BioRN

BioRN Annual Conference 2019

Artificial Intelligence meets Health
-from desk to bench to bedside-

ABSTRACT BOOK

11 November 2019, Heidelberg

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Welcome

Dear colleagues, members and friends,

On behalf of the BioRN Cluster, we would like to welcome you all in Heidelberg, to the BioRN Annual Conference 2019. The German Cancer Research Center kindly acts this year as the host for the event.

This year's Annual Conference titled "Artificial Intelligence meets Health - from desk to bench to bedside -" aims to provide an overview on current and future application of artificial intelligence and machine learning contributing to improve health, at different stages. Current and future breakthroughs in artificial intelligence and machine learning have taken root in biotech and have huge potential to change how healthcare is delivered.

We are delighted that Stefan Hell accepted our invitation to open the conference with a keynote lecture. In 2014, he was awarded the Nobel Prize in Chemistry for his pioneering work in high resolution light microscopy and is currently Director of the Max Planck Institute for Medical Research in Heidelberg & Max Planck Institute for Biophysical Chemistry in Göttingen.

A big 'Thank You' goes of course to all speakers, who accepted our invitation to share their exciting research and are at the heart of the meeting. We also would like to thank our host and sponsors for their dedication and financial support which allowed us to organize an excellent program.

And last but not least, we have to thank all our members, some have been with us since BioRN was founded more than 20 years ago, others only joined in the past year. Being part of our network means investing into the development of the region into a world-leading life science cluster. Together we drive a rich academic and translational ecosystem, attract top global talents and open up new markets. BioRN is currently leading a range of translational initiatives to support and expand our regional ecosystem and to lay foundations for future growth. This is only possible because BioRN can build on such a strong (and ever growing!) member base, very active boards and individuals who feel passionate about our life science region!

But now: let's get inspired by the exciting field of artificial intelligence and its latest applications from basic research to drug discovery! Enjoy the BioRN Annual Conference 2019 and its excellent networking opportunities – and do let us know what you would like to see at an Annual Conference in the near future – a conference from BioRN members for BioRN members!

Gitte Neubauer	**Michael Boutros**	**Julia Schaft**
Chair	Chair	Managing Director
BioRN	BioRN	BioRN

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Julia Schaft

Managing Director
BioRN Network e.V., Germany

After completing her PhD in molecular and developmental biology at the University of Giessen and the European Molecular Biology Laboratory in Heidelberg (Germany) in 2002, Julia continued her scientific research on the differentiation of human embryonic stem cells at Genea Ltd in Sydney Australia, an IVF clinic with a strong focus on research and innovation in the IVF and human stem cell field. Julia then took over leadership responsibilities in scientific project management and the supervision of all of Genea's embryo research licences. In 2014 Julia relocated back to Germany and took on an administrative role at the European Molecular Biology Laboratory in Heidelberg (Germany) building up the philanthropic fundraising program, the Friends of EMBL. She then joined BioRN as a project manager for international R&D and translational initiatives in the life sciences sector. Since October 2018 Julia is Managing Director of BioRN where she is also taking on BioRN strategic business development and partnering responsibilities.

Welcome and Wrap-up

Gitte Neubauer

Chair
BioRN Network e.V., Germany

Gitte Neubauer is a scientific founder of Cellzome. She graduated from Imperial College, London in Biochemistry and completed her PhD thesis with Matthias Mann at the European Molecular Biology Laboratory. After the acquisition of Cellzome by GSK in May 2012, Gitte Neubauer took over leadership of the company. She is Director of the Board of BioPro Baden-Württemberg, Director of the Board of the Centre for European Economic Research (Mannheim), a member of the industrial advisory board of the Biotechnology faculty of the University of Applied Sciences in Mannheim and member of the BioRN board since 2014 and chair of the BioRN executive board since 2018.

Michael Boutros

Vice Chair
BioRN Network e.V., Germany

Michael Boutros is the Head of the Division Signaling and Functional Genomics and Coordinator of the Functional and Structural Genomics Program at the German Cancer Research Center (DKFZ). He is also Professor for Cell and Molecular Biology at Heidelberg University. After his PhD at the European Molecular Biology Laboratory (EMBL), he joined Harvard Medical School in Boston as a postdoctoral fellow. In 2003, he started his independent group at the DKFZ in Heidelberg funded by an Emmy-Noether Grant of the German Research Foundation (DFG). He was also supported by the EMBO Young Investigator Program. He later became Head of Division and full Professor at Heidelberg University. Michael Boutros' research interests include functional genomic approaches to understand the regulation of cellular signaling in normal and cancer cells. His laboratory further develops and applies high-throughput screening and multi-omic data integration methodologies to dissect genetic networks and genotype-specific vulnerabilities in cancer. He is supported by the European Research Council (ERC) and is an elected member of the European Molecular Biology Organisation (EMBO). He is a member of the BioRN executive board since 2018.

Keynotes

Stefan W. Hell

Director
Max Planck Institute for Medical Research, Heidelberg & Max Planck Institute for Biophysical Chemistry, Göttingen, Germany

Stefan W. Hell is a physicist recognized for his pioneering research in far-field optical nanoscopy, also known as super-resolution microscopy. Hell was the first to demonstrate how one can decouple the resolution of a lens-based fluorescence microscope from diffraction and increase it down to a fraction of the wavelength of light, to the nanometer scale. Ever since the work of Ernst Abbe (1873) this feat had been believed impossible. After studies in Heidelberg (PhD in 1990) and postdoctoral work at the European Molecular Biology Laboratory, Hell laid out the principle of STED microscopy while on a research fellowship in Turku, Finland (1994). STED (standing for Stimulated Emission Depletion of the molecular fluorescent state) became the first viable proposal for a diffraction-unlimited fluorescence microscopy. The underlying idea, namely of discerning molecules (at subdiffraction length scales) by transiently preparing a subset of them in a non-signaling state, underlies all the practical diffraction-unlimited super-resolution fluorescence microscopy concepts to date. For these achievements and their significance for other fields, Hell has received numerous awards. In 2014 he shared the Kavli Prize in Nanoscience and the Nobel Prize in Chemistry. A recent breakthrough achievement, molecule-size resolution on the order of 1 nanometer with a concept termed MINFLUX, has enabled the ultimate level of resolution to be reached. 3D fluorescence “nanoscopy” with ~1-nm resolution is expected to have profound impact in the life and materials sciences, affording novel measurement opportunities for structure and dynamics at yet unchartered length and time scales.

The resolution revolution and the consequences for Heidelberg

Based on fundamental conceptual insights, the recently invented MINFLUX fluorescence nanoscopy has enabled the ultimate level of resolution for optical microscopy to be reached: resolution of the very size of a molecule (~1 nanometer). This breakthrough goes much beyond the typically 20-30 nanometer resolution demonstrated by 2014, at the time the Nobel Prize was given. MINFLUX is poised to open a new chapter in the imaging of protein complexes and distributions in fixed and living cells.

Heidelberg is the ideal place to realize the full potential of this transformative imaging concept for the life sciences. Heidelberg and the wider region, with its many outstanding researchers will be great partners in this endeavor. The Max Planck Society has recently announced a major investment in a new additional building for the MPI for Medical Research. This will be found in prominent location at the very entrance to the Neuenheimer Feld Campus, right at the Neckar river. Strong synergies are expected with neighboring partners such as the ZMBH of Heidelberg University, to enable work at the forefront of nanoscale biology.

Lindsay Edwards

VP AI Research
GlaxoSmithKline

Lindsay Edwards is VP Artificial Intelligence and Machine Learning (AI/ML) for GSK Pharma R&D, having previously led the Digital, Data & Analytics Unit for Respiratory. Originally a specialist in systems biology, he joined GSK in 2014 from a Lectureship in Physiology at King's College London. His background spans human physiology and biochemistry, metabolomics, computational biology and data science; he has extensive experience of applying novel analytical methods (including machine learning) to biological datasets. He has previously held academic appointments in both Australia and the UK. His interests currently centre on the use of contemporary analytical tools (including AI) to bring transformational change to drug discovery. He is a GSK Senior Fellow, holds a DPhil in Physiology from Oxford, has published more than 40 articles in peer-reviewed journals, and speaks regularly at international conferences.
Alongside his job at GSK, he is a Fellow of the Royal Society of Biology, a member of the scientific strategy board of the Xtreme Everest Project and has been an Academic Editor for Nature Scientific Reports. He is a former Google SciFoo attendee (2015).

Artificial intelligence: What exactly is it, and how can it support drug discovery?

The rise of Artificial Intelligence (AI) - principally deep learning - and its influence in our everyday lives is plain. Yet despite significant progress in computer vision and natural language processing, the promised impact of AI in drug discovery (and biomedicine generally) has been slow to emerge. I will start by outlining what exactly I mean by AI (and machine learning) and briefly introduce deep learning and its canonical applications. The focus of my talk will then be on how AI is being used to tackle fundamental problems in drug discovery, as well as the application of visualisation to problems in AI research.

