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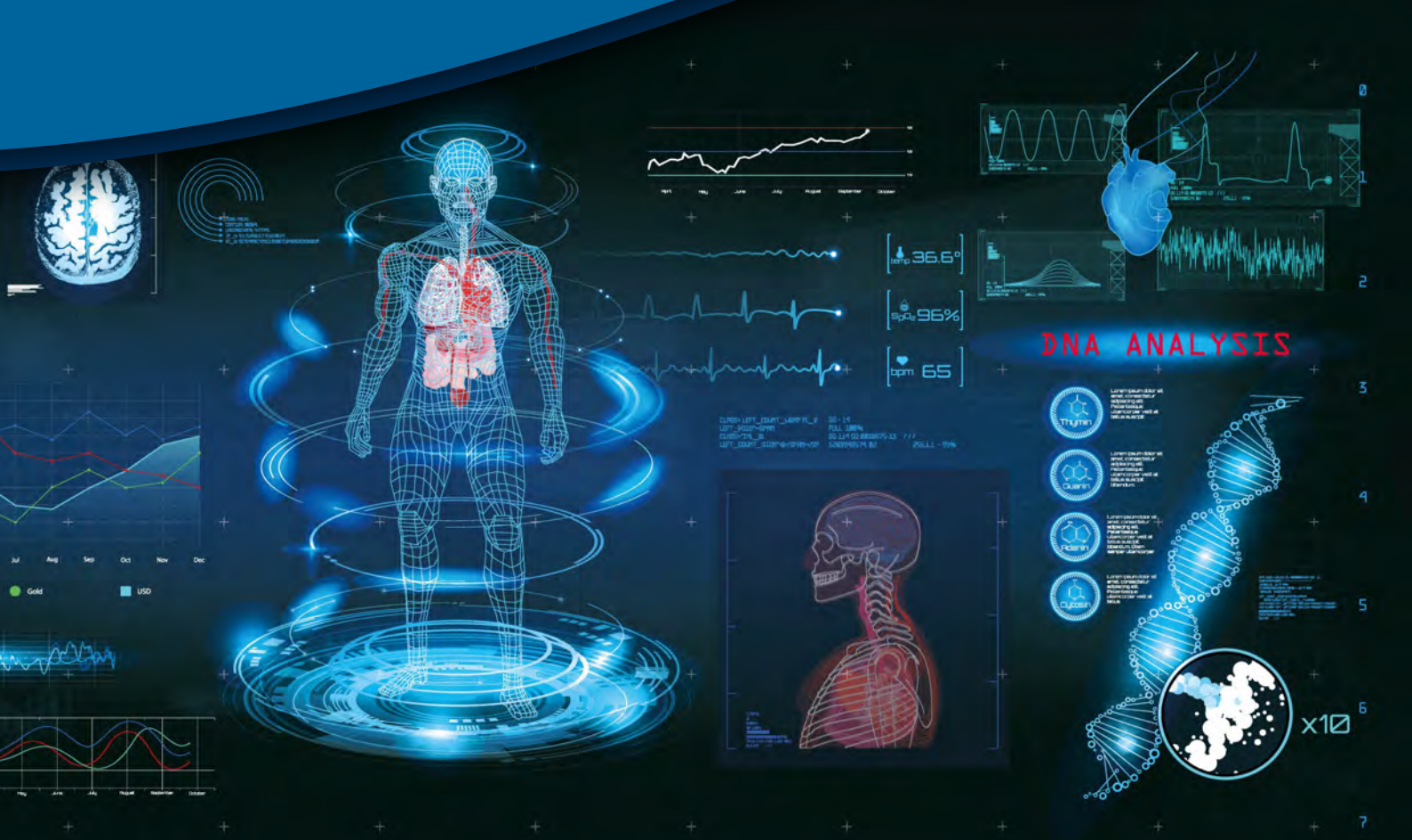

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is dedicated to finding solutions for today's most important challenges in health care focusing on Digital Health and Systems Medicine, two young disciplines that are considered to form the medicine of the future. The key is the combination of laboratory research data of different kinds with real-world data – from bench to bed-site. Innovative technologies and methods will pave the way for more precise predictions and personalised therapy. Already today, this approach is successfully used in Oncology and will be extended to other diseases in the future. Here, the establishment of robust and standardized IT infrastructure plays a major role to allow for the secure exchange of patient data with research teams. Read the magazine gesundhyte.de to find out how this innovative branch of science works to provide solutions for our current and future challenges in medicine.

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Greetings

Dear Readers,

Imagine yourself going to the doctor a few years from now. While you're talking to your doctor, speech recognition software records your acute symptoms and enters them into your medical file. At the same time, the AI-based programme analyses previous entries as well as the most recent health data from your smartwatch and compares relevant information with the latest medical publications. This enables an entirely new level of data analysis. Finally, the software proposes more specific diagnostic tests or creates a personalized treatment plan. It provides your doctor with comprehensive support, enabling them to make smarter decisions and use more streamlined processes that save resources.

More digital technology, better personalization and more targeted prevention – these three major trends will lift health care to an unprecedented level of quality.

At the Federal Ministry of Research, Technology and Space, we have launched various initiatives to support this development in the long-term. We fund, for example, the development of AI models for predicting cancer progression in individuals and designing tailored treatments. Reliable data is the most important prerequisite for developing such AI-based tools for medical practice. Making health data available across institutions and locations is a central objective of the Medical Informatics Initiative. To this end, the initiative will establish medical data integration centres in cooperation with the Network of University Medicine, enabling the development of innovative software solutions for databased health research.

This edition of gesundhyte.de looks to the future of medicine – a future where we can redefine the way in which we understand, treat and prevent disease.

I hope you enjoy an interesting read.

Prof. Dr. Veronika von Messling
Director-General Life Sciences
Federal Ministry of Research, Technology and Space

Photo: Prof. Dr. Veronika von Messling

Greetings

Dear Readers,

With over 100 departments and institutes, Charité is the largest university hospital in Europe. Like many other players in the healthcare sector, we are facing a number of challenges that need to be solved in the coming years. One of the most pressing issues is how the healthcare system will respond to demographic change – the ageing of the population. This has a significant impact on hospital operations as the so-called baby boomers retire from the labor market aggravating the already existing shortage of skilled workers. At the same time, the number of patients is increasing.

Demographic change and the associated social change present us with major challenges that require structural adjustments to hospital and research operations from both an economic and ecological perspective. We are convinced that prevention, innovation and digitalization are crucial to successfully overcoming these problems and securing healthcare for the future. In this issue of gesundhyte.de, we would like to give you an outlook on the urgently needed changes in the German healthcare system under the theme *"Health in transition!"*.

A key requirement for the medicine of tomorrow is the close integration of research and clinical medicine. Charité's Strategy 2030 *"Rethinking Health"* aims to achieve this. In particular, the use of artificial intelligence, and its application for health data, offers the potential to meet the upcoming structural change in prevention and care as well as in the development of new therapeutic approaches.

I would like to invite you to embark on a journey through the diverse and dynamic world of health research. Let's explore solutions for current and future challenges together.

Yours sincerely,

Prof. Dr. Heyo K. Kroemer
Chief Executive Officer of Charité – Universitätsmedizin Berlin

Photo: Wiebke Peitz / Charité

Foreword

Dear Readers,

"It is not said that things will get better if they are different. But if things are to get better, they have to change."

This saying by Georg Christoph Lichtenberg (1742-1799), aphorist and physicist who taught in Göttingen, arose from the story that an old, somewhat rickety catheder in one of the lecture theatres had been replaced by a new, more stylish model. When Lichtenberg saw the new catheder for the first time, he examined it closely, sat down, knocked on it and then said dryly to his students: *"Well, gentlemen, the catheter has changed, but whether it is better remains to be seen."*

His saying reminds us that not every innovation leads to progress, but that real progress is impossible without change. This also applies to modern healthcare research, which is undergoing rapid change. In just a few years, the interplay of sheer endless amounts of data from healthcare and research with modern artificial intelligence methods has completely turned healthcare research on its head.

Just because something is new and different does not automatically mean that it is better. It depends on whether the change actually represents an improvement. The focus of this issue, *"Health in transition!"*, promises exciting and compelling insights into the colourful new world of data-driven health research, which has been further fuelled by the rapid developments in artificial intelligence. We can marvel at how AI is driving the development of medicines, enabling the international exchange of algorithms and helping to increase the diversity of health data collections.

I hope you enjoy reading the 16th issue of gesundhyte.de and wish you many exciting moments.

Yours sincerely,

Prof. Dr. Roland Eils
Editor in Chief gesundhyte.de

Photo: Sebastian Runge

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Can AI help us develop new drugs?

A view from the structural biology perspective

by Gregor Popowicz

AI is changing every aspect of life in a way that can only be compared to the internet revolution. Despite fears and ethical concerns, the technology continues to evolve and amaze us with new capabilities on an almost daily basis. To our surprise, we have yet to see an AI breakthrough in the discovery of new drugs. The complexity of developing a new drug seems to be beyond AI's capabilities so far. But will it stay that way? Or are we on the verge of AI discovering new drugs for previously incurable diseases?

The world needs new medicines, and it needs them faster. There are still serious incurable diseases in developing countries, and in highly developed countries the problems of drug resistance are becoming increasingly serious and life-threatening. Climate change is leading to an increased spread of tropical diseases around the world. Nevertheless, only around 50 new drugs have been approved each year over the last ten years. At the same time, the cost of developing drugs is exploding, amounting to between 1 and 3 billion US dollars. This is mainly due to the cost of failed projects.

There is no doubt that this situation is far from ideal. Various means of improving this appalling situation are being proposed and implemented. Great hopes are pinned on the introduction of computer-assisted methods in drug research. Computer simulation of the effects of drugs in the body costs only a tiny fraction of the actual trial costs, does not require a wet laboratory and does not involve complex administrative overheads for chemical and biological safety, ethics and laboratory management. The increasing use of computational methods in drug discovery therefore offers the opportunity to lower the cost and barrier to entry into drug research, thereby democratizing the process and allowing more than just financially and administratively privileged players to participate. In addition, all stakeholders can engage in riskier strategies, as they lose fewer resources if the project fails.

Target- or phenotype-based development?

There are two very different approaches to drug discovery. In the phenotypic approach, the behavior of a biological disease model system is observed: Cells, tissues, organoids, *ex-vivo* or *in-vivo* models. The exact molecular target is usually of secondary importance as long as the observed phenotype is desired. In contrast, the target-based approach utilizes the known mechanistic function of a particular molecular target to focus drug discovery. An excellent example is the dysregulated Bcr-Abl kinase protein, which causes chronic myeloid leukemia. Targeted inhibition of Bcr-Abl by a small molecule inhibitor such as imatinib (Gleevec; Figure 1) led to a complete hematologic response in 98% of patients in a five-year study (Kurzrock *et.al.,* 2003). While phenotypic development has produced more approved drugs in the past, target-based development is becoming increasingly popular.

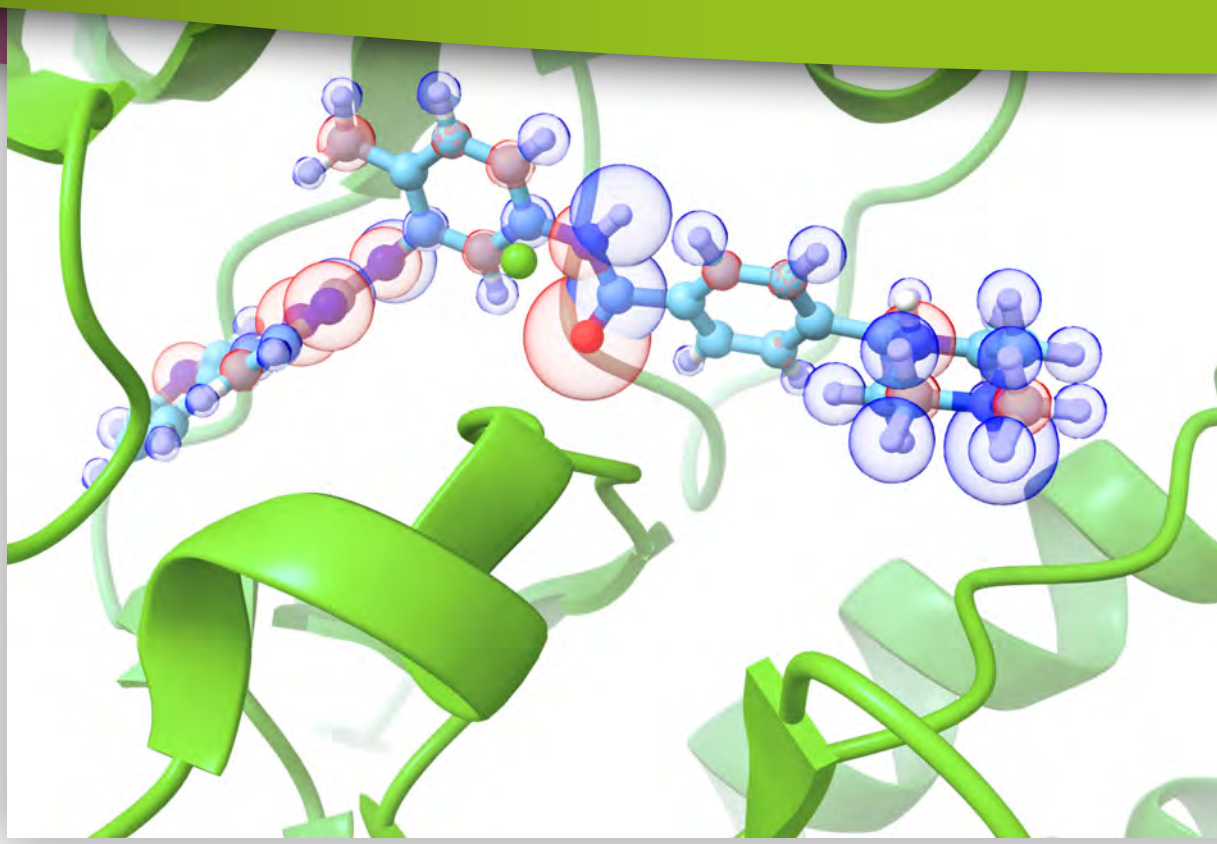
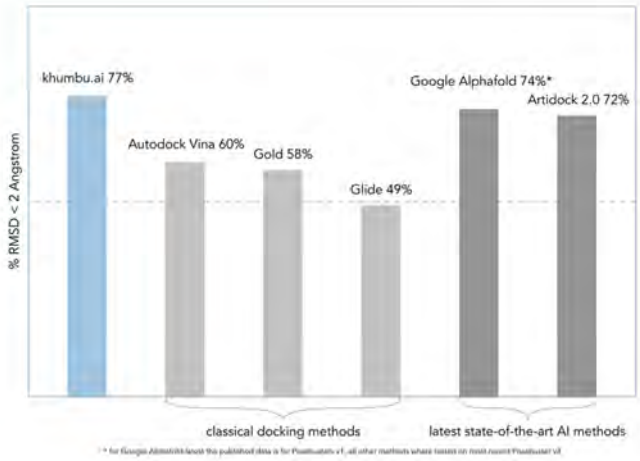


Figure 1: The molecular structure of imatinib (Gleevec) bound to its biological target – an abnormal, oncogenic kinase Bcr-Abl. The transparent spheres show the partial interaction energy calculated using quantum chemistry (red – repulsive, blue – attractive). Despite the precision of the interaction model at the atomic level, its dynamic behavior cannot be modeled completely and with sufficient accuracy using classical methods (Source: Grzegorz Popowicz).

The target-based approach usually involves the structural biology of the molecules under investigation. Here, the three-dimensional structure of the biomolecule is investigated together with the drug candidates using biophysical means. Ideally, it is possible to obtain an atomically resolved structure that explains all interactions between the biomolecular target and the drug. Of course, one would expect that with such precise structural information, the development of a new molecule would be a simple task. If you know the exact structure of a lock, it should be easy to design a key. However, the binding between drug and biomolecule is a complex, dynamic phenomenon that requires interpretation at the quantum level to obtain meaningful results. Due to the dynamic nature of the interaction, changes caused by the binding partner and experimental artifacts, our understanding of drug-biomolecule binding is not precise enough to be fully relied upon for drug discovery.

Quantum physics as a saviour in times of need

Early computer models applied Newtonian physics and treated the molecular forces as a series of springs that push the atoms in different dimensions (force fields). Although this approach makes it possible to analyse the dynamics of large biomolecular systems, it only provides a very rough picture of intermolecular interactions. The next level of precision is to analyse the electron-electron interactions within the system, which generally provides an approximate solution to the differential Schrödinger equation. The quantum approach for a highly dynamic system with many parameters is therefore computationally intensive and prone to misinterpretation. All these factors limit the usefulness of structural data in drug discovery. While structure shows medicinal chemists how to avoid obvious mistakes in the development of a drug, it offers little rational guidance for its improvement.



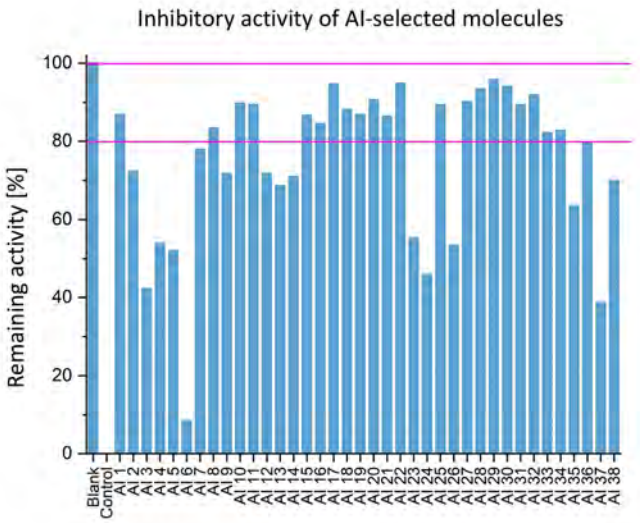


Figure 2: Accuracy of the prediction of drug biomolecule binding. (above) AI technologies developed by the consortium of Helmholtz Munich and Khumbu.AI GmbH, enable greater precision than conventional software tools.
(bottom) Results of the AI screening were tested experimentally. Almost all AI-selected compounds reduce the activity of a target biomolecule. (Source: Grzegorz Popowicz/Khumbu.AI GmbH).

Here, AI-based solutions offer the opportunity to overcome these problems and significantly improve the effectiveness of drug discovery. It has been shown that a properly constructed AI model can "understand" the physics of a system and reduce it to a minimal set of parameters required to describe it (Chen *et.al.,* 2022). The success of protein structure prediction by systems such as AlfaFold2 is impressive. Although they can predict the binding of small molecules, the accuracy is still below the requirements of drug discovery (Figure 2).

Our contribution to drug discovery

At Helmholtz Munich, we have carried out a number of projects to improve the accuracy of computational tools for drug discovery. The BMBF-funded SURPREME project is based on Target Preference Mapping (TPM) technology, which has already been patented by our team. In principle, we use AI models to predict what the biomolecular receptor "wants". Instead of predicting the interaction mode and energy, we "ask" the biomolecule what it wants. This approach works very well for rigid targets such as the antitumor kinase BcrAbl, but there is room for improvement. In particular, the dynamic character of the receptor still needs to be taken into account.

SURPREME aims to develop new cancer therapeutics using AI methods. With a good understanding of the dynamics of the target and the electronic properties of the ligands, we can now move on to obtaining and testing actual molecules for our targets. Preliminary results show that the molecules selected by AI screening are active against a target kinase, but not against structurally similar kinases that were not targeted. We can therefore assume that we will not only achieve a high screening success, but also be able to solve selectivity problems.

Our results in the use of AI-TPM technology have already been licensed out to Khumbu.AI GmbH. This has led to the development of virtual screening software that by far outperforms all benchmark products, including AlfaFold2, in terms of accuracy and speed. The company also has several drug candidates in the internal pipeline.

To train a new generation of AI models for drug discovery, we have established a public training archive called MISATO (Molecular Interactions Structurally Optimized, Figure 3). This dataset contains molecular dynamics data for nearly 20,000 biomolecules and a complete quantum

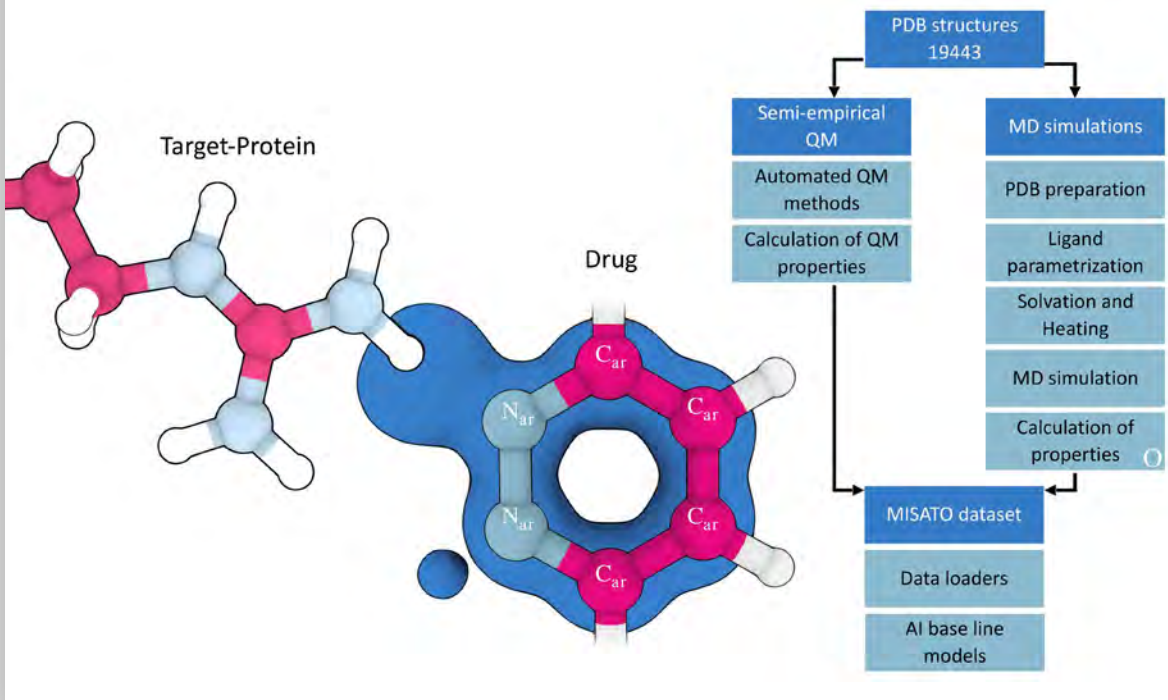


Figure 3: The concept of the MISATO dataset. The biomolecule (left) is represented by an atomistic, dynamic model. The drug molecule is represented by its full electronic representation derived from quantum chemical calculations. The complete curation and provision of the dataset is optimized for easy access (Source: Grzegorz Popowicz).

chemical characterization of their corresponding small molecule inhibitors. We have concluded that the architecture of biomolecules consisting of only a few building blocks (amino acids, nucleotides), can be successfully captured by AI models at the atomic level. The extremely diverse architecture of small molecules, on the other hand, requires a complete electronic (quantum chemical) description. This data is now available to AI developers with just two lines of code. The development of MISATO was published in the renowned Nature Computational Sciences Journal (Siebenmorgen *et.al.,* 2024). The development of the dataset was driven forward as a community project. It gathered an active team of AI experts and enthusiasts from all over the world. To capitalize on this momentum, we received a separate BMBF funding as part of the DATIpilot program.

