic lateral sclerosis (ALS)**
Jochen Springer, Stefan D. Anker; Herzzentrum Göttingen, Germany

1a-2 **Cytokine Loaded Particles in Hyaluronic Acid for Treating Osteoarthritis**
Michael Sittinger, Kristin Andreas, Jochen Ringe; Med. Klinik Rheumatologie und Klinische Immunologie CCM und Berlin-Brandenburger Centrum für Regenerative Therapien (BCRT), Berlin, Germany

1a-3 **A New Generation of Painkillers**
Christoph Stein, Simone Scheffel; Klinik für Anästhesiologie m.S. operative Intensivmedizin, Berlin, Germany

1a-4 **Highly effective anticancer agent**
Dagmar Gieseler, Max Lehmann-Matthaei; PVA SH GmbH, Kiel, Germany

1a-5 **CAAI – Covalent-allosteric AKT inhibitors**
Daniel Rauh, Rajesh Gontla, Jörn Weisner; Technische Universität Dortmund, Germany

1a-6 **Peripherally acting NMDAR Antagonists as new Antidiabetic Medication**
Eckhard Lammert, Alena Welters, Diran Herebian, Jan Marquard, Ertan Mayatepek, Thomas Meissner, Silke Otter; Heinrich-Heine-Universität Düsseldorf, Germany

1a-7 **NHR2 inhibitors**
Holger Gohlke[1], Manuel Grez[2], Alexander Metz[1], Julia Schanda[2], Christian Wichmann[2]; [1] Heinrich-Heine-Universität Düsseldorf, Germany; [2] Georg-Speyer-Haus, Frankfurt, Germany

1a-8 **Multiple Sclerosis (MS) therapy with humanized anti-CCR2 antibody through depletion of CCR2+ monocytes with proof of concept in primates**
Carlos Güntner; MBM ScienceBridge GmbH, Göttingen, Germany

1a-9 **How does the additional benefit extent of Orphan Drugs impact Price Negotiations in the German outpatient Sector?**
M. Freiberg, R. Schwarz; Quintiles Commercial GmbH, Mannheim, Germany

1a-10 **BARs for highly specific treatment of B-cell malignancies**
Nicole Comtesse; Universität des Saarlandes WuT GmbH, Saarbrücken, Germany

POSTER OVERVIEW

Session 1c: Diagnostics

1c-1 **AutoMax needs only single-stack regular FISH documentation images for automatic reading and scoring**
Joachim Moecks[1], Alexander Dressel[1], Pham Dinh Tuan[2], Hans-Ulrich Schildhaus[3]; [1] bioMcon GmbH, Mannheim, Germany; [2] Mathematical Consultant, Toulouse, France; Department of Pathology, [3] Medical Faculty Göttingen, Göttingen, Germany

1c-2 **ReadMax: A Novel Showcase Approach for FISH Biomarkers**
Joachim Moecks; bioMcon GmbH, Mannheim, Germany

1c-3 **Molecular pathology biomarkers:"Big Bang" of personalized medicine? Pros, cons, gaps, and traps**
Joachim Moecks ; bioMcon GmbH, Mannheim, Germany

1c-4 **Small molecule MNK inhibitors as cancer therapeutics**
Andy Merritt, Ed McIver; MRC Technology, London, UK

1c-5 **Small molecule PAICS inhibitors for metastatic breast cancers**
Debbie Taylor[1], Daniel Peeper[2]; [1] MRC Technology, London, UK; [2] Netherlands Cancer Institute (NKI), Amsterdam, The Netherlands

1c-6 **Innovative method for detecting co-occurring histone modifications in a single step using hybrid proteins**
Albert Jeltsch, Goran Kungulovski, Rebekka Mauser; Institute of Technical Biochemistry, Stuttgart, Germany

1c-7 **Direct, bisulfite-free detection of epigenetic cytosine modifications at user defined loci using TALEs**
Daniel Summerer, Grzegorz Kubik, Moritz Schmidt; Department of Chemistry, Konstanz, Germany

1c-8 **Modulation of the TLR4-signaling pathway**
Antje Ostareck-Lederer[1], Dirk H. Ostareck[1], Gernot Marx[1], Anke Liepelt[2], Jana C. Mossanen[1]; [1] Department of Intensive Care and Intermediate Care, [2] current Dept. of Internal Medicine III, University Hospital, RWTH Aachen University, Aachen, Germany

1c-9 **Differential diagnosis of Parkinson's disease and dementia with Lewy bodies**
Carlos Güntner, Stefan Uhle; MBM ScienceBridge GmbH, Göttinger, Germany

1c-10 **Self-assembly nanoantennas for fluorescence signal amplification in molecular diagnostics**
Andreas Speckbacher; EZN Erfinderzentrum Norddeutschland GmbH, Hannover, Germany

POSTER OVERVIEW

Session 2a: Up- and Downstream Developments

2a-1 **Novel cyclodextrins for hydrophobic drug delivery**
Nicole Comtesse; Universität des Saarlandes WuT GmbH, Saarbrücken, Germany

2a-2 **The application of model based design of experiments (MBDoE) and dynamic simulations to biotechnological production processes**
Sonja Jost[1], Mathis Gruber[1], M. Nicolas Cruz B.[2]; [1] DexLeChem GmbH, Berlin, Germany; [2] Bioprocess Engineering TU Berlin, Germany