Speakers and Abstracts

Oliver Stegle

Division Head
DKFZ and EMBL Heidelberg

Oliver Stegle is the Head of the Computational Genomics and Systems Genetics Division at the German Cancer Research Center (DKFZ) and group leader at EMBL in Heidelberg, Germany.
His group's main interest lies in computational methods to unravel the genotype–phenotype map on a genome-wide scale. To address this question, the team carries out research at the interface of statistical inference, machine learning and computational biology. A current direction in the lab is to extend the boundaries of single-cell analysis to integrate single-cell RNA-seq with somatic mutations and clonal substructure in tissues. This project will provide pertinent datasets and biological questions to further develop and apply these techniques in the context of a major biologist system.
Oliver obtained his PhD from the University of Cambridge in Physics in 2009 and worked as a postdoc at the Max Planck Institute for Intelligent Systems in Tübingen. He was a group leader at the EMBL European Bioinformatics before joining DKFZ as Division Head in July 2018.

Computational single-cell genomics - advances and translational opportunities

Rebecca Wade

Group leader / Professor
Heidelberg Institute for Theoretical Studies (HITS) and Heidelberg University

Rebecca Wade leads the Molecular and Cellular Modeling group at Heidelberg Institute for Theoretical Studies (HITS) and is Professor of Computational Structural Biology at the Center for Molecular Biology at Heidelberg University (ZMBH). Rebecca Wade studied at Oxford University and, following postdoctoral research at the universities of Houston and Illinois, became a group leader at the European Molecular Biology Laboratory (EMBL) in Heidelberg in 1992. She moved to HITS in 2001. Rebecca Wade's research is focused on the development and application of computer-aided methods to model and simulate biomolecular interactions. Her research group has developed protein structure-based methods for drug discovery and protein engineering, as well as computational approaches to investigate macromolecular association and the effects of macromolecular crowding. Rebecca Wade's research has resulted in over 250 scientific publications, as well as software programs and web servers that are used world-wide. She is an Associate Editor of the Journal of Molecular Recognition and PloS Computational Biology. She was the recipient of the 2004 Hansch Award of the QSAR and Modelling Society and the 2016 International Society of Quantum Biology and Pharmacology (ISQBP) Award in Computational Biology (www.h-its.org/mcm).

Machine Learning in Computer-aided Drug Design

Recent advances in machine learning methods have led to a huge burst in their application to computer-aided drug design (CADD). Despite the opportunities, there are many challenges and potential pitfalls to the application of machine learning in CADD. I will discuss how we are applying machine learning approaches, in combination with molecular modelling and simulation techniques, to structure-based drug design to assess protein druggability and to compute drug-target binding affinities and residence times (1,2).

[1] Kokh DB, Kaufmann T, Kister B, Wade RC. Machine Learning Analysis of τRAMD Trajectories to Decipher Molecular Determinants of Drug-Target Residence Times, Frontiers. Mol. Biosci. 2019, 6: 36.

[2] Ganotra GK, Wade RC. Prediction of Drug–Target Binding Kinetics by Comparative Binding Energy Analysis. ACS Medicinal Chemistry Letters 2018, 9: 1134–1139.

Adrian Carter

Vice President and Global Head of Discovery Research Coordination
Boeringer Ingelheim

Adrian Carter is vice president and global head of Discovery Research Coordination at Boehringer Ingelheim where he is responsible for guiding research policy, leading strategic and operational initiatives, and overseeing competitive intelligence activities. He graduated from the University of Wales in Cardiff with an honours degree in applied biology, has a Ph.D. in pharmacology from the Department of Medicine at the University of Nottingham, and an executive MBA from the University of Mainz. His career at Boehringer Ingelheim spans over 33 years including 8 years as head of neuropharmacology. Adrian subsequently spent 10 years in business development where he led the negotiations for several large licensing collaborations, co-commercialization deals, and patent agreements. Adrian represents Boehringer Ingelheim on the board of trustees for the Structural Genomics Consortium (SGC), the board of trustees of the Scientific and Medical Institute (NMI) in Reutlingen, as well as being vice chairperson of the Research and Innovation Strategy (RIS) Working Group of EFPIA and a member of the strategic advisory board of the Biotech Cluster Rhein-Neckar (BioRN).

opnMe.com, a digital platform for sharing open tools

Openly sharing pharmacological tools such as chemical probes is transforming the biomedical research landscape. The collective term “Open Tools” describes a broad variety of different unencumbered assets that are openly shared. We have created an easy-to-use digital portal, called opnMe.com, for sharing chemical probes with the scientific community. We also provide access to opnMINER, a powerful semantic search tool that allows the simultaneous search of multiple data sets and sources. Since its launch, opnMe.com has provided hundreds of external scientists with unrestricted access to validated chemical probes and their accompanying datasets via the molecules-to-order programme. We believe that the success of opnMe.com depends on the enthusiastic commitment of the R&D organization, a broad external communication and social media campaign, and a reliable, user-friendly web platform.

Lars Greiffenberg

Director R&D IT und Translational Informatics
AbbVie

Lars Greiffenberg holds a M.S. in Biology and a Ph.D. in Microbiology and has more than 15 years of experience in the field of integrated R&D IT solutions and translational informatics. He held different R&D IT management positions at Aventis Pharma and Sanofi-Aventis in Frankfurt before relocating to the Sanofi site in Toulouse, France where he was Global Head of Solution Center Translational Medicine with responsibility to manage and lead a global program to enable translational science at Sanofi. In 2014 he joined AbbVie in Ludwigshafen (Germany) as director of R&D IT and Translational Informatics. In this role he is heading business IT support covering data and solutions from early discovery up to Medical Affairs. In 2017 he extended his responsibilities including now global Library Sciences at AbbVie. He is driven by the ambition to transform the way we access, consume and leverage literature in the future. He recently established a team at AbbVie, dedicated to use modern methods and algorithms to extract and visualize mechanistic disease information from literature content. In 2018 he further enlarged his area of responsibility to incorporate the Academic Partnerships Organization which is leveraging an AbbVie Campus at the University of Illinois Urbana-Champaign. Lars is active in several pre-competitive organizations including IMI, PRISME Forum, Pistoia Alliance and EIT Health.

Value and Challenges of Data-Explosion in Pharma R&D

Digitalization is generating a gigantic data tsunami. Although the hype of big data has been transformed into expectations for the application of artificial intelligence – generating clear value out of these promises remains a challenge. This talk outlines several aspects of modern knowledge extraction and shows examples where these methods generating value for AbbVie R&D already today.

Maria de Kleijn

SVP Analytical Services
Elsevier B.V.

Maria is Senior Vice President Analytical Services for Elsevier. In this role she is responsible for bespoke analytical services to universities, funding bodies and governments worldwide, advising them on research performance, international collaboration, gender in research and research impact. Prior to joining Elsevier, Maria has worked for McKinsey and Company, for the Dutch government, and in the power and gas sector, in various analytical roles to combining big data to inform decisions. Maria holds a master's degree with distinction in Applied Physics from Delft University of Technology, and an MBA with distinction from Oxford University.

Artificial Intelligence - Benchmarking research in the Rhein-Neckar Region and implications for Life Science Players

Historically, Artificial Intelligence has been thought of as a research area within Computer Science. While significant conceptual and methodological breakthroughs have been made in the 20th century already, real-life application only really took off in the past 10 years or so. The main reason for that is that the current generation of AI is essentially machine learning, which requires vast quantities of data and computing power – which has only become available at the needed scale since the early 00s.

Where does this data come from? From the application domains, like medicine and life sciences. So this is also where the research has moved – which makes it hard to actually figure out how much research is done, where, and with what impact. To make it worse, experts agree there is no common definition of AI at all, and the AI label is sometimes applied very liberally. But, like today, many organisations – governments, corporations, research institutions – want to know what's going on and how they compare.

At Elsevier, through our Scopus database, we have a wealth of data and knowledge about which research is done where, how it builds on research done by others, and with what impact. And we have a large number of data scientists working on AI and machine learning in our own solutions. So we decided to assist the research community by benchmarking AI research, knowing we have the technology, the data and the people to do this.

And today I will show you the results for the Rhein-Neckar region, how the region compares with others, who the key AI players are with a focus on medicine and life sciences, and who they collaborate with.

Friedrich Rippmann

Director, Computational Chemsitry & Biology
Merck Healthcare KGaA

Friedrich Rippmann is Director of Computational Chemistry & Biology at Merck in Darmstadt, Germany. Previously he was head of Bio- and Chemoinformatics at Merck, with responsibility for groups in Germany, France and Switzerland. He was also responsible for the set-up of bioinformatics and protein crystallography at Merck in Darmstadt.
In his academic career he worked at the National Institute for Medical Research, MRC London, and at the German Cancer Research Center in Heidelberg, Germany. He is also a lecturer of Bioinformatics, at the University of Mannheim. Several major software developments originated in his group, among them RELIBASE, a comprehensive database of protein-ligand complexes; and more recently DoGSite Scorer, a druggability prediction server; TRAPP, a webtool for analysis of transient binding pockets in proteins; and a panel of methods for selective kinase inhibitor generation.
Currently he is working on digitizing many aspects of early discovery research, including the integration into coherent workflows. Machine Learning, especially Deep Learning, and Artificial Intelligence are key aspects of this. Another key interest is the “invention” of novel molecules, matching a predefined target profile, by AI techniques.