In the next steps, we will integrate fragment screening and de novo ligand generation into our AI system. Fragments are much smaller than drug-like molecules. The limited mass means that combinatorial diversity is lower. Fragments are also freer to adapt their shape and orientation to the target biomolecule. Nevertheless, it is not easy to develop a fragment into an effective drug-like molecule. This is usually due to the fact that it is difficult to obtain structural information for a weakly binding fragment. The AI system we have developed is particularly accurate in determining the pose of the bound fragment.

With an accurate prediction of target "wishes" and fragment poses, we can attempt to create a generative AI model that will provide us with new chemical molecules as drug candidates.

Conclusion

The AI revolution is still in its infancy. While enormous progress has been made in the processing and generation of natural language and image data as well as in the prediction of biomolecular structures, the world is still waiting for the first AI-generated drugs. The development of such models is not trivial. We have found that one of the limiting steps is the availability of

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(Photo: AdobeStock Green Creator).

curated, heuristically augmented interaction data and have developed MISATO to mitigate this problem. At the same time, the biomolecule-drug interaction models already exceed the accuracy of conventional calculations. We hope that with some further improvements we will be able to develop a fully computational drug discovery pipeline whose accuracy and success rate outperforms the experimental approach.

Research project in brief:

SURPREME – Superfine structure and fragment-based inhibitor design

The project has been funded by the Federal Ministry of Education and Research (BMBF) from 2021 to 2024 as part of the CompLS funding program.

SURPREME focuses on the development of new, AI-based software for analyzing and predicting biomolecule-drug interactions. This forms a starting point for the development of new drugs.

www.gesundheitsforschung-bmbf.de/de/surpreme-superfeine-struktur-und-fragment-basierte-inhibitor-gestaltung-13651.php

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Contact:

Dr. Gregor Popowicz
Structure-based Drug Discovery Group
Helmholtz Munich
grzegorz.popowicz@helmholtz-munich.de

www.helmholtz-munich.de/en/stb/research-groups/popowicz-lab

Photo: Popowicz: privat

AI for drug development

Applications, potentials and challenges

by Klemens Budde, Jean-Enno Charton, Björn Eskofier, Dagmar Krefting, Maren Lang, Wolfgang Nejdl, Matthieu-P. Schapranow and Thomas Zahn

Drug development is complex and time-consuming: It often takes more than a decade from inception to market launch, with average development costs of around 2.8 billion US dollars. This process can be made more efficient through the use of artificial intelligence (AI), saving years of work and costly investments. Examples of applications include systematic analyses in the identification of suitable drug candidates or the performance of clinical trials. The article outlines the prerequisites for the use of AI in drug development, emerging potentials, but also current challenges.

Challenges in drug development

Drugs are indispensable for modern medical care; in Germany, an average of one drug is prescribed for every visit to the doctor. Since the 1950s, however, there has been a clear trend in drug development: The development of new drugs is becoming increasingly expensive. On average, development costs of around 2.8 billion US dollars (approx. 2.7 billion euros) are incurred for each new drug; this also includes the costs for a large number of drug candidates that do not make it onto the market. In contrast to Moore's Law, productivity in the field of drug development is now halved every five years, which is referred to as Eroom's Law (Scannell *et al.*, 2012).

The reasons for this include the increasing complexity of products and study designs, the increasing requirements for documentation and safety during development and the recruitment of participants for clinical trials.

In addition to the economic challenges for companies in the pharmaceutical and biotechnology sector, this also creates disadvantages for patients. Cost pressure means that development focuses primarily on supposedly highly profitable diseases. Rare diseases that only affect relatively few people in a population are less economically attractive. In Germany, cancer and immunological diseases accounted for almost 50 percent of clinical trials for testing new drugs in 2021.

The use of artificial intelligence (AI) is now also becoming increasingly widespread in the pharmaceutical industry in order to overcome such challenges. This is due to the numerous technological developments in this area, especially since 2017. According to a survey, almost one in four pharmaceutical companies uses AI in drug development (Schulte, 2022). An analysis also shows that, depending on the available prior knowledge regarding the development goal, time and financial savings of 25 to 50 percent are possible in drug development through AI (BCG, 2023).

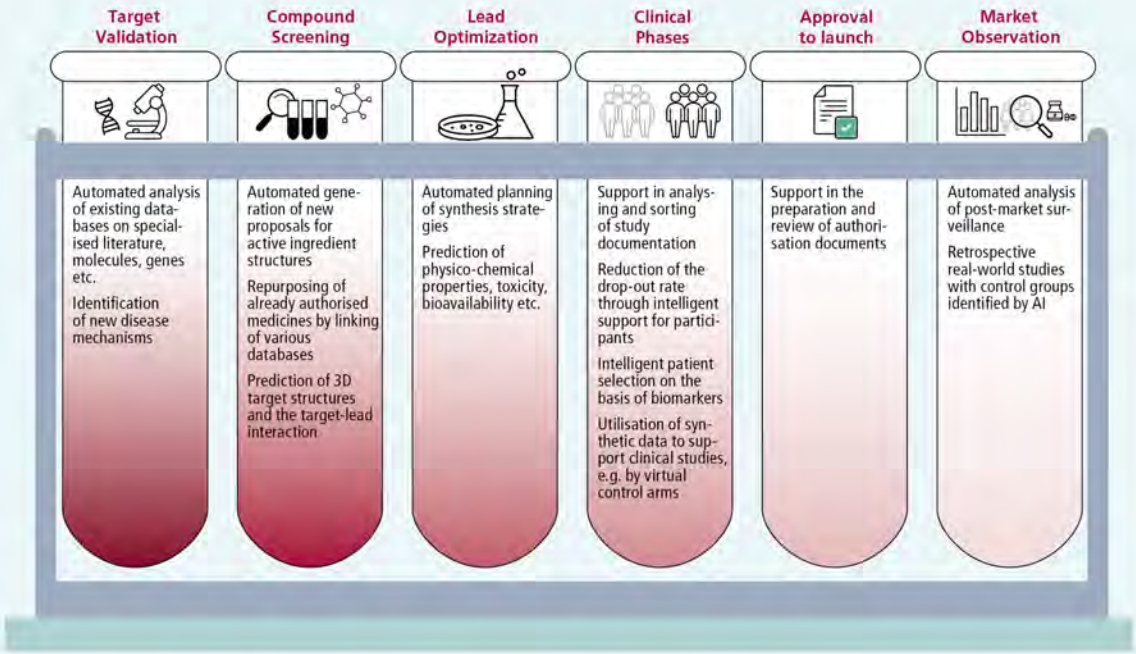


Figure 1: Possible applications of AI in the individual phases of drug development.
(Source: Budde, K. *et al.*, 2024).

Starting points for AI in drug development

Drug development takes place in the following phases: From a large pool of potential drug candidates and their combinations, the selection is narrowed down further and further during the process until finally a specific drug or combination of drugs receives marketing approval. Based on the identification of the drug target for influencing the course of the disease, various drug candidates are tested for their efficacy (screening) and their structure is optimized in terms of the pharmacological properties. In the clinical phases, the dosage and efficacy of the drug as well as possible side effects during administration are investigated. This is followed by approval and market observation with regard to drug safety. The use of AI can generate added value in all phases (DPI, 2022) (see Figure 1).

The many possible applications of AI in the field of drug development are illustrated below using three specific examples. The AlphaFold software developed by DeepMind, including its successor AlphaFold2, enables the AI-based prediction of protein structures within a few hours and with high accuracy; knowledge of these structures is essential as target structures for the development of drugs. To achieve comparable accuracy and resolution, these structures previously had to be researched experimentally, sometimes over months. The biotechnology company Insilico Medicine from the USA was able to develop a drug candidate against fibrosis to the preclinical phase with AI support for less than 850,000 US dollars, compared to average costs of around 664 million US dollars in conventional development. The pharmaceutical tech company Standigm from South Korea has developed an AI-based platform for the identification of drugs with new mechanisms of action, which enables the identification of these structures within an average of seven months compared to an average of 30 months in conventional development (DPI, 2022).

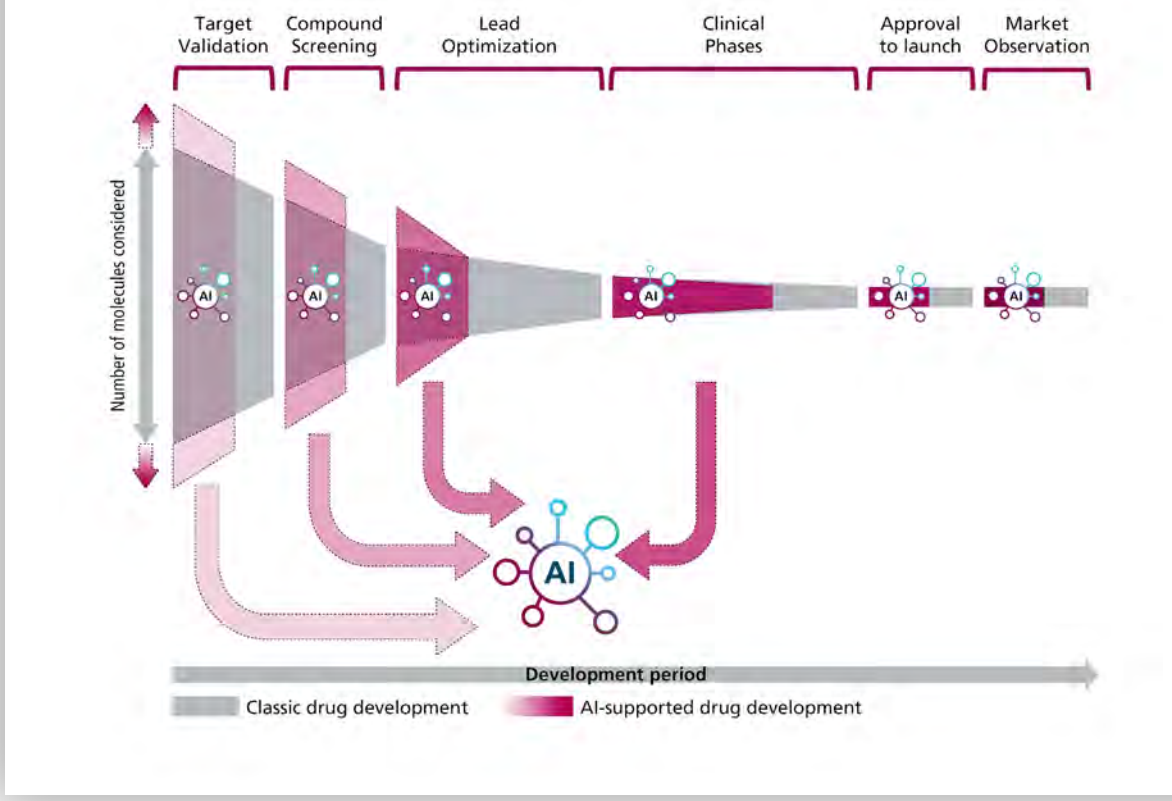


Figure 2: Schematic representation of the advantages of using AI in drug development across all development phases: shorter development phases, more easily accessible molecules and the utilization of all generated data to train the AI. (Source: Budde, K. *et al.*, 2024).

Figure 2 shows the advantages of using AI in drug development. In principle, the use of AI in the early development phases allows significantly more molecules to be analyzed, both in terms of targets and potential drug candidates. To date, only just under 700 usable targets have been identified for drug development in humans, while more than 10,000 disease-relevant proteins can potentially be influenced by drugs based on AI-supported predictions. In terms of potential drug structures, the traditional screening libraries in pharmaceutical companies contain only a few million compounds, while AI can sometimes access data on several hundred million compounds for development and virtual screening libraries can even contain several billion compounds. However, it should be borne in mind that some of these compounds are not as comprehensively characterized as in real libraries.

Besides to the additional accessible molecules, the use of AI enables significantly more efficient and potentially faster drug development. This applies to all development phases, as many time-consuming and labor-intensive steps in the laboratory can be simulated *in silico* in advance or at least partially supported in the future.

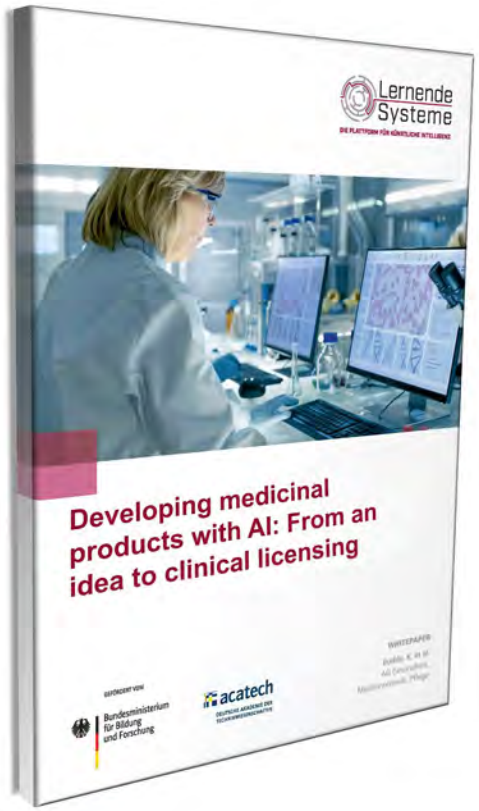
In conventional drug development, a single authorised drug is created from an average of 10,000 compounds at the beginning of the development process. However, important data is also collected on the remaining compounds that do not meet the development criteria and are therefore not pursued further in development. By integrating AI into the development process, the data from these compounds could also be used to improve the model by expanding the database for training.

Potential and challenges

The use of AI in drug development creates new challenges, but also potential in terms of economic implementation, the necessary data availability and the associated regulatory framework.

For companies, there are opportunities for new business models and the development of a digital ecosystem for collaborative data use, provided there is a willingness and ability to share data without compromising the competitiveness of companies. The exchange of metadata could represent a middle way here, for example by not sharing the actual structures of the respective active ingredients, but only the chemical differences between molecules.

Drug development with AI benefits above all from the increased availability of data on human biology, i.e. patient data. Sensitive data in particular, e.g. from genome analyses, form the basis for personalized therapy approaches. However, this also requires a willingness of the population to share data, particularly with industry.



In terms of regulation, the use of AI in drug development potentially leads to more applications and increased costs due to faster development cycles. However, AI can also be used by the authorities themselves to speed up review processes or make approval procedures more dynamic.

Outlook: Promotion of data availability and further development of the regulatory framework

To leverage the potential of AI in drug development, there are various starting points in the area of data availability for research and development and in relation to the regulatory framework for drug approval. Data availability could be promoted through expanded data exchange both between authorities and companies (e.g. the data transmitted to the BfArM in Phase IV) and between companies (e.g. sharing data from placebo groups in clinical trials). Further starting points for increasing data availability include making genome data available for research or the utilization of healthcare data collected after the approval of drugs, so-called Real World Evidence (RWE). However, uniform internationally recognized data formats and standards for the collection of this data as well as ontologies for the harmonization of data from different healthcare systems and countries must be used to ensure interoperability and international connectivity. In general, though, it is important to avoid bias in the database when using patient data,

This article was written on the basis of the white paper **Developing medicinal products with AI: From an idea to clinical licensing.** Munich, 2024. It was created by members of the working group Health, Medical Technology, Care of the Learning Systems Platform. https://doi.org/10.48669/pls_2024-1 (Source: Budde, K. *et al.*, 2024).

as this can potentially be replicated by AI. This requires specific details on the database used for an AI model, guidelines for the use of AI models and the further development of methods to detect bias.

The regulatory framework in the context of medicinal products should be further developed with a view to equal consideration and legally secure utilization of the results from AI-supported drug development, e.g. with regard to the use of smaller study groups based on intelligent patient selection or AI-based identification of surrogate parameters as clinical endpoints.

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Contact:

Prof. Dr. med. Klemens Budde
is Co-Head of the Working Group on Health Care, Medical Technology, Care of Plattform Lernende Systeme and Deputy Medical Director of the Medical Department, Division of Nephrology and Internal Intensive Care Medicine at Charité – Universitätsmedizin Berlin.

klemens.budde@charite.de

https://nephrologie-intensivmedizin.charite.de/metas/person/person/address_detail/prof_dr_med_klemens_budde/

Photo: Wiebke Peitz

Federal Ministry
of Research, Technology
and Space

News from the BMFTR

Dangerous brain tumours – computer model determines individual risk of relapse

Glioblastoma is the most common type of malignant brain tumour. In Germany, around 4,800 people are diagnosed every year. The tumour often grows unnoticed over a long period of time; by the time the first symptoms such as visual disturbances or epileptic seizures appear, the glioblastoma may already have reached a diameter of several centimetres. Once diagnosed, the first step is to remove the brain tumour surgically, if its location allows. This is followed by radiotherapy and chemotherapy. Despite this intensive initial treatment, the life expectancy of affected people is less than two years. In many cases, the tumour even returns within the first year after the surgery. An international research team with partner institutions from Germany, Luxembourg, France and Italy is developing a computer model to predict the individual risk of relapse for each patient so that countermeasures can be taken more quickly. The Federal Ministry of Research, Technology and Space (BMFTR) is supporting the project as part of the European ERACoSysMed funding measure.

There are several reasons why the treatment of glioblastomas is so difficult. Chemotherapeutic agents often do not respond equally well to all cells of the tumour, as they are very variable and therefore sometimes very resistant. As a result, the treatment does not always reach all areas of the brain tumour. This is similar to the effect of radiotherapy, to which the tumour cells can also react differently. In addition, individual cells in the peripheral area of glioblastomas also spread to the surrounding, still healthy tissue. If glioblastomas are located in regions of the brain that are particularly important for brain function, these extensions of the tumour cannot be completely removed during surgery.

Cells at the edge of the tumour are crucial for disease progression

In general, surgeons cannot remove the same wide margin of safety as they can in other parts of the body. This is because it is important not only to remove the tumour but also to avoid further damaging the brain. “Despite optimized surgical procedures, a small margin is almost inevitably left, which the tumour could use as a starting point to invade the rest of the tissue,” explains project coordinator Dr. Peter Raab from the Hannover Medical School. The neuroradiologist and his colleagues in the international research team are therefore particularly interested in the behavior of the glioblastoma cells at the edge of the tumor. “Because this can be decisive for the further behavior of the tumour,” says Raab. “The more precisely we can make a prognosis for this, the more accurately the aftercare can be adapted and treatment planning optimized.”

In order to predict the behavior of tumour cells as accurately as possible, the researchers used new computer-based methods to analyze and evaluate different data from patients.

The scientists “fed” and trained a computer model with these large amounts of data, including from cross-sectional images of the tumor and informa-

Glioblastomas occur in all regions of the brain. This often makes surgery difficult, as it may affect important brain functions.

Image credit: Adobe Stock/Gorodenkoff

tion from histological examinations of the tissue from the edge of the tumour. In doing so, they benefited from the interdisciplinary collaboration between separate biomedical disciplines and with experts from mathematics and bioinformatics.

Optimize the timing of therapy

Is there a risk that the tumour will grow back in the same place? Has the glioblastoma already spread to the surrounding tissue? In the future, the data-driven model will be able to answer these and other key questions for each individual patient during the aftercare, thus enabling individual risk assessments for the further course of the disease. “This newly acquired knowledge will make a significant contribution to improving future treatment decisions and optimizing the timing of aftercare examinations, further operations and the use of radiotherapy and chemotherapy,” says Raab. The analysis tool could soon be used in the participating medical centers in Hanover and Luxembourg. In a few years, the researchers hope that the new approach will also be widely used in clinical practice. In the meantime, they will continue to improve the model on the basis of further data sets.

However, further perspectives are already opening up. As part of the project, the research team also investigated the interaction of the tumour cells with the immune cells in the brain. “We have found evidence that certain immune cells in the brain can partially promote tumour growth,” explains Professor Dr. Friedrich Feuerhake from the Institute of Neuropathology at the Hannover Medical School. “If these assumptions are confirmed, it could open up completely new approaches to the treatment of glioblastoma. For example, it would be possible to use new types of drugs that target the immune system in order to indirectly slow down the spread and growth of the tumour.”

Further information can be found at:

gesundheitsforschung-bmbf.de
→ Shaping research
→ Digitalization and artificial intelligence

AI tool improves dementia diagnosis

Around 55 million people worldwide suffer from dementia. According to current estimates, this number will triple in the next 30 years. More than half of all patients suffer from Alzheimer's disease, the most common form of dementia. But there are several other types. Depending on the type of dementia, the stage of the disease and the individual's state of health, different medications and therapies can be considered. At the beginning, however, the symptoms of the various forms of the disease are very similar, which has so far made a differentiated diagnosis difficult.

A team of researchers at the Technical University of Munich wants to change this: The scientists are developing an AI tool that can quickly and reliably determine the form of dementia in its early stages. The Federal Ministry Research, Technology and Space (BMFTR) is supporting the “DeepMentia” project as part of the “Computational Life Sciences – CompLS” funding initiative.

Before an initial diagnosis is made, patients undergo a series of examinations that generate a lot of data. This includes image data such as MRI scans of the brain, but also the results of psychiatric tests and genetic information. “We fed and trained our AI model with this wide range of different data,” explains Professor Dr. Christian Wachinger from the Technical University of Munich. “We were able to access a data set of several hundred dementia patients.” In the future, the AI tool should reliably support doctors in diagnosing the four most common forms of dementia. These include vascular dementia, Lewy body dementia and frontotemporal dementia in addition to Alzheimer’s disease.

“Every type of dementia has its own pattern”

For the accurate analysis, the researchers have developed a novel AI method that can reconstruct the surface of the so-called cortex within seconds. The cortex, also known as the cerebral cortex, is a layer on the surface of the brain. The thickness of this layer decreases in dementia. “We can measure in which regions of the brain the cortex has thinned,” says Wachinger. “This provides information about the type of dementia, because each type of dementia has its own pattern.” These results, along with other data, are included in the diagnosis.

It is also important to the scientists that the AI analysis is comprehensible for the users. “Until now, AI tools have generally been like a black box. Nobody knows exactly on what basis they have arrived at a certain result,” says Wachinger. The Munich research team, on the other hand, visualizes the AI's decision-making processes with the help of diagrams and image data. “This allows doctors to see exactly which information contributed to the diagnosis,” explains Wachinger. The researchers are confident that this will also significantly increase acceptance of the tool. “It has been very well received by the physicians we work with.”

Wachinger expects the model to be ready for use in three years at the latest. By then, the researchers hope to have a company on board that already offers common software for everyday use in hospitals or doctors' surgeries. The AI tool for diagnosing dementia could then simply be integrated into this system. And Wachinger is sure: “Then it has an even better chance of being accepted by doctors.”

Further information can be found at:

gesundheitsforschung-bmbf.de
→ Shaping research
→ Digitalization and artificial intelligence

Making better use of data – treating cancer more effectively

PM4Onco stands for “Personalized Medicine for Oncology”. It analyzes the molecular characteristics of tumours, identifies specific targets and uses the most promising treatment option against them – because every tumour reacts differently. Only the overall picture of a cancer enables doctors to combine different drugs or radiotherapy to achieve the best possible treatment. In oncology centers, “tumour boards” – teams of doctors from different disciplines and scientific experts – analyze a wide range of information, from radiological findings and genetic analyses to new findings from cancer research, in order to choose the right treatment for each patient. In the future, intelligent IT solutions will support their work by organizing and visualizing all relevant data. Doctors will be able to see all the information at a glance and can quickly identify the therapy with the best chance of success.

Combining data from oncology centers and regional providers

However, the necessary clinical and biomedical data of many patients are often isolated from each other in clinics, radiology, oncology or general practice settings - and in different formats. The PM4Onco project, launched in May 2023 and funded by the Federal Ministry of Research, Technology and Space (BMFTR) with around 10 million euros until 2027, aims to make this data available for the personalized treatment of cancer patients - always in compliance with all data protection and data security requirements.

