NEXT-GENERATION Cell and Gene Therapies

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We set the bar high for innovation. Inspired by patients, driven by science and powered by our growing global community of partners, we're working hard to discover and develop the next generation of transformative medicines. Together we can learn more, do more and achieve more and get the next breakthroughs to patients faster.

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Programme

08:30	Coffee & Registration
09:00	Welcome & Introduction **Michael Boutros**, Vice-chair of the executive board, BioRN **Eckart Würzner**, Mayor, City of Heidelberg **Julia Schaft**, Managing Director, BioRN
09:30	"From vaccines to adoptive T cell therapy of cancer" **Michael Platten, German Cancer Research Center and Tcelltech** "Clinical development of a BCMA-directed CAR-T Therapy for the treatment of Patients with Multiple Myeloma" **Yunsi Olyslager, The Janssen Pharmaceutical Companies of Johnson & Johnson**
10:10	Coffee & Exhibition
11:10	"The landscape of emerging therapies for hematological malignancies in Heidelberg" **Carsten Müller-Tidow, Heidelberg University Hospital** "AAV gene therapy – challenges of a rapidly growing field" **Katja Betts PROGEN**
12:00	Lunch & Exhibition

13:30		**Young Scientists Pitch Competition** moderated by **Angelika Vlachou**, HTGF *Selected projects in Cell & Gene Therapy will be presented by PhD Students, Postdoctoral fellows and Junior PIs and compete for the audience prize.*
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	2	'Beneath the Surface': unveiling novel targets for Chimeric Antigen Receptor (CAR) T cell therapies in acute myeloid leukemia - **Josephine J. Brysting**, Molecular Medicine Partnership Unit (MMPU), Heidelberg
	3	Searching the Hairpin in the Haystack: Tracing the Impact of AAV-ITR Mutations - **Felix Bubeck**, BioQuant & University of Heidelberg
	4	AAViTOP - a novel screening approach to identify antagonists for improved clinical antibody/CAR T therapy safety - **Sarah Glenz**, NCT & DKFZ Heidelberg
	5	Preclinical studies of ABCB5+ human skin-derived stem cells to facilitate liver regeneration during acute on chronic liver disease - **Seddik Hammad**, Medical Faculty Mannheim, Heidelberg University
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14:30		**Keynote**: "Targeting illnesses at their source – the Cell & Gene Therapy commitment at Bayer" **Anke M. Schulte, Bayer Pharma**
15:15		Young Scientists Pitch Competition: **Award Ceremony** Closing Remarks: **Gitte Neubauer**, Chair of the executive board, BioRN
15:45		**Happy Hour & Speed-Networking with Live Music**
17:00		End of the Conference

Welcome

Dear BioRN Members and Friends,

On behalf of the BioRN Cluster, we would like to welcome you to the BioRN Annual Conference 2023: “NEXT-GENERATION Cell & Gene Therapies”.

In 2016 the first gene therapy (being still on the market) was made available to patients in Europe. A historic action, showing the great potential of this technology to transform medicine. Due to the high complexity together with issues to meeting the quality, safety, and efficacy standards set by the regulatory authorities, the field has experienced a slow growth. However, the constant investment in R&D, clinical trials and bioproduction led to the momentum now. Five additional FDA-approved therapies were added in 2022 and could be doubled in 2023, setting a new pace in the field.
While these technologies were initially developed to treat rare diseases caused by a single faulty gene, a variety of gene and cell-based therapies for both rare and common diseases are currently in development. Cell & Gene Therapies might be able to shift the paradigm from treating symptoms to curing diseases. This years’ BioRN Annual Conference will highlight next-generation approaches in the field. We are excited to have such renowned speakers from the field who will share with us their latest results and are at the heart of the meeting. Congratulations as well to the scientists who applied for the ‘Young Scientists’ Pitch Competition’ and can present their cutting-edge research at the conference.

We also would like to thank our sponsors for their dedication and financial support which allowed us to organize an outstanding program.

At the interface of academia and industry, where innovation happens - BioRN facilitates cooperations and successful development of ideas into application. Let’s jointly make life science matter and innovation happens.

Connect, bridge, and exchange ideas!
We wish you all an inspiring conference day.

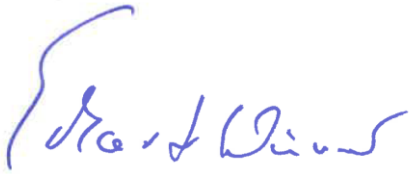
Gitte Neubauer	**Michael Boutros**	**Julia Schaft**
Chair	Vice Chair	Managing Director
BioRN	BioRN	BioRN

Greetings – City of Heidelberg

Greetings on the 15th birthday of BioRN Cluster Management GmbH! As the Mayor of Heidelberg, I am honored to celebrate this remarkable organization's growth and achievements. Our partnership with BioRN has been pivotal in shaping the life sciences ecosystem. Together with other key individuals, we have transformed BioRN into a strong pillar for strategic development. Its significant funding successes and inclusion in the prestigious InnoLife consortium are testament to its global significance. We take pride in supporting the annual BioRN conference, which has grown remarkably, and we envision it becoming a leading life science event in Germany and Europe. The recent achievement of BioLabs Heidelberg showcases the strength of our partnership. We remain committed to further successes and a brighter future for the Life Science Region. Congratulations to BioRN Cluster Management GmbH!

Prof. Dr. Eckart Würzner

Mayor, City of Heidelberg



Moderation

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.

Angelika Vlachou

Partner
HTGF, High-Tech Gründerfonds

Dr. Angelika Vlachou has been investing venture capital in biotech, pharma and life science start-ups for over 10 years. Over the course of her career, she has managed many transactions ranging from seed-stage venture capital and growth financing to licensing agreements, trade sale transactions and IPOs. Her expertise is also based on her virology-molecular biology research experience. One of her strengths is to combine scientific innovation with commercial potential. She is a valued sparring partner for founders, investors and stakeholders. With a doctorate in biology, she started her professional career in investment banking.

