

ANNUAL REPORT 2025

FOREWORD

Dear readers,

The most significant advances in health research often lie hidden: in tiny molecular changes, fleeting signals between cells, or data patterns that only become visible through modern analytical methods combined with AI. Our institute has the task to develop such analytical technologies and integrate them into high-performance measurement strategies for precision medicine.

The year 2025 has once again confirmed that we are on the right track – also from the perspective of an independent commission. Following the evaluation commissioned by the Leibniz Association in the previous year, the Commission reached a highly positive conclusion in the summer of 2025: It acknowledged the positive development of ISAS and recommended continued joint funding by the federal and state governments.

We are delighted that our scientific findings have been well received and that we are able to continue our work in collaboration with partners from universities, hospitals and industry. At the same time, we see this evaluation as an incentive to consistently advance our research and establish new partnerships.

Colleagues from a variety of disciplines, nationalities and career stages work together at our institute. What unites them is the shared goal of contributing to patient welfare through their research. Some scientists work exclusively with human samples or methods that do not involve animal testing, while others rely on studies involving mice and animal samples. Transparency and open dialogue about animal research therefore remain important issues for us, which we continued to address intensively in 2025.

Another topic that has been engaging us at ISAS for several years is how we can make our work even more sustainable. Sustainability is not only a matter for our research – such as our ‘green AI’, a climate-friendly energy concept and the responsible use of resources in the laboratory – but also to the way in which we make information accessible. We are therefore continuously developing our communication formats and expanding our digital offerings. With our ISAS Kompakt section on our website, we have already created additional space for science communication that is accessible to the general public. We intend to consistently pursue this digital path in the future.

I hope you enjoy reading our Annual Report!



A handwritten signature in black ink, appearing to read 'Albert Sickmann'.

Prof. Dr Albert Sickmann

PATHOMECHANISMS

New Drug Candidates for the Treatment of Heart Failure	26
Gut Flora & Stroke: How Microorganisms Influence Our Immune System	29
“Our findings suggest that a healthy microbiota may have a negative impact on the course of a stroke.”	31

JUNIOR SCIENTISTS

Microbiome Research: EU Network METAMIC 3 for PhD Students	33
Copenhagen: Different Molecules, New Perspectives?	35
What’s going on here, Luisa Speicher?	39

MS-BASED IMAGING

Endogenous Antioxidant Promotes Breast Cancer Cells in Lungs	40
Effective Stress-coping Strategies Enable Tumour Cells to Survive in the Lung	43

ORGANISATION

Organisation Chart	47
Boards	48
ISAS Memberships in Scientific Associations	51
Funding Sources	52

Imprint	53
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FROM HUMAN STEM CELLS TO MICE: RESEARCH INTO NEW TREATMENTS FOR HEART FAILURE



Few topics in research are as controversial as animal testing. At ISAS, scientists are fully aware of the significant ethical responsibility that this entails. Whenever possible, they opt for alternative methods rather than conducting experiments on mice. However, animal testing is currently necessary for many questions relating to cardiovascular diseases. This includes research into heart failure. Of the four million people affected in Germany, the diagnosis not only severely restricts their daily lives; it is also a life-threatening condition and the sixth leading cause of death.¹ For around half of patients, treatment with currently available drugs is not an option, or these drugs are simply not effective enough. This is where the HI-FIVE research project (► p. 07) comes in. Scientists and clinicians are working on a new drug-based therapeutic approach designed to close the existing gap in care for those affected. To this end, their research encompasses cell cultures, human stem cells, experiments with mice and a clinical trial involving patients.

Not all cases of heart failure are the same. In women, impaired relaxation of the heart muscle is more commonly the cause of reduced filling of the left ventricle, whereas in men, the most common cause of heart failure is reduced cardiac output. These different manifestations of the condition make it difficult to provide

appropriate treatment with currently available drugs. In the HI-FIVE project, researchers are further optimising GRK5 inhibitors – active substances that inhibit the key enzyme GRK5 which is up-regulated in heart failure – to pave the way for a new, targeted drug therapy. In doing so, they consider sex- and age-specific aspects of heart failure.

¹ https://www.dgpk.org/wp-content/uploads/Herzbericht-Update-2024-Gesamt_Final-2024-08-1.pdf



In addition to water, food, and bedding, mice in animal facilities are provided with play materials (known as 'environmental enrichment') to support species-appropriate housing: The red shelter and nesting material allow the animals to shape their environment and create a place to retreat. The wooden ball and the transparent tube provide important opportunities for stimulation and activity. The latter also enables positive 'handling' interactions between the animals and animal care staff, for example when the mice are picked up and held.

Pluripotent stem cells from patients' blood samples

The initial focus is on the effect of GRK5 inhibitors on human cardiomyocytes (heart muscle cells) and endothelial cells (cells lining the walls of blood vessels). The researchers isolate pluripotent stem cells from blood samples taken from patients and healthy individuals, which can be developed into various cell types in the laboratory. They then use these to produce the specialised cells required for their research. This allows potential positive and negative effects to be identified at the cell culture stage, before deciding whether the active substances need to be tested in living organisms in the next step.

Wherever possible, researchers at HI-FIVE opt for animal-free alternatives rather than conducting experiments on mice. For certain research questions, however, so-called mouse models are necessary because no viable alternative methods currently exist. For example, complex mechanisms of action within a living organism cannot be studied in a Petri dish. "Under the Animal

Welfare Act, animal testing is only permitted if it is indispensable – that is, if there are no alternative methods available for gaining knowledge," explains Prof. Dr Gero Hilken, Animal Welfare Officer at ISAS and Head of the Central Animal Laboratory at University Hospital Essen.

” Under the Animal Welfare Act, animal testing is only permitted if it is indispensable.

Researchers at HI-FIVE plan all animal experiments in consultation with the Animal Welfare Officer. Before the State Office for Consumer Protection and Food Safety of North Rhine-Westphalia (Landesamt für Verbraucherschutz und Ernährung NRW, LAVE) can approve ▶

an animal study, researchers must provide a detailed justification demonstrating that the study is indispensable, and that no alternative method can answer the research question. “Experiments cannot be approved if the distress caused to the mice is disproportionate to the knowledge gained,” says Hilken. The 3R principle – replace, reduce, refine – applies to every experiment in the EU.

In order to assess the effects of treatment with GRK5 inhibitors in women and men with heart failure, the researchers are also studying male and female mice of various ages with different forms of the condition.



Prof. Dr Gero Hilken, Animal Welfare Officer at ISAS and Head of Central Animal Laboratory at University Hospital Essen.

“ We conduct research for the benefit of people and are fully aware of the profound responsibility that comes with conducting experiments on mice.

“We conduct research for the benefit of people and are fully aware of the profound responsibility that comes with conducting experiments on mice,” emphasises Prof. Dr Kristina Lorenz, pharmacologist and Head of the Translational Research department at ISAS. She coordinates the HI-FIVE project. Only researchers on her team who have completed intensive training and are qualified to perform specific procedures are permitted to conduct experiments with mice. “Approximately four million people in Germany suffer from heart failure. For this serious condition, our research is making an important contribution to the development of urgently needed new therapeutic options,” says Lorenz.

For their analyses, the scientists induce various characteristics of heart failure in the mice, such as increased cardiac workload or metabolic changes, to assess typical disease progression and different manifestations. Echocardiography, pressure and volume measure-



Prof. Dr Kristina Lorenz heads the department of Translational Research and the Cardiovascular Pharmacology research group at ISAS.



ments, ECG analyses and tissue examinations help to investigate the effect of GRK5 inhibitors on heart function, heart growth and the risk of cardiac arrhythmias.

**Another component of the research project:
a study with patients**

Additionally, a clinical study involving patients is being conducted to analyse data on cardiac function, exercise capacity, and comorbidities such as chronic kidney disease. By combining these data with findings from experiments with human stem cells and mouse studies, researchers and clinicians gain a more comprehensive understanding. This enables them to identify which GRK5 inhibitors show the greatest promise as preclinical drug candidates for the development of new therapeutic approaches.