AI in Drug Discovery at Merck: benefits and perspectives

Artificial Intelligence has found numerous applications in drug discovery. Predictive models, i.e. models which have been trained on compound structures and their respective activities, are now used routinely to assess, before synthesis, whether a compound idea will have the desired properties, e.g. being active on ABC kinase, not active on XYZ kinase, be soluble, free of cardiac toxicity (hERG binding), and many more. Some of these models are so highly predictive, that the respective assays have been discontinued at Merck for newly synthesized compounds, where routinely a number of properties were experimentally measured. Deep Learning has shown game-changing performance in tasks like image or speech recognition, and they have proven useful to predict drug properties as well. Currently we have about 300 such models available for all researchers in Discovery Research at Merck, and great care has been applied to make their use easy and attractive, e.g. by allowing to immediately store and register a compound idea in the corporate database. Current activities centre on making Deep Neural Network predictions interpretable. Here we have published a versatile approach which maps the positive or negative contributions of parts of a molecule visually to its structure. This immediately gives the chemist ideas where to change a molecule to get rid of an unwanted property. Currently, training data for predictive models are limited to public and single-company inhouse information. To overcome this limitation, we have initiated a large EU-IMI project: the objective of MELLODDY is to go beyond each individual company’s limited chemical space, regarding predictive models, by accessing the information in each other’s chemical space, WITHOUT EVER SEEING each other’s compounds or assays.
The next level, which we currently actively exploit in collaboration, is to let the computer suggest totally novel compound, which are then screened against a predefined desired target profile. This is conceptually similar to recently published applications where images are e.g. morphed into the style of a famous artist.

Brandon Malone

Senior Researcher
NEC Laboratories Europe GmbH

Brandon Malone is a Senior Researcher at NEC Laboratories Europe GmbH. He received his Ph.D. at Mississippi State University and held postdoc positions at the University of Helsinki, the Max Plank Institute for the Biology of Ageing, and Heidelberg University Hospital before joining NEC. His research interests include application and design of novel graph-based machine learning approaches for the biomedical domain, including probabilistic graphical models, graph neural networks, and knowledge graphs.

Robust Tumor Heterogeneity Characterization from Single-cell Sequencing with Graph-based Artificial Intelligence

Cells in a tumor sample from a patient frequently display heterogeneous phenotypes. This heterogeneity can make seemingly-identical cell types respond differently (or not at all) to therapeutic drugs. Single-cell RNA sequencing (scRNA-seq) methods are emerging as an important new approach to dissect the cellular gene expression heterogeneity within tumor samples. One application of scRNA-seq in precision medicine is identifying responding and non-responding cell subtypes for a particular patient and therapeutic drug. The gene expression analysis by scRNA-seq holds promise for progress on this problem since it reveals the transcriptome and drug response of the cellular subpopulations within a tumor. However, the scRNA-seq data for individual cells are often noisy due to technical artifacts, and it is challenging to identify the functionally-relevant features from a differential gene expression analysis.
One approach to address this problem is to integrate the wealth of additional knowledge on the cellular transcriptome that resides in academic publications, manually-curated databases, and other sources. For example, genes have been annotated with respect to their biological functions and pathways. Furthermore, gene regulatory networks (GRNs) can be constructed to characterize the relationships among regulatory genes and targets. In a joint collaboration between NEC and DKFZ, we have developed an approach for uniting such rich domain knowledge with scRNA-seq data to identify common cellular subpopulations across samples. The method utilizes state-of-the-art graph neural networks to identify meaningful gene modules from the GRNs and domain knowledge. These gene modules are then used to characterize cell subpopulations. As an exemplary scRNA-seq data set, leukemia cells treated with a drug were analyzed to illustrate how sequencing artifacts, such as information on missing genes, can be compensated and changes in gene expression profiles can be assigned to gene modules.

Selected research short-talks

Robust small molecule-protein interaction inference reveals unknown drug off-targets

Nils Kurzawa[1,2], Isabelle Becher[1], Srishti Dar[3], Holger Franken[4], Carola Doce[4], Simon Anders[5], Markus Bantscheff[4], Wolfgang Huber[1], Mikhail M. Savitski[1]

[1]European Molecular Biology Laboratory, Genome Biology Unit
[2]Candidate for joint PhD between EMBL and Heidelberg University, Faculty of Biosciences
[3]European Molecular Biology Laboratory, Developmental Biology Unit
[4]Cellzome GmbH, GlaxoSmithKline
[5]Center for Molecular Biology of Heidelberg University (ZMBH)

Detection of proteins interacting with ligands such as drugs is a major challenge in biomedical research and drug discovery. Thermal proteome profiling (TPP) is a mass spectrometry-based assay that addresses this task by monitoring ligand-induced proteome-wide thermal stability shifts. Robust statistical methods have been developed and made available as open-source software for the analysis of TPP temperature range experiments. However, a more sensitive version of the assay (2D-TPP), measuring thermal stability in response to different ligand concentrations over a temperature range, is lacking rigorous, false discovery rate (FDR)-controlled analysis approaches. Here we present a method which applies concepts from functional statistics to robustly detect protein-ligand interactions from 2D-TPP datasets while controlling the FDR. Through reanalysis of several published datasets assaying drugs in human and bacterial cells and lysates, we find that our method detects known targets and reveals new drug-protein interactions that were previously not detected. We believe that this development is crucial to enable sensitive exploration of small molecule targets and thus has the potential to decrease clinical trial failure and enhance possibilities of drug repurposing.

- Savitski, M. M. et al. Tracking cancer drugs in living cells by thermal profiling of the proteome. Science 346, 1255784 (2014).
- Becher, I. et al. Thermal profiling reveals phenylalanine hydroxylase as an off-target of panobinostat. Nat Chem Biol 12, 908–910 (2016).
- Perrin, J. et al. Proteome thermal stability reflects organ physiology and identifies drug-target engagement in vivo. bioRxiv (2018)

DIY Research to Routine: Translation of Deep Learning into Radiological Practice using only Open Source Software

Jens Petersen[1], Fabian Isensee[1], Gianluca Brugnara[2], Martin Bendszus[2], Klaus H. Maier-Hein[1], Philipp Kickingereder[2]

[1]Division of Medical Image Computing, German Cancer Research Center
[2]Department of Neuroradiology, Heidelberg University Hospital

In recent years, deep learning or specifically convolutional neural networks have undoubtedly revolutionized computer vision and related disciplines, outperforming previous state-of-the-art methods by large margins both within and beyond medical image analysis. While virtually every phone can now make use of many of those models in real time, for example to detect faces in a photo, they have yet to have a similar impact in clinical use. There are a variety of reasons for this, but one presents a particular dilemma: We don't want to deploy a model to the real world before testing it, but to test it we need to deploy it to the real world.
We present a novel infrastructural solution that facilitates the translation of state-of-the-art medical image computing research to clinical routine, and in doing so, adheres to the following principles:
1) The system operates parallel to clinical routine and does not interfere with established processes and workflows.
2) Intellectual property is protected as image data remains within the clinic, while methods and models are exchanged in the form of Docker images with compiled routines.
3) Deployment of new models requires minimal effort from researchers and absolutely no technical expertise from clinicians.
On top of this, our system is based entirely on existing open-source software and is agnostic of the existing infrastructure. As such, it can be integrated by anyone at negligible cost.
The system we describe is currently used in the Neuroradiology Department at Heidelberg University Heidelberg to apply state-of-the-art glioma segmentation [2] for the purpose of longitudinally monitoring patients' tumor burden. We demonstrated in a retrospective study that automatic volumetric assessments are superior to manual assessments [1]. The current prospective testing with now over 1000 processed cases is a critical step towards automated and improved monitoring of patients suffering from glioma.

[1] "Automated quantitative tumour response assessment of MRI in neuro-oncology with artificial neural networks: a multicentre, retrospective study" Kickingereder et al., The Lancet Oncology 20(5), 2019
[2] "nnU-Net: Breaking the Spell on Successful Medical Image Segmentation" Isensee et al., arXiv, 2019, https://arxiv.org/abs/1904.08128

PRECOG: an ML-based web-server to predict, visually inspect and design GPCR couplings

Gurdeep Singh[1,2], Asuka Inoue[3], J Silvio Gutkind[4], Robert B Russell[1,2], Francesco Raimondi[1,2]

[1]CellNetworks, BioQuant, Heidelberg University
[2]Biochemie Zentrum Heidelberg (BZH), Heidelberg University
[3]Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, Miyagi 980-8578, Japan
[4]Department of Pharmacology and Moores Cancer Center, University of California, San Diego, La Jolla, CA 92093, USA

G-protein coupled receptors control multiple physiological and disease states by transducing virtually any extra-cellular stimuli into the cell by coupling to intra-cellular hetero-trimeric G-proteins. Here, we present PRECOG1 (http://precog.russelllab.org/), a web-server for a new machine learning-based predictor of GPCR couplings that allows users to: 1) predict with higher confidence the coupling probabilities of a given input sequence for individual G-proteins instead of families; 2) visually inspect the protein sequence and structural features that are responsible for a particular coupling; 3) suggest mutations to rationally design artificial GPCRs with new coupling properties (i.e. DREADD).
As a part of the most systematic quantification of GPCR coupling selectivity to date2, PRECOG was built by exploiting experimental binding affinities of 144 Class A human GPCRs for 11 chimeric G-proteins using a set of sequence- and structure-based features. The web-server has two options: “Make Predictions” or “Design a GPCR”. While the former allows to predict the coupling preferences for input, both Wild Type (WT) or mutated, the latter exploits instead feature information to automatically suggest the mutations more likely to switch a particular coupling. In either case, with the help of the sequence and structure viewers, the user can visualize features that are more significantly associated to a given G-protein. Information about interaction contacts, either involving ligand or G-protein binding interfaces, or the network of intra-molecular contacts can also be optionally visualized.
PRECOG outperforms previous methods not just in terms of results, but also, by way of the web interface, in the ability to interrogate predictions for putative mechanistic explanations that can be used potentially to alter coupling or design receptors de novo for particular signaling effects. Besides predicting the coupling preferences of all human GPCRs, PRECOG has been successfully exploited to design the first GNA12 specific DREADD2.