Session 2b: Biopharmaceutical Drug Formats / Developments

2b-1 **Gold(I)-Alkin-Complexes for the treatment of cancer, rheumatoid arthritis or infectious diseases**
Susanne Deutsch; EZN Erfinderzentrum Norddeutschland GmbH, Hannover, Germany

Session 2c: Upcoming Technologies

2c-1 **Neuroprosthetic device for tremor management without motoneuron stimulation**
Carlos Güntner; MBM ScienceBridge GmbH, Göttingen, Germany

2c-2 **Thermo-induction and identification of ion channel activity by dyes for high throughput application**
Andreas Speckbacher; EZN Erfinderzentrum Norddeutschland GmbH, Hannover, Germany

POSTER SESSION 1A: THERAPEUTICS

1a-1 **S- Oxprenolol for treating amyotrophic lateral sclerosis (ALS)**
Jochen Springer, Stefan D. Anker
Herzzentrum Göttingen, Germany

Amyotrophic lateral sclerosis (ALS) is an orphan neurodegenerative disease characterized by progressive muscular paralysis reflecting degeneration of motor neurons in the brain and spinal cord. The median age of disease onset is 55 years. Disease frequency increases with age until age of 75. 50% of the patients die within the first three years since the first clinical manifestation.

Riluzole, approved for treating ALS, delays the onset of ventilator dependence and prolongs life by two to three months. Nevertheless, there is a high medical need for novel drug candidates improving survival and quality of life.

S-Enantiomer enriched compositions of beta blockers, in particular S-Oxprenolol have been shown to be good drug candidates for treating ALS. Treatment of ALS-mice (animal model SOD G93A) with 10mg/kg/d S-Oxprenolol promotes a prolongation of survival life time by 33% compared to Placebo treated mice. The daily waste of muscle and body mass can be reduced after disease onset. Moreover, S-Oxprenolol (20mg/kg/d) treated ALS-mice significantly survive longer than Riluzole- treated mice. S-Oxprenolol is also superior in survival to either R-Oxprenolol or racemate Oxprenolol comprising both enantiomers.

1a-2 Cytokine Loaded Particles in Hyaluronic Acid for Treating Osteoarthritis

Michael Sittinger, Kristin Andreas, Jochen Ringe
Med. Klinik Rheumatologie und Klinische Immunologie CCM und Berlin-Brandenburger Centrum für Regenerative Therapien (BCRT), Berlin, Germany

So far the intra-articular injection of hyaluronic acid (HA) is the gold standard for treating patients with osteoarthritis as it has been shown to delay the degeneration of cartilage. In this regard, HA is a well-tolerated visco-supplementation of the synovial fluid for mild and moderate osteoarthritic joints. Until now however, there is no treatment option which is both able to delay or stop degeneration and which has regenerative potential.

A novel approach for the treatment of osteoarthritis and other cartilage defects is to inject biodegradable chemokine-loaded microparticles (e.g. PLGA-based) in a suspension of HA into the joint cavity. The microparticles ensure that the chemokines are released in a controlled manner (not at once) over a defined period of time thereby establishing stable chemo-attracting gradients that are required for effective stem cell recruitment to the site of cartilage defect. In vitro results surprisingly show that the combined administration of HA and the chemokine CCL25 (thymus expressed chemokine) or CXCL12 (stromal cell-derived factor-1α) synergistically promote the migration of human stem- and/or progenitor cells. Animal experiments in an osteoarthritis disease model of guinea pigs have been started.

POSTER SESSION 1A: THERAPEUTICS

1a-3 A New Generation of Painkillers

Christoph Stein, Simone Scheffel
Klinik für Anästhesiologie m.S. operative Intensivmedizin, Berlin, Germany

Opioids are considered the "gold standard" of intermediate to strong acting analgesic drugs and are regularly administered in acute and cancer pain. However, conventional analgesics are limited by detrimental side effects, inefficacy in certain chronic pain syndromes and widespread abuse. Opioids such as morphine produce apnoea, sedation or addiction in the central nervous system (CNS) and constipation via intestinal myenteric neurons. Although pain research has identified a plethora of relevant molecules, no truly innovative analgesics have reached the market. We are pursuing an innovative approach to design novel opioid agonists acting outside the CNS and intestine, explicitly activating peripheral opioid receptors in injured/inflamed tissues. In collaboration with the ZUSE-Institute Berlin we developed the proprietary IN-SILICO-EVOLUTION (ISE) method for the analysis of conformational changes of molecular systems. Thereby we designed in silico the first suitable drug candidate Fluor (F)-fentanyl which was effective for the treatment of acute and chronic pain without the generation of harmful side effects in our preclinical in vivo and in vitro experiments.

1a-4 Highly effective anticancer agent

Dagmar Gieseler, Max Lehmann-Matthaei
PVA SH GmbH, Kiel, Germany

After decades of intensive research in the field of cytostatically active benzo [c] phenanthridines and his aza-analogs the new *pyrido [3,4-c][1,9] phenanthroline* and *11,12 dihydropyrido [3,4 c][1,9] phenanthroline derivatives* with *nano-molar in vitro antitumor activity* have been obtained.

Furthermore, the pyrido [3,4-c][1,9] phenanthroline derivative "P8 D 6OEthNCH32" has been identified as a promising drug candidate.