(EH & SR) ■



HI-FIVE

In the HI-FIVE research project, scientists and clinicians from ISAS, Lead Discovery Center GmbH and Herz- und Diabeteszentrum NRW are collaborating on a new therapeutic approach for the treatment of heart failure. The focus is on GRK5 inhibitors which specifically block a key enzyme that becomes overactive in heart failure. The aim of the project is to develop new options for more precise treatment of heart failure, particularly in cases where existing drugs are not sufficiently effective. The collaborative project began in 2025. It will run for three years and is funded with around 2.1 million euros by the European Union and the State of North Rhine-Westphalia.



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Editorial note

As a member of the Leibniz Association, ISAS supports the “Initiative Transparente Tierversuche” and “Tierversuche verstehen – Eine Informationsinitiative der Wissenschaft”. Where animal testing is indispensable, ISAS relies on new analytical methods combined with artificial intelligence to significantly reduce the number of mice used, in line with the 3R principle. In addition, the scientists are developing various complementary analytical methods to extract a high level of information from a smaller number of animal samples.

MULTI-OMICS

The aim of the Multi-Omics research programme is to develop bioanalytical and computational technologies for prognostic, diagnostic, and predictive biomarkers. The scientists research methods which can be used to more effectively detect markers in complex biological matrices. These biological markers are intended for cardiovascular diseases (CVDs), cancer, and metabolic disorders.

More information about this research program is available online.



GRK 2989 TARGETING CELLULAR INTERFACES IN REPERFUSED ACUTE MYOCARDIAL INFARCTION (TCI REPAMI)

The Research Training Group TCI repAMI is funded by the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) and focuses on the consequential damages of heart attacks. While the rapid reopening of a blocked coronary artery is lifesaving,

it can also trigger inflammatory processes. These reactions are caused by an interaction between specific immune, vascular, and heart muscle cells.

The Research Training Group aims to improve the understanding of these processes and to identify new therapeutic approaches for patients.

TCI repAMI operates according to the bed-to-bench-to-bed principle, moving from clinical questions to laboratory-based research and back to the patient's bedside.

A key component of the graduate programme is its interdisciplinary training.

To this end, a total of 33 doctoral researchers are jointly supervised by tandem teams comprising two experts – one from clinical practice and one from basic research.



What is the focus of your work within the DFG Research Training Group TCI repAMI, Nora?

Nora Pauly (27) is working alongside 32 other doctoral candidates to investigate the potential long-term consequences of heart attacks. The immunologist is pursuing her doctorate in the Research Training Group "RTG 2989 Targeting Cellular Interfaces in Reperfused Acute Myocardial Infarction" (TCI repAMI) (see info box). To learn more about her work, the editorial team asked her to complete the following sentences.

Nora Pauly is a PhD student in the Bioimaging group at ISAS.

I am doing my PhD at ISAS on ...

a specific type of immune cell: macrophages. I am particularly interested in the differences between various subtypes of macrophages before and after a heart attack. We suspect that these subtypes perform different functions during a heart attack and are influenced by a specific cytokine, the macrophage migration inhibitory factor (MIF). I intend to investigate this process in more detail by "switching off" this factor and examining its impact on the various macrophage subtypes in the hearts of mice after a heart attack, using a confocal microscope, for example.

This is important for research on heart attacks because ...

MIF could be a potential therapeutic target for reducing consequential damage. Previous research has revealed how reperfusion injury - the damage that occurs after blood supply is restored to a previously occluded vessel - develops. However, it remains unclear how this damage can be reduced.

In the laboratory, I work with ...

three different devices. Using a confocal microscope, I can examine the spatial distribution of macrophage subtypes in detail. For example, I can see whether they are in the atrium, ventricle or apex of the heart. After a heart attack, the microscope allows me to clearly see where the dead heart muscle cells are and where the vessel has been constricted. I can identify individual subtypes using a flow cytometer. Although

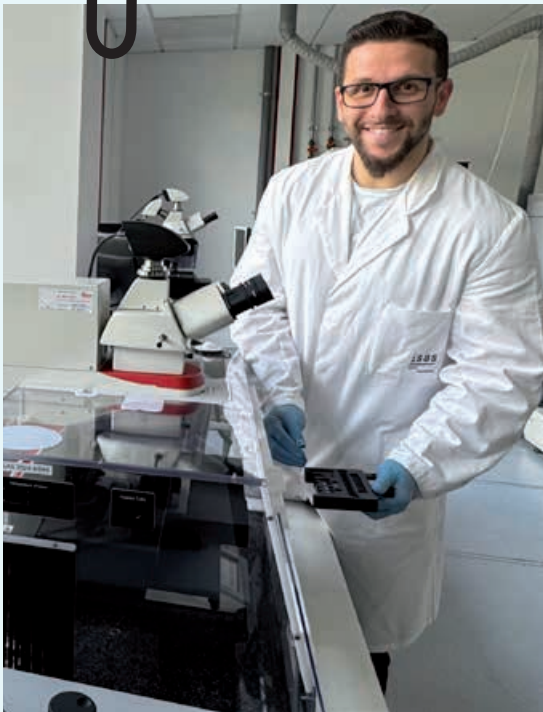


I cannot distinguish areas of the heart as clearly with the flow cytometer as with the confocal microscope, the analysis is more sensitive and provides information about the number of subtypes present. In addition, I will soon be working with a light-sheet fluorescence microscope. This will enable me to examine the entire heart of a mouse at once and view the macrophage populations in three dimensions.

Through the Research Training Group of the German Research Foundation I gain ...

very detailed insight and a wealth of background knowledge on heart attack research. This is thanks to numerous lectures designed to bring doctoral students from ISAS and the clinic up to the same level of knowledge. Clinic visits, which take place twice a year, also provide an opportunity to learn first-hand about the processes involved in patient care. Feedback at seminars, where we present the status of our research, and at various meetings with professors helps me stay on track scientifically and get the most out of my dissertation project.

(Protokoll: AB) ■



What is the focus of your work within the DFG Research Training Group TCI repAMI, Kevin?

Kevin Hau (28) works in the Proteomics research group at ISAS. After completing both his bachelor's and master's theses, he is now pursuing a doctorate at ISAS. As a PhD student, he conducts research within the Research Training Group "GRK 2989 Targeting Cellular Interfaces in Reperfused Acute Myocardial Infarction" (TCI repAMI) (see info box, p.08), focusing on damage caused by myocardial infarction. To learn more about his research, the editorial team asked him to complete the following sentences.

Kevin Hau is conducting research at ISAS on the long-term consequences of heart attacks.



For my doctoral thesis at ISAS, I am investigating ...

the changes in heart muscle cells before and after relief with a left ventricular assist device (LVAD). Clinicians use these cardiac support systems when advanced heart failure occurs following a myocardial infarction. I am particularly interested in how using an LVAD affects the cellular mechanisms that enable the heart to recover after a heart attack.

In the laboratory, I work with ...

various omics analyses for three different classes of molecules: lipids (fats), metabolites, and proteins. For my analyses, I use technologies such as mass spectrometry-based imaging, matrix-assisted laser desorption/ionisation (MALDI), and liquid chromatography-tandem mass spectrometry. One of the challenges, in addition to applying the methods themselves, is integrating the data. For example, I need to combine MALDI images of metabolites with quantitative protein data. My aim is to gain comprehensive insight into the metabolic processes of heart muscle cells by combining different analytical methods.

Through the DFG Research Training Group, I have already been able to ...

gain in-depth insight into everyday clinical practice through our collaboration with University Hospital Essen. For instance, I was able to observe the implantation of an LVAD and the transplantation of a fully artificial heart. This gave me a different perspective on the samples that I would later work with in the laboratory, as I could see where they came from.

I have been at ISAS since writing my bachelor's thesis because ...

the team spirit in our research group is excellent and I really enjoy the atmosphere at ISAS. It is also special to work with state-of-the-art technology in well-equipped laboratories. And finally, I enjoy the professional and personal networking opportunities at ISAS - I have made many friends here over the past years.