Welcome and Closing

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.

Keynote

Anke M Schulte

Cell & Gene Therapy, Head of Research & preclinical Development
Bayer Pharma

Dr Anke M Schulte is the Head of Research and preclinical Development within the Cell & Gene Therapy Unit since July, 2021 - when she joined Bayer. Previously, Dr Schulte worked 20 years at Sanofi in Frankfurt/Main, Germany in changing assignments. Starting as head of the Molecular Pathology group, joining Sanofi´s Diabetes Research Unit as head of the Islet Biology Cluster, being the project leader of the "Beta Cell Replacement Therapy" Program, and leading the IMI2 INNODIA collaboration "Translational approaches to disease modifying therapy of type 1 diabetes". Dr Schulte studied Biology at the Johann Wolfgang University in Frankfurt/Main, Germany and received her PhD from the Technical University in Darmstadt, Germany. She trained as postdoc fellow at Georgetown University and worked as Assistant Professor at the Lombardi Cancer Center in Washington D.C., USA where she spent 8 years. Dr Schulte has published more than 40 publications, invited chapters and reviews.

Targeting illnesses at their source – the Cell & Gene Therapy commitment at Bayer

By targeting illnesses at their source, we have the potential to shift from treating symptoms to curing diseases. Our approach to medicine and how we diagnose, treat and beat diseases has changed remarkably over the last hundred years. From x-rays to DNA sequencing, rapid advances in both our knowledge and technology have meant illnesses that were once considered life sentences can now be overcome or at least managed more effectively. However, despite this incredible improvement, there remain many diseases and disorders that are incurable and continue to be hugely destructive to so many people's lives. But what if there was a way of beating these previously untreatable illnesses? What if we could get to the root cause of the illness and stop it at its source? This is what Cell and Gene Therapy (CGT) seeks to do. Scientists are on the cusp of huge breakthroughs in a new field of medicine that would create a new paradigm for healthcare – one that could potentially cure even the most difficult diseases by focusing on the building blocks of our bodies, our genes and cells. Cell and gene therapy look at illness at a molecular level, seeking to replace damaged or dysfunctional molecules.
The idea of transferring viable cells to a patient in order to lessen or cure a disease is not new – blood transfusions have been around for almost a century and the first bone marrow transplant was more than 50 years ago. But in the past couple of decades major advances in research around stem cells have made it possible to grow and reprogram cells in order to help the body repair itself by replacing damaged cells with healthy new ones. BlueRock Therapeutics, Bayer´s arm´s length Cell Therapy company, is using iPSCs as a platform to manufacture and replace lost or damaged cells that the body needs to repair itself due to neurological, cardiovascular or

immune disorders. To reverse or halt the symptoms of devastating conditions like Parkinson's disease – the fastest growing neurodegenerative disorder in the world – is one lead program in clinical trial.

Many diseases are caused by a dysfunctional gene and/or a mutation that leads to a certain condition such as Hemophilia, Huntington disease or Sickle Cell Anemia. Gene therapies focus on the use of genetic material as a drug, correcting or replacing the abnormal gene function causing it. Asklepios BioPharmaceutical (AskBio), Bayer´s arm´s length Gene Therapy company, is a pioneer in in vivo gene therapy. AskBio's scientific co-founder, Jude Samulski, was the first to demonstrate that an adeno-associated virus (AAV) could be cloned for therapeutic purposes. AAV is a harmless virus bioengineered to carry a healthy gene to target cells in a patient with a genetic disease. Several clinical programs are underway addressing devastating diseases as Huntington´s, Parkinson´s, Congestive Heart Failure, and Pompe – just to name a few.

Strengthen Bayer's commitment to Cell & Gene therapy even further, a partnership was recently announced with Mammoth Biosciences, a company that is harnessing the diversity of nature to power the next-generation CRISPR products. Gene editing serves as a key enabler for cell therapies when used outside the living body (ex vivo) and allows therapeutic targeting of a wide range of genetic diseases with a high unmet medical need when used inside the living body (in vivo). Under the partnership the collaboration starts with a focus on liver-targeted diseases.

In the presentation, Bayer´s commitment to C&GT will be layed out and exemplified by concrete examples.

Plenary

Katja Betts

CEO, PROGEN

In 2016, Katja joined PROGEN and took over the role as CEO in 2019. Together with the PROGEN team, she forwards PROGEN´s commitment to support the gene therapy community in improving and expanding safe and reliable treatments for their patients.

Katja has a strong background within international marketing communications in the scientific sector, having held positions at EMBO and Newcastle University (UK) amongst others. She completed her Executive Master in Communications Management at USI Switzerland, UCLA USA and SMU Singapore and lived in the UK for more than 6 years.

AAV gene therapy – challenges of a rapidly growing field

AAV-based gene therapy represents one of the most promising approaches in modern medicine to date. This development is reflected by the great influx of companies and technologies into the field as well as the rapidly growing number of AAV gene therapies entering clinical trials. The fast growth of the entire AAV landscape is accompanied by many new findings and approaches leading to constant review and adaption of regulatory guidelines concerning viral based gene therapy. It is a major challenge to keep up with this quick development affecting indispensable comparability and safety concerns.
In this presentation, we present market data and give insight into the state of the AAV gene therapy field. Furthermore, we are going to address some of the challenges that the community is facing right now and which challenges companies in the AAV field need to prepare for in the future. While introducing these topics the presentation will take a closer look at currently available analytical tools that can help to ensure data comparability and the necessity of proper safety evaluations.