To further improve the cancer research database, PM4Onco will work with clinical partners, cancer registries and patients to collect all relevant information about the treatment and follow-up of cancer patients - known as follow-up data. This data strengthens analyses of the effectiveness of

Memory problems, absent-mindedness, speech difficulties – these are often the first symptoms of the onset of dementia. However, the type of dementia can vary.

Image credit: Adobe Stock/LIGHTFIELD STUDIOS

new therapies. And this is important for scientifically proving the potential benefits of treatments that are often still experimental. The better and earlier this is achieved, the faster new therapies can be incorporated into standard care, so that as many people as possible can benefit from medical progress.

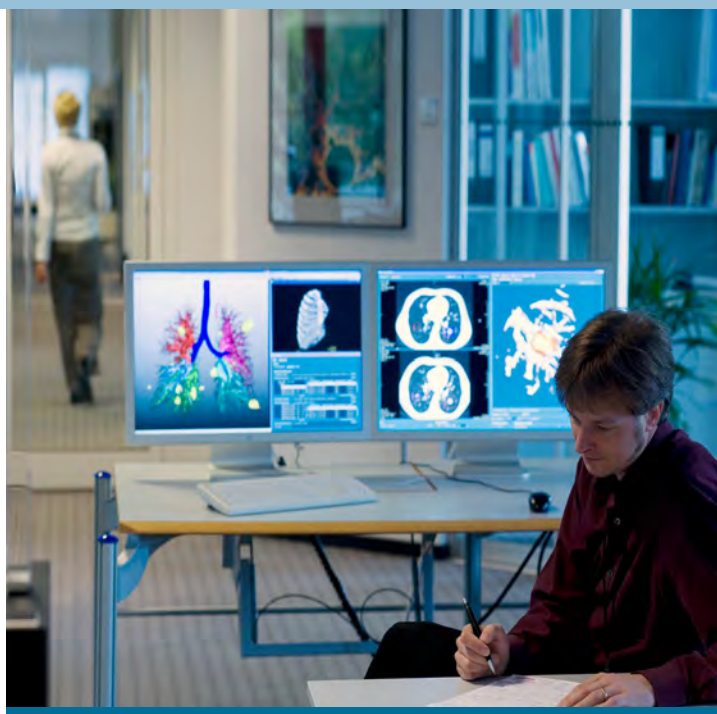
Involving patients – promoting young scientists

As with all BMFTR projects under the National Decade against Cancer and the clinical use cases of the Medical Informatics Initiative, the needs of patients are taken into account from the outset through cooperation with patient representatives. For example, the treatment results assessed by the patients themselves – known as Patient-Reported Outcome Measures (PROMs) are included in the projects. Workshops with patients and other stakeholders will also be held regularly. For example, the data analyses are explained, new results are presented and their potential use in healthcare is discussed with citizens. Young scientists are also supported: Junior oncology groups established at the MII will be integrated into PM4Onco in order to share research results and develop synergies.

Medical Informatics Initiative – the key data

Networking data, improving health research and patient care - this is what the MII stands for. It creates the conditions for the cross-locational use of data from research and care. To achieve this, the MII is working together with the Network of University Medicine to establish data integration centers at university hospitals and partner institutions. The medical added value of these infrastructures for research and medical care is demonstrated by a variety of use cases.

On this basis, the MII will become the engine and driving force of a decentralized research data infrastructure in Germany. An important component of this infrastructure is the German Portal for Medical Research Data (FDPG). The FDPG serves as a central point of contact for all scientists who want to conduct research with MII data. At the same time, it informs citizens about all ongoing projects that use patient data from the MII.



The analysis of data from oncology centers and regional players helps doctors to find the best possible treatment for each tumour.

Picture credits: DLR Project Management Agency/BMFTR
Source: Philipps University Marburg

The BMFTR has been funding the MII with a total of over 480 million euros since 2018.

Further information can be found at:

medizininformatik-initiative.de/en

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Digital innovations for improved patient care in rural areas

An IT platform as a bridge between university clinics, medical practices, hospitals and patients

by Torsten Panholzer

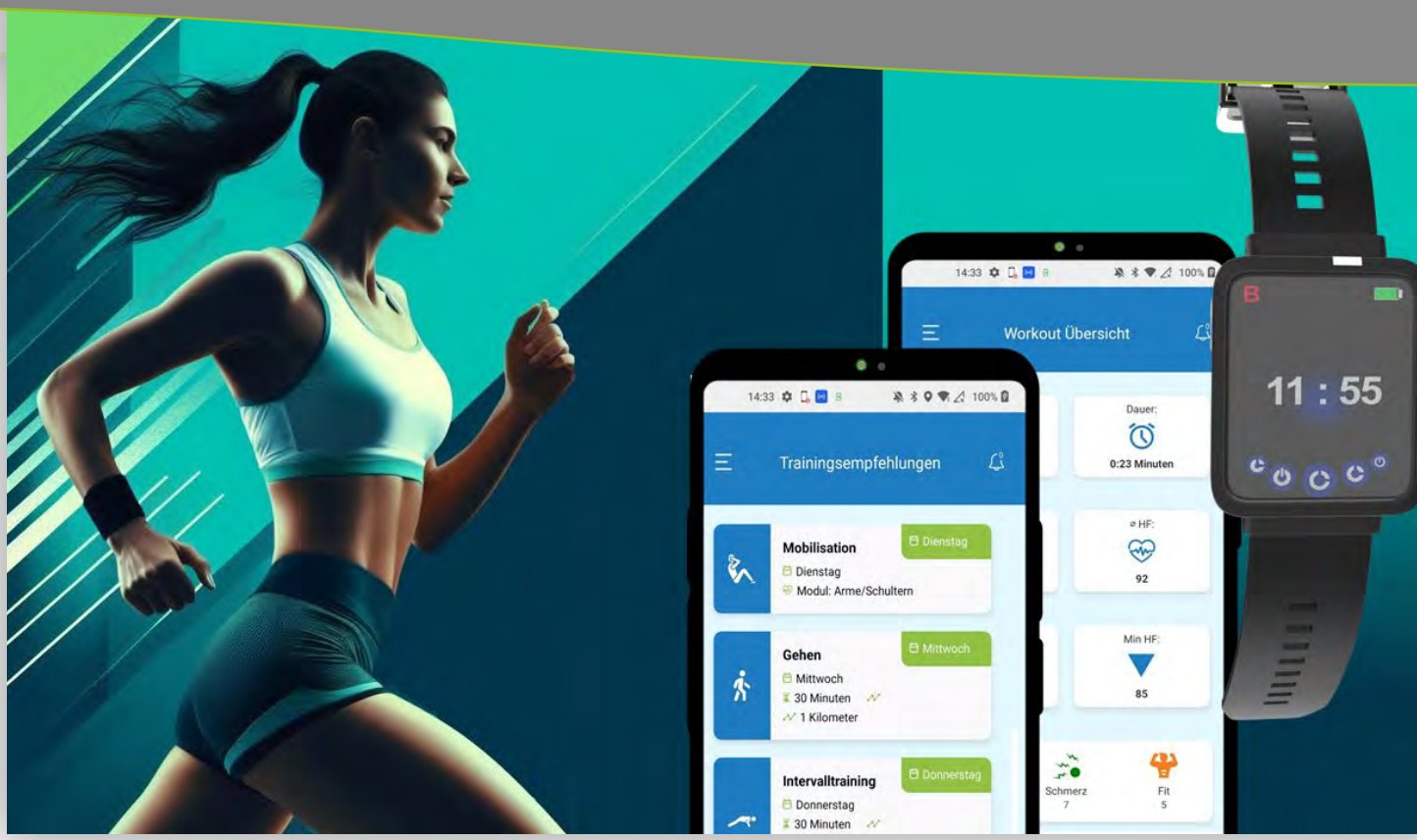
Together with regional hospitals, physicians in private practice or self-help groups, the Mainz University Medical Center is developing and testing model solutions in the Digital Hub DECIDE to provide the best possible care for people in rural regions and to use the data obtained for research.

DECIDE - short for **"Decentralized Digital Environment for Consultation, Data Integration, Decision Making and Patient Empowerment"** - focuses on cancer and depression, diseases that affect many people. DECIDE is testing processes and technical options to support regional healthcare providers and their patients so that treatment can be offered at a high level even in structurally disadvantaged areas. On the one hand, an exchange on diagnosis and therapy finding and, on the other, joint treatment between local providers and specialists at the university hospital can be made possible. This means that patients in the region also benefit from the expertise of university medicine. The Federal Ministry of Research, Technology and Space is funding the Digital Hub, which was launched in 2021, as part of its Medical Informatics Initiative (MII) until 2025.

Exercise as an accompanying telemedical therapy

In one use case for the DECIDE structures, additional movement therapy is offered alongside the treatment of cancer and depression. This is because physical activity is a valuable complementary therapy for many cancer patients. It can alleviate side effects such as fatigue or muscle weakness caused by chemotherapy. Exercise programs can also help to counteract depressive episodes. As there is often a lack of such services in rural areas, DECIDE is developing a personalized therapy that is delivered remotely via telemedicine.

The training is planned and carried out by the Department of Sports Medicine at the Sports Institute at Johannes Gutenberg University Mainz. After being referred by the physician to the sports therapist, the patient first undergoes a sports medical examination with stress test in Mainz. Based on this, an individual training plan is drawn up. The therapy can then be carried out remotely.



During movement therapy in DECIDE, the wearable device (right) sends sensor data to the developed smartphone app, which forwards it to the therapist. The training plan and other information are also provided via the app.
(Photo: MCS Data Labs).

Training with app and wearable device

The patient can perform the movement therapy at home at any time. The smartphone app developed in DECIDE provides information and instructions in addition to the training plan. He also receives a wearable device whose sensors on the wrist collect data during training. The device sends this data to the Digital Hub at the Mainz University Medical Center via the DECIDE app. The activity can then be monitored by the therapist. After a training session, the patient uses the wearable device to provide feedback on how strenuous the training was. This feedback and the sensor data are evaluated by an assistance system. It can draw attention to irregularities and support the therapist in adjusting the training plan if necessary.

"In DECIDE, we want to use innovative digital solutions to improve healthcare regardless of where people live and also obtain data for research."

Dr. Torsten Panholzer
Coordinator of DECIDE and Head of the Department of Medical Informatics at the IMBEI of the Mainz University Medical Center

The wearable device, smartphone app and secure data transfer to the Digital Hub were developed by MCS Data Labs GmbH, Berlin, in collaboration with the Institute of Medical Statistics, Epidemiology and Informatics (IMBEI) at the Mainz University Medical Center. The Fraunhofer Institute for Industrial Mathematics ITWM in Kaiserslautern created the assistance system for the therapist. This expert system contains knowledge from treatment guidelines and current study results.

Patient empowerment

The technical possibilities in DECIDE can also lead to greater patient participation in treatment (empowerment). For example, the patient is better informed about the therapy measures with the smartphone app

and can track the training values measured by the wearable device on the smartphone app. Achieving certain goals can serve as an incentive. Overall, this promotes the patient's active participation in the course of their treatment.

The app is also used in the DECIDE oncology and depression use cases. It provides treatment plans and information. In addition, questionnaires can be regularly sent to the app to obtain patient feedback. This is an important factor for monitoring and assessing the course of treatment.

Integration of artificial intelligence (AI)

As mentioned, an AI-powered assistance system is utilized to recommend possible adjustments to the training plan for the sports therapist. It can also support the physician in finding a therapy and drawing up a treatment plan in the areas of depression and lung and colorectal cancer.

Data must be available as a basis for the latter. As it is still not easy to exchange structured data between practice and hospital systems, DECIDE attempts to extract data from free text in existing medical letters. New large language models are used for this purpose.

Cross-institutional data for research

Data integration centers have been set up at university hospitals in Germany as part of the MII to bring together treatment data within a university hospital and make it available for health research. The newly created Digital Hub is now expanding the circle to include patients who are treated outside a university hospital. If they agree, the data collected during treatment can be transferred to the data integration center and made available for research purposes. This enables a more comprehensive overview of a patient's course of treatment with different providers.

Contact:

Dr. Torsten Panholzer
Projektcoordinator DECIDE
Mainz University Medical Center
Mainz
torsten.panholzer@unimedizin-mainz.de

https://decide.imbei.uni-mainz.de

Photo: Panholzer: private

THE RESEARCH PROJECT IN BRIEF

The Digital Hub DECIDE tests procedures and tools of telemedicine, artificial intelligence, apps and wrist sensors to treat cancer and depression in structurally weak areas at the highest level. To this end, regional care providers can use the technical possibilities for therapy determination with decision support as well as for therapy monitoring in cooperation with the Mainz University Medical Center. In addition, movement therapy can be carried out remotely. The treatment data can also be used for medical research purposes, provided that patients give their consent.

In addition to the Mainz University Medical Center with its Departments of Medical Informatics, Oncology and Psychiatry, the Sports Institute at Johannes Gutenberg University Mainz, Fraunhofer IWTM Kaiserslautern and the company MCS Data Labs Berlin as well as regional medical providers are also involved in the project. The Federal Ministry of Research, Technology and Space (BMFTR) is funding the project as part of the Medical Informatics Initiative.

The Digital Hub DECIDE has won the innovation competition "Digital Landmarks in the Land of Ideas 2023" in the Health category.
(from left to right: competition patron Daniela Kluckert, Parliamentary State Secretary to the Federal Minister for Digital and Transport, Dr. Torsten Panholzer, DECIDE Coordinator, Mainz University Medical Center, Kira Enders and Dr. Alexandra Brahmer, Sports Institute, Johannes Gutenberg University Mainz, Andreas Pfisterer, CEO Deutsche Glasfaser)
(Photo: © Laurin Schmid / Deutsche Glasfaser).

DIGITAL PLACE 2023

In November 2023, DECIDE was recognized for its telemedical movement therapy at an award ceremony in Berlin.

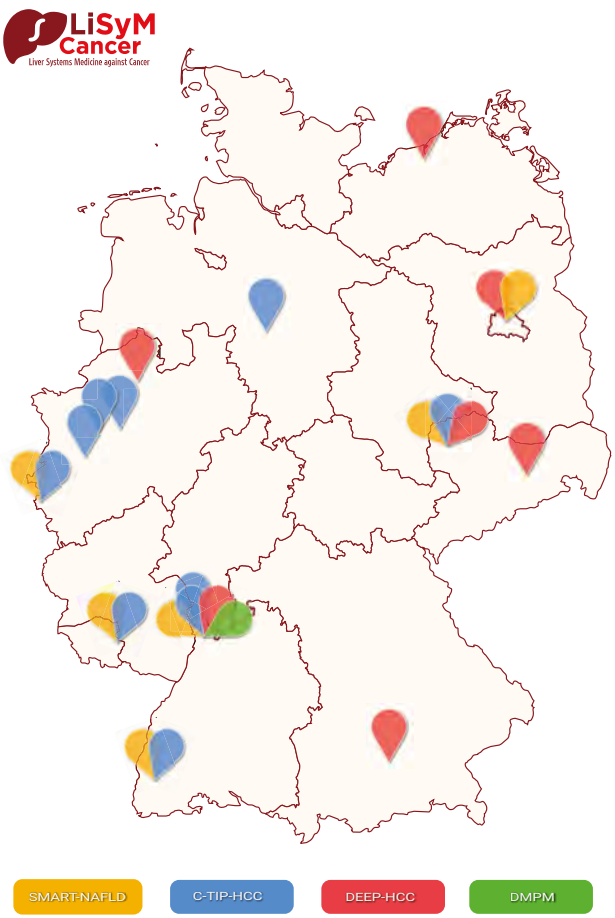
In the innovation competition "Digital Landmarks in the Land of Ideas" under the patronage of the Federal Ministry for Digital and Transport, DECIDE won in the health category. Out of more than 170 applications, 15 projects from all over Germany were nominated for the final. A jury with representatives from business, science, politics and society selected the winners in the categories of education, municipality, mobility, smart municipality and health. The competition, which was jointly organized by the "Germany - Land of Ideas" initiative and the Deutsche Glasfaser Group, honours outstanding digital solutions for rural areas every year.

Detecting and preventing liver cancer

LiSyM-Cancer: A systems medicine research network for the early detection and prevention of liver cancer

by Ina Biermayer, Sebastian Burbano de Lara, Steven Dooley, Susan Eckerle, Ursula Klingmüller, Beat Müllhaupt and the LiSyM-Cancer Network

Hepatocellular carcinoma (HCC) is one of the deadliest types of cancer worldwide. In Western countries, it is usually a consequence of liver cirrhosis due to steatotic liver disease (fatty liver) such as alcohol associated or metabolic dysfunctionassociated steatotic liver disease (MASLD). The problem of MASLD will continue to rise by the growing number of overweight people. Patients are often only diagnosed at an advanced stage of the tumor. There is therefore an urgent need to improve controls and develop early detection strategies for patients at high risk of HCC. Early detection enables treatment and improves the chances for cure.

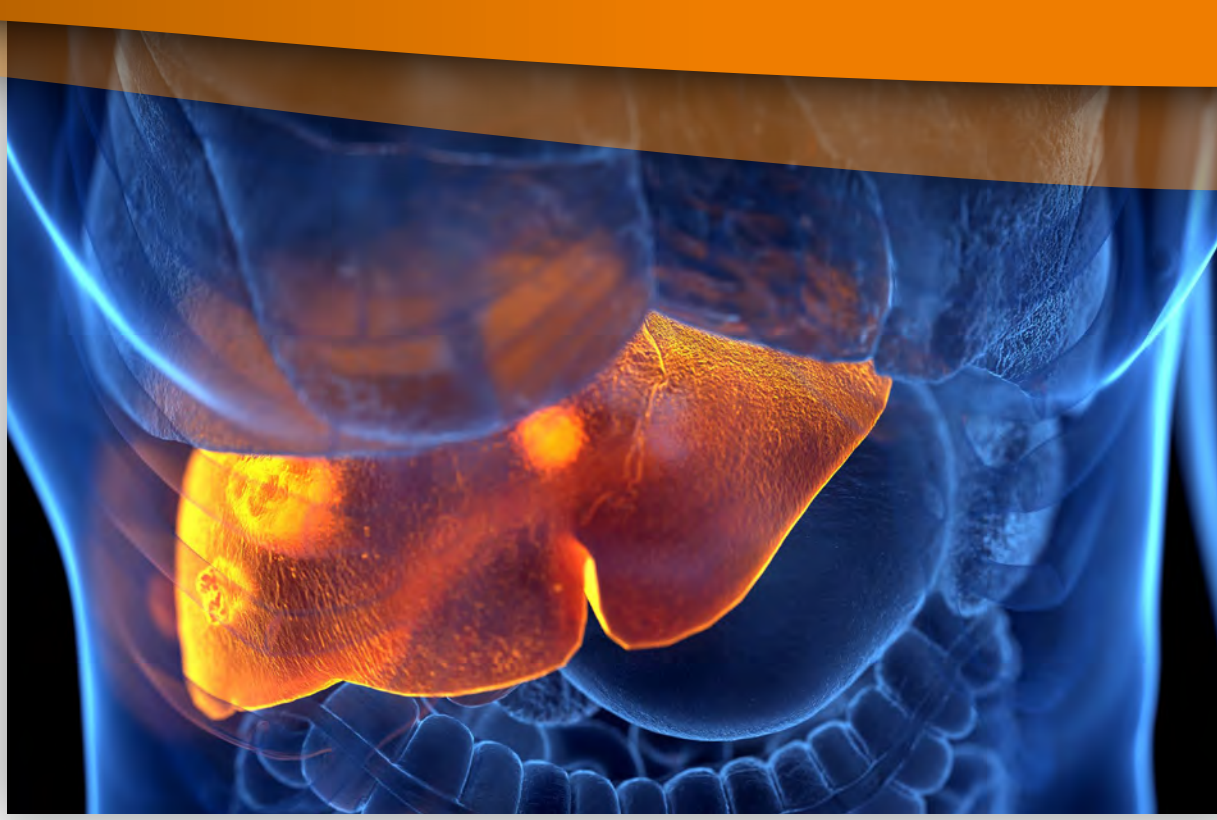


Interdisciplinary collaboration to understand mechanisms

The BMFTR-funded research network LiSyM-Cancer – Liver Systems Medicine against Cancer - brings together biologists, clinical researchers and mathematical modeling experts from all over Germany to investigate the development of hepatocellular carcinoma (HCC). The aim is to improve the early detection and prevention of hepatocellular carcinoma both against the background of MASLD and in the context of liver cirrhosis.

LiSyM-Cancer consists of the SMART-NAFLD, C-TIP-HCC and DEEP-HCC consortia as well as the central program and data management (Figure 1).

Figure1: The LiSyM-Cancer network with the SMART-NAFLD, C-TIP-HCC and DEEP-HCC projects, as well as the program and data management, brings together experts from all over Germany (Figure: LiSyM-Cancer, www.lisym-cancer.org).



The main objective of this collaborative project is to use a systems medicine approach to identify patients with chronic liver disease who are at high risk of developing hepatocellular carcinoma using non-invasive, blood- and image-based testing methods to improve early detection (Source: AdobeStock Sebastian Kaulitzki).

The systems medicine approach analyzes tissue remodeling, cell interactions and signaling networks to understand HCC development in the non-cirrhotic (SMART-NAFLD) and cirrhotic (C-TIP HCC and DEEP-HCC) liver.

The main objective of this collaborative project is to use a systems medicine approach to identify patients with chronic liver disease who are at high risk of developing hepatocellular carcinoma using non-invasive, blood- and image-based testing methods to improve early detection. This systems medicine approach is used to investigate dynamic tissue remodeling, the interactions of parenchymal (hepatocytes=liver parenchymal cells) and non-parenchymal cells (endothelial cells, stellate cells, Kupffer cells, etc.), the influence of extracellular matrix composition (connective tissue) and the interactions of metabolism, inflammation, proliferation and signal transduction on HCC formation.

Understanding the mechanisms that promote these early changes in metabolic and signaling networks is crucial to identify patients with chronic liver disease based on MASLD with and without cirrhosis who are at high risk of developing HCC. An integrative mathematical modeling approach will help to better understand the underlying complex mechanisms, reduce them to the essential steps and thus model them. In the LiSyM-Cancer project, dynamic signaling pathway models, network models and multi-scale models of tissue architecture are being developed to simulate the course of the disease in general and individually and to estimate the risk of HCC.