(Protokoll: AB) ■

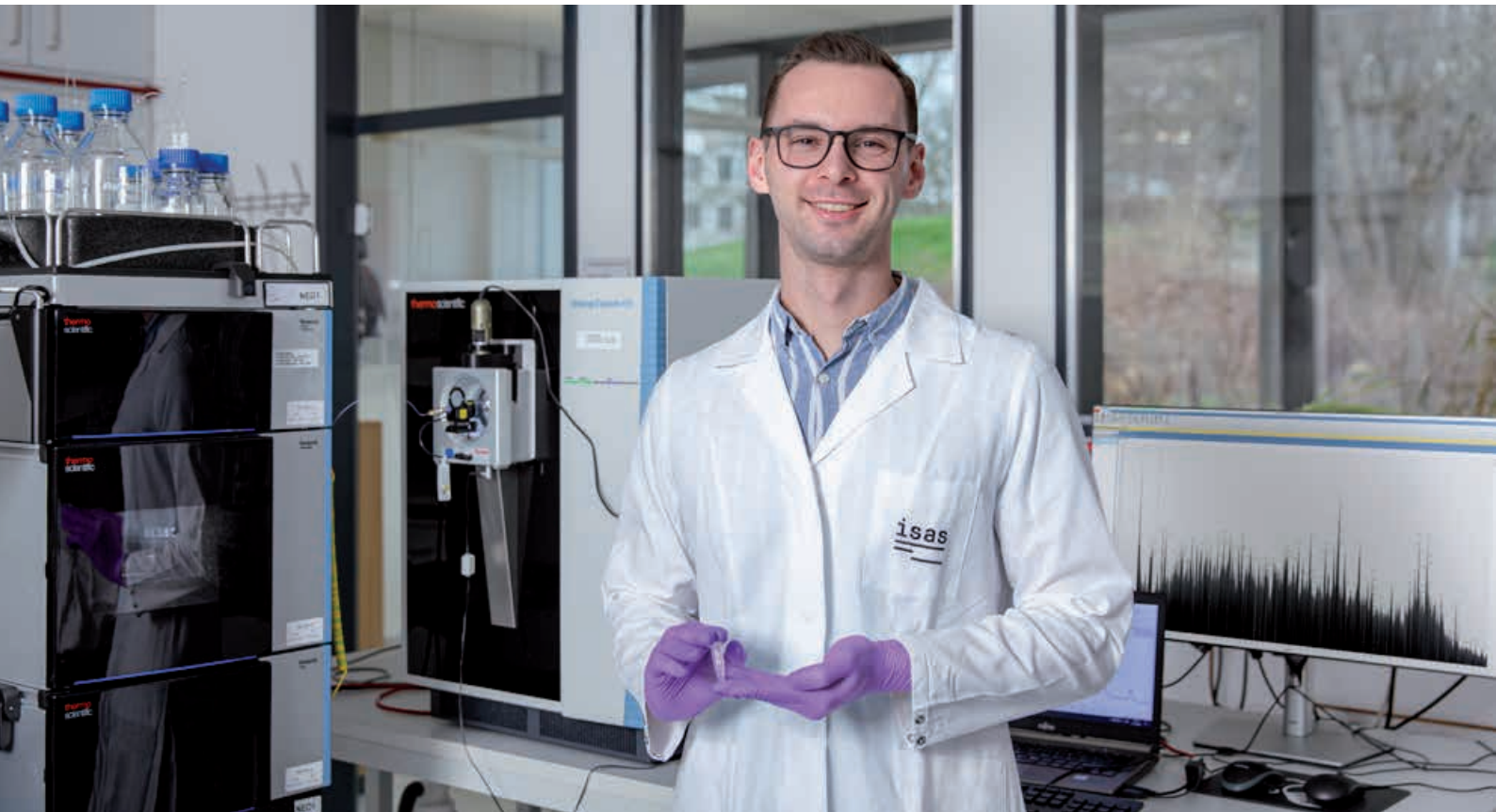
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DFG

3 Questions for ... Dr Tobias Lerchner



Dr Tobias Lerchner, a junior doctor specialising in internal medicine and cardiology at University Hospital Essen, conducts research at the interface between cardiology and immunology. His research focuses on immune-mediated processes that contribute to the development and progression of heart diseases. As a junior clinician scientist at the University Medicine Essen Academy, the 30-year-old worked as a guest scientist in the Proteomics research group at ISAS for three months during 2025.

Dr Tobias Lerchner is a junior doctor specialising in internal medicine and cardiology at University Hospital Essen. Since 2024, he has been working in the Cardiology and Angiology Clinic (headed by Prof. Dr h.c. Tienush Rassaf). The 30-year-old is currently conducting research as a DFG Walter Benjamin Fellow at the Cardiovascular Research Institute Maastricht (CARIM) within the Structural Heart Failure programme in the research group of Prof. Dr Stephane Heymans.

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1 What new opportunities for your research did the proteomics analyses – from sample preparation to mass spectrometry – open up?

Lerchner: For me, my time at ISAS was my first in-depth encounter with omics technologies, particularly proteomics analyses. Using liquid chromatography coupled with mass spectrometry, I was able to investigate heart transplant rejection at the molecular level. In clinical practice, rejection after heart transplantation has so far been assessed primarily using endomyocardial biopsies – that is, tissue samples taken from the heart muscle. This involves examining whether immune cells have migrated into the heart tissue and whether changes in the tissue structure indicate a rejection reaction. Proteomics analyses opens up a new perspective: it provides a detailed profile of all the proteins in the sample, revealing which ones are altered during rejection.

2 What role does the molecular information generated by proteomics analysis play in heart transplantation? Can it also help improve the treatment of a diseased heart?

Lerchner: The molecular data can help to identify potential biomarkers for monitoring disease progression after heart transplantation. Proteomics analyses, for example, can reveal whether the observed changes primarily affect proteins in the heart muscle or mitochondrial processes. In heart transplants, the data could also help to categorise patients based on molecular similarities. This could enable the identification of patterns that provide insights into the risk of subsequent rejection. The aim is to develop more targeted and highly personalised diagnostic and therapeutic approaches.

3 You are currently conducting research as a Walter Benjamin Fellow of the German Research Foundation, DFG, at the Dutch Cardiovascular Research Institute Maastricht, CARIM. What do you see as the greatest benefit and the greatest challenge of combining clinical practice with work in the laboratory?

Lerchner: As a clinician scientist, I can investigate questions arising from day-to-day clinical practice directly in the laboratory and translate the findings back into patient care, following the bed-to-bench-to-bed principle. I see the close connection between clinical practice and basic research as particularly valuable, because I want my work to contribute to improving patient care in the long term. Another benefit is the opportunity to work alongside many ambitious and motivated colleagues, both in the clinic and in the laboratory.

The biggest challenge is to do justice to both areas. Combining research and clinical practice at a high level is an incredibly fulfilling professional endeavour, one that requires perseverance. But challenges are there to be overcome! For me, the advantages of working as a doctor in a clinically relevant, translational field of research clearly outweigh the disadvantages.

(The interview was conducted by SSL.) ■

A Natural Helper for Stiffened Heart Muscles

Around two million people¹ in Germany suffer from heart failure with preserved ejection fraction, known as HFpEF. This form of heart failure is difficult to diagnose because the heart appears to be functioning normally. It is even more difficult to treat. Worldwide, up to 80 per cent of those affected are admitted to a hospital within five years, and around 50 per cent die.² Effective treatments are still rare. A research team led by PD Dr Anna Klinke from the Herz- und Diabeteszentrum NRW (Heart and Diabetes Centre North Rhine-Westphalia), with the involvement of ISAS, has shown in mice that nitro-oleic acid, a naturally occurring molecule, can significantly improve heart function in HFpEF. The researchers published their findings in the journal *Nature Communications*.