Yunsi Olyslager

Director, Clinical Scientist Leader Oncology
Janssen, Pharmaceutical Companies of Johnson & Johnson

Yunsi Olyslager joined Janssen in 2005 and is Clinical Scientist Leader in Oncology R&D. At Janssen, she has been leading and contributing to the design and execution of phase 1-3 clinical trials, in various hematologic malignancies, including Multiple Myeloma and Lymphoma, across the Heme Oncology portfolio. More recently she is focused on the Clinical Development Programs in Cell Therapy and T-cell Redirecting Therapies. Yunsi received her master's degree in biomedical sciences from the University of Antwerp.

Development of CARVYKTI™ (Ciltacabtagene autoleucel), a BCMA-directed CAR-T Therapy for the treatment of Patients with Multiple Myeloma

With advancements in technology and research, the next generation in cell therapies is emerging as a promising approach for effective treatment across a wide range of diseases.
During this session we will address the unmet needs of patients living with multiple myeloma as we will explore Janssen's novel therapeutic strategies that are advancing treatment goals and improving patients' lives.
Cilta-cel was Janssen's first approved CAR-T therapy and is continued being studied in a comprehensive clinical development program for the treatment of patients with relapsed or refractory multiple myeloma and in earlier lines of treatment. The design consists of a structurally differentiated CAR-T with two BCMA-targeting single domain antibodies. Cilta-cel has demonstrated sustained efficacy with durable responses and was approved for the treatment of relapsed/refractory multiple myeloma (RRMM) after ≥3 or ≥4 lines of therapy, including a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 antibody, based on the phase 1b/2 CARTITUDE-1 trial (NCT03548207).
This sets the stage for further innovation in cell therapy and advancing the science of multiple myeloma, building on developing and delivering innovative medicines for patients with this incurable blood cancer.

Carsten Müller-Tidow

Director Department of Medicine V, Speaker Heidelberg Center for Cell and Gene Therapy
Heidelberg University Hospital

Carsten Müller-Tidow is Professor of Medicine at Heidelberg University and Director of the Department of Hematology, Oncology and Rheumatology at Heidelberg University Hospital. He graduated from the University of Bonn in 1994 followed by an internship at the Department of Internal Medicine A at the University of Münster Subsequent to a three year postdocoral fellowship in Los Angeles he returned in 1999 to the University Hospital Münster to complete residency and fellowship in Internal Medicine/Hematology and Oncology. He became full professor in 2009 In 2014 he was appointed Director of the Department of Medicine IV at Halle (Saale) University Hospital and headed the state center for cell and gene therapy. Since 2017 he works as Professor at Heidelberg University Hospital and is a group leader of the MMPU of EMBL & Heidelberg University Hospital. He received various honors and awards, among them a Heisenberg Career Development Award by the DFG. He is the Speaker of the NCT Heidelberg Comprehensive Cancer Center (CCC). Carsten Müller-Tidow´s research interests focus on the development of novel treatments in hematological malignancies including clinical trials with a special emphasis on cancer stem cells and novel therapy approaches. He is founding member and Speaker of the recently established Heidelberg Center for Cell and Gene Therapy.

The landscape of emerging therapies for hematological malignancies in Heidelberg

Cancer therapies are driving medical innovations. Advanced cellular and gene therapies are currently revolutionizing the landscape of therapy options for until recently untreatable diseases. Here, I am going to outline the main developments in the field of hematological malignancies with a specific focus on clinical treatments, research and development in Heidelberg. These exciting advances were also one driver of the newly established Heidelberg Center for Cell and Gene Therapy. These developments and the perspectives for cell and gene therapy from the University Hospital perspective will be discussed.
This short talk explores a venture capitalist’s view on the field as an attractive target for a venture creation investment thesis.

Michael Platten

Professor of Neurology, Division Chair and Founder of Tcelltech
German Cancer Research Center

Michael Platten is Head of the Department of Neuroimmunology and Brain Tumor Immunology coordinator of the research topic Immunology and Cancer at the German Cancer Research Center (DKFZ) in Heidelberg. He is also a Professor of Neurology and Chairman of the Department of Neurology at the University Hospital in Mannheim. Michael serves as the vice chair of the German Neurooncology Working Group (NOA), the Management Board of the Helmholtz Institute for Translational Oncology (HiTRON) and the Scientific Committee of the European Association of Neurooncology (EANO). Michael has received his MD from the University of Bonn, Germany and his postdoctoral training at the Universities of Tübingen, Germany and Stanford University, USA. He and his team discovered novel pathways involved in immune regulation in gliomas and pioneered the development of novel therapeutic strategies for the immunotherapy of gliomas and other types of cancer currently tested in early multicenter trials. Michaels main scientific focus includes glioma immunogenicity, immune suppression, heterogeneity and personalized treatment strategies. He has published more than 350 articles in peer-reviewed journals including Nature, Nature Cancer, Nature Medicine, Science, Cancer Cell, PNAS, JCI, NEJM, Lancet Oncology and JCO and is listed as a Highly Cited Researcher. More recently he has founded Tcelltech, a spin-out of the DKFZ that develops personalised adoptive cell therapies against cancer.

From vaccines to adoptive T cell therapy of cancer

Personalized tumor immunotherapy - vaccines and T cell therapies - requires the selection of only a few immunogenic epitopes recognized by tumor-reactive T cell receptors (TCRs) from thousands of potential epitopes generated from tumor antigens or tumor-associated antigens in each tumor. This selection is a huge challenge, particularly in brain tumors, where access to tumor tissue is limited and tumor-infiltrating T cells are limited. We have in the past identified shared driver mutations as immunogenic epitopes for targeting tumor-reactive T cells to gliomas. We have developed a vaccine targeting shared clonal driver mutations in glioma, conducted phase 1 first-in-human clinical trials and found, that vaccine-induced neoepitope-reactive tumor-infiltrating T cells are characterized by a distinct transcriptional signature, separating them from bystander T cells. Based on this observation we have developed an antigen-agnostic classifier to identify and harness tumor-reactive TCR from T cells infiltrating unperturbed tumors for personalized T cell therapy using TCR-transgenic T cells. This approach can significantly cut down discovery time (from months to weeks) and will also obviate the necessity for testing cross-reactivity as such TCRs are derived from the patient itself.