- “Automated quantitative tumour response assessment of MRI in neuro-oncology with artificial neural networks: a multicentre, retrospective study” Kickingereder et al., The Lancet Oncology 20(5), 2019
- “nnU-Net: Breaking the Spell on Successful Medical Image Segmentation” Isensee et al., arXiv, 2019, https://arxiv.org/abs/1904.08128

Rematch-AI – Cloud AI for drug discovery and drug repurposing

Florian Heigwer, Christian Scheeder and Michael Boutros

German Cancer Research Center (DKFZ), Division Signalling and Functional Genomics and Heidelberg University

High overall costs in the development of new drugs in part stems from failure of drugs late in the development process due to side effects or lack of efficacy. A potential strategy to avoid late failures is to deeply characterize small molecules early in development using assays that generate information rich phenotypic profiles, such as by image-based high-content assays. Such assays provide a wealth of information that can interpreted with machine learning to predict the drug's MoA, toxicity, off-target and other adverse effects. With more performant hardware for image acquisition, high-content screening campaigns that profile very large libraries are now feasible. However, a major hurdle remains the processing, analysis and interpretation of imaging data that can easily exceed tens of terabytes of raw data. As part of an ERC-proof of concept project, we developed REmatch-AI to provide a fast and resource efficient software pipeline and knowledge-base to accelerate drug discovery. Our solution relies on cloud-computing solutions and enables tailored analysis pipelines. In the past months, we characterized more than 100.000 drug effects in diverse cell contexts, demonstrated the analysis capabilities and built a knowledge-base of small molecule profiles to facilitate the identification of drug repurposing potentials. We are currently evaluating a commercialization strategy for REmatch-AI to provide solutions for image-based drug profiling and machine learning for phenotypic drug discovery.

- Scheeder C., Heigwer F. and Boutros M., Current Opinion in Systems Biology, 2018 (doi 10.1016/j.coisb.2018.05.004.)
- Heigwer F. et al., eLIFE, 2018 (doi: 10.7554/eLife.40174.)

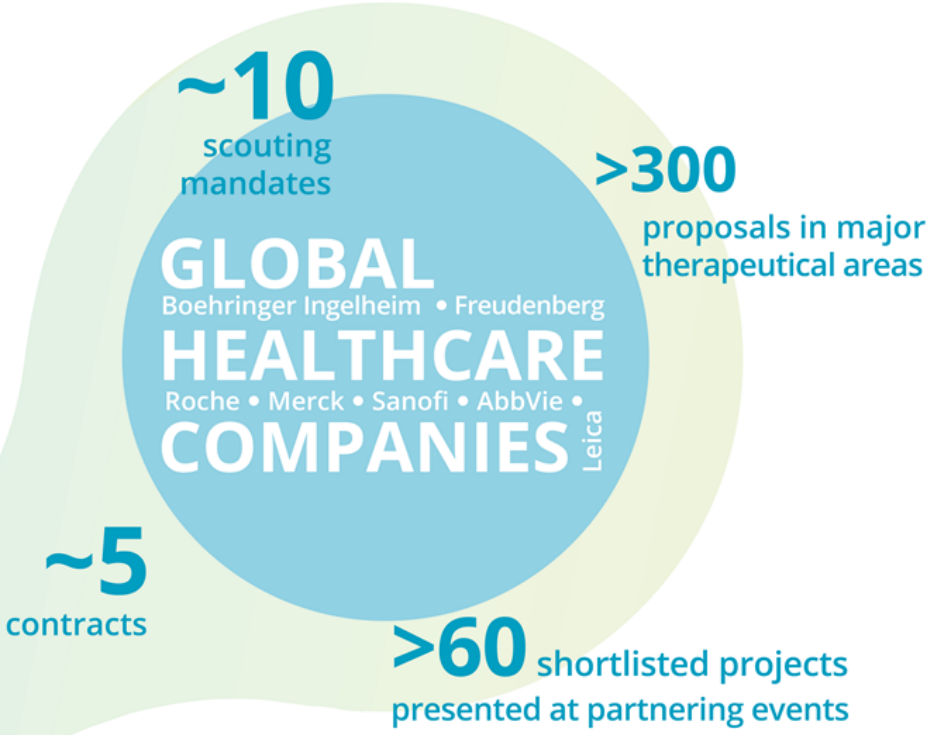
Boutros M., Heigwer F., Laufer C., Cell 2015 (doi: 10.1016/j.cell.2015.11.007)

HAEP

HEALTH AXIS EUROPE
PARTNERING

Tap a vast pool of innovators to feed your pipeline!

The HAEP partnering programme by the BioRN life science cluster joins major regional and European networks to effectively match health care innovation seekers with innovators.



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HAEP Session

Friedemann Loos

Innovation Manager
BioRN

Focusing on genome engineering and transgenesis, Friedemann earned his PhD in 2015 from the Erasmus Medical Center in Rotterdam. He followed up by conducting postdoctoral research in the lab of Guido Kroemer at Institut Gustave Roussy and the Centre de Recherche des Cordeliers in Paris. Working at the interface of immuno-oncology and autophagy, he introduced new genome editing tools and acted as manager of the LabEx Immuno-Oncology, a high-profile French research consortium of leading immuno-oncology labs (including amongst others Guido Kroemer, Laurence Zitvogel, Jessica Zucman-Rossi and Catherine Sautès-Fridman). Friedemann also worked for the Research Executive Agency of the European Commission, where he was involved in the evaluation of project proposals under the framework of FET-Open, a program to support potentially disruptive technologies. In January 2019 Friedemann joined BioRN to support translation of research from our Network.

HAEP – A novel format to foster Partnership

HAEP is an innovation scouting service and stands for Health Axis Europe Partnering. BioRN as the Rhine-Neckar Life Science Cluster has over 3000 innovators in reach and can directly access them without formal requirements. By tailoring our scouting to the searching company's search profile, we help both innovation seekers and innovators not only with identifying the best matches, we also help to save time by preventing lengthy follow-ups of out of strategy projects. Our strong and manifold ties to all regional and national stakeholders and via Health Axis Europe to additional life science clusters in Leuven, Maastricht and Copenhagen moreover allows us to detect very early-stage projects first and to score hits which usually would stay off-radar. BioRN's proven track record of scouting technologies and organizing partnering events for global health care companies stands for itself and enables companies to feed their pipelines as well as establish and nurture networks in Heidelberg, Germany and the Health Axis Europe. At the same time it helps innovators to establish contacts to the industry which without HAEP might be difficult to establish.

Patrick Most

Head of unit, Division of Molecular and Translational Cardiology University Hospital Heidelberg, AaviGen GmbH and Jefferson University

Prof. Most is a Co-founder and CEO of InoCard GmbH, a cardiovascular gene therapy company, which was acquired by uniQure NV in August 2014, and served as Managing Director of uniQure Germany GmbH and uniQure NL leadership team member until 2017. In 2018, he devised and co-founded the Biotech Startup AaviGen GmbH, a personalized gene therapy company, for which he serves as CEO. Prof. Most has nearly 20 years of experience in molecular cardiovascular research, a field in which he has become a key opinion leader, authoring numerous scientific articles in peer-reviewed journals, holding several patents and having received a large number of awards and stipends for his outstanding work, including, most recently, the Health Axis Europe Accelerator - Investors Choice Award and the Albert Fraenkel Award of the DGK. He is currently a Full Professor for Molecular and Translational Medicine at the Department of Internal Medicine III of the University of Heidelberg. In addition, Prof. Most holds an Adjunct Associate Professorship for Translational Medicine at Thomas Jefferson University, Philadelphia.

Closing the gap between "episteme" and "techne": challenges for successful biotechnology transfer

The paper will discuss the challenges and address potential solutions for successful biotechnology transfer from the academic to the post-academic and bioindustrial/biopharmaceutical space. To this end, the presentation will highlight personal experiences of the author as a serial entrepreneur and founder of biomed start-ups, their development towards successful investments and exit strategies, as well as his view on managing activities in biotech with an educational background as physician-scientist. The presentation will further reflect on the specific challenges for an academic breeding ground to translate medical research findings into innovative therapeutic and diagnostic prototypes for clinical development.