A healthy heart beats at a rate of around 60 to 80 beats per minute at rest.³ However, even a heart affected by HFpEF often beats without any noticeable abnormalities. An ultrasound scan reveals that the heart contracts regularly. The problem lies in the relaxation phase. After each heartbeat, the heart muscle must relax to allow the chambers to fill with blood. In HFpEF, this relaxation is impaired: The heart muscle becomes increasingly stiff, which hinders the filling of the ventricles. As a result, the heart can no longer pump enough blood during physical exertion. Those affected experience increasing shortness of breath, tire easily and struggle to climb stairs. Because this only becomes apparent when doctors carry out targeted investigations using specialised equipment and tests, many patients do not receive a clear diagnosis until the disease is at an advanced stage.⁴

Heart failure resulting from obesity and diabetes

The condition disproportionately affects people who are overweight or have diabetes. As both conditions

become more common, the number of HFpEF cases is also increasing globally. In Germany, HFpEF accounts for around half of all cases of heart failure⁵ – making it more common than Parkinson's disease and multiple sclerosis combined.⁶ The first drugs for HFpEF were authorised in Europe in 2022.⁷ However, “there are still far fewer treatment options than for other forms of heart failure,” says PD Dr Anna Klinke, who heads the Agnes Wittenborg Institute for Translational Cardiovascular Research at the Herz- und Diabeteszentrum NRW, and is the study's corresponding author. According to her, heart failure is often associated with older people, but patients with HFpEF – particularly those with diabetes – may also develop the condition at a younger age.



1 <https://www.aerztezeitung.de/Nachrichten/HFpEF-in-der-kardiologischen-Versorgung--447945.html>

2 <https://pubmed.ncbi.nlm.nih.gov/38944348/>

3 <https://herzstiftung.de/ihre-herzgesundheit/anzeichen-fuer-herzprobleme-erkennen/welcher-puls-ist-normal> + <https://herzmedizin.de/fuer-patienten-und-interessierte/wissen/blutdruck/herz-puls-optimaler-ruhepuls>

4 <https://www.ajmc.com/view/experts-sound-alarm-on-underrecognized-heart-failure-subtype-as-costs-readmissions-soar>

5 <https://www.aerztezeitung.de/Nachrichten/HFpEF-in-der-kardiologischen-Versorgung--447945.html>

6 <https://inspire.parkinsonnetzwerk.de/parkinson-krankheit/parkinson-verstehen/> + <https://www.dmsg.de/multiple-sklerose/ms-erforschen/grafiken-des-quartals/monats>

7 <https://www.boehringer-ingelheim.com/human-health/crm-health/cardiova...ealth/heart-failure/preserved-heart-failure-treatment-approval-europe>



PD Dr Anna Klinke heads the Agnes Wittenborg Institute for Translational Cardiovascular Research at the Herz- und Diabeteszentrum NRW.

The molecule that Klinke and her colleagues investigated is produced naturally in the body. Nitro-oleic acid (NO₂-OA) can form when oleic acid – a monounsaturated fatty acid also found in many vegetable oils – encounters nitrite in the acidic environment of the stomach. Nitrite is present in foods such as green vegetables and pickled food. The nitrite binds to the oleic acid. This chemical modification transforms the fatty acid into a biological signalling molecule that influences the energy metabolism of cells.

“We knew that the efficacy profile would be a very good fit.”

Nitro-oleic acid can also be produced synthetically and then administered therapeutically in larger quantities.

Klinke has been researching the compound for several years. Before investigating its potential in HFpEF, the pharmacist had already studied nitro-oleic acid in atrial fibrillation, ventricular arrhythmias and pulmonary hypertension. “We knew that the efficacy profile would be a very good fit,” reports Klinke.

In the study published in 2025, mice were initially given a high-fat diet combined with a substance that inhibits vasodilation. After eleven weeks, the animals’ hearts had stiffened, relaxed less effectively, and their physical endurance had declined – closely resembling HFpEF in humans. One group of mice was then given nitro-oleic acid for four weeks, whilst the control group received a placebo. The effect of the nitro-oleic acid was measurable: The hearts of the treated mice relaxed more easily again, and the mice were able to run for a longer time on the treadmill.

Two classes of lipids in the focus of the analysis

The analysis of heart tissue using liquid chromatography-mass spectrometry (LC-MS) and Raman spectroscopy was carried out by researchers from the Lipidomics and Cardiovascular Pharmacology research groups at ISAS. The focus was on two classes of lipids: triglycerides, which are routinely measured in blood tests, and ceramides. Both are elevated in hearts affected by HFpEF. “The increase in triglycerides within the heart muscle in particular indicates that the cells there are no longer fully and efficiently utilising the energy they need to function,” explains Prof. Dr Sven Heiles, Head of the Lipidomics research group. Ceramide levels often rise alongside triglycerides and, at sufficiently high concentrations, can become toxic to cells. ▶



Prof. Dr. Sven Heiles holds a junior professorship at the University of Duisburg-Essen and leads the Lipidomics junior research group at ISAS. He also coordinates the MS-Based Imaging research programme.

HFpEF: Nitro-oleic acid promotes mitochondrial formation

Although triglycerides and ceramides were still elevated in the hearts of the mice treated with nitro-oleic acid, their heart muscle cells stored less fat on average. Furthermore, significantly more mitochondria were found in their heart tissue than in untreated animals. Mitochondria are regarded as the powerhouses of the cell: these intracellular structures convert fats and sugars into energy, which is then available to the heart muscle for pumping. Apparently, nitro-oleic acid activates a molecular switch known as AMPK (adenosine monophosphate-activated protein kinase), which promotes the formation of new mitochondria and increases the breakdown of excess fat stores in the heart muscle cells. “If more healthy mitochondria are present, the heart can simply produce more energy,” says Klinke.

Next, Klinke and her colleagues at Herz- und Diabeteszentrum NRW plan to investigate the therapeutic effects of nitro-oleic acid in patients with HFpEF. Nitro-oleic acid is already considered to be well tolerated, and it also shows therapeutic potential in several other diseases. Phase 2 clinical trials are currently underway in the United States for obesity-associated asthma, while

a study in patients with Parkinson’s disease has recently begun in Norway. “Very few adverse effects have been observed so far. Mild diarrhoea occasionally occurs, but it has been so minor that no participant has withdrawn from a clinical trial because of it,” says Klinke. If nitro-oleic acid also proves effective in HFpEF, clinicians would finally have an additional treatment option for patients who currently have very few effective therapies available.

(UE) ■

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Lüdtke, S., Düfer, M., Tolstik, E., Dierks, J., Lorenz, K.,
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Freeman, B.A., Rudolph, V., Schlomann, U., Klinke, A.**

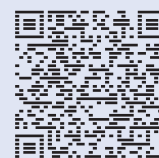
(2025) Nitro-oleic acid enhances mitochondrial metabolism and ameliorates heart failure with preserved ejection fraction in mice. *Nature Communications*, 16:3933.

<https://doi.org/10.1038/s41467-025-59192-5>

3D-MOLECULAR PATHOLOGY

Modern imaging methods are regarded as a key technology in first-class medical research. At ISAS, the research programme 3D Molecular Pathology focuses on temporally and spatially high resolution visualisations and measurements of physiological and pathological states in whole organs, the tissue structures and cells of which they are composed of, down to the molecular components which are essential for the function of the cells.

More information about this research program is available online.



New Framework for Efficient Image Data Analysis in Biomedicine

When developing data-centric artificial intelligence (AI), the focus is on optimising training data. This approach is less common in biomedical research than model-centric AI applications. A team led by Dr Jianxu Chen from ISAS, with researchers from China, Germany and the USA, aims to change this and establish data-centric AI applications in bioimaging research. To this end, they have published a so-called framework (open source) in the journal *npj imaging*. The framework is intended to make it easier for scientists from the bioimaging community to apply AI in the analysis of image data.



Dr Jianxu Chen heads the AMBIOM junior research group at ISAS.

Reliable AI systems are based on reliable data – that is the basic idea behind data-centric AI applications. Instead of constantly improving the model, researchers manually optimise the quality and representativeness of the training data with the support of AI applications. For example, they examine whether the data is clean, complete and balanced. This allows to continuously improve a defined AI model with refined measurement data. The counterpart to this is model-centric AI applications. Here, researchers use a fixed dataset to improve the AI model.

“Our framework is intended to serve as a common language for AI experts and biomedical researchers.”