The new pyrido [3,4-c][1,9] phenanthrolines can be easily obtained using the straight-forward one pot synthesis followed by derivatization of the amino group via facile reaction steps.

The new pyrido [3,4-c][1,9] phenanthrolines and 11,12 dihydropyrido [3,4 c][1,9] phenanthrolines, the method of producing them and a pharmaceutical composition comprising the new compounds are protected via US 9,062,054 B2 (granted), EP 13717459, JP 2015-503894, CA 2,869,426, AU 2013244918 and DE 102012006903 (all pending).

Licensing/selling of this invention is sought to a company that will produce, bring to market and distribute the patented compounds. PVA SH GmbH will further assist by arranging contact with the inventors on request.

1a-5 CAAI – Covalent-allosteric AKT inhibitors

Daniel Rauh, Rajesh Gontla, Jörn Weisner
Technische Universität Dortmund, Germany

The development of new drugs in oncology has shifted from unspecific cytotoxic drugs to highly specific substances with known targets and modes of action. A prominent group of these target specific cancer drugs are the kinase inhibitors. The invented substances are inhibitors of the kinase AKT which is involved in several pathways regulating cell functions in cancer, e.g. survival and proliferation. The particular novelty of the invented compounds is based on their combined covalent-allosteric binding mode. These are first-in-class modulators of AKT with a novel mode of inhibition. Covalent-allosteric inhibitors show extended drug-target residence times. Binding specificity as well as an IC_{50} of 0.2 nM for the most promising compound have been determined by *in vitro* experiments. Currently, mice studies are conducted.

1a-6 Peripherally acting NMDAR Antagonists as new Antidiabetic Medication

Eckhard Lammert, Alena Welters, Diran Herebian, Jan Marquard, Ertan Mayatepek, Thomas Meissner, Silke Otter
Heinrich-Heine-Universität Düsseldorf, Germany

According to the International Diabetes Federation *(IDF)*, diabetes affects close to 400 million people worldwide and caused 500 billion Euros in health expenditure in 2013. Most of the costs are associated with the treatment of subsequent disorders that, to a large extent, are caused by chronic hyperglycaemia. Diabetes is progressive with worsening hyperglycaemia likely caused by progressive decline of pancreatic beta cells, which cannot be stopped by current medication. In preclinical and clinical trials, the NMDA receptor antagonist dextrorphan (DXO) and its prodrug dextromethorphan have been shown to harbor antidiabetic properties (Marquard et al., *Nat Med* 2015). In addition, DXO was shown to protect mouse and human pancreatic beta cells from cell death during a diabetogenic setting. DXO is well tolerated and sold as over-the-counter (OTC) medication for more than 50 years. However, adverse events are observed, which are likely caused by the action of DXO on the central nervous system (CNS). Here, the scientists developed DXO-derivatives that do not efficiently pass the blood brain barrier (BBB), and thus should cause fewer adverse effects on the CNS, but maintain their antidiabetic properties. Therefore, the derivatives might maintain the good safety profile and antidiabetic properties of its starting substance dextrorphan, but with fewer adverse effects. As suggested by recent phase 2a clinical trials using DXO, also the novel compounds may be combined with existing antidiabetic drugs exerting a synergistic effect (Marquard et al., *Diabetes Obes Metab 2015*).

1a-7 NHR2 inhibitors

Holger Gohlke[1], Manuel Grez[2], Alexander Metz[1], Julia Schanda[2], Christian Wichmann[2]
[1] Heinrich-Heine-Universität Düsseldorf, Germany
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The formation and onset of the prevalent form of acute myeloid leukemia (AML, FAB subtype M2) requires RUNX1/ETO, the product of the t(8;21) chromosomal translocation. Tetramerization through the nervy homology region 2 (NHR2) of ETO is essential for the RUNX1/ETO-mediated transformation. We have demonstrated that inhibition of NHR2 tetramerization by first-in-class small molecules is a viable entry point for the treatment of AML. Drug candidates have been identified by a small-molecule *in silico* screening and have been validated in cellular assays. Several compounds proved to be successful in inhibiting NHR2 tetramerization. Preferred compound **7.44** was able to slow tumor growth in a xenograft mouse model (SKNO 1 xenograft).

1a-8 Multiple Sclerosis (MS) therapy with humanized anti-CCR2 antibody through depletion of CCR2+ monocytes with proof of concept in primates

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MBM ScienceBridge GmbH, Göttingen, Germany

Worldwide it is estimated that there are 1 Mio. cases suffering from Multiple Sclerosis (MS). The world market has a two-digit annual growth rate. MS is thought to be an autoimmune disease affecting CNS and destroying the neuron protective myelin layer. MS involves repeated episodes of inflammation of nervous tissue. High dose steroids/glucocorticoid in acute MS do not how improvement of MS symptoms in 40% of patients. Highlights of our solution are:

We offer a proprietary technology:

- Fully humanized anti-CCR2 antibody (hum DOC-2).
- Target CCR2 receptor is linked to neurological inflammatory diseases.
- The hum DOC-2 reacts with both human and marmoset CCR2.
- Very good dosing and half-life of the hum DOC-2.
- The antibody depletes only CCR2 expressing monocytes specifically (through ADCC mechanism).
- Possible use also for rheumatoid arthritis and colitis.