Dynamic modeling approaches for molecular understanding

In the development of MASLD, the storage of lipids in the hepatocytes is a characteristic structural change. The molecular mechanisms responsible for the progression of the disease are not yet fully understood. A possible marker that can provide information about the health status of the liver has now been found in a cross-project work in the LiSyM-Cancer network (Burbano de Lara *et al.,* 2024). In a preclinical model, lipid accumulation was induced in mice with a high-fat and high-sugar diet. The researchers found increased basal MET phosphorylation (MET: hepatocyte growth factor (HGF) receptor) and a strong downregulation of HGF-induced signaling pathways in hepatocytes of these mice. These signaling pathways play a major role in cell division in hepatocytes. By applying dynamic modeling of HGF signaling in combination with global proteomics, an important factor for increased proliferation of steatotic hepatocytes could be identified. An increased basal MET phoshorylation rate

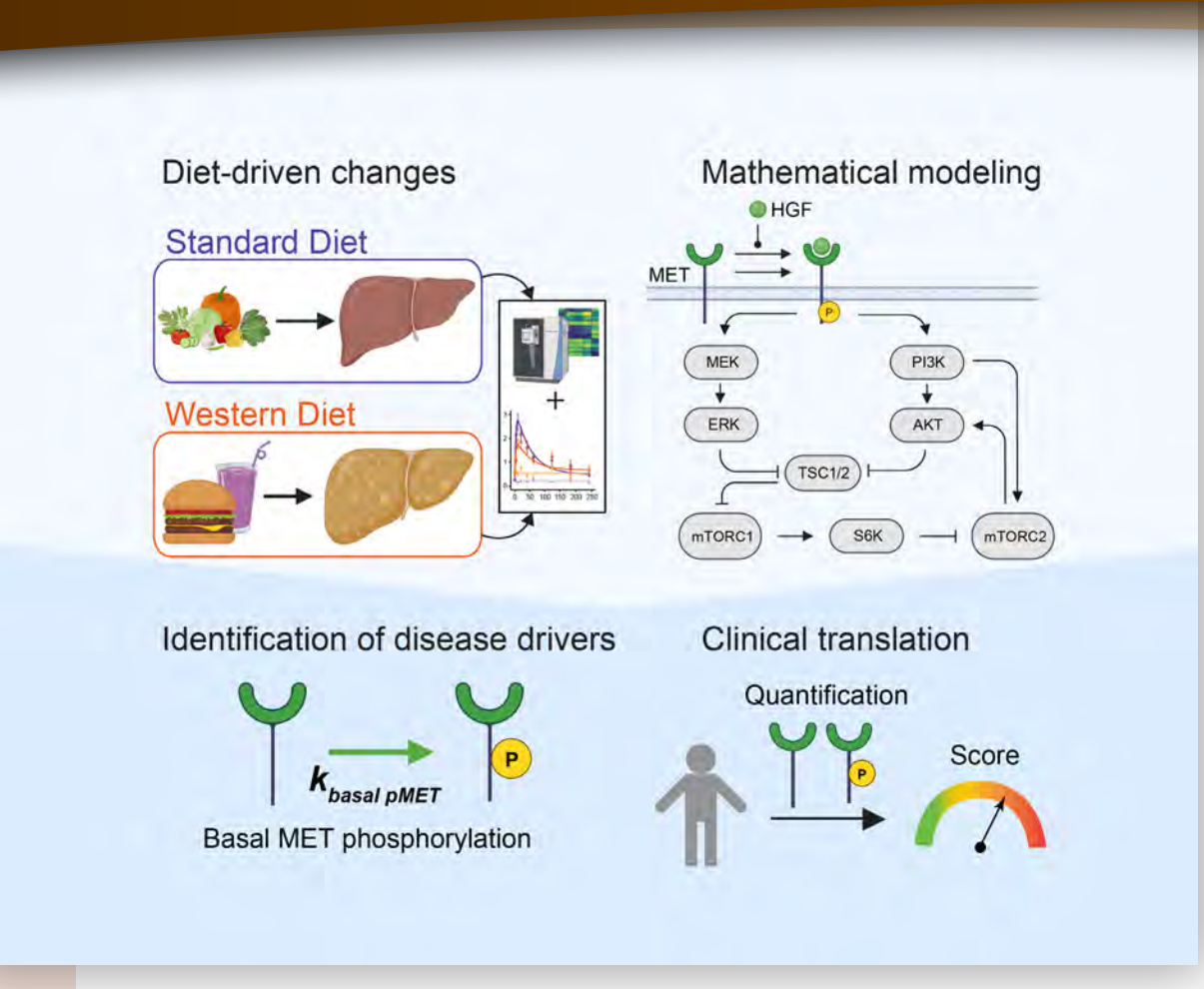


Figure 2: Nutrition-induced changes in hepatocytes are analyzed by mathematical modeling. Basal MET phosphorylation was identified as the main cause of the changes. The results could contribute to a decision support system in the clinic (Figure: Sebastian Burbano de Lara, Burbano de Lara *et al.*, 2024).

was the main cause for the altered signaling. The mathematical model was further fitted to data obtained from patients who underwent partial liver resection. The fitted model showed a patient-specific variability of basal MET phosphorylation that correlates with parameters of the patients' health status after liver surgery. Thus, dysregulated basal MET phosphorylation could be an indicator of the health status of the liver and thus provide information about a patient's risk of developing liver failure after surgery (see Figure 2). This identification of a potential biomarker was only possible through the collaboration of various disciplines in the LiSyM-Cancer network and years of funding in this field.

To further understand the changes that lead to HCC, new technologies such as pattern recognition using artificial intelligence (neural networks) and quantitative proteomics and metabolomics are also being used in the network. One focus is on the development of a coarse-grained modeling approach that considers only the essential metabolic reactions and combines these with dynamic signal transduction models such as the HGF model. By analyzing changes in metabolism and signaling pathways, signatures will be identified that indicate the risk for HCC development. These findings will be integrated into mathematical models and decision support systems will be developed to predict disease progression in MASLD patients, enable early detection and support treatment decisions.

OMICS data and image analysis for multiscale models

Another focus of the LiSyM-Cancer network is the investigation of the tumor environment and benign lesions in the non-cirrhotic and cirrhotic liver. Changes in the mechanical properties of the liver and the composition of the liver cell matrix during the course of the disease, as well as phenotypic changes in non-parenchymal cells and inflammatory cells influence the hepatocytes. To understand these processes, the activity of different signaling pathways and associated cellular parameters before and after the development of HCC will be investigated by

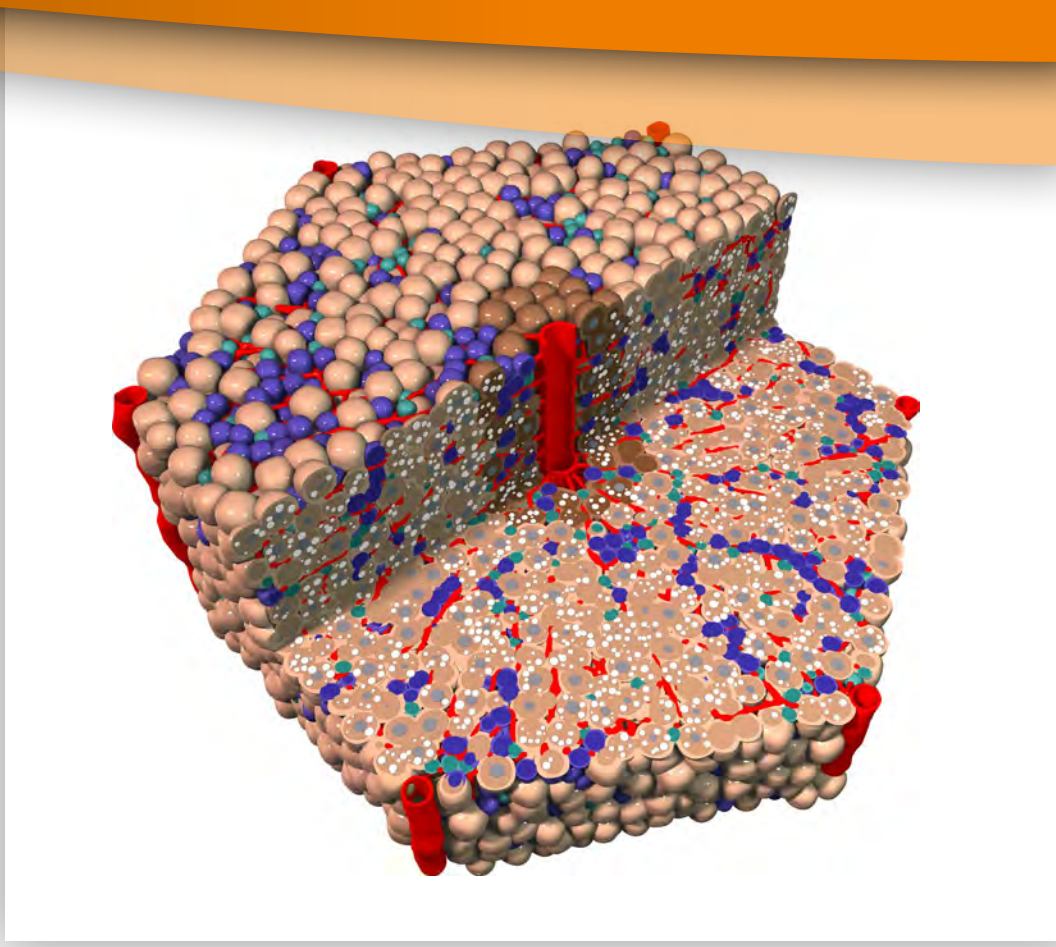


Figure 3: 3D liver tissue model with stained vessels (red, blue and orange), bile ducts (yellow) and different cell types: Healthy liver cells in brown with light blue cell nuclei and white small fat droplets; macrophages are dark blue; hepatic stellate cells involved in fibrosis are purple (Figure: Stefan Höhme, www.hoehme.com).

spatial analysis and quantitative imaging of human liver tissue. Bioinformatic analyses of the data obtained will then provide information on the different liver cell types involved in disease progression. In which phenotype are the cells present, in what quantity, where in the tissue are they localized and how do they communicate? The complex results are described in reductive compartment models (Figure 3). The researchers perform functional studies in primary cells, representative cell lines, 3D tissue culture models, organoids and mouse models to confirm or refute the model predictions. The identified mechanisms are then translated into blood- and image-based parameters and validated in longitudinal serum samples. All experimental data will be used for mathematical modeling at different scales. The project aims to develop a reliable data analysis pipeline for integrative network analysis to find a minimal indicator signature from the numerous candidates that identifies patients at risk of developing HCC. In addition, the mechanistic multiscale model will be used to propose strategies for targeted intervention that can prevent or delay the transition from tipping point to HCC, some of which are already being tested in preclinical mouse models as part of the project.

Multi- and Spatial-OMICS techniques and advanced imaging technologies contribute to the development of digital twin models by integrating mechanism-based dynamic pathway models, network models, kinetic models and tissue scale models. AI-based analyses support model development. The spatially resolved molecular analyses of human liver explants and resection samples provide insights into the different stages of HCC development. The establishment of patient-derived HCC organoids serves both for analysis and as a resource for the development of risk indicators. The optimized modeling approaches enable the discovery of new protein and lipid signatures for early HCC detection in blood.

Mathematical models of HCC development

HCC development is based on complex signaling networks and mechanisms. In order to decipher these, the LiSyM-Cancer project is focusing on the development of integrative mathematical models. The models should make it possible to predict HCC development using new blood- and histology-based signatures and imaging techniques. New indicators that show the risk of a tipping point and the development of HCC could make it possible to identify patients with a high risk of HCC at an early stage and monitor them more closely.

In summary, the researchers in LiSyM-Cancer are pursuing a comprehensive, multidisciplinary approach that aims to improve the early detection and prevention of hepatocellular carcinoma and optimize the efficiency and effectiveness of clinical decision-making. The development of software-based decision support systems and the integration of AI models will help to establish personalized monitoring strategies for patients with chronic liver diseases and thus improve the chances of treatment and cure. The developed decision support systems will be validated and standardized in proof-of-concept studies to prepare for clinical translation and to discuss the health economic potential. With its systems medicine approach, the LiSyM-Cancer network is driving forward the urgently needed early detection and prevention of liver cancer.

Further information about the research network and the partners involved: www.lisym-cancer.org

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Contact:

Prof. Dr. Beat Müllhaupt
Program Director LiSyM-Cancer
Head of Hepatology and Vice Chair –
Department of Gastroenterology and Hepatology,
University Hospital Zurich
beat.muellhaupt@usz.ch

www.lisym-cancer.org

Photo: Müllhaupt: private

Exchange program for algorithms

Distributed learning with AI in German hospitals

by Malte Tölle, Tim Seidler, Tim Friede, Sandy Engelhardt and the DZHK consortium FLOTO

People who do not speak the language in a foreign country often try to communicate with their hands and feet. However, some gestures that are polite in your own culture can easily be misunderstood. Without the right intercultural training, you are bound to put your foot in it. It is similar with AI algorithms: Models that have been trained on the data set from one hospital may perform worse on the data from another hospital or simply make poor decisions elsewhere. In medicine in particular, this can lead to undesirable or even serious consequences for patients.

Traveling to a foreign country can be tricky. For example, if you want to show the French baker that the baguette is exactly what you want despite your lack of knowledge of French, you can form a circle with your thumb and index finger. While this is a sign of satisfaction in Germany, the French baker would probably be very offended by this obscene gesture. One program that strengthens such mutual understanding through cultural exchange is ERASMUS.

Researchers at the German Center for Cardiovascular Diseases (DZHK) have now developed a comparable concept for AI algorithms - pioneering work in cardiovascular research. The simplest approach would be to store all the data from different clinics centrally on a server and train the algorithm there. However, as this data is very sensitive, data protection is correspondingly restrictive. In order to learn something about the other culture, similar to the ERASMUS program, you have to travel to the country or to the data. This is because the strength of an algorithm scales with the amount of data if it meets the relevant quality criteria. “There is no upper limit. The more, the better,” says Prof. Sandy Engelhardt, Head of the research group „Artificial Intelligence in Cardiovascular Medicine“ at University Hospital Heidelberg, a DZHK site. Even revolutionary technologies such as ChatGPT have only become possible by using such huge amounts of data. But how do you establish such a functioning consortium?

Let the algorithm travel, not the data

The pandemic period was characterized by little travel and reduced exchange. The AI/ML working group at the DZHK was founded on the initiative of Tim Friede, Professor of Biostatistics at the University of Göttingen, in order to strengthen this again. The group made good use of the time and wrote a review article on the use of artificial intelligence in cardiovascular medicine (Friedrich *et al.,* 2021). And extended the principle of exchange directly to the training process of AI algorithms. Previous work was often only trained and evaluated on data from one hospital. The generalization to the data of other hospitals was ignored.

Figure 1: The clinics involved in the project (Source: Tölle, Burger *et.al.,* 2024).

In practice, this is precisely the problem that still exists for many topics today: The data is widely distributed and is available in different formats. For example, if you want to train an AI algorithm that can recommend the best possible replacement valve for defective aortic valves based on computer tomography (CT) scans, you will find a few hundred data sets here, a few hundred there and perhaps around a thousand in Heidelberg. “If we only trained on our Heidelberg data, the algorithm would probably work for us, but not in other hospitals,” says Engelhardt.

These problems can now be solved by reversing the common principle of centralized data storage and training locally in the clinics instead. **“Let the algorithm travel not the data”** is the name of this approach; the corresponding technical term is **‘federated learning’**. With this mantra, Engelhardt's group has already succeeded in collecting over 8,000 CTs in the consortium across the locations. And this is by no means the end of the story. “We're aiming for ten thousand by the end of the year,” says Engelhardt, who has entrusted her doctoral student Malte Tölle with the project.

Making good use of the pandemic period

And he had work to do. Establishing such a network requires a great deal of effort, which often takes place behind the scenes. Every hospital needs a sufficient computing infrastructure and the data must be available in the same format everywhere. “For the connection of the nodes alone, we or Malte Tölle made over 200 support calls,” says Sandy Engelhardt. Standardizing the data was also difficult. They actually have the same format everywhere, but the project has brought to light some site-specific peculiarities that work well for each site, but make training difficult. These range from different manufacturers of the CT devices and therefore gray value distributions in the image to varying image sections. The examinations are parameterized slightly differently everywhere. “If we want to have an algorithm that can make helpful recommendations based on routine data, then it has to be trained with data from different facilities,” says Engelhardt.

As a pilot project, the DZHK group chose transcatheter aortic valve replacement (TAVI), more precisely the AI-based recommendation of suitable TAVI prostheses based on CT. “Despite sophisticated software for TAVI planning, the interpretation is limited to a sense of pro-

Prof. Dr. Sandy Engelhardt is researching multimodal AI algorithms at Heidelberg University Hospital, which are currently being trained and validated decentrally across eight clinics without the data being exchanged between them (Source: Heidelberg University Hospital).

portion and simple geometric measurements and thus depends heavily on the experience of the interventionalist," says Prof. Dr. Tim Seidler, Deputy Clinic Director of the Kerckhoff Clinic in Giessen, who proposed the initial idea from a medical perspective. Of course, the prosthesis recommendation does not cover all the important issues. In future, in combination with the ECG data, a probability for pacemaker dependency is to be determined on the basis of the previous experiments, as the implantation of the valves can impair the conduction system and thus make a second intervention necessary.

" Multicentric AI, whether distributed or centralized, will be of crucial importance in the German medical research landscape."

Prof. Dr. Sandy Engelhardt

Research project in brief

The DZHK project "Federated Learning of TAVI Outcomes (FLOTO)" is supported by the University Hospitals of Göttingen, Giessen, Heidelberg, Münster, Munich (LMU), Hamburg, Greifswald, Frankfurt and the Charité in Berlin (Figure 1). An expansion to other partner locations is planned. The team has already been able to show that distributed training of AI across 8 sites with diversely annotated data is possible using a transformer network architecture (Tölle, Garthe *et al.,* 2024) after structuring the input data (Tölle, Burger *et al.,* 2024). The approach is structured in such a modular way that it can easily be expanded with additional tasks or the network can be used efficiently in the sense of a foundation model. Figure 2 shows the result of a segmentation of the patient's individual heart and aorta from a CT data set. In addition, the model is able to detect important landmarks on the aortic valve and the outgoing vessels in order to help determine the size and type of the prosthesis to be implanted.

A promising project for the future

It is clear that the infrastructure will be extended to other projects after the test phase - whether in the DZHK, the umbrella organization DZG or possibly through other digital networks in German university medicine. A con-

nection to the Network of University Medicine (NUM) is also conceivable, which has so far pursued COVID projects but in principle provides suitable infrastructures. “There is now huge interest in the project. I really believe that it could be scaled up well,” says Engelhardt. However, the framework conditions have to be right. It needs sustainable funding - and motivated scientists, because technology alone does not lead to success. “We have come this far because we have worked together extremely well, and I would like to take this opportunity to thank all the researchers involved in the consortium.”

Just as ERASMUS has become an integral part of the German university landscape, the researchers are trying to establish the same successful concept for training algorithms.

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Contact:

Jun. Prof. Dr. Sandy Engelhardt
Head of research group
„Artificial Intelligence in Cardiovascular Medicine“
University Hospital Heidelberg,
Clinic for Cardiology, Angiology, and Pneumology and Clinic for Heart Surgery
Heidelberg
Sandy.engelhardt@med.uni-heidelberg.de

https://ukhd.de/aicm

Figure 2: Cardiac structures automatically segmented from the CT data (white) and the ascending and descending aorta (red). (Source: Sandy Engelhardt).

Photo: University Hospital Heidelberg

Revolutionizing cardiovascular care

Berlin cooperation sets new standards

by Stavroula Deoudi and Vivien Schubert

In a pioneering collaboration, Charité – Universitätsmedizin Berlin and the municipal hospital company Vivantes – Netzwerk für Gesundheit GmbH have launched a groundbreaking partnership that has the potential to fundamentally change cardiovascular care in Berlin and beyond. Under the motto of "**CA**rdiovascular Diseases – **E**nhancing **H**ealthcare through cross-Sectoral **R**outine data integration" (**CAEHR**), the two institutions are pooling their expertise to develop innovative digital solutions aimed at sustainably improving the efficiency and quality of treatment for patients with cardiovascular diseases.

The first patients have been recruited for research and study purposes as part of the project since spring 2024. A first milestone was reached in June 2024 when the collection of patient data via a joint portal was successfully launched. The network is to be further strengthened through the involvement of cooperating resident cardiologists in the Berlin area. As a result of this growth, the CAEHR sub-project, which is managed by Berlin Institute of Health at Charité (BIH), is gaining in profile.

Digital networking is made possible by the standardized use of data at Vivantes, while Charité has been setting up a data integration center since 2018 as part of the Medical Informatics Initiative, which promotes the cross-institutional use of medical data for research and care.

As part of the "outpatient care" use case of the CAEHR project, the BIH team and its partners have developed an IT architecture that enables the bidirectional

"The CAEHR digital progress hub brings the work of the Medical Informatics Initiative (MII) and the HiGHmed consortium to the everyday care of the Berlin population."

Dr. Mina Baumgarten
Head of Business Processes & Supply Innovation

Photo: Vivantes

exchange of structured patient data. This allows the partners in the resident cardiology practices to view their patients' treatment data from the clinic and in turn send the treatment data collected during the CAEHR visits in structured form (openEHR) to the Medical Data Integration Center (MeDIC). The IT solution developed at BIH was successfully introduced at Vivantes, so that both study teams at Charité and Vivantes work with the same portals. This strengthens the functions of both the MeDIC at Charité and the clinical data center currently being set up at Vivantes.

"A common goal is to transfer the knowledge and solutions gained within CAEHR to other regions and partners."

Prof. Dr. Roland Eils
Founding Director of the BIH – Center of Digital Health

Photo: Sebastian Runge

RESEARCH PROJECT PROFILE: CAEHR

CAEHR focuses on the flow of information between the various sectors of the healthcare system on the basis of three use cases:

- The use case "**Emergency care**" (Würzburg) is dedicated to the interface between acute inpatient and emergency care for stroke patients.
- The use case "**Rehabilitation**" (Göttingen and Hanover) focuses on the interface between inpatient care and rehabilitation for patients following aortic valve replacement using catheter technology.
- The use case "**Outpatient care**" (Berlin) focuses on the interface between inpatient and outpatient care for patients with chronic heart failure and coronary heart disease.

The resulting added value for patients, the healthcare professionals involved, the scientists involved and the healthcare system as a whole is to be demonstrated in the three use cases mentioned.

Consortium partners:

- D. Krefting, Universitätsmedizin Göttingen and Georg-August Universität Göttingen, consortium leader
- U. Bavendiek, Medizinische Hochschule Hannover, consortium leader
- R. Eils, Charité – Universitätsmedizin Berlin
- P. Heuschmann, Universitätsklinikum Würzburg
- U. Hübner, Hochschule Osnabrück
- S. Becker, HiGHmed e.V. Heidelberg
- N. Hellrung, Vitasystems GmbH Mannheim
- J. Seeger, AOK Niedersachsen
- P. Alexander, System Vertrieb Alexander GmbH Wiesbaden
- H. Schühlen, M. Baumgarten, Vivantes, Netzwerk für Gesundheit GmbH Berlin

Individual consultations, tailor-made solutions (Photo: AdobeStock hedgehog94).

This shows that the solutions developed as part of CAEHR can also be used for other projects to sustainably improve treatment options for cardiovascular patients, regardless of location.

This pilot project is already being supported by cooperation with other partners in order to develop digital solutions to improve treatment options, which can be extended to other regions in the long term and applied to various disease areas. By networking and sharing medical data, the aim is to optimize treatment options for cardiovascular diseases and reorganize collaboration between clinics. In this way, CAEHR could make a sustainable contribution to improving healthcare.

With this innovative approach, Berlin is setting new standards in digital healthcare and demonstrating how the future of medicine can be shaped through intersectoral cooperation and the use of state-of-the-art technologies.

Contact:

Stavroula Deoudi
Communication and Public Relation Manager
Project Management Office
HiGHmed
Stavroula.Deoudi@bioquant.uni-heidelberg.de

https://www.highmed.org

Dr. Vivien Schubert
Project Management CAEHR
BIH – Center of Digital Health
Berlin Institute of Health at Charité (BIH)
Berlin
Vivien.Schubert@bih-charite.de

News from the BIH

EBV may trigger autoreactivity and cause ME/CFS

The consortium project CURE-ME (Characterizing AUtoimmuneREsponses and Defining Targets in ME/CFS) between the Berlin Institute of Health at Charité (BIH), Charité –Universitätsmedizin Berlin, and the Technical University of Munich (TUM) will receive a total of €1,817,508 in grant funding from Germany's Federal Ministry of Research, Technology and Space (BMFTR) through 2027. Led by immunologist Prof. Birgit Sawitzki, the consortium aims to study the pathomechanisms of post-infectious ME/CFS, identify biomarkers for a more precise and early diagnosis, and develop innovative approaches for new treatment strategies. Its research will focus on examining the role of Epstein-Barr virus (EBV) as the driving force behind misdirected, autoreactive T and B cell responses, and thus as the cause of ME/CFS.