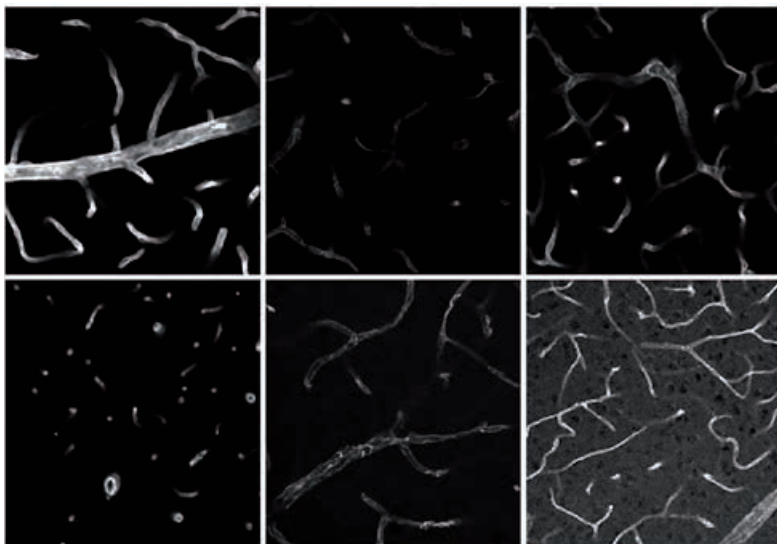
Dr Jianxu Chen, Head of the AMBIOM – Analysis of Microscopic BIOMedical Images junior research group at ISAS, is the corresponding author of the new publication. “Our framework is intended to serve as a common language for AI experts and biomedical researchers,” explains the expert in biomedical image analysis and deep learning. A framework describes a collection of programming tools and libraries that help developers to create and train AI models more easily. In this case, it provides an organized overview of all relevant AI methods and techniques in the context of

bioimaging that help biomedical scientists think through their bioimaging problems in a data-centric mindset.

Chen demonstrates the advantages of the new four-stage framework using an example that he developed with AI researchers worldwide and scientists from the field of biomedical research. For this purpose, he and his co-authors collected over 800 three-dimensional microscope images for the segmentation of a vascular structure. Rather than evaluating this large amount of data manually, as has been the norm for model-centric approaches to date, the researchers used the raw data to pre-train an AI model. Using this initial AI application, they identified the most representative images from the dataset to train an AI model for further evaluation. They then continuously improved this model by, for example, manually analysing microscope images that the model had difficulty with, using these to further enhance the model.

Framework builds a bridge between AI development and biomedical research

In the cited example, the researchers used basic algorithms that are accessible via GitHub. Integrating further complex algorithms is also a possibility for the future. Additionally, the framework could be applied to other research questions in biomedicine. The authors emphasise that model-centric and data-centric approaches are by no means mutually exclusive and could be combined in future research.



Examples showing the diversity of a vasculature dataset from a real biomedical study, with varying morphology, intensity, signal-to-noise ratio, etc. The “BioData-Centric AI” framework provides a systematic approach for biomedical researchers to tackle such real-life challenges.

The framework is intended to serve as a guide for two target groups in particular: scientists in biomedicine and developers of AI methods for biomedical research. “The framework helps biomedical scientists integrate AI applications into their research in a meaningful way, without requiring them to know everything about AI,” explains Chen. For developers, the paper provides an overview of the possibilities of data-centric AI and guidance for future developments.

(AB) ■



Cao, J., Wenzel, J., Zhang, S., Lampe, J., Wang, H., Yao, J., Zhang, Z., Zhao, S., Zhou, Y., Chen, C., Schwaninger, M., Yang, J., Chen, D.Z., Chen, J.
(2025) Rethinking deep learning in bioimaging through a data centric lens.
npj imaging, 3:29.

<https://doi.org/10.1038/s44303-025-00092-0>

Federal Ministry of Research, Technology and Space (Bundesministerium für Forschung, Technologie und Raumfahrt, BMFTR) is funding the MSCoreSys associated junior research group AMBIOM – Analysis of Microscopic BIOMedical Images under the funding code 161L0272.

Gefördert durch:



High-fidelity Image Compression Using Neural Networks

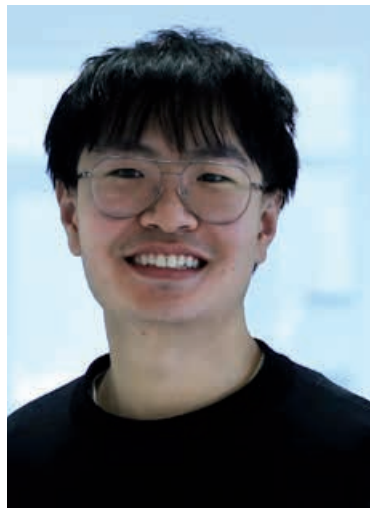
Modern microscopy provides high-resolution insights into complex biological structures and dynamic processes. The result is ever-growing volumes of data whose storage, exchange, management, and visualisation are becoming increasingly challenging. To address this issue, a German-Chinese research team, with the participation of ISAS, has developed a new AI-based method. Compared to conventional approaches, the method can not only compress microscopy images more efficiently but also preserve important detailed information. The authors described their method in *Nature Computational Science*.

High-resolution microscopy generates enormous and highly complex datasets, including information on three-dimensional structures, time series, and multichannel imaging. These massive volumes of data require substantial storage and computing capacities. Conventional compression methods such as JPEG 2000 or HEVC quickly reach their limits. While they can significantly reduce file size, it is often at the expense of image quality, which can lead to distortions of biological structures and undesirable artefacts such as blurring or image noise. As a result, there is a strong demand in biomedical research for new methods that can efficiently compress image data without losing biologically relevant details.

Neural image representation instead of pixel grids

With INIF (Implicit Neural Image Field), the researchers present a new open-source method for compressing biomedical imaging data. The corresponding code has been published as a Python code on GitHub.

INIF is based on Implicit Neural Representations (INR). Instead of storing an image as a pixel grid, the method describes it using a continuous, learned function. A neural network learns the underlying structure of the image and can reconstruct it based on this representation. The advantage is that high-resolution microscopy images can be stored while requiring significantly less



Yu Zhou is PhD student in the AMBIOM junior research group at ISAS. Prior to that, he studied biomedical engineering in Sweden and in Switzerland.

storage space. “The method combines neural image representation with a learned optimiser. This enables high detail fidelity alongside efficient compression for microscopy images of different dimensionalities,” explains Yu Zhou, a doctoral researcher in the AMBIOM – Analysis of Microscopic BIOMedical Images group and one of the study’s core contributors.

Learning-based optimisation as a key factor

A central component of the compression process in INIF is a “learned optimiser” (► p. 21). Unlike classical optimisation methods, it does not rely on fixed, pre-defined rules. Instead, it learns from data how model parameters can be efficiently adapted to image data.

The optimiser helps the neural network to adapt to the images quickly and adaptively, thereby facilitating the learning process. This makes training faster and more stable. During decompression, the image data can then be reconstructed with high fidelity and fine detail.

Application-specific, context-dependent data compression

“We were able to show that INIF produces less noise and distortion during decompression,” Zhou explains. The advantage is that, through training, INIF can distinguish between information-rich structures such as cell boundaries and less relevant regions. Individual image areas can also be selectively reconstructed during decompression without processing the entire dataset. This is particularly helpful for analyses focusing on specific structures or cellular regions.

Since, unlike conventional compression methods, INIF

learns the underlying image structure itself, compression, reconstruction, and analysis become more closely integrated. The method can help store and process large

“ We were able to show that INIF produces less noise and distortion during decompression.

microscopy datasets more efficiently. Ultimately, this may facilitate data exchange and collaboration between researchers. The researchers have released the code of the method as open source on GitHub: <https://github.com/MMV-Lab/INIF>.

(SSL) ■



LEARNED OPTIMISER

An optimiser is a method that adjusts the parameters of a neural network in such a way as to minimise the loss function – that is, the error between the prediction and the actual value. In this way, the neural network learns to solve tasks efficiently and reliably. The speed at which the neural network learns is determined by the learning rate (the size of the adjustment steps). A high learning rate speeds up the learning process, but can lead to unstable results. A low learning rate is more stable, but takes longer to find a good solution.