Results achieved successfully with hum DOC-2:

- IN VIVO PROOF of concept in primates (marmoset).
- Excellent efficacy.
- Significant improvement of clinical score in mice and primates treated.
- Prolonged survival of primates.
- Strong and sustained depletion of monocytes expressing CCR2 receptor.
- Very good plasma levels of hum DOC-2.
- Future treatment of MS will be less focused on beta interferon opening the door to novel therapies.

Status and next steps

- IP rights (all granted): EP2004692B1 (validated in DE, FR, GB), US, AU, CA.
- Developed up to advanced pre-clinics at the Universities of Göttingen and Regensburg, humanization step in collaboration with the MRCT.
- We are looking for a licensing partner.

1a-9 How does the additional benefit extent of Orphan Drugs impact Price Negotiations in the German outpatient Sector?

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Objective: For orphan drugs an additional benefit is granted by market authorization of the European Medicines Agency.[1] Although an additional benefit is granted companies have to demonstrate the extent of this additional benefit as basis for subsequent reimbursement price negotiations by submitting a simplified dossier to the Federal Joint Committee (Gemeinsamer Bundesausschuss).[2] In case orphan drugs exceed an annually turnover of 50m Euro in the outpatient sector (based on ex pharmacy prices incl. value added taxes) orphan drugs have to undergo an entire additional benefit assessment. Based on the results of the assessment pharmaceutical manufacturer and the head association of the statutory health insurance (GKV-Spitzenverband) negotiate prices and related rebates. The objective of this analysis was to assess whether the additional benefit extent of orphan drugs does impact the rebate size of the price negotiations.
The hypothesis indicated an inversely proportional association between additional benefit extend and negotiated rebate size.

Methodology: In a first step the orphan drug market was analyzed and substances affected by an assessment of additional benefit extent were identified within the German healthcare market. Association between additional benefit extent and rebate size of negotiations was analyzed by Spearman correlation analysis. Data were collected from public available information of the Federal Joint Committee as well as price information from the German pharmacy pricing data base LAUER-TAXE®.[3]
In a second step of the analysis a survey was conducted and market access experts of orphan drug manufacturers were interviewed.

Results: By February 2016, 84 orphan drugs with active orphan drug designation were identified in the European Union. 19 were currently distributed in the outpatient German healthcare market and underwent additional benefit extent assessment as well as price negotiations. Rebate sizes ranged from 9% up to almost 44%. Association between additional benefit extent and rebate size could only be identified if the category "not quantifiable additional benefit" was excluded. By inclusion of this category the hypothesis was rejected.
The hypothesis was also rejected by empirical analysis as approximately 70% of the respondents in the experienced group did not agree that there is an inversely proportional association between the extent of additional benefit and the rebate size negotiated. In addition to that further factors impacting the price negotiations were identified.

Conclusion: There is only limited association between the extent of additional benefit and rebate size for orphan drugs. This is mainly caused by a large rebate range for orphan drugs for which the additional benefit extend was not quantifiable.
Further factors impacting the price negotiation were identified as: European comparison prices, treatment area, negotiation management and prevalence of indication. Price negotiations for orphan drugs are not solely related to assessed additional benefit extend.

1 European Community, Regulation (EC) No 726/2004
2 Gemeinsamer Bundesausschuss, Nutzenbewertung nach § 35a SGB V, 1.06.2015 https://www.gba.de/informationen/nutzenbewertung
3 LAUER-TAXE®, 01.06.2015

POSTER SESSION 1A: THERAPEUTICS

1a-10 BARs for highly specific treatment of B-cell malignancies

Nicole Comtesse
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Unique treatment strategy for B-cell malignancies with highest specificity by use of B-cell receptor antigens for reverse targeting (BARs)

Effective treatment of B-cell malignancies is still hampered by the lack of specificity of the available therapeutic options, which often result in severe side effects and fail to effectively eliminate all malignant B-cells in the patient. Antibodies (e.g. rituximab) and antibody-conjugates, targeting cell surface molecules expressed on malignant B-cells have emerged. However, said cytotoxic antibodies are not sufficiently specific as they, too, target and kill other (healthy) B-cells expressing the same surface molecules.

Scientists of The Medical Faculty of Saarland University have developed a unique reverse targeting approach based on the systematic search for tumor-specific B-cell receptor (BCR) antigens. The so called BARS (B-cell receptor antigens for reverse targeting), which are e.g. toxin conjugated, bind to the BCR on the surface of the B-cell lymphoma cells. After internalization of the toxic BCR/BAR complex, the B-cell lymphoma cell is killed. Binding of BARs to normal B-cell with other BCR-specificity is not possible. BARs can be used in a whole variety of therapeutic strategies for B-cell lymphoma including but not limited to toxin-conjugation, radionucleotid-conjugation, BAR-CARs, and Bi-BARs (CD3-BAR, CD16-BAR).

The principle of reverse targeting with BARs can generally be used for treatment of all B-cell malignancies for which the BCR-antigen is known. BARs have been identified so far for a variety of B-cell lymphoma entities, including such with unmet medical need.