Sergey Biniaminov

CEO / Data Scientist
HS Analysis GmbH

Sergey Biniaminov graduated with a diploma in Economics and Political Science at Karlsruhe Institute of Technology and now he is managing shareholder at HS Analysis GmbH, based in Karlsruhe. HS Analysis means "High Scale Analysis" and stands for the management of Big Data in medicine, which focuses on the efficiency of drug development, predictions in companion diagnostics (CDx) and analysis of the growth of cultured cells in fluorescence or label free images. HS Analysis employs data scientists, biomedicine researchers and designers with the goal to secure trust in artificial intelligence in life science and medicine.
First HS Analysis develops software that investigates the efficacy of antibody therapies in the treatment of e.g. ovarian cancer and tumor shrinkage after e.g. bevacizumab combination therapy. As an example of personalized medicine, the quantification of stainings from the antigen of the thorium conjugate is considered to be target expression or target content in human lung tumors.
Second HS Analysis build up an on top database, to allow computational analysis of damaged tissue areas. The parameters allow to subclassify each disease in the future and make disease progression and rest life time of the organ as well as therapy responsiveness more predictable.
The current approach of HS Analysis used deep learning to detect the covered area over time in label free or fluorescence images and separate single cells instead of covered area or to detect cell cycle.

Artificial Intelligence: Deep Learning in Medicine, Myth or Reality?

For diagnostic purposes, it's important that microscopy images are not just images, diagnosis reports are not just unstructured information, molecular data are not just separated from results of image analysis. Doctors and pathologists would be supported best, if suspicious or malicious structures of tissue samples are identified at the early stages. In that case the doctors be able to apply their expert knowledge more efficiently and to focus on the illness itself.
This is exactly, what the HS Analysis GmbH does, when it comes to automated image analysis, structure reports and bring them with knowledge from molecular data. HS Analysis is working closely with different partners together, when digitization, digitalization and automation in life science is going to be a part of daily routine for the medicine. With the help of modern AI and Deep Learning supported methods, Sergey Biniaminov, CEO of HS Analysis, believes to seriously inspire diagnosis and research areas such as the early detection and therapy of cancer.
The discussed matters are highly user-oriented (physicians, clinicians, laboratories, medical centers and data scientists in medical field). Medical needs and compatibility with user processes (clinical routine) and the chances and risks of the integration of artificial intelligence from 2019 are key factors for the talk.
To discuss are the chances and risks of following technics in medicine and life science:

- DL (Deep Learning) for the automatic analysis of medical images.
- NLP (Natural language processing) for the structured reporting in the diagnostics
- DRL (Deep reinforcement learning) for the DNA-, RNA-, peptide-analysis
- ILP (Inductive logic programming) for the human machine collaboration

Ute Schepers

Professor and Group Leader
Karlsruhe Institute of Technology (KIT) and VasQlab

After studying chemistry, Ute Schepers received her doctorate from the University of Bonn. In 1998 she worked at the Department of Cell Biology at Harvard Medical School in Boston as a research associate. From 2001 to 2008, she starte a junior research group on organ-specific transport of bioactive molecules and drugs. Since 2009, she is heading her research group at the Karlsruhe Institute of Technology (KIT). In 2015, she was appointed as a senior scientist and professor of chemical biology.
Her research focus is the investigation of organ-specific transport of active substances and drugs. Since 2010 she has been working on the in vitro reconstruction of 3D organs on the chip. In the last years she has also been working on 3D bioprinting of human organs for drug testing. This research is currently being used to fund the KIT spin-off "vasQlab".

Organs-On-A-Chip And Artificial Intelligence Platforms In Personalized Medication Development

In addition to 2D cell culture models in plastic petri dishes animal, mainly rodents such as mice and rats, are used, which are despite their homology to the human genome not completely comparable to human patients giving rise to high failure rate in the clinical phase. To date, almost half of the newly approved drugs are biologics e.g. antibodies, which are not always cross-reactive in the animals. To direct the drug development process towards a personalized process, animal models have to be replaced by reconstructed humanized tissues such as organoids, matrix assisted 3D cell cultures or even sophisticated organ on chip systems, or a whole body on a chip. These systems have the advantage that they can exploit the whole portfolio of human cells for the reconstruction of humanized tissue, which resemble the genetic variability of different groups of patients by reprogramming adult somatic cells from biopsies into induced pluripotent stem cells (iPSCs). A recent screening technology patented by vasQlab@KIT, which is a spin-off of the Karlsruhe Institute of Technology (KIT), includes a 3D organ-on-a-chip system (vasQchip) based on humanized 3D vascularized tissues generated by 3D bioprinting of cells on a disposable microfluidic vasculature. The all in one vasQchip plug & play system can be applied in HT screenings of potential drugs. It was so far used to reconstruct many vascularized tissues such as liver, blood brain barrier, neurovascular unit of the brain, vascularized skin, and even the metastatic niche as well as several tumor models. The vasQchip has recently been exploited to develop a variety of functional bioinks for 3D bioprinting, which were tested for their endothelialization within the microvasculature. The technology platform can also be used for the development of immune tolerance inducing therapeutics for the treatment and ameliorization of autoimmune diseases such as systemic Lupus Erythematosus and multiple sclerosis (MS) using our model of the space of Dissé as the immune part of the liver.

Industry Poster Gallery

#1. Interrogated Knowledge Networks

Mark Griffiths[1], Mehmed Sariyildiz [1] , Brian Martin[2], Jennifer van Camp[2] and Lars Greiffenberg [1]

[1]AbbVie GmbH & Co. KG, Ludwigshafen, Germany
[2]Abbvie, Inc North Chicago, IL 60064, USA

Company: AbbVie www.abbvie.de

BACKGROUND/PURPOSE:

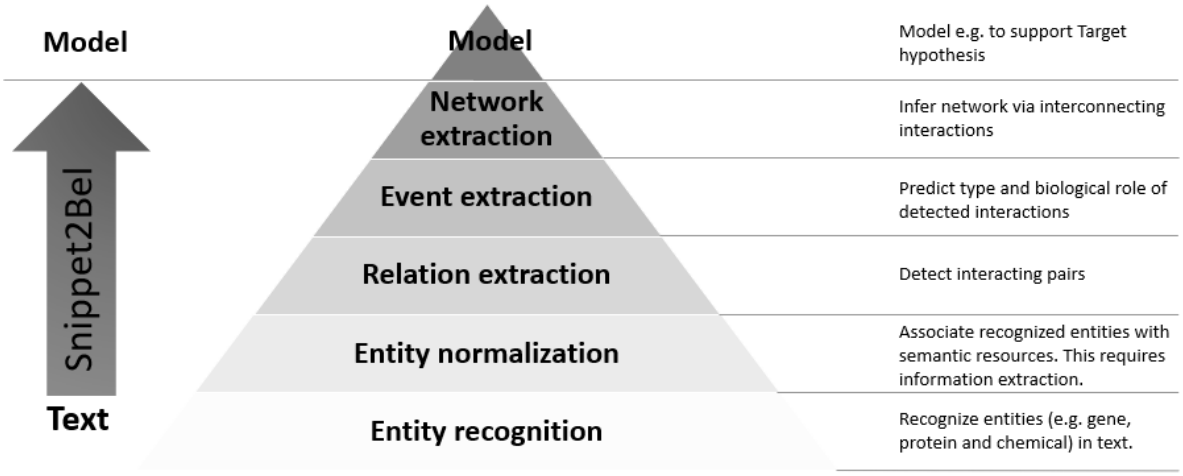
- Extracting knowledge from biomedical scientific literature to build a knowledge graph is by no means trivial [1]. We define such a graph as being composed of nodes that denote biomolecules/processes and edges between the nodes representing the interactions or reactions. Such a graph may be built from triples for example in the **B**iological **E**xpression **L**anguage (BEL) [2].
- Example BEL language triple

Causal

```
p(HGNC:CCND1) => act(p(HGNC:CDK4))
```

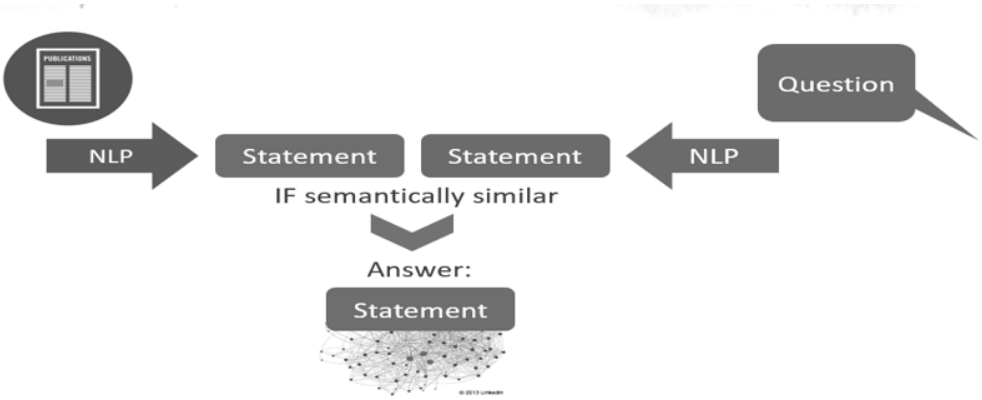
The abundance of the protein designated by *CCND1* in the HGNC namespace directly increases the activity of the abundance of the protein designated by *CDK4* in the HGNC namespace.