INIF uses a learned optimiser, i.e., a neural network that has been specifically trained on a large amount of optimisation problems. This controls the adjustment steps efficiently without empirical manual tweaking of the learning rate.

As a result, a highly detailed reconstruction can be achieved after just a few optimisation steps.



Dai, G., Zhang, R., Wuwu, Q., Tseng, C. C., Zhou Y., Wang, S., Qian, S., Lu, M., Tuz, A. A., Gunzer, M., Huang, T., Chen, J., Zhang, S.

(2025) Implicit neural image field for biological microscopy image compression.
Nature Computational Science, 5 (11), 1041–1050.

<https://doi.org/10.1038/s43588-025-00889-4>

Federal Ministry of Research, Technology and Space (Bundesministerium für Forschung, Technologie und Raumfahrt, BMFTR) is funding the MSCoreSys associated junior research group AMBIOM – Analysis of Microscopic BIOMedical Images under the funding code161L0272.

Gefördert durch:



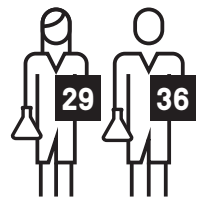
Bundesministerium
für Forschung, Technologie
und Raumfahrt

OUR YEAR IN FIGURES

161

employees

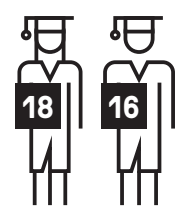
As at December 31, 2025, ISAS had 80 female and 81 male members of staff at its locations.



65

researchers (m/f/n-b)

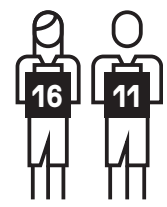
were employed at the institute in 2025, of whom 29 were women and 36 men.



34

doctoral candidates (m/f/n-b)

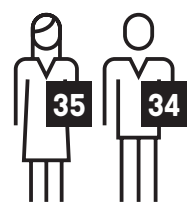
Among the researchers, there were 18 female and 16 male PhD students.



27

scientific technical staff members (m/f/n-b)

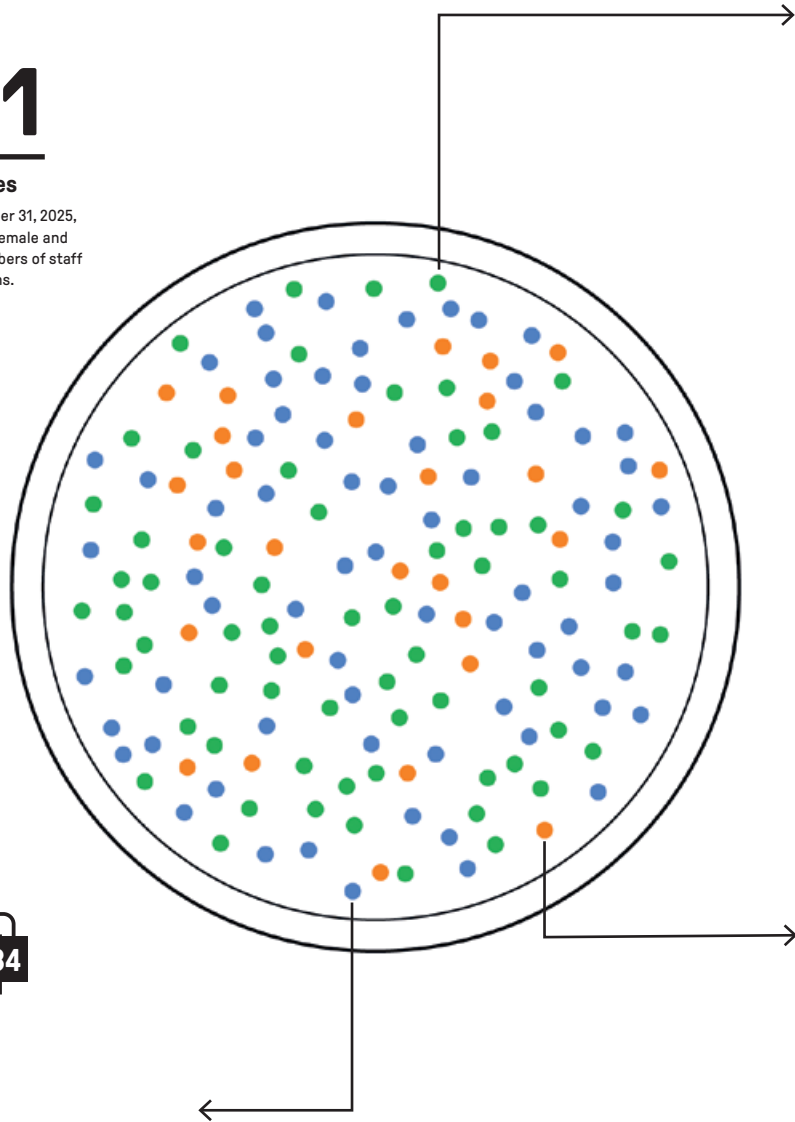
worked at ISAS, of whom 16 were women and 11 men.

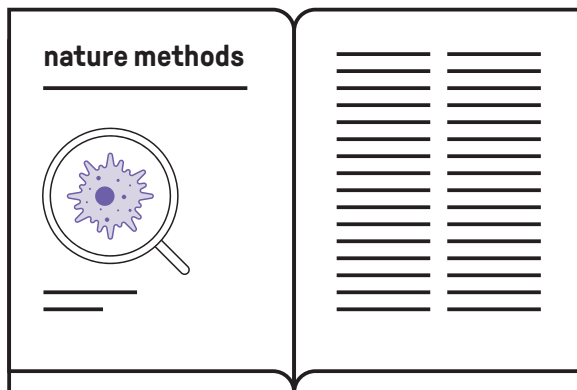


69

other staff members (m/f/n-b)

Among them were 35 female and 34 male employees.





9.03

impact factor

The average impact factor of the publications in peer-reviewed journals was 9.03.

46

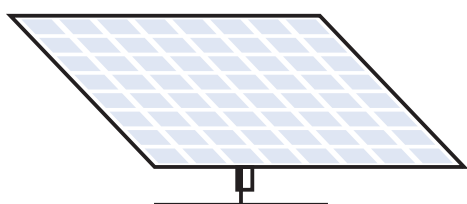
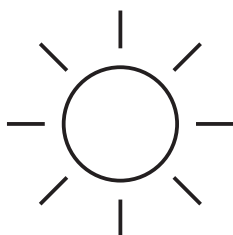
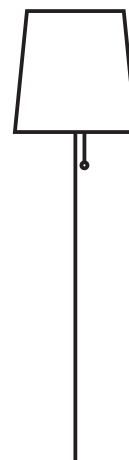
papers

with a lead or corresponding author from ISAS.

90

publications

were published in peer-reviewed journals.



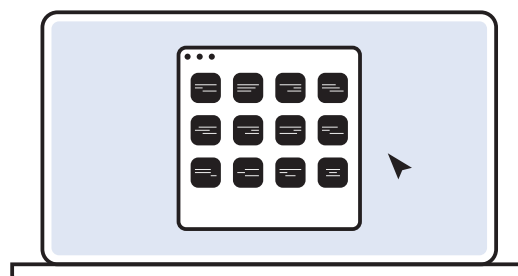
Approx. 1,236,600 kWh

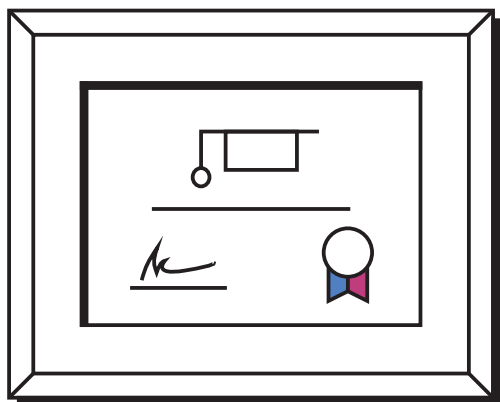
of electricity were produced by the ISAS City location, including approx. 935,000 kWh by the photovoltaic system and approx. 301,600 kWh by the cogeneration power plant.