POSTER SESSION 1C: DIAGNOSTICS

1c-1 AutoMax needs only single-stack regular FISH documentation images for automatic reading and scoring

Joachim Moecks[1], Alexander Dressel[1], Pham Dinh Tuan[2], Hans-Ulrich Schildhaus[3]

[1] bioMcon GmbH, Mannheim, Germany; [2] Mathematical Consultant, Toulouse, France; [3] Department of Pathology, Medical Faculty Göttingen, Göttingen, Germany

Introduction: Systems for computerized reading of FISH images usually require high quality multi-stack images for valid processing. For the clinical routine this may lead to an actual slower process than performed by the common manual processing. AutoMax is a novel proprietary system developed by bioMcon to provide solutions for automated FISH analysis taking the challenge to base the automatic analysis on a low quality standard. AutoMax bases the analysis on regular single-stack images as they arise e.g. by routine in the lab documentation. This enables integrating AutoMax into the standard workflow, while keeping the benefits of standardization and speed.

Material and Methods: The present analysis deals with images that were not produced on purpose for automatic analysis, but were the side product of the routine clinical assessment. AutoMax developed highly adaptive features in order to meet the wide variety of appearances of these images. Several color purifying steps enhance markedly the signal to noise ratio of the images and can cope also with low quality. AutoMax features a dual image analysis philosophy – aside of traditional image analysis approaches, AutoMax employs in addition novel methods from "topological" thinking.

Results: Validation of AutoMax for single-stack documentation images from clinical routine is at the time of this submission underway. The presentation will report results, strengths and issues with the AutoMax approach.

1c-2 ReadMax: A Novel Showcase Approach for FISH Biomarkers

Joachim Moecks
bioMcon GmbH, Mannheim, Germany

The recently published study[1] demonstrates that novel approaches can overcome hidden issues in widely accepted FISH scoring approaches. The study dealt with EGFR-scoring in NSCLC, where the established Colorado scoring was found to blur actual aberrance and failed as predictor in pivotal trials. ReadMax represents a 'maximizing strategy', where the reader strives for recording of most aberrant cells. The reading results underwent a systematic analysis to identify different types of aberrance and to evaluate their predictive power for treatment with erlotinib. It was a surprising finding that scorings of polysomy and/or co-amplification and not amplification were the winners in predictiveness. Other areas may share hidden issues HER2, MET in different cancer types tend to rely mainly on the 'ratio' as quantification – which is hazardous scientifically, as the role of polysomy and centromere co-amplification is disregarded, and is hazardous moneywise, as biomarker developments are based only on a narrow slice of the available aberrance information – not a wise bet.

The results of the ReadMax study are sketched and the methodological novelties are Illustrated. The extension of this methodology to other areas of FISH biomarkers is discussed and real data results are presented.

1 Moecks, Soulieres, Klughammer (2015): *"ReadMax – a novel reading and scoring approach for EGFR gene copy number to predict therapeutic benefit of erlotinib treatment in EGFR wild-type non-small-cell lung cancer", J Path: Clin Res* 2015, (wileyonlinelibrary.com).
DOI: 10.1002/cjp2.15 : http://onlinelibrary.wiley.com/doi/10.1002/cjp2.15/full

POSTER SESSION 1C: DIAGNOSTICS

1c-3 Molecular pathology biomarkers:"Big Bang" of personalized medicine? Pros, cons, gaps, and traps

Joachim Moecks
bioMcon GmbH, Mannheim, Germany

The big bang came so easy: To select patients with HER2 addicted tumors for trastuzumab therapy simply the Immuno-Histo-Chemical (IHC) tissue analysis needed to be conducted – this was in 1998. A subjective and semi-quantitative method to quantify the tissue images was established. Later in 2002 FISH-analysis of the Gene Copy Number was added as alternative biomarker – featuring the "ratio" to quantify gene amplification. Both over-simplistic approaches seemed to be sufficient.

The obvious success of this approach coined many development followers in the oncology area: trastuzumab and its biomarker approach became the ubiquitous blueprint for biomarker development using IHC and FISH.

The poster shows

- Pros and cons for IHC vs FISH for biomarker development
- Traps, how the big bang strategy failed for other genes
- Gaps, how the scoring strategy for HER2 FISH developed to fix prevailing gaps
- How molecular pathology biomarkers can be validly employed by sound bio-math approaches

Watch out, the big bang approach may lead to a black hole for development money.

1c-4 Small molecule MNK inhibitors as cancer therapeutics

Andy Merritt, Ed McIver
MRC Technology, London, UK

We are interested in MNK kinases as promising therapeutic targets for the development of new cancer drugs. MNK phosphorylates the eukaryotic translation initiation factor eIF4e, and is important for the expression of a number of key cancer-related proteins. Both MNK1 expression and eIF4e phosphorylation are upregulated in various human tumours. MNK1 expression is highly elevated in tumour cells compared with normal cells and MNK1/2 double knockout mice develop normally and are viable, again suggesting that therapeutic targeting of MNK may have minimal side effects. MNK proteins make an attractive drug target because they are at the convergence point between the Ras and mTOR pathways, so inhibiting MNK could simultaneously block two pathways crucial for tumour growth.

We have generated two novel series of small molecule MNK inhibitors that are active against both MNK1 and MNK2. The inhibitors have excellent potency and selectivity over other kinases in *in vitro* assays. The inhibitors also have desirable *in vivo* pharmacokinetic properties, with a long half life. Other groups have shown that MNK inhibition shows synergy with chemotherapy, and we are currently testing our MNK inhibitors in a combination therapy setting with docetaxel in mouse xenograft models. There is literature to suggest that MNK1 inhibitors will be effective in two tumour types with huge unmet medical need: glioblastoma and prostate cancer. There is also further potential to use MNK inhibitors to treat other cancer types, particularly where the tumour suppressor PTEN is mutated. We are interested in finding commerical partners to collaborate on or licence our MNK inhibitors to develop them further as cancer therapeutics.