Myalgic encephalomyelitis/chronic fatigue syndrome, or ME/CFS for short, is a chronic multisystemic disease that often leads to significant physical and mental impairment and in most cases develops following an acute infection. Currently, there are very limited treatment options for people living with ME/CFS, as scientists don't fully understand what causes the disease and have yet to develop a targeted therapy. The disease is associated with severely restricted social participation, especially in younger patients, but it's still completely unclear whether the responsible mechanisms are similar for adolescents and adults.

Across all age groups, however, the Epstein-Barr virus is associated with the occurrence of autoimmunity and the development of ME/CFS. *"EBV can contribute to the emergence of post-infectious ME/CFS in many ways, either directly through homologies to autoantigens as a result of a primary EBV infection or indirectly through the infection of autoreactive B cells"*, explained Birgit Sawitzki, BIH Professor for Translational Immunology. Working together with Charité's Prof. Carmen Scheibenbogen, Thomas Dörner, and Harald Prüß as well as Prof. Uta Behrends from the Technical University of Munich (TUM), she wants to not only identify EBV cross-reactive and other (e.g. neuronal) autoantibody profiles for a more precise and early diagnosis of the disease, but also to investigate the underlying dysregulations in T and B cell communication, with the aim of laying the basis for targeted therapies and facilitating translation into clinical practice. The study of disrupted T and B cell communication will focus on EBV-related changes in the balance between stimulating and inhibiting surface receptors, the so-called checkpoint molecules.

Prof. Birgit Sawitzki, BIH Professor for Translational Immunology
(Photo: © BIH / Thomas Rafalzyk).

The research results offer completely new possibilities for early detection (Photo: © Pixabay).

Proteins in the blood can predict the risk of developing more than 60 diseases

A new collaborative study by researchers from the Berlin Institute of Health at Charité (BIH), Queen Mary University of London, University College London, University of Cambridge, and the pharmaceutical company GlaxoSmithKline (GSK) shows that proteins measured in a single drop of blood can predict risk for a variety of diseases.

The research results, which were published in Nature Medicine, show that protein 'signatures', combinations of a small number of 5-20 proteins, predict the risk of 67 different diseases. These include multiple myeloma, non-Hodgkin's lymphoma, motor neuron disease, pulmonary fibrosis, and dilated cardiomyopathy.

Thousands of proteins can now be measured using just a small drop of blood and this new study shows how these can provide important insights into the risk of developing disease in the future. Using data generated by the UK Biobank PharmaProteomics (UKB-PPP) project, the largest proteomics study to date, the team analyzed data from around 3,000 plasma proteins from a randomly selected group of over 40,000 blood samples linked to disease diagnoses from participants' electronic health records.

New possibilities for timely diagnoses

Using state-of-the-art analytical methods, the researchers were able to identify which 5 to 20 proteins in the blood are the most relevant for predicting certain diseases. The protein prediction models were able to show better predictive accuracy than conventional models based on standard clinical information such as blood count, cholesterol, kidney function and diabetes tests. These findings opens up new prediction possibilities for a wide range of diseases, including rare diseases. Many can currently take months or years to be diagnosed. The research results offer new possibilities for prevention and earlier detection. The next step is validation of these protein signatures in different populations, including different ethnic groups.

" The measurement of proteins, for example troponin for the diagnosis of a heart attack, is standard clinical practice. It is a huge step that we can now identify new potential markers for screening and diagnosis from the thousands of proteins that circulate and can be measured in human blood. What we now urgently need are tests that can measure disease-relevant proteins using assays that fulfil clinical standards and are affordable."

Prof. Claudia Langenberg
Head of Computational Medicine group at the BIH and Director of the Institute of Precision Medicine at Queen Mary University of London, UK.

Recovery Cat Team (from left to right):
Alissa Maresa Rohrbach, Jakob Kaminski, Toni Muffel, Dennis Stratmann, Elisabeth Kress, Hanhoan Truong, Katrin Friedmann, Felix Machleid
(Photo: © Recovery Cat / Toni Muffel).

Recovery Cat, an app that helps with the treatment of severe mental illnesses, is now available to TK insurees

Recovery Cat is an app that provides digital therapy support to people with severe mental illnesses. Effective immediately, patients who are insured with Techniker Krankenkasse (TK) can use the Recovery Cat service free of charge. Further insurances will follow. A spin-off from the Berlin Institute of Health (BIH) and Charité – Universitätsmedizin Berlin, Recovery Cat is thus now being incorporated into real-life care settings. This once again demonstrates the success of Charité BIH Innovation's translational development programs, which provide tangible benefits to a broad spectrum of patients.

After release from inpatient treatment, people with severe mental illnesses frequently have to fend for themselves for a long period of time. This often leads them to break off their treatment, which can result in further crises that make it necessary to go back to the hospital. In order to help such people cope better with this situation, physicians and scientists at Charité's Department of Psychiatry and Neurosciences have worked closely with patients to develop the Recovery Cat app, which is designed to help patients, psychotherapists, and psychiatrists in treating and managing these illnesses. Since 2020, the team has been funded, mentored and supported as part of the BIH Digital Health Accelerator program at Charité BIH Innovation, the joint technology transfer unit of Charité and BIH.

"With our digital platform, we want to give patients more control and autonomy in dealing with their illness while supporting them in planning and evaluating the therapy process together with therapists and doctors."

Dr. Jakob Kaminski
Managing director and co-founder of Recovery Cat GmbH.

The aim of Recovery Cat is to improve patients' self-management. The app, which is certified as a medical device, offers the option of doing a daily check-in. Patients can record their symptoms, side effects, resources and early warning signs and receive visualizations for analysis purposes. These provide a precise overview of the course of the illness. Using this info, the app alerts the patients to changes and helps them evaluate symptoms and activate their individual resources. Simultaneously, a separate interface allows doctors and therapists to set up and customize the tool together with them, which makes therapy planning transparent.

In January 2025, Recovery Cat GmbH, which was spun off in 2022, started a cooperation with TK, Germany's largest health insurance company, through a selective contract. This enables therapists and physicians to integrate the app into day-to-day care and collaboratively involve patients in the therapy process.

Bettina Stark-Watzinger, former Federal Minister of Education and Research, receives the National Strategy for Gene- and Cell-Based Therapies from Prof. Dr. Christopher Baum, spokesperson of the National Strategy GCT and Chairman of the BIH Board of Directors (Photo: © Svea Pietschmann).

National Strategy for Gene and Cell Therapies presented to the BMBF

The Berlin Institute of Health at Charité (BIH) officially handed over the National Strategy for Gene-andCell-based Therapies to former Federal Research Minister Bettina Stark-Watzinger (FDP). Some 150 experts from various stakeholder groups drew up the paper and developed a road map for improving healthcare and strengthening Germany as a hub for gene and cell therapies. The former German Federal Ministry of Education and Research (BMBF) had commissioned the BIH to coordinate and oversee the drafting of the strategy. Some 250 stakeholders from science, business, politics and society from across Germany attended the handover event at the Futurium in Berlin.

Gene and cell therapies (GCTs) are some of the key technologies driving innovation in biomedical research and patient care. They are not only used to modulate disease processes and alleviate symptoms, but also directly address the genetic causes of diseases. This opens promising perspectives for patients suffering from severe and rare diseases for which no treatment currently exists.

In order to improve patient access to gene and cell therapies and to strengthen Germany as an international hub for research and innovation in this field, the former German Federal Ministry of Education and Research (BMBF) had commissioned the BIH in fall of 2022 to coordinate and oversee the development of a National Strategy for Gene and Cell Therapies.

Former Federal Research Minister Bettina Stark-Watzinger said: *"The National Strategy for Gene- and Cell-Based Therapies is an important step towards securing and expanding Germany's position as a centre of biomedical innovation. Our declared aim is to create new treatment options for patients in the long term. I am very pleased that we have succeeded in bringing together so many stakeholders from different areas and jointly developing the National Strategy. This collaboration between science, industry, the public sector and society is an important key to success. I would like to thank all those involved for their great commitment. With this spirit of optimism, we should now move forward together in a national network."*

Photos: © BIH / Thomas Rafalzyk, Elschner / private

Contact:

Konstanze Pflüger
Head of Communications
and Press Office
Berlin Institute of Health at Charité (BIH)

Katharina Kalhoff
Spokesperson, Editor for Science
Communication
Berlin Institute of Health at Charité (BIH)

Dr. Sophie Elschner
Editor for Science Communication
Berlin Institute of Health at Charité (BIH)

www.bihealth.org

Systems medicine research in lymphoma and leukemia

Tumor microenvironment and drug sensitivity profiling in the lab help to improve therapies

by Peter-Martin Bruch, Nora Liebers and Sascha Dietrich

Lymphomas and leukemias, also known colloquially as lymph node and blood cancer, affect each patient differently. While many patients have a very good prognosis thanks to modern therapies, too many people still suffer from lymphoma as a recurring, sometimes fatal disease. In order to further improve the treatment of lymphoma and leukemia patients, we are conducting our systems medicine research. This means that we try to bring together all the information about the patients, their disease, potential therapies and other factors in order to draw conclusions about the biology of the disease, the best individual therapy and the prognosis in each single case.

The response of patients with malignant diseases of the hematopoietic system (hematological neoplasms) to therapy is determined not only by the cancer cells themselves, but also by other factors, such as the surrounding healthy cells in the tissue, the tumor microenvironment. The interaction of these so-called *tumor extrinsic* factors with the properties of the cancer cells themselves (*tumor intrinsic*) is complex, as tumors are influenced by the microenvironment in their development and response to therapy, but conversely also influence their own surrounding. This complex interaction, together with genetic

Figure 1: Depending on the disease, cancer cells can be isolated by blood sampling, bone marrow aspiration or biopsy. These cells can then be treated outside the body with a variety of drugs to predict the most effective therapy. The direct application of this technology has not yet reached widespread clinical practice, but a large number of researchers are working on it (Source: Sascha Dietrich, designed by DrawImpacts).

changes in the tumor cells, determines the response to therapy and thus the long-term survival of patients. Here we present some examples of our research and its benefits for better patient care.

Testing the sensitivity of drugs *ex vivo*

Although many resistance mechanisms and prognostic markers are known today, one can still not predict with certainty how well patients will respond to certain drug therapies, which makes it difficult to select the best possible treatment. We have therefore chosen the strategy of testing primary leukemia and lymphoma cells with potential drugs in order to predict therapy response and determine the most effective therapy for individual cases.

We have conducted a clinical study called "SMARTrial", which investigated and established the use of drug response profiling in clinical practice. Profiling here means testing the treatment response to various chemotherapeutic and targeted agents in an individual patient. These tests are carried out on cancer cells previously taken from the person outside the human body (*ex vivo*) so that the patient is not exposed to stress.

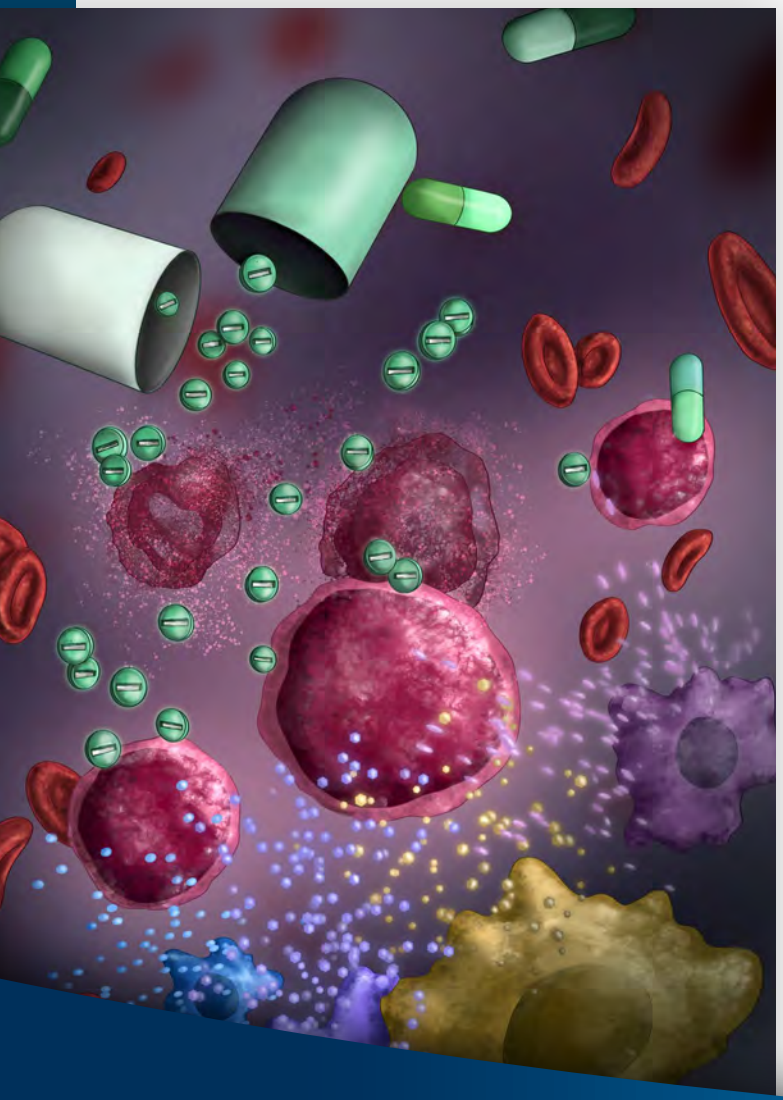
The cancer cells were collected during standard-of-care diagnostic procedures such as blood sampling, bone marrow aspiration or surgical biopsy and treated with a wide range of potentially effective drugs (Figure 1). On average, drug response profiling results were available within three days. This is important in order to make this test useful for everyday clinical practice, as treatment decisions usually have to be made very quickly in acute leukemias and aggressive lymphomas, for example.

One advantage is that significantly more drugs can be tested *ex vivo* in this way than are used in patients. Such large-scale screening studies are made possible by highly automated pipetting processes that perform hundreds of tests in parallel.

Utilizing mathematical models, we compared the treatment response of each patient to the various standard drugs and experimental drugs with the response of all other study patients to the same drugs. The experimentally predicted treatment response was then compared with the actual effect of the treatment selected by the treating physician. The result in each case is an individual profile of drug effects, which allows individual vulnerabilities of the cancer cells to be identified, from which a therapy option can immediately follow.

In patients with acute myeloid leukemia (AML), the largest single group in this study, the effect of standard therapy with the two drugs daunorubicin and cytarabine could also be predicted beyond the already known genetic risks. In particular, among patients with an unfavorable genetic risk profile (according to ELN-22 guidelines) we identified individuals who could have benefited from an alternative therapy.

For example, a study participant with aggressive lymphoma that had failed standard therapies was treated with methotrexate in an individualized therapy based on the drug response of his cancer cells determined *ex vivo*. This therapy showed a clear effect and made it possible to perform a stem cell transplant in this patient, which led to a good long-term response (Liebers *et al.*, 2023).



Further studies are needed to determine the exact status of this technique in clinical application, but the encouraging research results of recent years promise a significant improvement in the personalized treatment of blood cancer. With the help of drug response profiling, more people could be cured of their disease in the future and fewer unnecessary therapies with potentially severe side effects should be used.

Influence of the tumor microenvironment on the drug effect

As already mentioned in the beginning, the response to cancer therapy is not only influenced by the cancer cells themselves, but also by other factors. For example, healthy cells in the tissue, which together form the tumor microenvironment, can lead to resistance to chemotherapy and targeted drugs.

In further studies, we are therefore also integrating these effects of the tumor microenvironment into the investigation of drug effects. For example, we have analyzed the influence of soluble factors of the microenvironment on the effect of chemotherapy and targeted drugs in chronic lymphocytic leukemia (CLL) (Figure 2). This revealed clear differences between the leukemia cells of the individual patients. In particular, the functional *ex vivo* studies enabled us to identify a group of patients who suffered significantly faster progression of their disease (Bruch *et al.,* 2022). We combined this functional characterization with genetic data, which allowed

Figure 2: Soluble factors of the microenvironment influence leukemia cells in their *ex vivo* drug sensitivity. Cover illustration Molecular Systems Biology August 2023 for the publication (Source: Bruch *et al.,* 2022, designed by DrawImpacts).

us to demonstrate the influence of tumor cell mutations on microenvironment effects. In addition, the effect of the microenvironment on clinically relevant drugs such as chemotherapies and B-cell receptor inhibitors was investigated. Here, interleukin-4, a messenger substance produced by immune cells in the lymphoma, led to the strongest resistance to the therapies investigated.

Various immune and connective tissue cells (so-called stromal cells) form soluble factors that act on the tumor cells. However, direct cellular interactions between stromal cells and cancer cells in particular can influence the effect of drugs. In a complex coculture model, we have therefore also investigated the influence of these cell-cell interactions. It is difficult to measure these effects, as healthy cells are also influenced by the drugs. We therefore observed and measured the interaction using confocal high-throughput microscopes. In fact, the healthy cells massively influenced the effect of the drugs on cancer cells. The insights into cell-cell interactions gained in this way are particularly important for the development of new drugs, which are usually first tested in the laboratory and only later in animals and humans (Herbst *et al.,* 2023).

The association of genetic changes, the functional measurements on the leukemia cells and the clinical course of the disease makes it possible to draw conclusions about the mechanisms of the different genetic alterations. This deep biological understanding of the disease should allow even more individualized, targeted therapies in the future and thus enable more people to survive with the disease for longer or be cured.

Investigation of the tumor microenvironment in cancer tissue

The functional investigation of cancer and microenvironment cells can provide important insights into the mechanisms of therapy resistance, but these investigations are very complex and difficult to carry out in everyday clinical practice outside of university hospitals. Furthermore, in the laboratory it is often only possible to map interactions between individual components of the complex situation in humans.

In order to investigate the exact influence of the entire microenvironment, we analyze diagnostic biopsies, which are regularly taken from almost every patient. These tissue samples are used for diagnostic purposes and can also be exploited for scientific purposes with the patient's consent. In particular, we examine the immune cells present in the tissue alongside the cancer cells. In fact immune cells are able to prevent the development of cancer. However, faulty functions of these immune cells or evasion mechanisms of cancer cells can lead to people becoming ill. Conversely, immune cells can be reactivated by modern therapies, so-called immunotherapies, in order to attack cancer cells. This complex picture of pro- and anti-cancer effects arises because many different subgroups of immune cells are present in the tissue and fulfill different functions. Understanding this composition of immune cells is an important step towards improving future therapies.

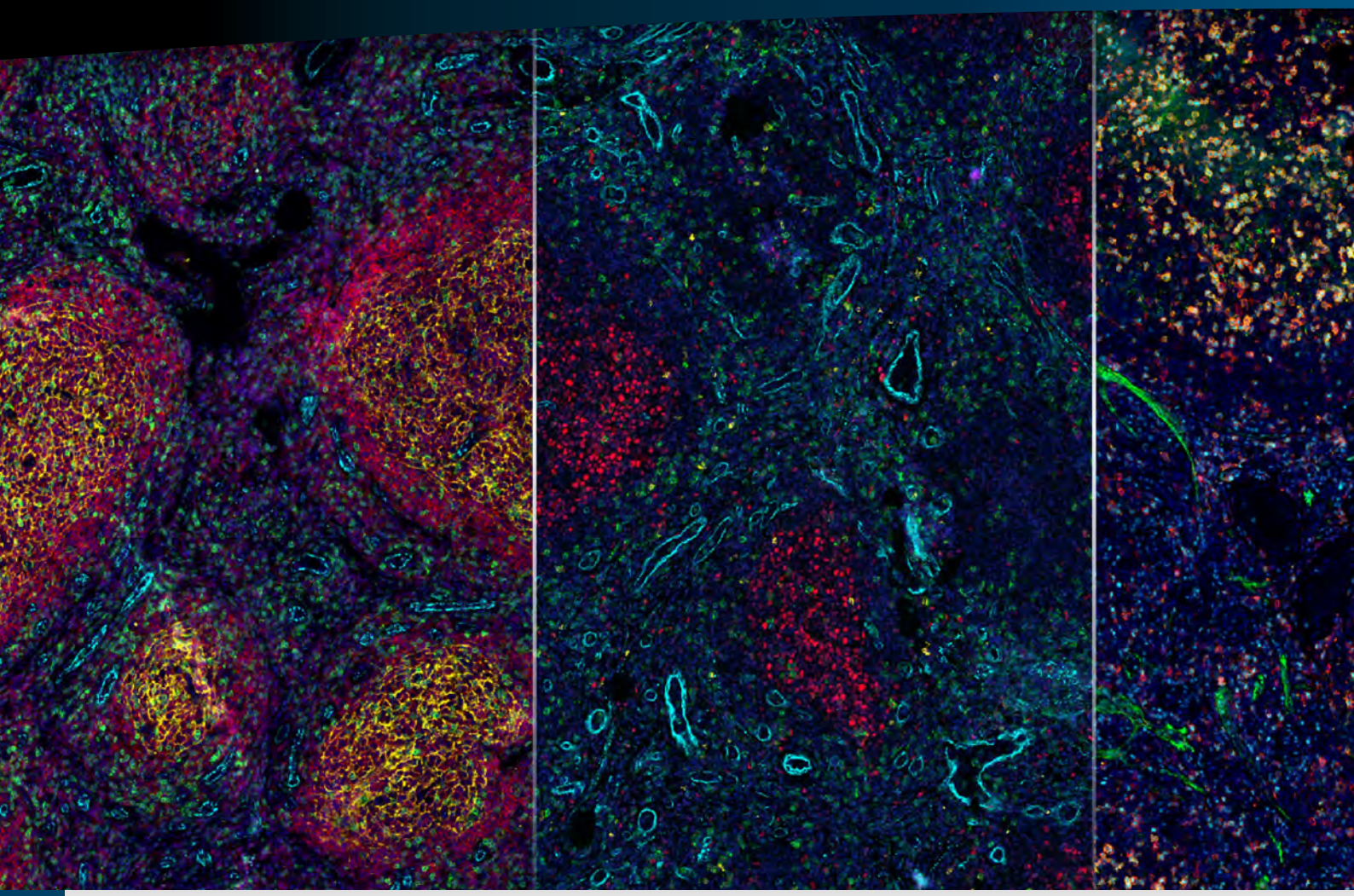
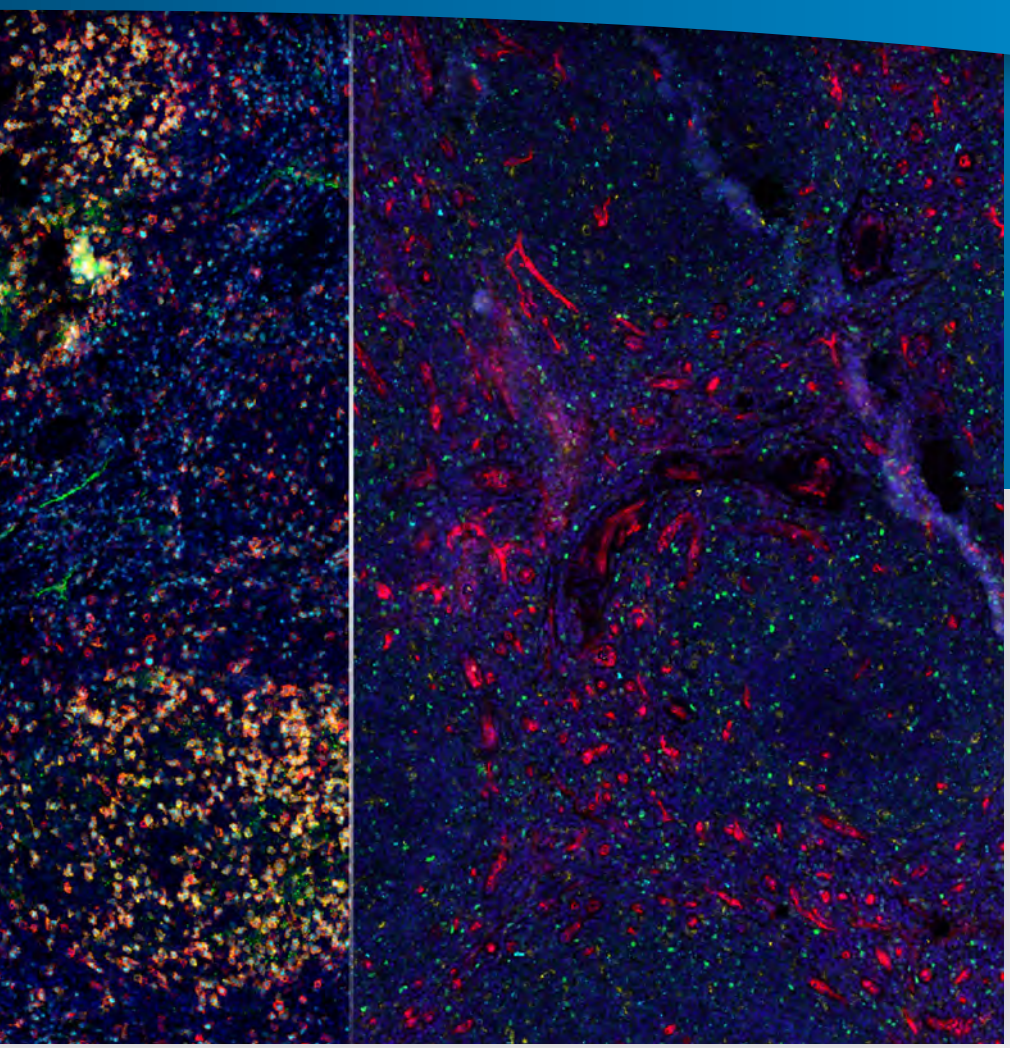


Figure 3: Multiparametric immunofluorescence staining of cells in a follicular lymphoma. The different colors in the four panels represent different surface molecules. By combining this information, the different cells in the tissue can be recognized (Source: Sascha Dietrich).