5

software & tools (open source)

were published by the AI experts and bioinformaticians in 2025.





35

academic qualifications

Of the 35 final theses, 12 were internal.*

22

PhD theses

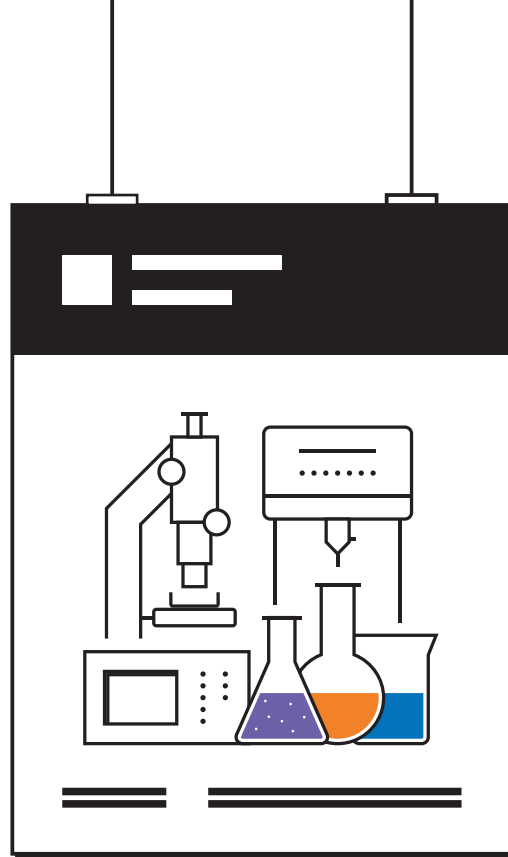
Of these PhD dissertations, 7 were written at ISAS.*

13

BSc, MSc

These included 2 bachelor's and 3 master's students who wrote their final theses at ISAS.*

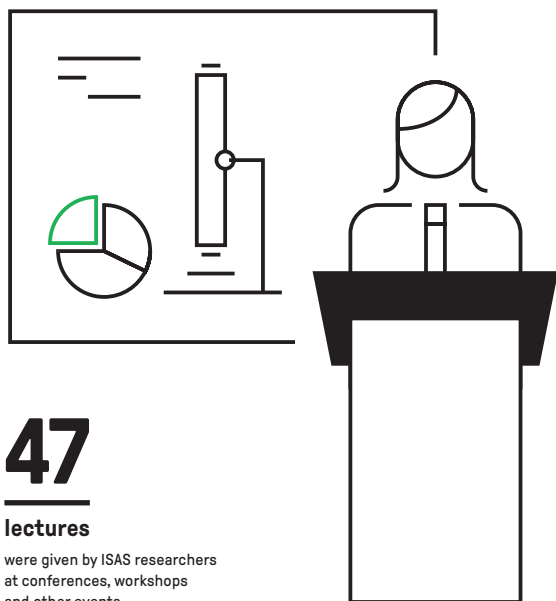
* The other projects were external expert assessments.



40

poster presentations

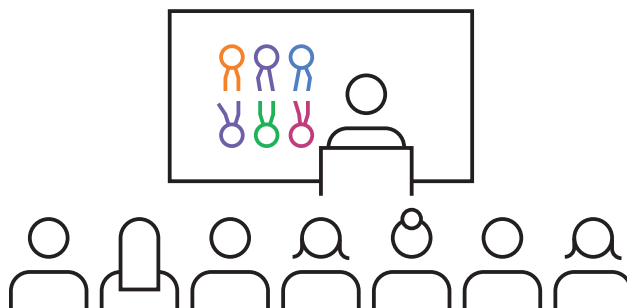
were held by researchers from ISAS in 2025.



47

lectures

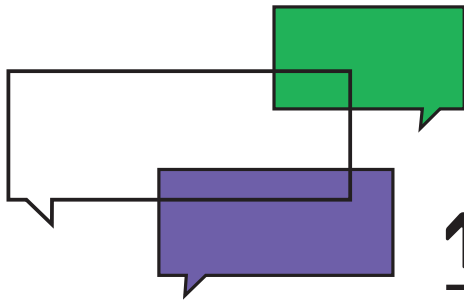
were given by ISAS researchers at conferences, workshops and other events.



8

scientific events

were (co-)organised by ISAS in 2025.



13

colloquia at ISAS

with international and national guests took place in 2025.



37

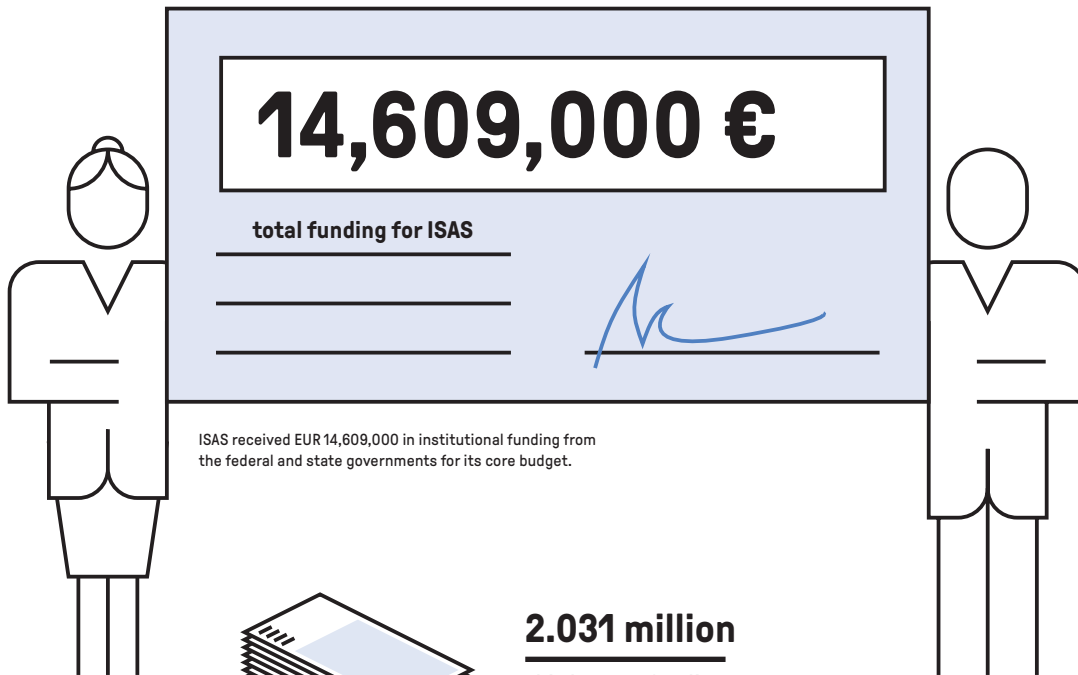
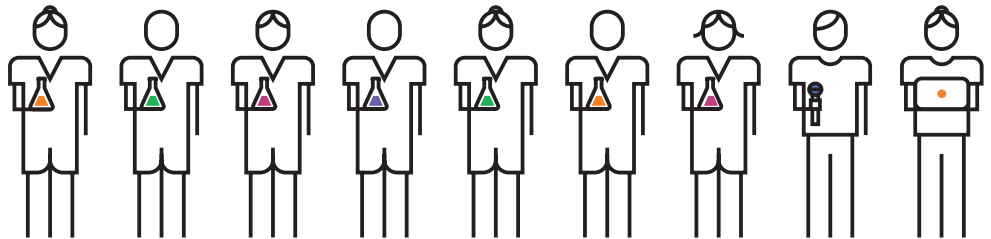
conferences

In 2025, ISAS researchers presented their work at 37 scientific conferences.

17

interns (m/f/n-b)

were introduced to the work at ISAS in 2025. 14 interns gained practical insight into the research. 3 interns were in the Communications team, where they familiarised themselves with all matters concerning press and public relations.



14,609,000 €

total funding for ISAS

ISAS received EUR 14,609,000 in institutional funding from the federal and state governments for its core budget.

2.031 million

third-party funding

In addition, the institute received EUR 2,030,781 in third-party funding for 2025.