1c-5 Small molecule PAICS inhibitors for metastatic breast cancers

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The gene PAICS (phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase) encodes a bifunctional enzyme that catalyses two consecutive steps of a metabolic pathway, the de novo purine biosynthesis pathway. Metabolic targets for cancer are appealing since rapidly dividing cancer cells have higher metabolic demands than normal cells. PAICS is a novel cancer target that is overexpressed in human breast cancer cell lines compared with non-tumourigenic breast epithelial cells, and knockdown of PAICS expression can inhibit tumour growth and metastasis in mouse models.

We have carried out a fragment screen to identify molecules that bind PAICS. Synthetic medicinal chemistry has yielded a novel series of small molecules that potently inhibit PAICS in *in vitro* assays, with an IC50 ~3nM and have good pharmacokinetic properties. We have also shown target engagement of PAICS by the small molecules by analysis of the metabolites from PAICS-treated cells. The compounds show inhibition of 2D proliferation of breast cancer cell lines, as well as anchorage independent 3D cell growth but do not cause cytotoxicity. The inhibitors also reduce the migration of breast cancer cells. The inhibitors are currently being tested in *in vivo* metastatic models and in a number of different cancer cell lines from the CLIMB panel.

Beyond breast cancer, there is further potential to use PAICS inhibitors in other cancer types where PAICS is overexpressed, for example, PAICS is also overexpressed in melanoma. We are interested in finding commerical partners interested in collaborating on or licencing our PAICS molecules for further preclinical and clinical development.

1c-6 Innovative method for detecting co-occurring histone modifications in a single step using hybrid proteins

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Background

The last two decades have seen an enormous increase of insight into the role of **epigenetics** in a vast array of diseases such as cancer, mental retardation and diabetes. In fact, the study of epigenetic mechanisms has become one of the most rapidly growing fields of biology, generating growing interest of the pharmaceutical industry. Amongst others, epigenetic alterations involve **post-transcriptional histone modifications (PTMs)**. Occurring in complex patterns, they form the so-called ´histone code`. In order to decipher said code and unravel its involvement in disease, the characterization of co-occurring histone modifications is considered to be an important cornerstone. Currently, co-occurring histone modifications are studied by the isolation of nucleosomes using consecutive chromatin immunoprecipitation (ChIP). This technique carries several serious drawbacks: it is time consuming, requires a lot of starting material and is difficult to perform. Furthermore, ChIP assays have poor sensitivity and, at present, DNA gained from the process cannot be investigated using next-generation sequencing.

Solution

Scientists at the University of Stuttgart developed an innovative method, in which two or more highly specific histone modification binding proteins are fused to form **bi-or multispecific hybrid proteins**. This construct allows the detection of co-occurring histone modifications in one single step. The DNA gathered from the process can be analyzed using next-generation sequencing. Thus, it enables the **investigation of co-occurring histone modification patterns on a genome-wide or locus-specific scale**. Contrary to conventional methods, the technique offers much improved sensitivity, is easy to perform and features consistent quality. A European Patent (EP) application was filed on 30 March 2015. The inventors currently set up a spin-off company on the basis of the technology.

1c-7 Direct, bisulfite-free detection of epigenetic cytosine modifications at user defined loci using TALEs

Daniel Summerer, Grzegorz Kubik, Moritz Schmidt
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Background

Scientific breakthroughs over the last 20 years have shown that epigenetic **5-cytosine modifications** play pivotal roles in the regulation of **gene expression, genome stability and a great variety of diseases**. Currently, they are detected using methods such as bisulfite conversion or anti-body-based techniques (e.g. (h) MeDIP). However, present methods do not offer programmable sequence selectivity, require harsh conditions (bisulfite conversion) or only produce qualitative information at low resolution ((h) MeDIP).

Solution

Scientists at the University of Constance, Germany, have now developed a **direct (no prior chemical modification of the DNA sample needed) and accurate method** allowing the detection of epigenetic modifications (5mC and 5hmC) in **any user defined sequence**. Using TALEs (transcription-activator-like effectors), which feature high flexibility, the recognition of the target sequences is achieved by means of two amino acid residues per module (repeat variable di-residue or RVD). Thus, the status and level of 5mC or 5hmC alterations can be analyzed. A European Patent (EP) application was filed in June 2013. The US nationalization and EP regionalization based upon a PCT application have been filed shortly.

For further information on these technologies please contact:
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1c-8 Modulation of the TLR4-signaling pathway

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Background:
Besides cardiovascular diseases and cancer, sepsis is the third leading cause of death. Critical ill patients suffer from inflammation associated with uncontrolled release of inflammatory cytokines, which leads to sepsis and high lethality. Macrophages, the first line of innate immune defense, can be activated by Lipopolysaccharides (LPS) of gram-negative bacteria, which interact with Toll-like receptor 4 (TLR4). Signaling pathways that emanate from activated TLR4, involving Transforming growth factor-ß-activated kinase 1 (TAK1) as a central branch-point, induce cytokine expression to stimulate inflammatory immune responses. The synthesis and activity of TLR4 downstream molecules modulates inflammatory cytokine expression, which is disturbed in severe inflammation and sepsis.