The next 150 years start here

Seit 150 Jahren sind die Menschen am Roche-Standort in Mannheim treibende Kraft hinter innovativen Therapien und diagnostischen Tests – für Patient:innen auf der ganzen Welt. Inmitten Europas, an zwei Flüssen: Roche in Mannheim ist so lebendig, erfinderisch und vielfältig wie die Quadratestadt selbst. Hightech trifft Herz und Machermentalität. Auch für die nächsten 150 Jahre.

www.roche.de/mannheim

Young Scientists' Pitch Competition

How it works?

1. Young Scientists have replied to a call of abstracts launched in early summer and now present their research live in a short pitch at 13:30 about their research work (10')
2. The onsite audience selects the best research pitch, through live voting:
    - Go to slido.com and include the code #BioRNConference or scan the QR code here under to access the live voting system
    - Select your favorite Research Pitch and submit your vote – Voting closes around 15:00 (end of Keynote).
3. The winner will be announced during the award ceremony after the Keynote

Slido.com

#BioRNConference

#1 A combination approach of a cellular library and single-cell microfluidics analysis for rapid identification of functional CARs

Eren Boga[1], Toros Tasgin[2], Robert Embacher[3], Alicia Roig-Merino[4], Richard Harbottle[2], Dirk Jäger[1,5], Patrick Schmidt[1,5]

[1] Clinical Cooperation Unit "Applied Tumor Immunity", National Center for Tumor Diseases (NCT) and German Cancer Research Center (DKFZ), Heidelberg, Germany
[2] DNA-Vector Lab, German Cancer Research Center (DKFZ), Heidelberg, Germany
[3] Berkeley Lights, Emeryville, CA, USA
[4] MaxCyte Inc, Gaithersburg, MD, USA
[5] Department of Medical Oncology, National Center for Tumor Diseases (NCT) and University Hospital Heidelberg, Heidelberg, Germany

Research group- DNA Vectors (dkfz.de) & Applied Tumor-Immunity (dkfz.de)

Long lasting complete responses have been achieved for the treatment of B cell malignancies by using CAR T cells targeting prominent B cell markers. However, more CAR constructs need to be screened for functionality and specificity to make CAR T cell therapy more applicable for broader cohort of patients. Currently, scFv phage display libraries are the golden standard for CAR identification, but reaching the final product is laborious and time consuming. Moreover, not every isolated scFv could give rise to a functional CAR molecule and the constructed CARs have potential to have tonic signaling. Therefore, alternative screening platforms are needed to shorten the CAR isolation process in order for patients to receive a personalized treatment in a reasonable timeframe. In this project, we propose an innovative approach that would accelerate isolation of functional CAR constructs. To do so, we generate a "cellular" CAR library by engrafting a plasmid CAR library into a reporter Jurkat cell line. For this purpose, we first cultivated a highly sensitive single-cell derived reporter Jurkat clone. This clone is then transfected with a plasmid CAR library that is generated by cloning a randomly assembled scFv repertoire into a functional CAR backbone. Since CAR library is engrafted into the reporter cells directly, tonic signaling CARs can easily be identified as they will activate the cells in the absence of antigen-specific stimulation and can be excluded from further analysis. Consequently, remaining library is ready to be screened for any antigen of interest on a single-cell level by using Phenomex Lightning™ device. Positive hits can be identified by induced reporter expression and be exported from the Lightning™ device to have their CAR molecules sequenced. We envision above mentioned process can be done in as little as 2 weeks. Once the cellular library is established, aliquots can be frozen to be thawed later for on demand screening against a TAA of interest.

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Daniel B. Goodman et al., Pooled screening of CAR T cells identifies diverse immune signaling domains for next-generation immunotherapies. *Sci. Transl. Med.***14**, eabm1463 (2022). DOI: 10.1126/scitranslmed.abm1463

#2 'Beneath the Surface': unveiling novel targets for Chimeric Antigen Receptor (CAR) T cell therapies in acute myeloid leukemia

Josephine J. Brysting[1], Yi Liu[1,2], Christian Rohde[1,2], Jennifer Schwarze[3], Frank Stein[3], Simon Renders[4], Julia Unglaub[2], Tim Sauer[2], Judith B. Zaugg [2,3], Carsten Muller-Tidow[1,3]

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[4] Department of Stem Cells and Cancer, Cancer Research Center and Heidelberg InsKtute for Stem Cell Technologies and Experimental Medicine (HI-STEM GmBH), Heidelberg, Germany

Epigenetics, Epitranscriptomics and Novel Therapy Approaches in AML

Introduction: Acute myeloid leukemia (AML), is a haematological malignancy that disproportionately affects elderly patients with poor prognosis; < 15% 5-year survival rate and high levels of relapse. The use of CAR-T cell therapies for these patients is thus a promising strategy but their clinical success against current cell surface targets is thus far hampered by severe on-target, off-tumor toxicities. We show the most promising strategy to date for unveiling novel CAR-T targets that combines cutting-edge technology with a clinically-relevant treatment approach.
Innovative Approaches: We show the use of a clinically implemented hypomethylating drug, 5-azacitidine (5-aza, approved as SOC in AML in combination with Venetoclax), to upregulate the expression of cell surface molecules suitable for CAR-T targeting in AML. We unveil novel biologically relevant cell surface molecules by “multi-molecule glyco-cell surface capture” (MM-CSC) method in AML patient samples. To date, we have produced a unique cell surface glyco-proteome dataset in untreated and 5-aza treated AML patient cells and the first cell surface glyco-RNAome of AML with the same treatment conditions. Both these datasets provide unique resources for target mining.
New discoveries: We have shortlisted a handful of promising novel plasma membrane-anchored proteins for targeting by CAR-T cells. Critically, these targets demonstrate low normal tissue expression and are enriched in cells harboring leukemic stem cell phenotypes and high mutational complexities. Their specificity and relevance in AML pathogenesis further highlight their therapeutic potential.
Conclusion: Taken together, we demonstrate an unparalleled approach for discovering novel CAR-T targets and propose a viable clinical therapeutic strategy for treating AML patients with very limited treatment options.