- There are many steps involved in a standard text-mining project to build such a model. Errors at each stage propagate to the next reducing overall accuracy. In addition, manual curation of the network is currently required to achieve acceptable levels of quality and consistency.
- Snippet2BEL approach is included for comparison which bypasses these steps.



- Once such a model has been built it can be used in the form of an interrogated Knowledge Network.

Figure 2. Interrogated Knowledge Network



Plain text is converted into triples (*entities and relationships*) which can then be used to search for other or similar triples in a triple store.

- You will notice that both sides of this equation involve turning text into triples.
- Since the current processes requires a large effort and manual curation, we decided to try a novel approach. The idea we had is to treat this problem like a translation problem such as English into Chinese characters. We first tried an encoder/decoder model but found that a decoder model yields the best results. The model was trained against various data sources, converting if required the input to BEL.
- The approach works and we were able to build a POC application based where you can enter a

CONCLUSIONS:

- By treating this as a translation problem we were able to train decoder models with a high accuracy (up to 96%) that can turn text directly into a BEL triple bypassing the conventional steps of a text mining project.
- This has the potential to open the door to rapid generation of Knowledge Graph models based on literature to support discovery projects with minimal manual curation, in the ideal case none.
- Such models could also play a role supporting recommender systems via the generation of a “knowledge fingerprint” for articles of interest.

REFERENCES:

[1] https://doi.org/10.1093/bioinformatics/bty114

[2] https://github.com/OpenBEL/language

#2. Clinical data science services for patient stratification in oncology

Garrit Jentsch, Pinar Boyraz Jentsch

Company: BAST GmbH www.bastde.com

At BAST we enable our clients from the pharmaceutical and biotech industry to make informed decisions and mitigate risks by providing state-of-the art data analysis services, which range from stand-alone data analyses to long-term strategic project support.

Apart from providing fit-for-purpose biometric and pharmacometric modelling expertise for its clients, BAST devotes some of its time to the development of computational tools for clinical development. In recent months BAST has developed a prototype proprietary machine learning platform, which uses omics data to identify survival subgroups in oncology. The platform consists of two modules: The first module employs a deep learning autoencoder and k-means clustering to infer patient subgroups with significant differences in overall survival. In the second validation module machine learning techniques are used to build a classification model, which identifies omics-features that are linked to the differential survival of patients. The prototype was developed and tested on publicly available mRNA-sequencing data from the cancer genome atlas (TCGA). In the future, BAST hopes to deploy this framework in clinical development projects to improve the understanding of the molecular mechanisms in oncology and assist in the development of personalized treatments.

#3. Challenges of the Clinical Trials Supply Chain

Giuseppe Tricarico, George Gibbons

Company: Biocair www.biocair.com

Advancing technologies, data security concerns, increasing complexity of treatment strategies and the growing focus on patient centricity are all impacting the way in which clinical trials are managed.

Today patient recruitment and retention over the trial are still the biggest concern for the sponsors. Failures in the supply chain are to be avoided by all means. These factors have led to the outsourcing of clinical trial supply and logistics and a growing number of full-service clinical supply chain experts, like Biocair. Success will mean that the clinical trial supply chain is efficient, effective and compliant with the necessary regulations as well as maintaining the highest levels of patient safety. As a resulting benefit we should also not forget costs reductions in the long run if all the above-mentioned criteria are satisfied. A delay in the timeline of a clinical trial has in fact a significant financial impact.

In order to ensure a flawless supply chain, it is key to involve the distribution partners quite early in the process and approach possible challenges from different angles with a specific expertise. Sometimes a small change in the set-up of the supply chain can have a significant impact on the overall structure.

#4. Novel systems for robust screening of autoantigens in autoimmune disease

Yonatan Herzig, Jing Zhang, Veronica Pinamonti, Nathan Felix, John Lindner

Company: Biomed X www.bio.mx

T cells are the key effectors of cellular adaptive immune reactions and become activated when their T-cell receptor (TCR) engages an antigen presented on the surface of antigen-presenting cells (APCs). Newly generated T cells each express a single TCR from a theoretical repertoire size of 1018 unique receptors. To minimize the inherent potential for self-reactivity, the T-cell repertoire is carefully curated through tolerogenic processes. Indeed, failure to distinguish self from non-self can result in devastating autoimmune diseases. While the general mechanisms of immune tolerance and how their breakdown results in autoimmunity are now better understood, there is still only limited knowledge of the identity of the targeted antigens in many autoimmune diseases.

Here we propose a robust and versatile strategy to 'de-orphanize' patient-specific self-reactive TCRs, effectively uncovering the range of targeted antigens in any autoimmune disease of interest. We aim to generate a highly parallel system, capitalizing on patient-specific APCs, engineered to express tissue-specific antigens, and screen for potential activation of interacting T cells expressing patient-specific TCRs. We will first generate state-of-the-art donor-specific APC lines enabling expansion, molecular manipulation, and antigen presentation. Utilizing automated droplet-based microfluidic chambers, single APCs and T cells will be co-cultured and systematically screened for interacting dyads, resulting in T-cell activation. This will thus enable us to deconvolute the identity of disease-specific autoantigens, leading to the rational design of novel therapeutic strategies.

#5. Using Euro-BioImaging services and tools to generate data for AI projects

Kelly Sheehan-Rooney and Frauke Leitner

Company: Euro-BioImaging (EMBL) www.eurobioimaging.com

Image data is an untapped resource in the field of AI and Euro-BioImaging is an easy way to generate this data for your AI projects!

Visit the Euro-BioImaging poster if you work for a company or organisation that uses/would like to use imaging in your research. We have a range of imaging technologies that you can access across Europe, with expert staff who will support your project's pipeline from setup to analysis. For the pharmaceutical and biotechnology sectors, accessing Euro-BioImaging's technologies and services holds huge, cost-effective potential for company's R&D and can be a great way to explore new, potentially high risk, avenues of research.

By visiting the Euro-BioImaging poster you will also hear about how we can provide expertise and support in the fields data reusability and accessibility as well as access to data work sets and development of tools – all of which are important factors in successful AI projects.

As the pan-European research infrastructure for biological and biomedical imaging, Euro-BioImaging has a lot to offer the in the field of imaging-associated AI.

#6. GELITA TUFT-IT®: the first gelatin-based non-woven hemostat - Case series report in open and laparoscopic liver surgery

Cletus Sali, Marcus Murnauer

Company: GELITA MEDICAL GmbH www.gelitamedical.com

Blood loss has been and still is absolutely a central risk issue in the liver surgery with intra- and postoperative blood loss and transfusion having a significant impact on mortality, morbidity and length of hospital stay with the resultant socio-economic malaise3. Liver surgeons must implore strategies to reduce blood loss and transfusion in order to improve outcomes in liver surgery2 Blood loss reduction in liver surgery is still an arduous task despite technological advancement in recent years. TUFT-IT®, a novel non-woven gelatin based hemostat, was introduced lately to the University Hospital Augsburg and the hemostatic and handling properties of TUFT-IT® in series of liver surgeries was evaluated. Their experience shows that the products is easy to use in open and laparoscopic surgeries. It adapts fully to irregular resection sites due to its flexibility and stretchability thereby providing very good hemostasis in a variety of liver resections. This is especially advantageous in more challenging types of resection sites where there is a very rough and irregular, inconsistent surface with deeper craters. Additionally, TUFT-IT® significantly lowers the cost of the surgical procedures.

[1]Hallet et al., The impact of red blood cell transfusions on perioperative outcomes in the contemporary era of liver resection. Surgery. 2016;159:1591-9.

[2]Kooby et al., Influence of transfusions on perioperative and long-term outcome in patient following hepatic resection for colorectal metastases. Ann Surg. 2003;237:860-9.

#7. Autonomous AI systems for pre- and clinical research and diagnostic purposes

Sergey Biniaminov and Christian Lamberz

Company: HS Analysis GmbH www. hs-analysis.com

For pre- and clinical research and diagnostic purposes, it's important that microscopy images are not just images, research and diagnosis reports are not just unstructured information, and molecular data are not just separated from results of image analysis. Researchers and doctors are supported best when all necessary information is provided in an accessible and well organized way. In such a scenario, researchers and doctors will be able to apply their expert knowledge more efficiently, to focus on the essentials.

In science and medicine a big challenge lies in the loss of information and expertise that takes place when PhDs and doctors that have built up considerable inside knowledge on specific tasks are leaving their workplace in pursuit of their careers. If information were to be stored digitally, in a standardized and easily accessible form, even better if complex and time taking analyses of imagery or molecular data were to be simplified by the help of advanced AI technology and the resulting data included in a system that incorporates the handling of information from recording to publishing. This is exactly, what autonomous AI systems from HS Analysis does.