For example, in a recent study on B-cell lymphomas, the most common group of lymph node cancers, we were able to observe the infiltration of immune cells and link it to the clinical progression of the disease. It has been shown that exhausted T cells in particular, which show less activity against cancer cells, are associated with a poorer prognosis for patients. This may be due to the fact that the T cells, which should normally recognize and destroy cancer cells, are no longer able to control the disease due to their exhaustion (Roider *et al.,* 2024).

In addition to the composition of the immune cells, the spatial representation of the tissue is also crucial. After all, the immune cells must first reach the cancer cells before they can attack them. To characterize these tissue samples, we use multiparametric immunofluorescence staining (Figure 3). This technique allows us to visualize a variety of surface molecules and thus identify the cell types in the tissue. The resulting information on the frequency, spatial distribution, and activity of different immune cells allows us to draw conclusions about the biological processes in the tumor tissue.

In summary, by closely examining cancer cells and the surrounding tissue, we are trying to better understand the development of cancer and its response to therapies. This biological understanding is the basis for the development of targeted therapies to date and should also lead to further improvements in therapies in the future, thereby improving patients' chances of recovery.



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Contact:

Prof. Dr. med. Sascha Dietrich
University Hospital Düsseldorf
Director of Hematology, Oncology and Clinical Immunology
Klinikleitung.Haematologie@med.uni-duesseldorf.de

https://uniklinik-duesseldorf.de/dietrichlab
https://www.sys-med.de/en/junior-research-groups/sympathy

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e:Med SYSTEMS MEDICINE

Photo: © University Hospital Düsseldorf

A breath of fresh minds in systems medicine – young talents shape the future

Talking with Silke Szymczak and Julie George

A particular focus of the e:Med systems medicine research concept, which has been funded by the BMFTR since 2013, is the support and promotion of young researchers. They specialize in medically relevant topics during their studies, as doctoral candidates and post-doctoral researchers and are therefore an important part of the e:Med research community.

The e:Med modules "junior research alliances" and "junior research groups" give young scientists the opportunity to acquire third-party funds in order to implement their research at an institution and to thus establish themselves as independent researchers. Additionally, they are also given the chance to develop scientifically as part of "research alliances" which are active across locations and the application-oriented "demonstrator projects".

The success is remarkable: following their BMFTR funding through e:Med, more than 43% of young e:Med researchers received a professorship. Often new professorships were explicitly established for topics on systems medicine or personalized medicine. The leadership and teaching skills of young researchers were further strengthened by providing funds for e:Med "summer schools".

Who are the young scientists that have taken up a professorship with the e:Med program?

Here, two of them talk about their career paths and their thoughts on promoting young talents:
Prof. Dr. Julie George, University of Cologne and
Prof. Dr. Silke Szymczak, University of Lübeck.

gesundhyte.de: *Professor Szymczak, you very successfully led the e:Med junior research group ComorbSysMed. What was the research focus of this project?*

Professor Dr. Silke Szymczak: In ComorbSysMed we combined machine learning methods and omics technologies in a systems medicine approach to investigate comorbidities in inflammatory skin diseases. The long-term goal is to make individualized decisions for therapy, prognosis or prevention, based on the large amounts of measured data available nowadays. Selecting the appropriate statistical and computational methods is especially crucial for high-dimensional omics data sets (Degenhardt *et al.,* 2019).

Beyond the e:Med junior research group I am involved in developing approaches for specific methodological research questions, for example how to include measure-

Prof. Dr. Silke Szymczak also writes scripts and evaluates data herself (Photo: Wiebke Bergmann).

ments that change over time, or how to deal with missing data. "Integrative models" are another aspect: how can the predictions of different models be combined in a meaningful way when each of the individual models is trained on a specific type of data, e.g. clinical information, genetic variants or gene expression.

gesundhyte.de: *In your workshop "Artificial Intelligence – Learning through play", which you developed for the e:Med event EXPLORE Precision Medicine, school children represented data points.*

Professor Dr. Silke Szymczak: Yes, that worked very well. Professor Helena Zacharias from MH Hannover and I ran the workshop together. We wanted to teach basic knowledge about training and validating prediction models. The underlying methods are approaches from machine learning, a subfield of artificial intelligence (AI). AI is now a commonly known term, so we have given the workshop this name. However I usually refer to my own research area as "machine learning for precision medicine".

gesundhyte.de: *Which brings us to the heart of your research and of the promotion of young talents. Before we go into this I am curious: did you already want to be a researcher when you were at school?*

Professor Dr. Silke Szymczak: At school, I was overwhelmed by the many career opportunities. I didn't have a clear idea of the options and thus I had to find my way around. When I look back, I always took one step at a time. I always decided early on what the next step should be, and then implemented it. But it's also a matter of luck that opportunities keep arising.

gesundhyte.de: *What would you recommend to young researchers?*

Professor Dr. Silke Szymczak: What I can recommend: You have to be prepared, then you are in a position to seize the opportunity when it arises. For example, while working on my diploma thesis I proactively emailed professors to see if I could be a doctoral candidate in their team. As a postdoc, I started early to apply for professorships to get to know the process. I was nervous at first, but later on I knew the procedure and was able to use the experience to my advantage.

gesundhyte.de: *What were your steps so far leading up to your professorship?*

Professor Dr. Silke Szymczak: I decided at an early stage that I would like to go abroad after my doctorate, as I didn't do that during my studies. When the opportunity arose, I was ready. As a doctoral student, I was also able to attend international conferences and started to build a network. Established professors came to the poster sessions and spoke specifically with the young people, always approachable and interested. I also experience this in the well-organized systems medicine community. That's how I ended up at the NIH in Baltimore, USA.

gesundhyte.de: *The NIH was certainly a great experience, but you didn't stay there, why?*

Professor Dr. Silke Szymczak: The group was like a big family and there were many interesting and exciting projects. Everything was great professionally, but USA is a disaster without a driver's license. I decided early on that I wanted to return to Germany. I was really looking forward to come to Kiel. I already felt very comfortable in northern Germany near the Baltic Sea during my doctorate in Lübeck.

At the UKSH in Kiel, I first worked with Prof. Dr. André Franke at the Institute of Clinical Molecular Biology, then with Prof. Dr. Michael Krawczak at the Institute of Medical Mathematics and Statistics. If I remember correctly, he was the one who drew my attention to the e:Med call. It came at the right time and I was very happy that my first own application was funded. I believe that this funding was important for my further career.

gesundhyte.de: *Your next step, a professorship, was already clear then?*

Professor Dr. Silke Szymczak: Not at first. I always liked the academic setting, I was enthusiastic about the freedom of research. Even as a doctoral student, I was able to work on projects and topics that interested me. I've always enjoyed teaching, too. However, it was foreseeable that it would hardly be possible to get a permanent position in the "Mittelbau". So I decided to aim for a professorship. The e:Med junior research group was perfect because there was no need to do a habilitation. And I already had staff and budget responsibility. I took the didactics courses required for a habilitation nevertheless.

" The e:Med program is special and I like it for various reasons. In the systems medicine community, people know each other over time. And what I also find exciting is that it brings together people from so many different disciplines. Otherwise you often stay in your community bubble."

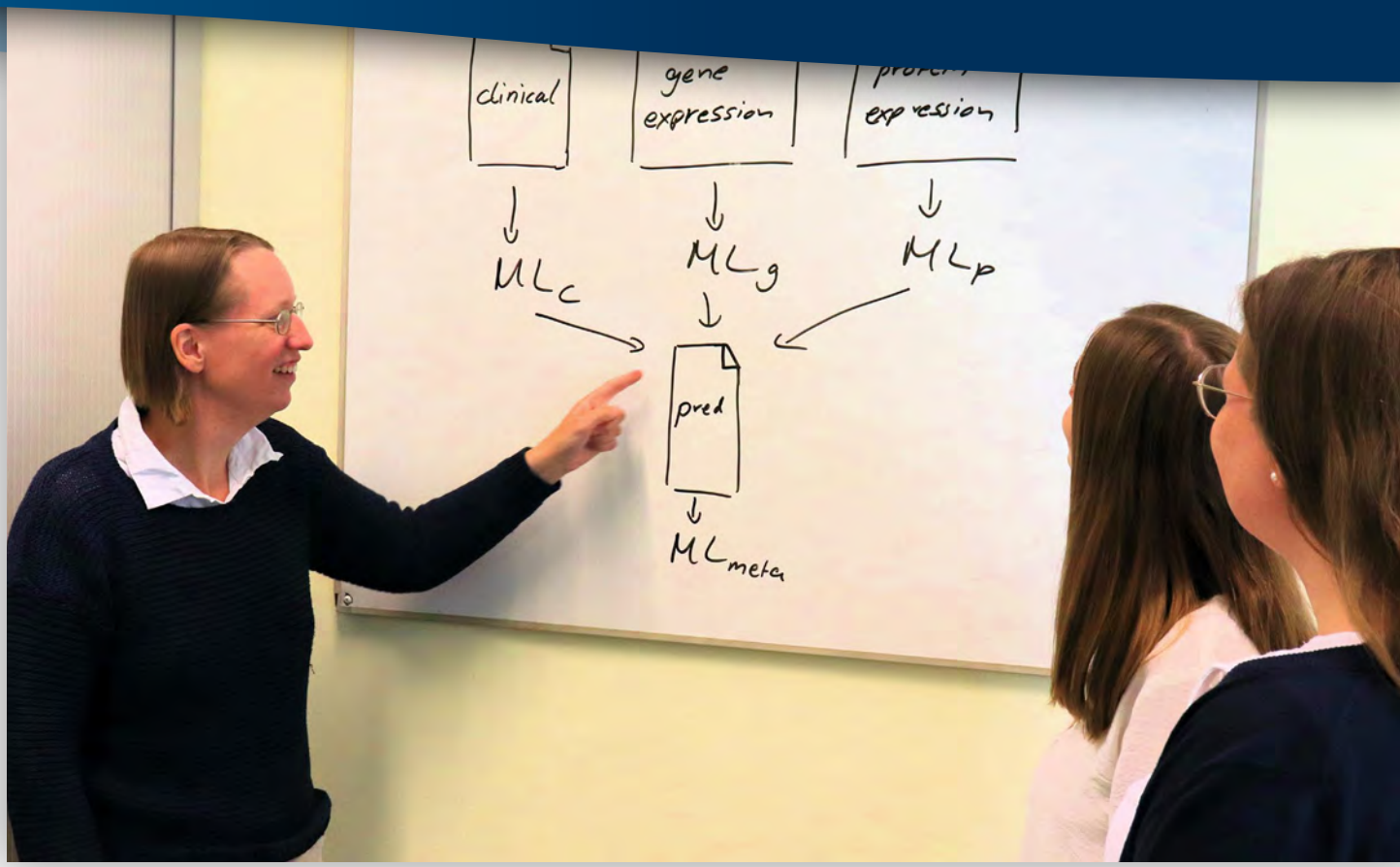
Professor Dr. Silke Szymczak
University of Lübeck

gesundhyte.de: *Professor Szymczak, you were involved in several e:Med projects in parallel.*

Professor Dr. Silke Szymczak: Yes, exactly, besides my ComorbSysMed junior research group I was also involved in the coNfirm research alliance led by Tanja Zeller from the UKE Hamburg. I already knew her from my time as a doctoral student. We had worked together on the data from the Gutenberg Heart Study. In addition, I am a PI in the GUIDE-IBD project led by Prof. Dr. Stefan Schreiber, Kiel.

The e:Med program is special and I like it for various reasons. In the systems medicine community people know each other over time. And it is also exciting that it brings together people from so many different disciplines. Otherwise you often stay in your community bubble.

Many people at e:Med tend to be younger. So the promotion of young talent has worked wonderfully. I was a lecturer at Tanja Zeller's summer school "COME" three times, which was very interdisciplinary. Biologists, methodologists and clinicians had to work on a project together. On the first day, they realized that "we can't even talk to each other!" How valuable to experience this in a protected environment already during the doctorate!



Regular meetings and discussions with staff members are an important part of the working life of Silke Szymczak (Photo: Wiebke Bergmann).

There are many networking opportunities, such as the annual conferences. You meet again every year, ask who you brought with you, talk about your current research and come up with ideas for new projects. It's the same when someone comes to the poster, the high level of interdisciplinarity means that only a small aspect serves as a starting point. You have to explain your research on a completely different level. That is very helpful and offers new perspectives.

With the events for the public, e:Med has also given opportunity to introduce schoolchildren to systems medicine. We were happy to participate in this and held the workshop mentioned at the beginning several times. It was great to experience the enthusiasm of the children. And they asked a lot of really good questions.

gesundhyte.de: *You became involved in didactics and teaching early on, do you have any ideas for us about what future promotion of young talents could benefit from?*

Professor Dr. Silke Szymczak: Time for individual career support could already be specified in the call for applications. There is often not enough time to discuss possible career paths and the next steps with the young researchers. The contracts are short, employees should start thinking about their goals at an early stage. If I know their goals, I can support them better, suggest further training courses and involve them more closely. Time for exchange and discussion is also important to plan and write successful grant proposals.

I think a mentoring program is very useful. It can run for two to three years, and bring researchers from very different disciplines and institutions together, to enable an open discussion.

I had local support from a professor who went through the applications and application documents with me and helped with her wealth of experience. I now do the same with my team members, of course transparently from my perspective.

To make it easier to find out about different career paths, we invite former team members to speak at our research colloquium.

I also think the development of establishing permanent positions below the professorship makes sense. If there were more such positions, there would be professional flexibility at this level as an alternative perspective.

Professor George has accepted the newly created Professorship for Molecular Head and Neck Oncology at the Medical Faculty of the University of Cologne. She works in the field of head and neck oncology at the Clinic for ENT (ear, nose, and throat) Medicine. She is also associated with the Department of Translational Genomics under the direction of Professor Dr. Roman Thomas, with whom she also jointly heads a research project in the e:Med alliance InCa.

gesundhyte.de: *What are you currently working on?*

Professor Dr. Julie George: The main aim of my work is to gain a mechanistic understanding of tumor biology in order to discover new therapeutic targets for cancer patients.

My work focuses on cancers of the lung and the head and neck, both of which are among the most common types of cancer. Lung cancer in particular is the most common cause of cancer-related death globally.

This includes small cell lung cancer (SCLC), a highly aggressive tumor of the lung, which is frequently diagnosed in heavy smokers. Due to the rapid spread of this tumor disease, most patients can only be treated with systemic chemotherapy, which initially works very well. In a long-term study on patients with small cell lung cancer, we recently discovered a key mechanism of recurrence and resistance: The therapy has a good effect on the cancer cell population prevailing at the time of diagnosis, but there are numerous other different cancer cells that are resistant to therapy and continue to multiply unrestrained. This finding is sobering, but very important for future treatment strategies (George *et al.,* 2024).

In the e:Med alliance InCa (systemic approach to the investigation of heterotypic interactions of lung cancer cells with their microenvironment) we are investigating the determination of cellular components in lung cancer. This joint project focusses on the study of non-small cell lung cancer (NSCLC), which comprises several types of lung cancer.

We characterize tumor cells and the non-tumoral cellular infiltrates in samples from patients receiving therapeutic treatment with immune checkpoint inhibitors (ICI), which in recent years has been administered in combination with chemotherapy. By relating the type and quantity of the tumor infiltrate to the genomic profile of the tumor, we try to determine to what extent the genomic profile influences the immune cell infiltration and recognition.

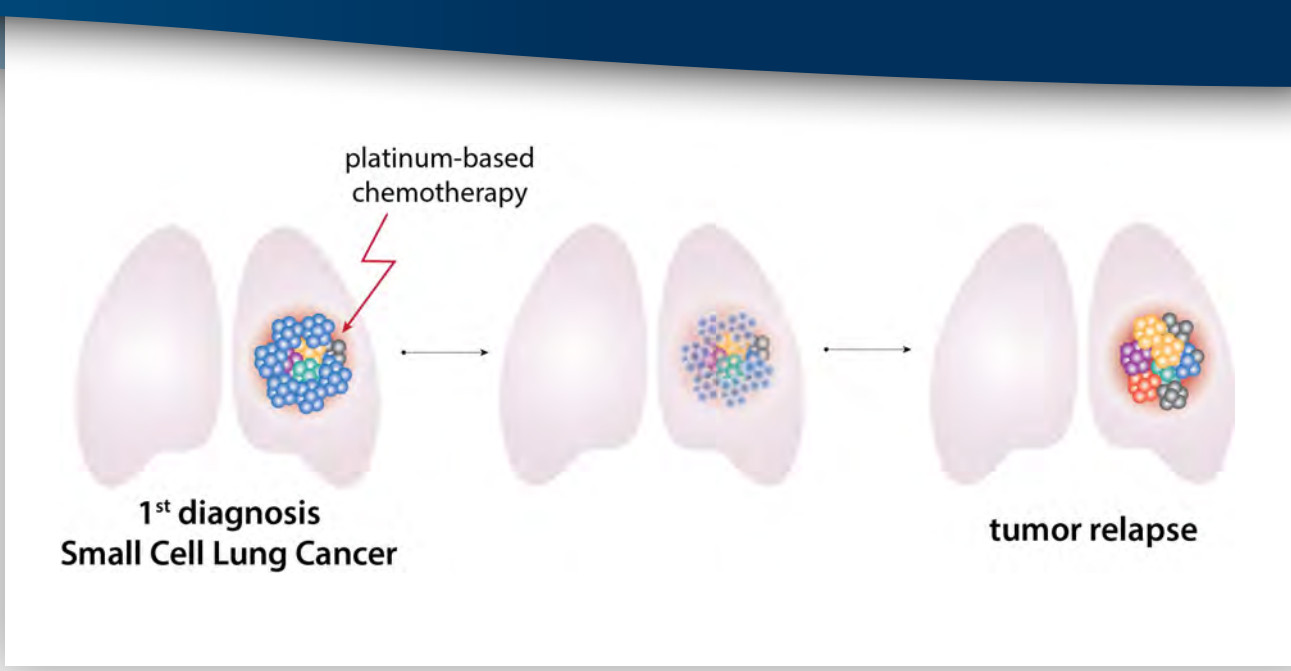
gesundhyte.de: *You took up your professorship in 2021, exactly ten years after your doctorate. You are working with technologies that have only been established in recent years. Was it your goal as a student to become a professor?*

Professor Dr. Julie George: I was interested in so many things. I found it particularly fascinating to understand and explore mechanisms of diseases and the medical context in detail, and this with completely new methods of omics research.

When I started studying, the first interdisciplinary Bachelor's and Master's degree programs were launched in Germany. That was crucial for me. It was extremely attractive for me to cover different scientific areas during my studies and to obtain a degree that would allow me to work internationally.

" The main aim of my work is to develop a mechanistic understanding of tumor biology in order to discover new therapeutic targets for cancer patients."

Professor Dr. Julie George
University of Cologne



Treatment of small cell lung cancer: initially good response to platinum-based chemotherapy, but rapid occurrence of tumor relapse. Comparative analyses show that the tumor consists predominantly of one dominant tumor clone at the time of initial diagnosis, but that many other tumor subclones already exist, which dominate at tumor recurrence (Source: Julie George, University of Cologne).

The study program focusing on Molecular Life Sciences was introduced at that time, which was then further developed: to keep a translational and interdisciplinary research focus, also in English, that was very tempting. There were only a couple of universities that offered these programs at that time and the Medical University in Lübeck provided what I was particularly interested in, topics on drug design and structural biology. Five years later, many universities were offering such courses.

gesundhyte.de: *These were the details you were looking for, the basis for going into more depth.*

Professor Dr. Julie George: Yes, exactly. After my Master's, I decided to stay in Germany and pursued a PhD at the German Cancer Research Center in Heidelberg. I studied the immune system, structurally and functionally. This was before the success of immune checkpoint inhibitors; investigating the immune system has always been a topic in cancer research.

As I had finished my Bachelor's, Master's and PhD relatively quickly, I was not frightened to engage in a new research topic as a postdoctoral fellow. It was important to me to expand my knowledge, to not just remain working in one area of research, and this also applies to my future research direction.

gesundhyte.de: *There is also the possibility of becoming active in a company or a start-up. But you haven't decided to do that yet.*

Professor Dr. Julie George: I have sometimes thought about possibly taking up positions in science management or business. In a start-up, you may at first focus on specific applications or approaches. It's very exciting and the goal is important, the teamwork is great, but so far I preferred keeping a broader perspective. I am excited about tackling larger projects which are often best explored in an academic environment.

"Working as a young scientist in the e:Med alliance InCa gave me the opportunity to work on my questions from an even broader perspective of the overall question in exchange with many highly competent colleagues. This was not only fun, but also helped me to make great progress in terms of content and perspective."