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#3 Searching the Hairpin in the Haystack: Tracing the Impact of AAV-ITR Mutations

Felix Bubeck[1,2], Conradin Baumgartl[1,2], Dirk Grimm[1,2,3]

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[2]BioQuant, University of Heidelberg, Heidelberg, Germany
[3]German Center for Infection Research (DZIF) and German Center for Cardiovascular Research (DZHK), Heidelberg, Germany

Viral Vector Technologies, Medical Faculty, University of Heidelberg https://grimm-labs.com/

In Adeno-associated viral (AAV) vectors, engineering of the ITR (inverted terminal repeat, i.e., replication and packaging cis element) sequences may enhance vector productivity, safety and efficacy. Strikingly, however, the impact of the ITR sequence and structure on these parameters remains largely unexplored. To facilitate manipulation of the ITRs, we developed a toolbox for AAV ITR engineering which includes a vector construct design that allows easy modification of plasmid ITR sequences. This is complemented by a strategy for plasmid ITR sequence confirmation that can be used with conventional Sanger sequencing chemistry. To trace the ITR mutants during production and transduction, each ITR variant is associated with a specific DNA barcode in the 5‘ UTR of a transgene cassette on the virus genome. The integrity of the produced viral genomes and the presence of ITR mutants was examined by Nanopore sequencing. There, we discovered a previously undescribed trans-acting ITR-repair mechanism in which ITR variants derived from different plasmids can serve as repair template. This ITR repair mechanism can be circumvented, permitting AAV vector generation with mutant ITRs that are maintained in the virus genome. Subsequent barcode interrogation by deep sequencing enables the determination of barcode distribution at high resolution, which, in turn, allows to quantify the impact of the mutations on AAV genome replication and packaging. Barcode sequencing in extracted RNA can also serve as a qualitative and quantitative measure for effects of the ITR on vector transduction efficiency, despite the potential loss of the ITR by recombination in the nucleus. Altogether, the novel pipeline for ITR modification and tracing reported here forms the basis for the comprehensive analysis of alternative ITR designs and their function during AAV production and transduction, which should ultimately benefit the creation and optimization of next-generation AAV vectors.

#4 AAViTOP - a novel screening approach to identify antagonists for improved clinical antibody/CAR T therapy safety

Sarah Glenz[1], Patrick Schmidt[1,2], Inka Zörnig[2], Dirk Jäger[1,2], Silke Uhrig-Schmidt[2]

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[2]Department of Medical Oncology, National Center for Tumor Diseases (NCT) and University Hospital Heidelberg, Heidelberg, Germany

Applied Tumor Immunity, DKFZ,https://www.dkfz.de/en/angewandte-tumor-immunitaet/Applied-Tumor-Immunity/Applied-Tumor-Immunity-Group.html

#5 Preclinical studies of ABCB5+ human skin-derived stem cells to facilitate liver regeneration during acute on chronic liver disease

Seddik Hammad[1], Matthias Gerstner[2], Lukas Neckermann[1], Pia Erdoesi[1], Matthias Lemmer[1], Toa Lin[1], Riu Liu[1], Matthias Ebert[3,4,5], Andreas Kluth[2], Kathrin Dieter[2], Steven Dooley[1]

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Chronic liver disease (CLD) patients often succumb to acute organ failure triggered by factors like drug or alcohol use on top of their condition. The incidence of acute-on-chronic liver failure (ACLF) is increasing and characterized by high short-term mortality in more than 30% of cases at 28 days after hospitalization (Golden window) as previously reported (Clin Liver Dis (Hoboken); 2019; 14(5): 171–5). Urgent clinical needs for ACLF patients include early detection and therapeutic strategies, yet there is a lack of experimental models for preclinical validation. To address this, we established a mouse model combining a genetically modified liver (Abcb4/Mdr2-/-; 60-65 weeks old) with chemically-induced acute liver failure using CCl4. This novel model replicates key features of human ACLF, including a critical 24h mortality period (Golden window) and extrahepatic organ injury i.e. kidney besides signs of CLD. Single nuclei sequencing of liver identifies a cluster of CXCL2-expressing hepatocytes in poor (short-term mortality) mice only. Enrichment pathway analysis identified JAK-STAT, NF-kappa B, and Glucagon signaling pathways as significantly enriched in these mice. In vitro experiments

demonstrated that supernatants from macrophage-stimulated ABCB5+ stem cells derived from human skin enhance essential hepatic functions like albumin production. Therefore, we are investigating the impact of ABCB5+ stem cells on clinical outcomes and liver regeneration in Abcb4/Mdr2-/- ACLF. Macrophage-stimulatedABCB5+ stem cells or their secretome are being injected intravenously or intraperitoneally in Abcb4/Mdr2-/- ACLF mice, respectively to increase the survival rates. Detailed evaluation will encompass tissue and blood damage parameters, especially in the liver, wound healing, regeneration, and inflammation. This comprehensive analysis aims to uncover the pro-regenerative and hepatic functional capabilities of ABCB5+ stem cells as novel cell therapeutic approaches for ACLF.