Combining automated image analysis with the structuring of reports and bringing them together with knowledge from molecular data. HS Analysis is working closely together with different partners, as digitalization and automation in life science is going to be a part of daily routine for medical researchers

#8. Independent Top 10 Pharma Trial of Voice-to-Text Technologies

Guru Singh

Company: Labtwin www.labtwin.com

A top 10 pharma company decided to test 5 voice-to-text technologies and LabTwin won hands down. LabTwin scored more than twice as high as the nearest competitor. The top 10 pharma scientists dictated a scientific protocol and compared how the five technologies transcribed it. To make direct comparisons easy, they color-coded the results.

LabTwin is the world's first voice- and AI-powered digital lab assistant. It is designed to accurately transcribe scientific language, including difficult-to-spell reagents and appropriate units of measurement. LabTwin uses machine learning to continually adapt to individual scientists needs and will become even more accurate as its user base grows.

#9. Cognitive neurorehabilitation with virtual reality

Barbara Stegmann, Julian Specht

Company: Living Brain GmbH www.livingbrain.com

More than 30 million people in Europe suffer from long lasting mild cognitive impairment due to neurological disorders that current cognitive trainings and neurorehabilitation therapies cannot solve. Paper-and-pencil exercises and computerised exercises are standard of care, but lack a solid theoretical framework regarding the selection of tasks. They are not tailored to the patient specific needs and also not related to activities of daily life, not reproducing the richness of multi-stimuli present in real-world settings which greatly compromise patient recovery.

Living Brain develops a virtual-reality based cognitive training software. The novelty of the solution stands in the fact that Living Brain's VR software is scientifically based on the principles of neural plasticity and psychological learning strategies, providing immersive 3D scenarios that optimally reproduce the multi-stimuli environment of activities of daily life speeding up cognitive recovery. The concept is in clinical evaluation at university hospital Göttingen at the moment, a feasibility study is running at university hospital Freiburg.

#10. Automated scanning and diagnostic pre-classification with Convolutional Neural Networks in cytology, microbiology and histopathology

Siegfried Hänselmann, David Christensen

Company: MetaSystems Hard & Software GmbH www.metasystems-international.com

Automated image analysis of biological material has always been facing the double challenge of high sample variability on the one hand and high demands on reliability and robustness of results by routine laboratories on the other. Consequently, software development cycles tend to be long, and only relatively few very specialized applications are making it to routine use.

With the availability of Deep Learning techniques, object detection and classification no longer relies on the tedious identification and extraction of suitable object features. Instead, Deep Neural Networks (DNNs) are trained with large numbers of pre-classified images directly, which significantly accelerates algorithm development.

MetaSystems' high-throughput slide scanning platform Metafer provides an ideal setting for Deep Learning based solution development. It supports easy generation and pre-classification of microscopy images as a prerequisite for DNN training. Trained DNNs can then be applied during the scan to analyze captured images on the fly, thus avoiding unnecessary transmission and storage of whole digital slides.

Among the applications currently being addressed are bacteria detection in Gram stained slides, leukocyte classification from bone marrow smears, mycobacteria screening, chromosome classification from blood and bone marrow preparations, tumor detection from brain tissue sections, and more.

#11. AI-driven software to predict clinical development success

Sonia Vivas, Blanca Baez, Alena Blank-Giwojna, Rudolf Caspary, Markus Hartenfeller, Tabitha Müller, Leo Nesme, Uri Olivares, Lucia Santoso, Alexander Strigun, Bernhard Sulzer, Ulrike Ziehm, Armin Schneider.

Company: Molecular Health www.molecularhealth.com

A drug development project is successful only in 1 out of 11 cases, resulting in estimated costs of around $2-3 billion per approved drug. The success rate of clinical trials has remained unchanged over the last 25 years implying that we do not learn sufficiently from past trials. Machine learning / artificial intelligence now offers the means for learning from large datasets around clinical trials. Insights drawn from such unbiased statistical models may support subject matter experts in the pharmaceutical industry in better estimating the probability of technical success (PTS) of a program and optimize various parameters.

Molecular Health Predict (MH Predict) is an AI-based application which predicts clinical trial success, defined as a trial having achieved its primary endpoint(s). The algorithm draws information from feature domains such as sponsor company, drug, target or trial design and operations to make its prediction. Currently more than 60,000 trials are predictable with the engine.

Functionalities beyond the mere prediction of the PTS of a trial allow users to analyse and benchmark trial sets of interest, simulate effects of changing trial parameters and analyse the drivers of trial success/failures by means of state-of-the-art interpretable machine learning methodologies derived from game theory. We believe that the offerings of this product bring value to portfolio management, clinical trial design, clinical operations and asset search and evaluation.

#12. Precision Immunotherapy with Graph Neural Networks

Brandon Malone, Yoshiko Yamashita, Kousuke Onoue, Yuki Tanaka, Timo Sztyler.

Company: NEC Laboratories Europe GmbH
https://uk.nec.com/en_GB/emea/about/neclab_eu

Immunotherapy is a promising therapeutic approach for combating cancer by teaching the patient's own immune system to recognize and destroy cancerous cells. However, each patient is unique, and precision medicine approaches are needed to give each patient the best chance for a positive outcome.

In this work, we propose graph neural networks (GNNs) as a precision medicine framework which integrates patient-specific data with public domain knowledge culled from the literature. In particular, we demonstrate how GNNs can be used to rank patient-specific, somatic variants in cancer (neoantigens) as candidates for use in personalized immunotherapy, such as cancer vaccines or adoptive cell transfer therapy.

Additionally, we describe a bioinformatics pipeline which extracts candidate neoantigens from genomic and transcriptomic sequencing data. In addition to the GNN input, the pipeline extracts a variety of patient-specific parameters about each candidate neoantigen like its abundance in the sequencing data.

Empirically, we demonstrate that GNNs lead to better neoantigen rankings compared to existing state-of-the-art approaches including deep neural networks and gradient-boosted trees. Our pipeline, which integrates patient-specific parameters, further improves the rankings.

#13. AI facilitating assessment of biomedical research quality

Björn Gerlach, Christoph H. Emmerich, Martin C. Michel, Anton Bespalov, Andre Der Avakian, Rob Miller, Dan Deaver, Patricia Kabitzke

Company: PAASP GmbH / PAASP US LLC www.paasp.net

Drug development success rate has declined over the past decade. One factor that is thought to contribute to the high rate of preclinical-to-clinical translation failures is the robustness of preclinical evidence.

To address these concerns, a fit-for-purpose quality system for non-regulated drug discovery research is being developed by a private-public consortium called EQIPD (European Quality In Preclinical Data) under the umbrella of the Innovative Medicine Initiative. A total of 29 consortium partners have designed a system dedicated for the preclinical research environment combining the needs for an effective and lean approach.

One of the main challenges associated with implementing a quality system in early-stage drug discovery research environment is the lack of a performance assessment mechanism. This mechanism would fit the purpose of the general quality system intended for a broad deployment in biomedical research – an assessment being easily accessible, lean and affordable.

Independently of EQIPD, PAASP US LLC has received support from the U.S. National Institute on Drug Abuse to develop an AI-based assessment protocol. The objective of this project is to develop an online self-assessment tool based on PAASPort®, an established tool for operational risk management and research quality evaluation. The next generation PAASPort® will use a neuronal-network-learning technology to improve and accelerate the output.

#14. FUBIS is an alendronate-5-Fluorodeoxyuridine duplex drug with strong anti-resorptive activity and reduced systemic toxicity.

Tiwari S, Tower RJ, Kneissl P, Rambow A-C, Campbell GM, Desel C, Damm T, Heilmann T, Fuchs S, Zuharya M, Trauzold A, Glüer CC, Schem C, Schott S

Company: PEKKIP Oncology Alliance AG www.pekkip-oncology.com

We present the latest research and considerations for our molecule FUBIS, a bisphosphonate (alendronate) conjugated to the anti-metabolite 5-Fluorodeoxyuridine. Ultimately, this project aims at a development of an anti-resorptive and anti-tumor drug for the treatment of bone metastases in various cancer situations.

Background: Nitrogen-containing bisphosphonates (N-BPs) exert their anti-resorptive activity through inhibition of farnesyl pyrophosphate synthase (FPPS), which is ultimately toxic to osteoclast cells. High exposure of N-BPs can damage epithelial layers and give rise to renal toxicity and gastro-intestinal tract toxicity. Increasing reports in the literature associate toxicity to different cell types, including osteoblast, with administration of N-BPs. A bone-seeking agent which maintains anti-resorptive properties but with improved safety profile will allow for higher dosing with beneficial effects on bone health.

Results: In this study we tested FUBIS, a bisphosphonate duplex drug consisting of alendronate conjugated to the anti-metabolite 5-Fluorodeoxyuridine in a preclinical mouse model of bone metastases. In vitro, FUBIS does not inhibit FPPS but cells accumulate in the S and G2/M phase of the cell cycle. Cell toxicity assays reveal FUBIS to be less toxic to breast cancer cells than alendronate, but for multiple myeloma cell lines FUBIS has greater toxicity. In vivo, FUBIS retains anti-resorptive activity but in contrast to alendronate treatment does not decrease serum levels of the bone formation marker osteocalcin. Furthermore, molar doses of 1000 fold greater than alendronate do not affect renal function as assayed by measurement of the glomerular filtration rate.