Solution:
To understand the molecular mechanisms that regulate TLR4 signaling molecule synthesis in LPS-activated macrophages post-transcriptionally, at the level of mRNA stability and mRNA translation, we analyzed mRNA interactions with regulatory RNA binding proteins. We identified TAK1 mRNA as regulatory target of hnRNP K and validated hnRNP K-mediated regulation of TAK1 synthesis. A specific TAK1 mRNA 3'UTR sequence and KH domain 3 of hnRNP K enable the regulatory interaction. HnRNP K-mediated translational regulation of TAK1 mRNA modulates LPS-induced cytokine expression (Liepelt et al., 2014 *RNA* 20:899-91). The modulation of the hnRNP K-TAK1 mRNA interaction (PCT/EP2013/001513), and thereby TAK1 synthesis to balance inflammatory cytokine expression, possesses therapeutic potential to prevent systemic inflammation and sepsis.

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POSTER SESSION 1C: DIAGNOSTICS

1c-9 Differential diagnosis of Parkinson's disease and dementia with Lewy bodies

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Parkinson's disease (PD) is a neurodegenerative disorder affecting about 1% of the population over 65 years. Atypical Parkinson syndrome arise generally from other neurodegenerative diseases like Dementia with Lewy bodies (DLB). Recent studies reporting a prevalence range of DLB up to 22.8% of all dementia cases. The accurate distinction between PD, DLB and other non-α-synuclein variants with Parkinson syndrome is challenging due to an overlap of clinical symptoms and neuropathological changes. There is currently no assay or imaging method available that provides security for clinical diagnosis of PD and atypic Parkinson syndromes. As a consequence, atypic Parkinson syndromes like DLB are often misdiagnosed as idiopathic Parkinson disease, which may lead to long-lasting mistherapy. Accordingly, there is an unmet need for methods of differential diagnosis of PD, DLB and other non-α-synuclein variants with Parkinson-like syndromes.

We offer a proprietary technology:

- Scientists at the University of Göttingen, Medical Department developed a new diagnostic approach to differentiate between DLB, PD and other neuropathies.
- The methodology involves: (a) extracting exosomes from CSF patient samples, (b) counting number of exosomes and (c) measuring the amount of exosomal a-Synuclein.
- Results include: This differential diagnostic approach resulted in a high sensitivity (>0.85) and specificity (>0.80) to differentiate between DLB and PD, which is more than twice compared to analyzing CSF α-Synuclein total amount.

Status and next steps

- International IP rights have been filed.
- We are looking for a licensing partner.

1c-10 Self-assembly nanoantennas for fluorescence signal amplification in molecular diagnostics

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The invented technology describes a purely physical signal enhancement mechanism that can directly act on any identified target. It is able to place molecules specifically and targeted in the fluorescent hotspot of a nanoantenna, leading to a fluorescence enhancement signal of more than 100fold [1]. These nanoantennas for fluorescence enhancement are produced by placing a pair of gold metallic nanoparticles forming a dimer. Upon illumination, the nanoantenna focuses the incident light at the gap between the nanoparticles, typically around 20 nm. The structures are fabricated by self-assembly techniques and thus, paralleled synthesis of billions of structures is feasible. Probe molecules can easily be placed in the hotspot, because the nanoantennas are built from biocompatible DNA by using the so-called DNA origami approach.

Potential applications include, for example, molecular diagnostics and single-molecule DNA sequencing. A polymerase could be place at the hotspot and the order at which fluorescently labeled bases are incorporated into the synthesized DNA can be monitored using fluorescence techniques. The strong enhancement at the reduced hotspot means that only labeled bases at the hotspot will be detected enabling measurements at high concentrations [2].

1 G. P. Acuna et al., Science 338, 506 (2012).

2 G. P. Acuna et al., Journal of Biomedical Optics 18, 065001 (2013).

2a-1 Novel cyclodextrins for hydrophobic drug delivery

Nicole Comtesse
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Solubilization of active pharmaceutical ingredients (APIs) by novel water soluble 6-thioalkyl-cyclodextrins

Low aqueous solubility is the major problem encountered with formulation development of active pharmaceutical ingredients (APIs). Cyclodextrins are generally employed to increase the bioavailability of those APIs scarcely soluble in water. The observed solubilization of an API is generally based on the complexation of the hydrophobic part of the API molecule within the CD cavity. However, known cyclodextrins are often limited with regard to their applicability, load capacity, synthesis or solubility in water.

Scientists of Saarland University and Julius Maximilian University of Würzburg have developed novel water soluble 6-thioalkyl-cyclodextrins, which form highly stable complexes with APIs. The new cyclodextrins show low ion strength in solution and no pH dependence. They can be obtained in well-defined stoichiometry, no statistic, randomly substituted products are generated, thereby simplifying quality control and analysis. Even highly volatile substances such as the anesthetics halothane or sevoflurane can be complexed. For example, one of the new 6-thioalkyl-cyclodextrins showed the highest binding affinities sevoflurane and halothane, much higher than native cyclodextrins or and known cyclodextrin derivatives.