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#6 Tumor-derived cDC therapy to prevent relapse and metastasis in NSCLC

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Non-small cell lung cancer (NSCLC) is one of the cancers with the highest incidence and mortality. Novel therapies have improved the survival of these patients, nonetheless, the response rate

remains low and 30-60% of them still develop metastasis, indicating an urgent need for novel therapies.
The last years, we have shown that tumors harbor a heterogenous population of conventional dendritic cells (cDCs). In mice, tumors contain two cDC subsets able to mount an effective anti-tumor immune response. Indeed, prophylactic vaccination with tumor-derived cDCs could confer protection in several cancer models. To mimic a more clinically relevant situation, we inoculated mice with a metastatic NSCLC cell line, isolated cDCs from a surgically removed primary tumor and re-administered these tumor-derived cDC to the same mice.
Before surgically removing the tumor, the mice were treated with a combination of CD40 agonist and Flt3L to increase both cDC numbers and activation. Interestingly, tumor-derived cDC therapy resulted in reduced metastasis and significantly prolonged survival.
Further dissection of the cDC subsets indicated that CD200+ cDC2s are the main responsible for the anti-metastatic effect. Using scRNA-seq and flow cytometry, we have also confirmed the presence of these cDCs in patients with different types of cancer, including NSCLC.
Therefore, we propose a novel strategy whereby patients are treated with Flt3L and CD40 agonist before surgery, after which cDCs are isolated from their resected tumors and used as personalized therapy to induce an anti-tumor memory immune response, resulting in the active prevention of relapse and metastasis formation. Thereto, we aim to further optimize cDC isolation, ensuring quality and safety of the product for use in patients. With this, we take the last hurdles towards initiating a clinical trial to evaluate safety and efficacy of the tumorderived cDC vaccine in NSCLC patients to decrease relapse and increase survival.

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Booth no. 1

ARXUM® is a deep-tech blockchain technology company offering advanced infrastructure and versatile middleware that reduces the complexity of connecting existing IT systems with blockchain-based business logic. This enables highly complex, global and cross-enterprise industrial processes to run across heterogeneous IT systems in a completely transparent, tamper-proof and stable manner.

The solutions offered by ARXUM® are applied in the areas of pharmaceuticals, procurement, logistics, manufacturing and sales. The basis for this is an innovative solution suite based on state-of-the-art blockchain technology and deep industrial know-how.

Trusted by a wide range of organizations, from cutting-edge startups right up to big pharma, our success is founded on purpose-built and future-ready solutions.

Booth no. 2

BioEcho Life Sciences is a specialized solution provider for the extraction and analysis of nucleic acids. We create disruptive technologies, products, and workflows that make downstream processing of nucleic acids easier and faster, significantly increase throughput, and deliver reliable results. Our patented EchoLUTION™ technology enables the fastest DNA and RNA extraction on the market - in just one single step. It reduces the associated plastic consumption by up to 70 %.

BioEcho was founded in 2016 by leading industry experts. The headquarter in Cologne, Germany, is certified according to ISO 9001 and ISO 13485. BioEcho. The Nucleic Acid Experts.

Booth no. 3

BioIVT enables smarter science and accelerates medical breakthroughs by delivering high-quality personalized biospecimen solutions and research services to life science and diagnostic industries. Recognized as an industry leader, we specialize in control and disease state samples including human and animal tissues or preparations, cell and gene therapy products, blood, and other biofluids, as well as ADME contract research services from standalone bioanalytical support through tiered in vitro studies with submission-ready reports to customized consulting. By combining our technical expertise, exceptional customer service, and unmatched access to biological specimens, BioIVT serves the research community as a trusted partner in ELEVATING SCIENCE®.

Booth no. 4

BioLabs - Let's grow together & join the Heidelberg life-science ecosystem. BioLabs is a membership-based network of laboratory and office spaces located in key geographies with proven biotech innovation clusters. BioLabs offers beautifully designed coworking environments that pair fully equipped and supported lab, office, and event spaces with relevant programming and unparalleled access to capital and industry partners.

These fertile, supportive ecosystems allow young companies to shift their focus from start-up operations to experimentation and innovation so they can reach their scientific potential quickly and achieve business success. Companies can start with a single lab bench and scale-up as they grow. BioLabs regards itself as more than just a useful element of infrastructure.

Through its competitive approach, BioLabs generates a forward-looking culture of entrepreneurship, directly promoting the creation of networks and cooperation between regional and international companies and venture capitalists. As such, it is an important facilitator of growth, bridging the gap between biotech research and commercial success.

The expanding BioLabs and Affiliates US network of labs now comprises sites throughout the U.S. and is continuously developing additional domestic and international sites. In 2022 their first European site was opened in Heidelberg (Germany), and further sites in France will follow. BioLabs Heidelberg will be catalyst for growth and entrepreneurship in Germany's Rhine-Main-Neckar area, enabling the development of tomorrow's life-science

technologies. BioLabs Heidelberg will contribute significantly to the goal of bringing together all relevant stakeholders for sound growth in the region, thus providing an additional boost for Heidelberg as a top research location, for the Rhine-Neckar region as a life-sciences industry hub and to the city development in Heidelberg.

Booth no. 5

Founded by research scientists in 1999, Cell Signaling Technology (CST) is a private, family-owned company with over 400 employees worldwide. Active in the field of applied systems biology research, particularly as it relates to cancer, CST understands the importance of using antibodies with high levels of specificity and lot-to-lot consistency. That's why we produce all of our antibodies in house and perform painstaking validations for multiple applications. And the same CST scientists who produce our antibodies also provide technical support for customers, helping them design experiments, troubleshoot, and achieve reliable results.

Booth no. 6

The GxP document management and collaboration platform for pharmaceutical and biotech companies that enables seamless collaboration with third parties With Docuply, we enable pharmaceutical and biotech companies to run smooth and GxP-compliant day-to-day operations with third parties and distributed teams. This way, you avoid chaotic audits and downtime during an inspection. Ultimately, this leaves more time for what matters most: Making the world a little better with new medicines.