Discussion: The preclinical study indicates FUBIS to be a promising drug for treatment of bone metastases and multiple myeloma but further studies are required to elucidate mechanism of action and pharmacokinetics. Furthermore, we are looking into options to prove clinical efficacy through biomarkers and possible ways to delineate further information on the MOA from pre-clinical research.

#15. Image based precision diagnosis powered with machine learning

Yongsheng Cheng

Company: PixelBiotech GmbH www.pixelbiotech.com

PixelBiotech is providing a single-molecule genetic testing end-to-end tool, combining proprietary HuluFISH probe and AI-empowered data analysis. HuluFISH is breaking the multiplexity limit of traditional fluorescence-based assays, and bring tens to hundreds of targets to be analyzed in a single step. This will be a great validation tool for NGS data, quality control tool for cell therapy and gene therapy by controlling dozens of potential viral/bacterial contaminations. Our AI data analysis can help customers to get rid of the difficult image data analysis. Our products have been adopted by customers from developmental biology, biochemistry, tumor biology, infectious disease control, and cell therapy. The long term goal of PixelBiotech is developing an integrative platform HuluONE, which will combine HuluFISH staining, imaging, and AI image analysis into a single fully automated machine. This all-in-one platform will empower academic, clinic and industrial customers to generate accurate single-molecule gene detection tool in one standard.

#16. Predicting the onset of chronic kidney disease in patients with diabetes using electronic health records

S. Ravizza, T. Huschto, A. Adamov, L. Böhm, A. Büsser, F.F. Flöther, R. Hinzmann, H. König, S.M. McAhren, C. Ringemann, D.H. Robertson, T. Schleyer, B. Schneidinger, W. Petrich

Company: Roche Diabetes Care GmbH www.roche-diabetes-care.de

Traditionally, clinical trials serve as the gold standard to establish medical evidence and guide medical decision making. Nevertheless, it is known that there is a substantial gap between what is seen in clinical trials and what can be observed in routine care. The ever growing amount of medical data from electronic health records (EHRs), as well as the improvements in data analytics, offer an opportunity to substantially reduce this gap.

From longitudinal real world EHR data (RWD) of more than 600,000 people with diabetes from the IBM Explorys database and the Indiana Network for Patient Care (INPC), we built an algorithm to predict the risk of an individual patient to develop chronic kidney disease (CKD) within three years after the initial diagnosis of diabetes. The Explorys data was randomly split into a teaching and validation set, constituting the basis of building a logistic regression model with forward selection for feature reduction. The INPC data was used for independent validation. Particular focus was placed on the robustness of the model as the Explorys and INPC database reflect distinct sources of EHRs.

Comparisons with prediction algorithms derived from major clinical trials data (ONTARGET, ORIGIN, RENAAL and ADVANCE) showed the superiority of our prediction model, even if applied to only a sub-cohort of patients mimicking the original cohort of the clinical trials.

Based on this comparison with literature algorithms, we conclude that in this particular case algorithms based on RWD achieve a superior performance in predicting the risk of diabetes patients to develop CKD. We speculate that the diverse nature of RWD is the main driver of this difference, but caution that further investigations are necessary before such a statement should be generalized.

#17. Expert in standardized & individual Cold Chain Solutions

Moritz Brummer, Markus Hoffmann, Carsten Wolf

Company: THERMOCON www.thermocon-coldchain.com

The Schaumaplast Group produces molded parts and packaging made of EPS (Styrofoam®), EPP, E-TPU and other particle foams. Today, Schaumaplast operates in Germany, Poland and the USA.

With THERMOCON, Schaumaplast has its own business unit for the development, production and qualification of passive thermal packaging.

GDP-COMPLIANT TRANSPORT.
Schaumaplast develops pre-qualified thermal packaging solutions especially for pharmaceutical, biotech and medical products. They consist of a thermo box, cooling elements, outer carton and thermal documentation. The systems have been tested in the company's own climate chambers according to difficile and standardized temperature profiles. Customer-specific solutions can also be developed, produced and reliably implemented.

EASY. COMPATIBLE.
Special feature of the THERMOCON systems are their modular and expandable options. Many systems can be flexibly enlarged using stacking frames. Different temperature ranges and running times can be achieved only by changing the refrigerants. This simplifies handling, reduces storage and purchasing costs.

YOUR PROJECTS. OUR COMPONENTS.
THERMOCON offers a wide range of different refrigerant types: from the inexpensive gel pack to the safe alternative for dry ice, the PCM pack. As well as EPS thermo boxes in different sizes from 1.3 to 1275 litres capacity. Optionally, they can also be made of Biomass Balance Styrofoam.

As an expert in thermal packaging, we're happy to advise you on your individual Cold Chain Project!

#18. Efficiency in Clinical Research through Quality by Design – How QbD will help in defining your Clinical Development Strategy

Björn Bosse

Company: SCOPE International AG www.scope-international.com

Good quality in clinical trials is essential but there are many pitfalls along the way.

Achieving good quality of your data in clinical research can be challenging. We at SCOPE International, an internationally active full-service CRO, will help shedding light on the situation and to show ways and solutions to avoid classic mistakes right at the beginning of clinical development. In this poster we highlight the different requirements of big and medium pharma, biotech companies and start-ups with a special focus on regulatory and reimbursement aspects and outsourcing, where it is essential to find the right strategy for the respective development program.

Topics, to be covered:

- Early considerations for regulatory and reimbursement aspects in clinical development
- Outlining efficient study set-up with QbD
- Discussing how QbD supports your CRO and vendor selection strategy
- Defining efficient and high-quality Data Collection & Processing
- Efficient and guideline-conform reporting (Clinical Study Reports and Dossiers)

About the Organiser

BioRN is the science and industry cluster of the Rhine-Main-Neckar region around Heidelberg, one of Germany's strongest biotech hubs. It is a non-profit network fostering health innovations and serving its members by creating a rich translational ecosystem as well as promoting, representing and connecting the regional innovation stakeholders.

Our vision is to develop the region into a world-leading life science cluster attracting international investments and top global talent.

BioRN has about 100 institutional members, including the top academic and research institutions, 7 global pharmaceutical companies, a large range of small and medium-sized enterprises bolstering the life science ecosystem as well as local government organizations and interest groups.

Founded in 1996 BioRN has since raised more than 70 million € of public funding for its members. It was instrumental in the successful bid for the European Institute of Technology (EIT) KIC Healthy Living and Ageing in 2014 with a total grant of 700 million €

BioRN Cluster management establishes initiatives to nurture and extend networks between its members - the key regional innovation stakeholders. It stands for the promotion and visibility of the Life Science region and fosters connections to other regions of innovation worldwide.

BioRN is founding member of the Health Axis Europe (HAE), a strategic alliance between the leading life science hubs of BioRN, Leuven (Belgium), Maastricht (Netherlands) and Copenhagen (Denmark). The alliance aims to bundle and cross leverage the members' innovation resources and thus jointly increase international competitiveness.

The cluster is internationally recognized as an academic center of excellence in the field of cancer, immunology, cutting edge imaging and omics, holding an enormous potential for translation into health applications. By leveraging the unique combination of global pharma and leading academic institutions amongst its members, BioRN drives a range of translational initiatives in order to create an entrepreneurial ecosystem that can compete with other centers of excellence on an international level. These initiatives include tailored technology scouting activities between industry and academia (Health Axis Europe Partnering – HAEP), paving the way towards a fully equipped and professionally run life science startup incubator (BioLabs HD), and the implementation of funding instruments to finance the conversion of academic projects into industry ready assets (HDDiscovery).

General Information

Research Short-Talk Session – Vote for your favorite

To vote for your favorite candidate, go to www.sli.do and enter the code given to you at the end of the session. Vote for the best project by considering the scientific quality, innovativeness of idea, relevance and impact. You can vote until 16:00. The best project will be awarded during the 'Closing Remarks' around 17:00.

Photo and Video Recording

You are participating in an event during which the organizers will be taking photographs and videos that may contain your recognizable image. We will use these photographic and video recordings online, internally or externally (e.g. in press releases, on the BioRN websites, and in the LinkedIn and Twitter social networks) for a period of 10 years. The recordings will be deleted after 10 years. For more information about our privacy policy, please go to the BioRN websites (www.biorn.org). You may, of course, object to the use of the photographic and video recordings at any time during the event by talking to the photo/video team, or after the event by contacting

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Im Neuenheimer Feld 582
69120 Heidelberg
Email: info@biorn.org

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While we encourage your use of social media in and around the conference, we ask that you be aware of the following guidelines:
Follow the conference on Twitter (@BioRNCluster) and use the hashtag #BAC19 for this conference.
You are welcome to discuss the conference and what you are hearing and seeing, but please refrain from sharing raw data presented, as this may preclude subsequent publication of the data in a scholarly journal.

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