Professor Dr. Julie George
University of Cologne

Working as a young scientist in the e:Med alliance InCa gave me the opportunity to work on my area of research from an even broader perspective and interacting with many highly competent colleagues. We are constantly collaborating with national and international scientists, and exchange resources and technologies. This was not only fun, but also helped to make great progress in terms of content and perspective.

gesundhyte.de: *Looking back on your career, what ideas do you think are particularly important for young researchers?*

Professor Dr. Julie George: Good programs provide opportunities for different disciplines. Increasingly, the question is how to deepen and apply what's learned. e:Med also pursues these aspects. In addition to the instruments for promoting young researchers, I have found it important to give young researchers space and inspiration to pursue their own topic within a larger framework such as a research alliance or consortium.

I think it's important to take measures that promote young talents at their respective locations. Junior researchers have often made the leap to pursue their own research as part of their own working group to establish their research focus further. Measures that offer junior researchers opportunities over a period of five to eight years, and thus a real chance to position themselves with the team and topic are efficient. During this time, the junior researchers manage to recruit personnel, acquire expertise in the latest data, set up/ rebuild the laboratory, establish the experiment portfolio and, of course, the years of conduction, evaluation, testing, presentation and publication. A time frame of several years is essential for this.

Personally, excitement for academic research started for me as student, when working at international conferences, which allowed following many exciting presentations and latest findings. Lab visits are also valuable, i.e. visits to other working groups and collaborations. Several opportunities are existing for doctoral students and postdocs, which would also be beneficial for early career researchers, i.e. Bachelor students and student assistants. This would allow them to recognize at an early stage which direction they would like to take and prepare themselves accordingly. One possibility would be to incorporate this into the curriculum of the Master's degree programs.

" I think it's important to take measures that promote young talents at the location. Junior researchers have often already made the leap to pursuing their own research in their own working group and are now establishing themselves further. Measures that offer junior researchers opportunities over a period of five to eight years and thus a real chance to position themselves with the team and topic are efficient here."

Professor Dr. Julie George
University of Cologne

gesundhyte.de: *Thank you both very much for these inspiring conversations.*

Conclusion

Promoting early career researchers plays a crucial role in supporting young scientists on their career path and offering them a real opportunity to establish themselves. It is an important separate instrument, as is the scientific space within larger research networks. A capacity for mentoring is essential in order to provide targeted support for young researchers. In order to make this support sustainable, longer-term funding is necessary.

Prof. Dr. Julie George and PhD student Zurwa Uzun working in the laboratory (Photo: Oliver Siefer).

Early laboratory visits and student exchanges, even at the level of student assistants, Bachelor's and Master's students, are important measures for integrating and promoting early on young talents in the scientific community .

The interviews were conducted by Dr. Silke Argo.

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Contact:

Prof. Dr. Silke Szymczak
Institute of Medical Biometry and Statistics, University of Lübeck
University Hospital Schleswig-Holstein, Campus Lübeck
silke.szymczak@uni-luebeck.de
https://www.imbs.uni-luebeck.de/en/staff/academic-staff

Prof. Dr. Julie George
Department of Translational Genomics
University of Cologne
Clinic for ENT Medicine, Head and neck Oncology, University Hospital Cologne
jgeorge@uni-koeln.de
www.translational-genomics.de

https://hno.uk-koeln.de/forschung/arbeitsgruppen-labore/ag-molekulare-kopf-hals-onkologie/

" Promoting early career researchers plays a crucial role in supporting young scientists on their career path and offering them a real opportunity to establish themselves."

Photos: Silke Szymczak © Wiebke Bergmann; Julie George © private

Standard is the middle-aged man

An interview about diversity in medicine with Sophie Van Linthout

"The awareness of diversity in medicine is a prerequisite for appropriate translational research and personalized medicine". With this conviction, Prof. Dr. Sophie Van Linthout, head of the "Translational Immunocardiology" working group at the Berlin Institute of Health at Charité (BIH), conducts research and is committed to raising awareness of gender bias in research and the introduction of standards and guidelines that reduce gender discrimination in medical research.

gesundhyte.de: *What does diversity in medicine mean and why is diversity in medicine important?*

Prof. Dr. Sophie Van Linthout: Diversity in medicine means medicine in which all genders, backgrounds, ethnicities, beliefs and perspectives are appropriately represented in order to ensure the best possible care for each individual. In this sense, personalized medicine also includes the recognition and inclusion of diversity.

Diversity in medicine is important to open up opportunities for groups that are currently underrepresented in medicine, reduce inequalities in healthcare and improve patient outcomes.

Studies have shown that physicians from underrepresented minorities and women are more likely to provide care to underserved communities. In addition, it is known that promoting diversity not only improves staff engagement and retention, but also increases patient satisfaction and improves the handling of complex medical problems.

In research, where there is a sex and gender bias both preclinically and clinically, the inclusion of women is seen as beneficial to promote scientific progress in general and to advance women's health in particular. This is partly attributed to the greater openness of women to consider sex as a relevant biological variable in preclinical experiments and to explore gender-specific effects. In

"The recognition of diversity in medicine is a prerequisite for appropriate translational research and personalized medicine."

Prof. Dr. Sophie Van Linthout
Head of the research group "Translational Immunocardiology"
Berlin Institute of Health at Charité (BIH)

Photo: BIH/Thomas Rafalzyk

Groupphoto from Girls'Day 2024. ***Heartbeat in the lab: How does our body's engine work?***
(Photo: BIH)

this way, greater consideration of women in science can improve the quality and depth of research, as men and women can bring different skills and ways of thinking to the table.

gesundhyte.de: *When did you first come into contact with the topic yourself and how did diversity find its way into your work?*

Prof. Dr. Sophie Van Linthout: My first contact with the topic of diversity was the preparation of a position paper for the Working Group "Cellular Biology of the Heart" of the European Society of Cardiology (ESC), which addressed the importance of sex as a biological variable in cardiovascular research and provided recommendations to guide future research (Perrino *et al.,* 2020). Since then, part of my research has been focused on investigating the impact of biological sex and age in heart failure, and I am an active advocate for equity and diversity in the cardiovascular field. In my role as Chair of the Committee to promote gender equality of the Collaborative Research Center (CRC)1470 and as a member of the Heart Failure Association (HFA) Women in Heart Failure Working Group, I promote equity and diversity by raising awareness of gender/sex bias in research, of existing programs to promote women in science and by increasing the visibility of female scientists. In practice, I implemented and lead a seminar on gender bias in (cardiovascular) research at the Berlin School of Regenerative Therapies (BSRT). I also organize and contribute to congresses and sessions about/with women in heart failure (HFA Congress 2024, German Centre for Cardiovascular Research (DZHK) Science on Friday 2024, CRC1470 Satellite Symposium "Women in Heart Failure, Heart Failure in Women" 2024) and am actively involved in articles on this topic (Perrino *et al.,* 2020, Rosano *et al.,* 2024).

gesundhyte.de: *What does diversity mean in concrete terms in basic research, for example on fibroblasts?*

Prof. Dr. Sophie Van Linthout: Diversity in basic and translational research means that you take the impact of different characteristics (age, biological sex, strain, race,…) of your cells, animals, patients on the pathogenesis of the disease, therapy responsiveness, outcome into account. Unfortunately, even in an era of personalized medicine where stratification of patients is an important hallmark, sex bias in preclinical (cardiovascular) research is prevalent (Ramirez *et al.*, 2017). Mainly male mice are used in experimental studies, and in many cases the sex of the cells and animals is not even reported. The importance of addressing sex differences in experiments, or at least reporting the sex of your animals/cells, is supported by our findings with cardiac fibroblasts, which reflect sex differences in collagen production and inflammatory potential (Pappritz *et al.*, 2023) and provide insights into the different role of cardiac fibroblasts in the pathogenesis of heart failure between women and men. In addition, our research shows differences in the expression profiles of endomyocardial biopsy-derived fibroblasts from male and female patients, indicating the potential use of patient-specific endomyocardial biopsy-derived fibroblasts as screening platform to assess the efficacy of novel anti-fibrotic therapies in a biological sex-dependent manner.

gesundhyte.de: *Why is the topic important to you?*

Prof. Dr. Sophie Van Linthout: I firmly believe that the recognition of diversity is a prerequisite for appropriate translational research and personalized medicine.

With regard to cardiovascular research, I find it staggering that in 2025 there are still gender disparities in cardiovascular care to the detriment of women. This shows that greater awareness, integrated efforts, expanded research funding and specific guidelines for the prevention and treatment of cardiovascular disease in women are needed to close this gap.

gesundhyte.de: *How has the topic changed, what developments have there been in recent years?*

Prof. Dr. Sophie Van Linthout: The topic of diversity in medicine has gained raising recognition in recent years, which is among others reflected in the establishment of committees for diversity, equal opportunities and inclu-

"With regard to cardiovascular research, I find it staggering that in 2024 there is still a backlog in gender-specific cardiovascular care for women."

In the lab on Girls'Day 2024. ***Heartbeat in the lab: How does our body's engine work?***
(Photo: BIH)

sion in various societies/associations, the mandatory reporting of diversity metrics in studies and publications, the inclusion of diversity in research guidelines, the integration of cultural competence and diversity education into the curricula of medical faculties, and the existence of mentoring programs and diversity training.

Despite these developments, there is still a gender bias. While women are much more represented in medicine, they are still underrepresented in leadership positions, the so-called "leaky pipeline", i.e. the decreasing proportion of women in medicine and science with higher career levels. Women are underrepresented in clinical trials, and gender bias is still widespread in preclinical (cardiovascular) research.

gesundhyte.de: *Where do you see particular potential in this approach - also with a view to the future and treatment opportunities for patients?*

Prof. Dr. Sophie Van Linthout: Diversity is broad and complex. When it comes to sex/gender and my field of research, heart failure, a comprehensive understanding of the mechanisms underlying sex and gender differences in heart failure is key to progress towards the practical application of precision medicine.

I see particular potential in basic research that looks at biological sex differences, but also in the need to set specific inclusion thresholds for women in randomized controlled clinical trials or to conduct specific randomized

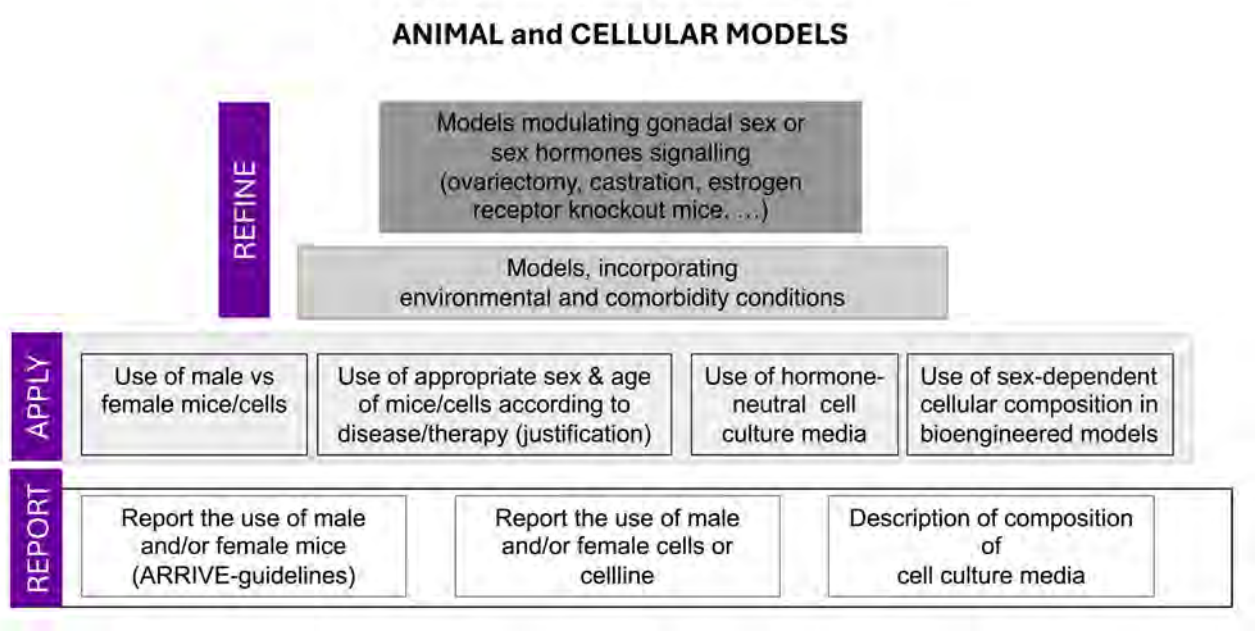

Figure 1: Exemplary standards for the use of animal and cell models to study sex-dependent differences in heart failure. From bottom to top: Minimum criteria *(Report)*, through criteria that set standards for experimental design to avoid sex bias in preclinical heart failure research *(Apply)*, to criteria that focus on specific understanding of sex differences in heart failure underlying mechanisms *(Refine)* (Graphic: Sophie Van Linthout).

controlled trials for treatments in order to enable a meaningful gender analysis that then provides well-documented evidence of gender differences or equality.

A translational institute such as the BIH has the opportunity and responsibility to facilitate diversity inclusion by promoting awareness and creating incentives that encourage research in this context.

gesundhyte.de: *What challenges do you see in preclinical research?*

Prof. Dr. Sophie Van Linthout: The challenges are manifold and show that scientists, healthcare professionals, universities, scientific societies, journal editors, peer reviewers and funding bodies need to act together to raise awareness of the importance of diversity in preclinical medical research, including the establishment of standards that provide guidance (see Figure 1).

The implementation of diversity in preclinical research is hampered by ethical, financial and statistical problems, which, for example, make the paired evaluation of female and male cells/animals impossible for all scientific questions. Therefore, in my opinion, scientists can only be recommended to use and compare both male and female mice/cells in their experiments. If this is not possible, researchers should use mice/cells of appropriate sex and age depending on the disease and therapy and justify this. As logical as this sounds, it is not common practice. Experiments with the opposite biological sex could be carried out as part of a consortium with other researchers. There are already minimum criteria and guidelines for specifying the sex of the animals, as set out in the ARRIVE guidelines (Animal Research: Reporting of In Vivo Experiments) (Kilkenny *et al.,* 2010). However, this does not yet apply to the sex of the cells, which in many cases is still not specified and in many cases is not known (Shah *et al.,* 2014). Recognizing the sex of cells is necessary to improve the applicability of biomedical

research discoveries. Awareness of this issue needs to be further raised, including the use of hormone-neutral cell culture media and sex-dependent cell composition in bioengineered models. Since the prevalence and impact of risk factors and various comorbidities differ between men and women, preclinical studies should further investigate the influence of these factors on the development of heart failure on a gender-specific basis. Finally, the influence of sex hormones on sex differences can be investigated in specific models that modulate the gonadal sex hormones. However, these studies are intended for specialist groups dealing with gender medicine and cannot be a prerequisite for all researchers.

In addition to the underrepresentation of female experimental models, mainly human cell lines from donors of European descent are currently used, indicating an underrepresentation of other groups in preclinical research. Efforts must be made to ensure that our preclinical research models reflect different population groups and therefore our patients in all their diversity.

gesundhyte.de: *What opportunities arise from your work at the BIH? What roles do collaborations play?*

Prof. Dr. Sophie Van Linthout: The BIH Excellence Award for Sex and Gender Aspects in Health Research enabled me to collaborate with the awardee Dr. Ralph Knöll (Astrazeneca), who is investigating the sex-dependent effects of constitutive myosin light chain phosphorylation on cardiac function. In a broader sense, my work at the BIH allows me to be active and contribute to initiatives within the BIH, but also in (inter)national societies, that give visibility and attention to this topic.

gesundhyte.de: *You also take part in campaigns such as Girls' Day and try to get girls interested in science. Is it possible to sensitize the participants to the topic?*

Prof. Dr. Sophie Van Linthout: I think so. In addition to the main aim of the initiative to inspire girls for science, it of course also offers the opportunity to address such topics and raise awareness of them. Specifically, we addressed the fact that women's and men's hearts are different and that heart failure has been considered a man's disease, even though it affects at least as many women as men, and that further research is needed to understand these differences and enable women to be treated accurately.

"The implementation of diversity in preclinical research is hampered by ethical, financial and statistical problems, which, for example, make the paired evaluation of female and male cells/animals impossible for all scientific questions."

Knowing that women are more receptive to such topics emphasizes even more how important it is to get girls interested in science!

The interview was conducted by Katharina Kalhoff.

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Contact:

Prof. Dr. Sophie Van Linthout
Head of Research Group Translational Immunocardiology
Berlin Institute of Health Center for Regenerative Therapies
Berlin Institute of Health at Charité (BIH)
Berlin
Sophie.van-linthout@bih-charite.de

www.bihealth.org/en/research/research-group/translational-immunocardiology

Photo: BIH/Thomas Rafalzyk

baseTraCE

The participatory project for training and further education in the Medical Informatics Initiative

by Dagmar Krefting and Carolin Bittner

The joint project "basic services for Training and Continuous Education within the Medical Informatics Initiative" (baseTraCE) serves as a central hub for the education and training activities of the Medical Informatics Initiative (MII).

The digitalization of medicine and the development and use of new information technologies are creating new and exciting fields of activity. Therefore, new digital skills are of great importance – especially the handling of clinical treatment data and decision support systems, as well as the employment of information and communication technologies for medicine.

In recent years, the Medical Informatics Initiative (MII) has made important progress in utilizing the potential of digitalization for better healthcare research and care (Semler *et al.,* 2024). An important component is the establishment of so-called data integration centers (DIC) at the participating university hospitals. The DIC staff ensure, that the inpatient treatment data is integrated and made available for research, taking into account all legal framework conditions, such as informational self-determination. With the progress of the MII, DIC are now also set up in the first non-university hospitals.

The staff members in the DIC require a wide range of skills: Many legal regulations must be observed and they must ensure that no one gains unauthorized access to sensitive health data. In addition, employees must be familiar with numerous technologies and software systems so that data can be found, and requested for use by researchers and ultimately made available for analysis.

There is presently a shortage of skilled labour in the DIC, combined with salaries and long-term prospects that currently cannot compete with the private sector. Therefore the overarching aim of baseTraCE is to ensure the sustainable operation of DIC.

In the previous funding phase of the MII, many concepts, offers and technical infrastructures for online learning and knowledge management have been developed. These include, for example, the "HiGHmeducation" courses, the MIRACUM-DIFUTURE colloquium and the catalogs of learning objectives developed in the SMITH consortium. In baseTraCE, we want to make these offers findable via

a common platform and reusable for as many interested parties as possible, continuously integrating new offers being developed in the current funding phase. The shared platform will also make it easier to find relevant information and further relevant education and training opportunities.

New training and further education courses will not be created within the baseTraCE project, as it is a project for structural support. Funding is provided for conception and coordination costs to provide and maintain basic structures such as the learning management system or an event calendar. This will make the courses and teaching materials offered by the respective experts better known and thus used more efficiently.

As already indicated above, the focus lies on the qualification of the DIC staff. A particular challenge is that the range of tasks and skills within a DIC is very heterogeneous and the distribution of tasks can vary greatly depending on the structure and size of the DIC. On the other hand, the skill profiles of new members are also very diverse. So depending on the matching of existing and required skills, different learning opportunities are needed to ensure an optimal start to the new job. An initial result of the project is a so-called Quickstart Guide, which provides an overview of the network structures in which the DIC are embedded, and the most important methods and technologies.

However, rapid technological progress, changes in the legal framework, the further development of the Medical Informatics Initiative and the research landscape require lifelong learning from DIC members.

This can only be reached in the long term through a lively and committed community in which MII members exchange ideas and share their experiences and knowledge. BaseTraCE aims to support this through suitable community tools and platforms.

The project relies on broad support from the community: on the one hand, by providing learning materials that have already been developed and by reporting events.

PROFILE RESEARCH PROJECT: BASETRACE

Name of the Project
basic services for Training and Continuous Education within the Medical Informatics Initiative

Acronym
baseTraCE

Duration
01.07.2023 until 30.06.2027

Funding
Federal Ministry of Research, Technology and Space, Germany (BMFTR)

Project partners
- Technical University of Applied Sciences Mannheim
- German Association of Medical Faculties
- Technical University of Munich
- Leipzig University
- University Medical Center Göttingen

Objective
Establishment of a central hub for MII training and further education activities

Target group
DIC staff members, MII members

Website
www.medizininformatik-initiative.de/en/basetrace

Joint meeting of the projects baseTraCE, EVA4MII, fit4translation and MII-Academy and the MFT at GMDS 2024: from left to right: Prof. Dr. med. Rainer Röhrig, Alexander Brenner, Dr. Birgit Schneider, Jun. Prof. Dr.-Ing. Myriam Lipprandt, Cornelia Dolling, Kai Günther, Dr. Michael Storck, Philipp Konhäuser, Erik Schiller, (Photo: Univ.-Prof. Dr. med. Rainer Röhrig).

On the other hand, through feedback from users in order to identify gaps in the learning offers and to align the further development with the needs. In particular baseTraCE relies on the development and provision of updated and new learning opportunities.

A preliminary collection of learning materials can be found on the following page:
https://github.com/medizininformatik-initiative/BaseTRACE

Reference:

Semler, S.C., Boeker, M., Eils, R., Krefting, D., Loeffler, M., Bussmann, J., Wissing, F., & Prokosch, H.U. (2024). Die Medizininformatik-Initiative im Überblick – Aufbau einer Gesundheitsforschungsdateninfrastruktur in Deutschland [The Medical Informatics Initiative at a glance-establishing a health research data infrastructure in Germany]. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz, 67(6), 616–628. https://doi.org/10.1007/s00103-024-03887-5

Contact:

Prof Dr. Dagmar Krefting
Project lead baseTraCE
Director of Medical Informatics
University Medical Center Göttingen
Göttingen
dagmar.krefting@med.uni-goettingen.de

Carolin Bittner
Project coordinator baseTraCE
Department of Medical Informatics
University Medical Center Göttingen
Göttingen
carolin.bittner@med.uni-goettingen.de

www.medizininformatik-initiative.de/de/basetrace

Photos: Medical Informatics\UMG

Events

BIH exhibition goes international

Exhibition “Berlin – Capital of Women Scientists”

by Katharina Kalhoff

The exhibition “Berlin – Capital of Women Scientists” is garnering international attention as it travels to Berlin’s partner cities. The exhibition tour – which has already included stops in Prague, Tokyo and Budapest – is organized in collaboration with Goethe Institute branches and the German Academic Exchange Service (DAAD).

The traveling exhibition is a continuation of the project **“Berlin – Capital of Women Scientists,”** which was launched under the auspices of Science Year 2021 as a cooperation between the Berlin Senate Chancellery and the Berlin Institute of Health at Charité (BIH). It all began with several edit-a-thons and writing workshops in which interested citizens, from pupils to pensioners, composed new Wikipedia entries and edited existing articles. Based on these new and improved biographies – more than 50 in all – a traveling exhibition was created that succinctly portrays the lives and careers of 22 women scientists and scholars from different eras and disciplines who were or are based in Berlin. The exhibition has already been shown at various locations in Berlin, such as at universities, libraries and town halls, and is also available online.

“In addition to dismantling structural barriers and supporting individual women scientists, it is very important to us as a research institute to play our part in increasing the visibility of women scientists through various projects” says Karin Höhne, Head of Equal Opportunity and Diversity at the BIH. “Women scientists who are made visible can change perceptions and serve as role models.” She is thrilled about the international collaboration, adding: “With 35 percent of professorships across the city held by women, Berlin is the capital of female scientists and scholars and the exhibition is a way to give some of them a voice.”

In collaboration with Goethe Institute branches and the DAAD, the exhibition is traveling to Berlin’s partner cities (Photo: © BIH/Katharina Kalhoff).

The exhibition was opened at Charles University in Prague (Photo: © BIH/Katharina Kalhoff).

On the occasion of the anniversary "30 years of city partnership Berlin-Tokyo 2024", the Goethe Institute invited the exhibition to Tokyo (Photo: © Yohta Kataoka).