Booth no. 7

Genscript is the world's leading biotech company providing life sciences services and products. With gene synthesis, peptide, protein, antibody and preclinical drug development service capabilities, we are providing life sciences services and products to over 200,000 scientists in over 100 countries worldwide. We have four major platforms including

(i) life-science services and products platform to provide one-stop solutions to global research communities,
(ii) a biologics contract development and manufacturing organization (the "CDMO") platform,
(iii) an industrial synthetic products platform, and
(iv) an integrated global cell therapy platform.

With global support from its loyal customers and over 5000 employees located across the globe, GenScript continues to strive towards their vision of being the most reliable biotech company in the world, in service of a better and healthier future.

Booth no. 8

GenScript ProBio, a subsidiary of GenScript Biotech Corporation, offers end-to-end CDMO services from drug discovery to commercialization with proactive strategies, professional solutions and efficient processes in CGT, vaccine and antibody protein drug, aiming to accelerate drug development for customers. GenScript ProBio has established companies in the United States, the Netherlands, South Korea, and China (Hong Kong, Shanghai, and Nanjing) and other regions to serve global customers, and has helped customers in the United States, Europe, Asia Pacific and other regions obtain more than 50 IND approvals since October 2017.
GenScript ProBio's total CGT solution covers CMC of plasmid and virus for IND filing as well as clinical manufacturing and commercial manufacturing. GenScript ProBio's innovative solutions for biologics discovery and development include therapeutic antibody discovery, antibody engineering and antibody characterization. In the biologics CDMO service, GenScript ProBio has built a DNA to GMP material platform, including stable cell line development, host cell commercial license, process development, analytical development to clinical and commercial manufacturing, and offer fed-batch and perfusion processes to meet the growing needs for antibody and protein drugs. GenScript ProBio has established GMP capacity that meets regulatory requirements of the US Food and Drug Administration (FDA), European Medicines Agency (EMA) and National Medical Products Administration (NMPA).

Booth no. 9

Gerresheimer is the global partner for pharmaceutics, biotech and healthcare with a very broad product range for pharmaceutical packaging solutions and drug delivery systems.
The company is an innovative solution provider from concept to delivery of the end product, with 11,000 employees, locations all around the globe and 36 manufacturing sites.
The division Gx Biological Solutions is especially dedicated to leverage the entire organization capabilities to serve its customers, from the lab to the patient
incl. life cycle management and associated services along the journey of clinical phases.
The experts of Gx Biological Solutions are designing the best containment and delivery strategy for successful drug development when related to primary packaging and drug delivery systems. It includes glass and COP platforms (vials & pre-filled syringes), delivery systems (syringes, auto-injectors, on-body devices) and associated services (compatibility, E&L, regulatory, …).
Gx Biological Solutions is the go to partner to increase patient adherence and facilitate your drug development journey from early stage to clinical phases.

Booth no. 10

Heidelberg ImmunoTherapeutics GmbH is a clinical stage biopharmaceutical company focusing on the clinical development of innovative antibody-based immunotherapeutic for the treatment of viral diseases and cancer.
The company was founded as spin-off from the German Cancer Research Center (DKFZ) and Heidelberg University Hospital in 2016. Our goal is to advance novel immunotherapeutic from preclinical research towards early phase I and II clinical trials. The company's lead product, HDIT101, is designed to treat herpes simplex virus infections, which affect millions of people. An initial human study demonstrating the pharmacokinetics, safety and tolerability has been completed. Two phase II studies are currently ongoing in patients with recurrent HSV-2 positive genital herpes and in patients with orolabial HSV-1 infections.

Booth no. 11

MANNHEIM 2
Medical Technology Cluster

Medical technology is an essential and innovative sector within the healthcare industry on which the city of Mannheim has set a focus to support the emergence of new medical products and the establishment and growth of companies. In 2011 the city launched the Mannheim Medical Technology Cluster which supports the networking of companies, startups, clinics, universities and research institutes in the region. The Cluster includes players in all subsectors of the healthcare industry within an hour's drive of Mannheim, aiming to work on the further development of innovation and the ecosystem. The Cluster Office is located on the Mannheim Medical Technology Campus which offers space for young, innovative companies – an area right beside the University Hospital of Mannheim. The strategic planning is managed by the Executive Board, including representatives of the city of Mannheim, as well as managing directors and executives of local and regional medtech companies, the Mannheim Medical Faculty of the University of Heidelberg, Mannheim University of Applied Sciences, the Institute of Medical Technology and the Fraunhofer Institute.

Booth no. 12

Metropolregion
Rhein-Neckar

The Rhine-Neckar metropolitan region with its 2.4 million inhabitants is one of Germany's most vital locations for business. The region ranks highly with its innovative spirit, reputation for academic excellence, a lively cultural scene, attractive options for living and shopping, striking and unspoiled natural resources and the can-do attitude of its local citizens. It is home to global businesses such as BASF, SAP and Bilfinger, along with SMEs and start-ups. In fact, the Rhine-Neckar triangle is a hot spot for business incubators; there are 15 such centres in the greater Heidelberg, Mannheim and Ludwigshafen areas alone. The core areas of industry for the region include biotech, IT, chemicals, automotive, mechanical engineering and systems engineering, plus a vital cultural and creative economy. An excellent local infrastructure combined with its location at the heart of Europe ensure the region enjoys optimum connections to networks of all kinds. Its huge capacity for innovation is built on a high level of education; Rhine-Neckar is among the top locations when it comes to highly qualified workers, and 16.7% of employees work in high-tech industries. The 22 universities and some 30 internationally renowned research institutes in the region maintain close contact with industry and thereby ensure broad transfer of knowledge.

Booth no. 13

BIMOVIS is an innovative startup with the ambition to make structural biology accessible to small and medium sized companies.