2a-2 The application of model based design of experiments (MBDoE) and dynamic simulations to biotechnological production processes

Sonja Jost[1], Mathis Gruber[1], Nicolas Cruz B.[2]
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Theoretical modeling and computer based dynamic simulations are valuable tools to design and optimize industrial processes. So far, these techniques are mainly used in chemical production, helping to identify ideal operation parameters, optimize the process or achieve better scale-up results. Technically, these methods are also applicable to biotechnological processes. However, in reality this is rarely the case.

Biotech processes show a very high complexity such that only an approximate model description of the real process is possible. It is important that all phenomena of interest are covered but the model parameters must still be identifiable. Here, model based design of experiment (MBDoE) is a powerful technique to determine the optimum setup that generates the necessary data.

Due to the challenges mentioned above, so far no easy to use toolbox for the modeling of fermentation processes is available. DexLeChem bridges this gap between science and industrial application by offering dynamic simulation services which employ MBDoE for biotech applications. In cooperation with the chair of Bioprocess Engineering lead by Prof. Neubauer, we combine knowledge from the fields of reaction engineering, process engineering, biotechnology and theoretical modeling, thus transferring scientific results towards industrial application.

We will present the resulting strategy how we model the complex behavior of biotechnological processes such that new optimization goals can be reached:

- Increase process robustness
- Minimize time to reach cell mass & cell concentration
- Maximize biomass production
- Maximize protein activity
- Controlled scale-up

About our cooperation partner:
The Chair of Bioprocess Engineering at the TU Berlin aims to advance bioprocesses, and, amongst others, successfully develops models for the dynamic simulation. These methods are capable to optimize biotech processes and deliver higher yields, shorter fermentation times and less unwanted byproducts. It was possible to obtain improvements of 20% and more for industrial processes.[1]

1 Neubauer, P. and Cruz, N. and Glauche, F. and Junne, S. and Knepper, A. and Raven, M. (2013). Consistent development of bioprocesses from microliter cultures to the industrial scale. *Engineering in Life Sciences*, 224-238.

2b-1 Gold(I)-Alkin-Complexes for the treatment of cancer, rheumatoid arthritis or infectious diseases

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Gold(I) complexes have been widely used for the therapy of rheumatoid arthritis for several decades. Further ailments that might be treated with these coordination compounds include among others tumors or infectious diseases (e.g. from bacterial or protozoal microorganisms). The invented technology describes coordination compounds consisting of a gold(I) central atom, an alkyne, and a phosphane or N-heterocyclic carbene (NHC) as ligands. These novel drug candidates show an appropriate stability for biomedical applications, represent strong and selective inhibitors of the enzyme thioredoxin reductase (TrxR) and trigger significant antiproliferative and anti-angiogenic effects. The advantages of the invention are related to the design and development of targeted drugs for the treatment of severe medical conditions such as cancer, rheumatoid arthritis or infectious diseases.

2c-1 Neuroprosthetic device for tremor management without motoneuron stimulation

Carlos Güntner
MBM ScienceBridge GmbH, Göttingen, Germany

Pathological tremor is the most common movement disorder and its incidence and prevalence are increasing with the aging of the population, affecting 15% of people aged between 50 and 89 years. Common causes are neurodegenerative diseases, like Parkinson.

We offer a proprietary technology:

- Novel neuroprosthetic device for monitoring and suppression of pathological tremor in a patient via stimulation of peripheral afferent pathways (sensory nerves).
- The device consists of a neuroprosthesis to reduce tremor, integrating all the electronics including bioelectrical sensors and electrodes for soft neurostimulation.
- Prototype available and tested in patients (pilot studies).
- Easy to wear and use.
- Portable, self-contained system (sensors + analysis unit + stimulation unit).
- Individually adaptable to each patient.
- No surgery required.

Uses

- Diagnosis, monitoring and treatment of Parkinson patients.
- Diagnosis, monitoring and treatment of patients with Essential tremor, etc.
- Replacement or complementary to pharmacological treatments.

Status and next steps

- IP rights (in proceedings): US and EP patent applications.
- Clinical proof of concept with patients using a prototype successfully achieved.
- Innovation and prototype developed in collaboration between Universitätsmedizin Göttingen and CSIC (Spain).
- We are looking for a licensing partner.

2c-2 Thermo-induction and identification of ion channel activity by dyes for high throughput application

Andreas Speckbacher
EZN Erfinderzentrum Norddeutschland GmbH, Hannover, Germany

Ion channels are relevant targets in drug discovery. The activation of ion channels allows to mediate specific ion transport along the concentration gradients whereas changes in the trans membrane potential can be quantified by the Nernst equation. A nonradioactive flux assay allows to study ion channel function by highthroughput methods since a hugh panel of chemical compounds are available which requires assay systems to analyze drug or side effect activities. In this context temperature can on one hand activate or deactivate channel activities and is in addition a multiplicator of the transport rate. Therefore it was analyzed whether the temperature is a trigger to study the ion channel function or is able to increase the transport rate. To proof this concept channel proteins were synthesized in E. coli cells and purified. The function of purified hemichannel channel hCx26 was analyzed by optical flux and electrophysiological measurements. It could be shown that the dye lucifer yellow was released from dye charged liposomes by hCx26 activity in temperature dependent manner. This approach allows the analysis of the channel activity by measuring transport rates, substrates and inihibitors using microtiter plates or microarrays. The inhibitory effects comparable to concentration as found by other methods. It is suggested, that this application can be used in general for analysis for agent screenings directed against to the channel function.

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