Exhibition opened in Prague and Tokyo in May, and in Budapest in June, 2024

In **Prague**, the joint project was kicked off in the Rectorate of Charles University by Prof. Milena Králíčková, the university's rector, and Dr. Helena Reichlová, an outstanding solid-state physicist. Reichlová currently heads the prestigious DIOSCURI research center at the Institute of Physics of the Czech Academy of Sciences, a program to promote scientific excellence initiated by the German Max Planck Society. The exhibition was on display for a month in the former cloister at the Rectorate of Charles University and included a particular highlight for school classes: a specially designed digital rally via the app Actionbound, which enabled kids to explore the exhibition interactively.

As part of the anniversary **"30 Years of City Partnership Berlin-Tokyo 2024,"** the exhibition was displayed in Japanese, English, and German in the foyer of the Goethe Institute **Tokyo** from May 7 to 17, 2024. As a side program, a Wikipedia edit-a-thon was held in Japanese on May 7 and 8, 2024 at the Goethe Institute's library. And on May 15, 2024 in Tokyo, the edit-a-thon participants presented the results of their workshops under the motto "Capitals of Women Scientists: The Gender Gap in Research and Society,". followed by a discussion in which experts from science and media provided valuable insights on the topic. This event was attended by the Governing Mayor of Berlin, Kai Wegner, and the President of the Berlin House of Representatives, Cornelia Seibeld.

In **Budapest**, the exhibition opening at the local Goethe Institute was held in conjunction with a panel entitled **"What women know – the role of women today in science and academia."** The aim was to examine the situation of female scientists and scholars in Hungary and Germany through two exhibitions and a discussion.

Prof. Christopher Baum, Chair of the BIH Board of Directors and Chief Translational Research Officer of Charité stresses: "As a research institute, we are delighted through this exhibition to be able to promote international exchange and raise the visibility of women scientists, which is something that is absolutely necessary."

Further collaborations are planned for 2025: The exhibition will open in Paris on April 8 and in Brussels on May 12.

Contact:

Katharina Kalhoff
Spokesperson, Editor for Science Communication
Berlin Institute of Health at Charité (BIH)

www.bihealth.org

Photo: © BIH / Thomas Rafalzyk

Events

Diversithon on board of the MS Wissenschaft

The BIH was once again a cooperation partner of the MS Wissenschaft

by Katharina Kalhoff

The Berlin Institute of Health at Charité (BIH) was a cooperation partner at the Diversithon on deck of the "MS Wissenschaft", the floating science center with exhibits for hands-on testing and participation on behalf of the Federal Ministry of Research, Technology and Space (BMFTR), with a stop in Cologne. Many people use Wikipedia to search for information. However, who does Wikipedia represent? And who writes and edits the entries? Just 19 percent of biographical entries on Wikipedia have women as their subjects. Most people you can find information about on Wikipedia are white and male.

The Diversithon - a writing workshop about female scientists on Wikipedia at the BMFTR's floating Science Center – was designed to at least slightly increase this proportion of women. Together with committed participants, articles about female scientists were edited, completely redesigned and rewritten.

"I work at a Max Planck Institute, meaning I work in science, and writing is my hobby. I enjoy to combine these two worlds, which is why I was keen to take part in the writing workshop," explained participant Male Arimond.

In keeping with the **"Freedom" theme** of the 2024 Year of Science, attendees also discussed how Wikipedia might better reflect the diversity of our society, building on experiences and ideas already developed since 2021 in the BIH writing workshops **"Berlin - Capital of Women Scientists"**. The digital version of this exhibition, which is now touring internationally, will accompany the MS Wissenschaft on this year's route through Germany

The BIH was once again a cooperation partner of the MS Wissenschaft (Photos: © BIH/Katharina Kalhoff).

In keeping with the "Freedom" theme of the 2024 Year of Science, the workshop participants also discussed how the diversity of our society might be reflected better in Wikipedia (Photo: © BIH/ Katharina Kalhoff).

Together with committed participants, articles about female scientists were edited, completely redesigned and rewritten (Photo: © BIH/Katharina Kalhoff).

and Austria. "The Berlin Institute of Health at Charité has been organizing the Diversithon since 2019 to help women and other underrepresented groups in science gain more visibility. Everyone uses Wikipedia, and if certain groups of people are missing there and we can't find anything about them, this is a distortion that we want to counteract with the writing workshops. The scientific achievements of women and other underrepresented groups need more attention, as without diversity there can be no new and groundbreaking findings," says Karin Höhne, Head of the Equal Opportunities Office at BIH.

National topics from science and research inspire a desire for more

As the right to information includes the freedom "to inform oneself without hindrance from generally accessible sources", it was very important for the Diversithon to reach out to people with no previous experience of writing in Wikipedia and to remove any barriers by providing both information and guidance. In this way, for example, it was possible to arouse the interest of participant Waltraud Kochhan: "I visit the MS Wissenschaft every year because I find the topics from science and research super exciting and what is shown and offered here is also of supra-regional importance. As the MS Wissenschaft can't dock in Aachen, today I just boarded the ship at a nearby station and I immediately found the Diversithon workshop interesting. I've already learned a lot today and now I am keen to write more articles about women scientists."

Photo: © BIH / Thomas Rafalzyk

Contact:

Katharina Kalhoff
Spokesperson, Editor for Science Communication
Berlin Institute of Health at Charité (BIH)

www.bihealth.org

Events

SBHD 2024 Modern Science in an ancient hall

16th annual international conference on Systems Biology of Human Disease

by Lucas Arnoldt, Khue Nguyen and Julius Upmeier zu Belzen

For the second time Vanderbilt University invited international researchers and trainees to the Systems Biology of Human Disease (SBHD) in early June 2024. After a brilliant first meeting in Nashville in 2022, attendees were eager to meet again and network face-to-face. Researchers and trainees from around the world brought their expertise and music spirit to the Capitol of Country Music, Nashville, USA, to discuss their scientific breakthroughs.

After the first day's meeting, attendees came together for a welcoming reception and a chance to network. The lively spirit of Nashville brought extra energy to the international community at the Vanderbilt Alumni Hall the next day.

The sixteenth annual SBHD meeting's planning crew, led by the Vanderbilt University Quantitative System Biology Center (QSBC), the Vanderbilt Diabetes Research and Training Center (DRTC), and the Berlin Institute of Health at Charité, designed each symposium to be grouped by today's hot topics in human disease research such as Diabetes, Cancer, Aging-related Diseases, Vision-related Diseases and Infection. Many distinguished speakers diversified and enriched each of the five symposia, among those were **Carlos Lopez** (Altos Labs), **Andrew Gentles** (Stanford University), **Cynthia Reinhart-King** (Vanderbilt University), **Benjamin Wild** (BIH @ Charité-Universitätsmedizin Berlin), and **Samuel Scarpino** (Northeastern University). By keeping the tradition of supporting young researchers, each symposium was designed to highlight both senior and junior investigators in a series of short talks.

Researchers of all levels participated in two poster sessions held throughout the 3-day event to discuss the current trends in systems biology research. Presenters shared hypotheses on cancer therapies and immunology, insulin resistance and obesity, genetic disease risk, and neurodegenerative disease. Selected abstracts were chosen by the planning committee to also give a short, fifteen-minute talk to summarize their research, along with the opportunity to engage with attendees via Q&A.

2024th Awardee of the Anne-Heidenthal Prize for Fluorescence Research, given by Chroma Technology Corp., was **Sabrina Spencer**, Associate Professor from the University of Colorado Boulder, for her presentation "Mechanisms

Award ceremony Anne Heidenthal-Prize for Fluorescence Research awarded by Chroma Tech. Inc.
2024th Anne-Heidenthal Prize for Fluorescence Research has been awarded to Sabrina Leigh Spencer from the University of Colorado. (from left to right: Dr. Georg Draude (Chroma), the awardee Sabrina Leigh Spencer and Prof. Dr. Roland Eils (chair SBDH) (Photo: © Jessica Kimber).

The two chairs of SBHD Roland Eils (left) and Vito Quaranta (right) present Nikolaos Meimetis (mid) with the prize for best short talk (Photo: © Jessica Kimber).

The last-minute venue change turned out to be a great thing! The new venue was perfect for the size of this year's event and was a beautiful setting to enable scientific exchange and discussions during poster sessions (Photo: © Jessica Kimber).

of Sensitivity and Adaptation to CDK2 Inhibitors". Her presented work contributes to understanding how cancer cells respond to CDK2 inhibitors, which is crucial for developing effective cancer therapies and overcoming cancer drug resistance.

The poster sessions provided another opportunity for networking and exchanging ideas among senior and junior researchers. The conference participants engaged with the junior presenters by voting for best poster presentations and short talks. Initially, there were two awards each for poster presentations and short talks. However, due to the exceptional quality of the presentations, determining just two top short talks proved challenging. Ultimately, two additional awards were given, resulting in six awards to outstanding trainees:

Best Short Talk

Nikolaos Meimetis, Masachusetts Institute of Technology

Title: Leveraging Machine Learning Modeling to Identify Cues for Improving Tissue-on-Chip Studies of Human Liver Disease

Best Short Talk (runner-up)

Marey Messingschlager, Berlin Institute of Health at Charité (BIH)

Title: SARS-CoV-2 Induced Alterations of the Upper Airway DNA Methylome Exert Long-Term Effects on Genes Involved in Ciliary Function

Best Poster

Joseph T. Benthal, Vanderbilt University Medical Center

Title: Identification of disrupted Gene Regulatory Networks in the Murine Sox10^{DOM} Enteric Nervous System via Single Cell Multiomics

Best Poster (runner-up)

Khue M. Nguyen, Berlin Institute of Health at Charité (BIH)

Title: Inference and Application of a Data-Driven Hierarchical Gene Ontology with Cell-Type Resolution Across the Human Body

Honorable Mentions

Pablo Naranjo Meneses, University Hospital Heidelberg & BioQuant

Title: Optimization of Chemotherapeutic Regimens Using Multi-Objective Reinforcement Learning

Bryan Glazer, Vanderbilt University

Title: TangleFlow: A Deep Learning Model of the Cellular Dynamics of Embryonic Development

The community looks forward to the SBHD 2025, held again in Berlin from June 16 to 18.

Contact:

Franziska Müller
Project Management and Editorial Office
gesundhyte.de
BIH Center of Digital Health
Franziska.mueller@bih-charite.de

https://www.hidih.org/events_sbhd

Photo: © BIH / Thomas Rafalzyk

News

Community Building for Disease Modeling

e:Med Online Seminar Series: Modeling Approaches for Disease Processes

by Sara Checa, Markus Morrison, Kevin Thurley and Jana Wolf, for the e:Med project group
Modeling approaches for disease processes

In the last decades, computational modeling has been successfully used to describe and elucidate fundamental biological processes. Different modeling approaches have been applied to derive a quantitative understanding of molecular and cellular processes and to integrate qualitative and quantitative data to elucidate underlying mechanisms.

More recently, the field has evolved to also address biomedical research topics in the framework of system medicine. Diseases are often characterized by multiple perturbations in various biological processes ranging from gene expression, metabolism, signaling within cells, to cell-cell communication, immune responses or tissue organization. Therefore, an interdisciplinary exchange of knowledge and expertise is highly necessary.

The e:Med Project Group ***Modeling Approaches for Disease Processes*** formed end of 2021 to build a community with the aim to connect scientists investigating different disease processes and modeling techniques. The focus is on various aspects of disease modeling, such as integration of different processes, modeling of perturbations, and consideration of patient heterogeneity. Moreover, an important research topic is currently the quantitative analysis and integration of high-dimensional data sets into mathematical models. These datasets result from single-cell sequencing over time-course transcriptomics and proteomics to high-content imaging data sets, which give insights into the spatial relations among highly individual cell types in complex tissues. Machine-learning tools including autoencoders, optimal transport and trained neural networks are instrumental in this highly dynamic research field. Moreover, methods to connect them to mechanistic modeling techniques are highly needed to gain interpretable and data-based descriptions of biological processes.

Within the ***Modeling Approaches for Disease Processes group***, we are building a community between modelers, bioinformatitians, computer- and data scientists as well as clinicians. We also bridge between modeling efforts and computational research in academia and pharmaceutical R&D. While we started to foster the exchange between e:Med groups in the beginning, we soon reached out to our wider community, both nationally and internationally. We strive to engage community members across all career stages from undergraduate students to senior group leaders.

Figure 1: Participants of the e:Med Satellite Workshop 'Modeling Approaches for Disease Processes' at the Systems Biology of Mammalian Cells Conference (SBMC), May 2022, Heidelberg (Photo: © Silke Argo, e:Med).

We started with an Online Seminar Series in January 2022 that has been taking takes place every 1st or 2nd Wednesday of the month since then. The focus of the seminars is the introduction, discussion and comparison of different mathematical modeling approaches. By winter 2025, we held 23 seminars, with video recordings of many past seminars made openly available. An in-person-meeting took place as a satellite workshop at the SBMC conference in Heidelberg, in May 2022 (Figure 1).

The program of the autumn/winter seminar series and information on additional activities of the community are kept up-to-date at https://www.sys-med.de/en/networking/pg-modeling-of-disease-processes/online-seminar-series.

The fruitful discussions within the group sparked the development of a special issue '*Mathematical Modeling of Disease Processes'* in the journal *'Current Opinion in Systems Biology'* which is currently being assembled.

Link to the publication:
https://www.sciencedirect.com/special-issue/10JBBNDV8TG

Contact:

Prof. Dr. Jana Wolf
Head Mathematical Modelling of Cellular Processes
Max Delbrueck Center for Molecular Medicine (MDC), Berlin
jana.wolf@mdc-berlin.de

Prof. Dr. Markus Morrison (Rehm)
Director, Institute of Cell Biology and Immunology
University of Stuttgart
markus.morrison@izi.uni-stuttgart.de

Prof. Dr. Kevin Thurley
Biomathematics, Institute of Experimental Oncology
University Hospital Bonn
kthurley@uni-bonn.de

News

The medicine of the future – visions

The new CHARITÉ season jumps to the year 2049

What will medicine look like in the future and what social issues will affect society? What challenges will doctors and nurses at the fictional Charité be facing in 2049? The fourth season of the ARD series ventures a look into the future. It tells of advanced climate change, a healthcare system under cost pressure and an unknown bacterium, as well as digitalization, innovative research and artificial intelligence in diagnostics and therapy.

Following the great success of the first three historically oriented seasons, six more episodes about Charité were launched at the beginning of April 2024. At the center of the story in midsummer 2049 is the microbiome and its research. Once again, a snapshot of the microcosm of university medicine has been created from various storylines. The successful ARD series was created in collaboration with ARTE and produced by UFA Fiction.

Six new episodes

The residents of Berlin experience an extreme climate: temperatures of up to 45 degrees and heavy rainfall are no longer a rarity. Charité continues to be a stronghold of medical excellence and research with state-of-the-art equipment. Artificial intelligence (AI) supports the teams in diagnosis, all patients have a digital twin for surgery simulation and organs come from the 3D printer. Innovative therapies offer hope and new drugs bring healing. Despite the efficient technologies, it is clear that it is the people – the nurses, doctors and technicians – who make the diagnoses and care for the patients.

Artificial intelligence (AI) will play an important role in future medicine (Photo: © ARD/MDR/BDA/Benno Kraehahn).

In the fourth season, people remain important in medicine despite new efficient technologies (Photo: © ARD/MDR/BDA/Benno Kraehahn).

The series once again focuses on successful women, above all microbiologist Maral Safadi (**Sesede Terziyan**), who comes to the Charité with her wife, gynecologist Julia Kowalczyk (**Angelina Häntsch**). For top researcher Dr. Safadi, it is a return from Boston to head the Institute of Microbiology at the Charité. Her first patient suffers from an infection caused by an unknown bacterium. When a second patient is admitted with the same symptoms, the race against time to find the cause begins.

In addition, a planned healthcare reform threatens to overturn the principle of solidarity and divide society: Health insurance companies will create a score for each person and collect data on health and life expectancy. This becomes the basis for medical treatment or non-treatment.

Microbiome as a topic for the future

For a season set in the future, the key question was: For which medical breakthrough could there be a Nobel Prize in 25 years' time? Current medical developments were considered further and, with the support of the advising Charité scientists, the microbiome - the complex interaction of thousands and thousands of bacteria in the body - was selected as a promising field of research. This choice is an interesting link to the first season of the series: In the 19th century, it was Robert Koch who discovered bacteria and their role in the development of diseases. In the present day, it is the microbiologist Dr. Safadi who triggers a potential medical revolution with the help of a bacterium.

Artificial intelligence in medicine

Prof. Dr. Heyo K. Kroemer, CEO of Charité, sees artificial intelligence as a great opportunity: "The use of artificial intelligence will also change medicine and expand treatment options. For example, AI can be used to analyse complex patterns in medical data, enabling even more precise diagnoses and individual, personalized therapies. Basically, I think that AI will be used in all areas of medicine. We are currently using AI to support radiology and pathology in particular. And yet we will still need medical professionals to guide, evaluate, confirm and support. Medicine remains a profession of people for people."

Contact:

Franziska Müller
Project Management and Editorial Office
gesundhyte.de
BIH Center of Digital Health
Franziska.mueller@bih-charite.de

Photo: © BIH / Thomas Rafalzyk

News

HDP4Germany

National access to health data for the EHDS

Since September 2023, the project **HDP4Germany** (Improving HealthData@EU-preparedness for Germany) has been funded under the European Commission's EU-4Health program with the aim to set up a national data access point for health data. The project thus makes a significant contribution to advancing the future European Health Data Space (EHDS) at the national level.

The EHDS aims to improve the cross-border use of health data within the European Union (EU) with the aim of providing all EU citizens with improved access to and more control over health data arising from primary use, but also to strengthen the use of this data for scientific purposes (secondary use) at the EU level.

An important step towards implementing the EHDS at national level is therefore the establishment of Health Data Access Bodies (HDABs), which play a central role in the networking of various data-holding bodies, such as the Health Research Data Center (FDZ) or individual registers. This is a basic prerequisite for enabling access to health data for research and development, both at national and European level. The aim is to establish a secure network for the harmonized use of health data in Europe.

One of the main tasks of HDP4Germany is therefore to develop and test the technical and organizational requirements for the national data access point. The first use case to be developed is linking health data at national level. As part of the project, the results of previous EHDS related EU projects (e.g. Joint Action: Towards the European Health Data Space, HealthData@EU pilot project), in which the FDZ is also actively involved, will be used as a basis for advancing German activities in line with the current European developments.

In HDP4Germany, the establishment of the national data access point is being implemented within the framework of five technical work packages with the following focal points:

1. the establishment of a national application management system
2. the provision of a national metadata catalog
3. the creation of a secure virtual environment for the processing of electronic health data
4. the establishment of a cross-border gateway to the HealthData@EU infrastructure
5. to improve the quality of the electronic health data to be provided by the data access point in the future

The consortium partners of HDP4Germany are the Federal Ministry of Health (coordination), the Health Research Data Center at the Federal Institute for Drugs and Medical Devices and Forschungszentrum Jülich GmbH/Projektträger Jülich. The project will run for four years (01.09.2023 to 31.08.2027). The project is co-funded by the European Union's 4th Health Program (2021-2027) under grant agreement no. 101128672.

Contact:

Rebecca Alvarado
FDZ/BfArM
Rebecca-Elizabeth.Alvarado@bfarm.de

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Redaktion:

Editor in Chief: Prof. Dr. Roland Eils
Berlin Institute of Health at Charité (BIH)
Editorial coordination: Franziska Müller
Berlin Institute of Health at Charité (BIH)
Editorial Team:
Dr. Silke Argo (e:Med), Melanie Bergs (PtJ), Prof. Dr. Lars Kaderali (Universität Greifswald), Katharina Kalhoff (BIH), Dr. Marco Leuer (DLR-PT), Dr. Miriam Engels (PtJ), Dr. Matthieu-P. Schapranow (Hasso-Plattner-Institut), Dr. Thomas Steiner (Plattform Lernende Systeme), Konstanze Pflüger (BIH), Dr. Jessica Rosenberg (DLR-PT) and Stavroula Deoudi (HiGHmed).

Address:
Editorial office gesundhyte.de
c/o Berlin Institute of Health at Charité (BIH)
Center of Digital Health
Luisenstr. 65, D-10117 Berlin, Germany

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c/o Berlin Institute of Health at Charité (BIH), Center of Digital Health
Luisenstr. 65, D-10117 Berlin, Germany
franziska.mueller@bih-charite.de

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The gesundhyte.de editorial team:

First row, left to right: Prof. Dr. Roland Eils (BIH), Franziska Müller (BIH), Dr. Silke Argo (e:Med), Melanie Bergs (PtJ), Prof. Dr. Lars Kaderali (University of Greifswald),
second row, left to right: Katharina Kalhoff (BIH), Dr. Marco Leuer (DLR-PT), Dr. Miriam Engels (PtJ), Dr. Matthieu-P. Schapranow (Hasso Plattner Institute), Dr. Thomas Steiner (Plattform Lernende Systeme),
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Contact

Berlin Institute of Health at Charité (BIH)
Editor in Chief: Prof. Dr. Roland Eils
Editorial coordination and ordering service:
Franziska Müller
c/o Berlin Institute of Health at Charité (BIH)
Center of Digital Health
Luisenstr. 65, D-10117 Berlin, Germany
E-Mail: franziska.mueller@bih-charite.de
www.hidih.org

Communication and Marketing, Press Office
Contact persons:
Konstanze Pflüger and Katharina Kalhoff
Anna-Louisa-Karsch-Str. 2, D-10178 Berlin, Germany
E-Mail: konstanze.pflueger@bih-charite.de and katharina.kalhoff@bih-charite.de
www.bihealth.org

Lernende Systeme – Germany's Platform for Artificial Intelligence
Contact person:
Dr. Thomas Steiner
Managing Office: c/o acatech
Karolinenplatz 4, D-80333 München, Germany
E-Mail: steiner@acatech.de
www.plattform-lernende-systeme.de

Project Management Jülich
Forschungszentrum Jülich GmbH
Sustainable Development and Innovation
Universities, Innovation Structures, Health (HIG)
Contact persons:
Melanie Bergs and Dr. Miriam Engels
D-52425 Jülich, Germany
E-Mail: m.bergs@ptj.de and mi.engels@ptj.de
www.ptj.de

German Aerospace Center (DLR)
Project Management Agency – Department Health
Contact persons:
Dr. Marco Leuer, Dr. Jessica Rosenberg and Dr. Bettina Koblenz
Heinrich-Konen-Str. 1, D-53227 Bonn, Germany
E-Mail: marco.leuer@dlr.de, jessica.rosenberg@dlr.de and
bettina.koblenz@drl.de
www.dlr-pt.de

e:Med Management Office
Managing Director:
Dr. Silke Argo
c/o Deutsches Krebsforschungszentrum (DKFZ) – V025
Im Neuenheimer Feld 581, D-69120 Heidelberg, Germany
E-Mail: s.argo@dkfz.de
www.sys-med.de

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KAISERIN FRIEDRICH-HAUS
ROBERT-KOCH-PLATZ 7
10115 BERLIN, GERMANY

ORGANIZED BY:

ROLAND EILS
BERLIN INSTITUTE OF HEALTH AT CHARITÉ (BIH), BERLIN, GERMANY

IRINA LEHMANN
BERLIN INSTITUTE OF HEALTH AT CHARITÉ (BIH), BERLIN, GERMANY

VITO QUARANTA
NORTHEASTERN UNIVERSITY, BOSTON, USA

KEYNOTE SPEAKERS:

PEER BORK
EUROPEAN MOLECULAR BIOLOGY LABORATORY, HEIDELBERG, GERMANY

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