Large companies often have a separate department for structural biology providing expertise for drug design, protein engineering, development of analytical methods, interpretation of special publications and marketing. For startups and SMEs, it is usually not economical to employ structural biologists and bioinformaticians, which represents a clear competitive disadvantage.

With BIMOVIS, we aim to close this gap and help companies utilize structural biology depending on the available resources. In addition to consultation and project coordination, we support our clients with tailor made training and courses to acquire internal expertise in the field of structural biology. Thus, our customers become increasingly independent in structural biology and ultimately more professional in protein science.

Booth no. 14

PROGEN was founded in 1983 by four scientists from Heidelberg, Germany, who joined forces to manufacture and supply high quality antibodies for biomedical research.

We help scientists worldwide drive biopharmaceutical and diagnostic progress to provide high-quality and reliable treatments for patients. Our mission is to make new therapies safe and affordable and to improve existing research processes.

The PROGEN team consists of bioscientists and adeno-associated virus (AAV) experts who collaborate with specialists around the world. Our products are essentials for research in science and industry.

We are more than just a manufacturer of antibodies, AAV gene therapy tools, density gradient media, and phage display technologies: We strive to understand the needs of scientists to develop solutions to jointly address challenges in academic research, biotechnology and pharma.

Booth no. 15

With a portfolio of more than 4,000 products covering the fields of genomics, protein analysis and expression, cellular analysis, drug discovery and genetic identity, Promega is a global leader in providing innovative solutions and technical support to life scientists in academic, industrial and government settings. Promega products are used by life scientists who are asking fundamental questions about biological processes as well as by scientists who are applying scientific knowledge to diagnose and treat diseases, discover new therapeutics, and use genetics and DNA testing for human identification. Since its founding in 1978, Promega has consistently integrated the values of corporate responsibility and sustainable business practices into all aspects of its corporate culture and activity. Promega realizes that its success depends upon the connections the company forges among its customers, community and employees. Since 1997 and with about 100 employees, Promega GmbH, as a subsidiary of the Promega Corp. is responsible for the distribution of Promega products in Germany, Austria, Poland and Eastern Europe.

Booth no. 16

ProtaGene CGT GmbH (former GeneWerk GmbH) is part of the world-leading analytic CRO ProtaGene which is partner for the biopharmaceutical and cell and gene therapy industries. As pioneers and industry leaders, we are setting the standards for vector safety and integration site analysis in preclinical and clinical development of gene therapies. Our strong bioinformatics as well as research and development capabilities complement the portfolio needed by our clients. GeneWerk's founders were leading experts in the field and involved in the safety assessment of many cell and gene therapy drug products, including Glybera®, the first gene therapy drug product approved in the western countries for treating Lipoprotein Lipase Deficient (LPLD). For more than 20 years, the team has worked alongside clients around the world and from research through product commercialization to develop novel cell and gene therapies that meet regulatory safety requirements. Our clients rely on our deep scientific, technical and regulatory expertise to de-risk their cell and gene therapy development pathway. As a credible partner with proven expertise in the field, we function as an extension to the client's internal teams to bring breakthrough therapies in development to market authorization.

Booth no. 17

SCHOTT Pharma designs solutions grounded in science to ensure that medications are safe and easy to use for people around the world – because human health matters. The portfolio comprises drug containment and delivery solutions for injectable drugs ranging from prefillable glass and polymer syringes to cartridges, vials, and ampoules. Every day, a team of around 4,700 people from over 65 nations works at SCHOTT Pharma to contribute to global healthcare. The company is represented in all main pharmaceutical hubs with 16 manufacturing sites in Europe, North and South America, and Asia. With over 1,000 patents and technologies developed in-house, a state-of-the-art R&D center in Switzerland, and around 130 employees in R&D, the company is focused on developing innovations for the future. SCHOTT Pharma AG & Co. KGaA, headquartered in Mainz, Germany, is part of SCHOTT AG that is owned by the Carl Zeiss Foundation. In light of this spirit, SCHOTT Pharma is committed to sustainable development for society and the environment and has the strategic goal of becoming climate-neutral by 2030.

Booth no. 18

Access to cutting-edge technology is key in modern life science to accelerate scientific discoveries. VIB Technologies has a unique approach which provides its research community a competitive advantage by offering access to state-of-the art technologies.
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Booth no. 19

YUMAB develops fully human antibodies from target to lead for clients and partners worldwide.

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Smoothie Bike

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About the Organiser

BioRN is a science and industry innovation cluster with a unique combination of all relevant innovation stakeholders in the Life Sciences around Heidelberg at the border between Baden-Württemberg, Rhineland-Palatinate and Hesse, and connected by the rivers Rhein, Main and Neckar.

BioRN is a non-profit network counting more than 140 members. It includes top universities, research institutions and Technology Parks. Ten global pharmaceutical companies have R&D sites or are active in the BioRN network. The ecosystem is completed by a large range of small and medium-sized enterprises as well as local government organizations and interest groups.

With the vision to make life science matter and innovation happen, the cluster management established a clear strategy to become the leading European life science cluster, attracting global investment and talent.

BioRN Cluster management establishes initiatives to nurture and extend networks, stands for the promotion and visibility of the Life Science region and fosters connections to other regions of innovation worldwide. BioRN initiates and manages different programmes to support the development of (academic) research ideas through all necessary development stages. BioRN recently supported the establishment of the Evotec's BRIDGE beLAB2122, a new public-private partnership to fund and execute novel disease modifying therapeutic projects in the region. BioRN is also initiator, project manager and Founding Partner of Biolabs Heidelberg, part of the global BioLabs network of co-working space for startups.

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We strongly encourage the use of social media in and around the conference.

Follow the conference on LinkedIn and Twitter (@BioRNCluster) and use the hashtag **#BioRNConference** 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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Notes

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