PATHOMECHANISMS

The research programme Pathomechanisms concentrates on the analysis of disease mechanisms with focus on cardiovascular diseases (CVDs), in particular heart failure due to myocardial infarction (heart attack), pathological cardiac hypertrophy (heart growth) or cardiotoxic cancer therapies. The overall goal of the programme is to identify molecular changes that are causative for the development of these diseases and are suitable as targets – and possibly as biomarkers.

More information about this research program is available online.



New Drug Candidates for the Treatment of Heart Failure

About four million people in Germany suffer from the life-threatening condition of heart failure. For 50 per cent of them, available drugs are not an option or are only partially effective. Researchers and cardiologists at the Leibniz-Institut für Analytische Wissenschaften – ISAS, Lead Discovery Center GmbH (LDC) and Herz- und Diabeteszentrum NRW (HDZ NRW) aim to expand the range of treatment options for heart failure. They are working on the development of new active substances to specifically improve patient care and quality of life. Their new research project ‘HI-FIVE – GRK5 inhibitors for the treatment of various heart failure entities’ (‘HI-FIVE – GRK5-Inhibitoren zur Therapie verschiedener Herzinsuffizienz-Entitäten’) is being funded by the North Rhine-Westphalia state government and the EU with approximately 2.1 million euros.

In heart failure, the heart no longer pumps enough blood through the body. As a result, organs are not supplied with sufficient oxygen and nutrients. Patients complain about loss of performance, shortness of

breath, fatigue and, in advanced stages of the disease, water retention. But not all cases of heart failure are the same; there are different forms: “While reduced cardiac output is the most common cause of heart failure in

men, in women, an impaired relaxation function of the heart muscle leads to reduced filling of the left ventricle,” explains Prof. Dr Tanja Rudolph, senior physician at the Clinic for General and Interventional Cardiology/Angiology at HDZ NRW.



Prof. Dr Tanja Rudolph is a cardiologist at HDZ NRW and clinical lead of the HI-FIVE research project.

New therapeutic approach targets key enzyme

The various manifestations of the disease make it difficult for half of those affected to receive adequate treatment with the drugs currently available. In a previous project, the researchers identified active substances that inhibit the key enzyme GRK5, which is upregulated in heart failure. The HI-FIVE project partners now want to further optimise these GRK5 inhibitors in order to pave the way for a new targeted therapy. “In this research project, we will take sex- and age-specific aspects of heart failure into account. This is urgently needed, as age and female sex as factors are still underrepresented in most preclinical and clinical studies,” says

Prof. Dr Kristina Lorenz, Head of the Department of Translational Research at ISAS. The pharmacologist is coordinating the HI-FIVE project.

Research towards preclinical development candidates

A great deal of research and development is still required before individuals with heart failure will benefit from a new treatment option. To ensure the successful translation of findings into application, scientists and physicians are working closely during the three-year preclinical research project. HI-FIVE builds on GRK5 inhibitor lead structures that LDC has previously identified using high-throughput screening, and subsequently validated. The most promising candidates, with good oral absorption, high target activity, and few side effects, are being further optimised in HI-FIVE. To gain a deeper understanding of heart failure, 500 patients at HDZ NRW will be examined for one year regarding symptoms and severity of their disease. To investigate



Prof. Dr Kristina Lorenz is a pharmacologist and Head of the Translational Research department at ISAS. She coordinates the HI-FIVE project.

the efficacy of GRK5 inhibitors, scientists are conducting research on human heart muscle cells derived from stem cells, as well as on mice. “At the end of the project, we want to reach the next important milestone towards clinical application – a preclinical development candidate – thereby creating new treatment options for millions of patients with heart failure,” adds Bert Klebl, CEO and CSO of LDC.

(SR) ■



Bert Klebl is CEO and CSO of the Lead Discovery Center GmbH.



INFORMATION PLATFORM ON HEART FAILURE

A brief insight into the research of HI-FIVE for non-specialists, including background information on heart failure and heart health in general, is available on the LinkedIn page www.linkedin.com/company/hi-five-forschung.

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The state government of North Rhine-Westphalia and the European Union are funding the project “HI-FIVE – GRK5-Inhibitoren zur Therapie verschiedener Herzinsuffizienz-Entitäten” with approximately 2.1 million euros.



Kofinanziert von der
Europäischen Union

Ministerium für Wirtschaft,
Industrie, Klimaschutz und Energie
des Landes Nordrhein-Westfalen



Gut Flora & Stroke: How Microorganisms Influence Our Immune System

The gut microbiota includes all the microorganisms that occur in the intestine. Scientists have long suspected a link between this intestinal flora and various immune cells. Researchers at University Hospital Essen and ISAS have recently demonstrated how the microbiota influences the activation of neutrophil granulocytes. This can negatively impact the brain after a stroke. The scientists published their findings in the *Journal of Neuroinflammation*.

In the study, the researchers compared neutrophils (see info box) from mice with healthy intestinal flora and those in which the microbiota had been reduced by antibiotics. For their analyses they used various techniques, including liquid chromatography-mass spectrometry (LC-MS), flow cytometry, and light sheet fluorescence microscopy. The researchers were able to establish that the analysed immune cells become more active when the intestinal flora is intact. In contrast, neutrophils are less active when there is a microbiota deficit. This inhibited activity protects the mice's brains from the consequences of a stroke. Consequently, fewer thrombi are found in the brain vessels and there is less inflammation of the nerve tissue after a cerebral infarct. The area of brain tissue affected by a stroke was also smaller when there was a microbiota deficit. ▶



NEUTROPHIL GRANULOCYTES

Neutrophil granulocytes are a specific type of white blood cells that is most frequently found in the blood. They primarily fight bacteria but are also present in increased quantities during acute or chronic inflammation.

Following a stroke, they are the first immune cells to arrive in the brain. When activated, they can negatively impact the recovery process. The molecular signals that lead to neutrophil activation have not yet been fully discovered. However, understanding them is crucial for combatting the neurotoxic functions of neutrophils in the future.

The results of the study suggest that the microbiota activates neutrophils, although the exact mechanism of this interaction remains unclear. If further research succeeds in exploring this mechanism, this finding could provide a potential starting point for the development of therapies for stroke patients.

(AB) ■



**Tuz, A. A., Ghosh, S., Karsch, L., Antler, M., Lakovic, V.,
Lohmann, S., Lehmann, A. H., Beer, A., Nagel, D.,
Jung, M., Hörenbaum, N., Kaygusuz, V., Qefalia, A.,
Alshaar, B., Amookazemi, N., Bolsega, S., Basic, M.,
Siveke, J. T., Heiles, S., Grüneboom, A., Lueong, S.,
Herz, J., Sickmann, A., Hagemann, N., Hasenberg, A.,
Hermann, D. M., Gunzer, M., Singh, V.**

(2025) Gut microbiota deficiency reduces neutrophil activation and is protective after ischemic stroke.

Journal of Neuroinflammation, 22:137.

<https://doi.org/10.1186/s12974-025-03448-w>



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Dr Susmita Ghosh analyses samples of neutrophil granulocytes using an ultrasensitive mass spectrometer. Her aim is to understand how immune cells behave after a stroke.

“Our findings suggest that a healthy microbiota may have a negative impact on the course of a stroke.”

Dr Susmita Ghosh conducts research in the Biofluorescence research group, and is one of three lead authors of a study published in the *Journal of Neuroinflammation* (► p. 30). Together with Dr Ali Ata Tuz (ISAS and University Hospital Essen) and Laura Karsch (University Hospital Essen), she investigated the connection between gut microbiota and neutrophil granulocytes. In this interview, the biologist discusses her research on proteins and the effect that neutrophils have on the brain following a stroke.

How did you come up with the link between gut microbiota, neutrophile activation and strokes?

Ghosh: In our previous papers, we observed that activated neutrophils have a negative impact on stroke outcomes. We wanted to find out why and identify the decisive factors. Meanwhile, Dr Vikramjeet Singh from University Hospital Essen was researching the link between gut microbiota and stroke outcomes. Together, we wanted to establish whether gut microbiota could trigger neutrophil activation upon stroke. To do this, Dr Ali Tuz, Laura Karsch and I divided the parts of the study equally. While Ali and Laura brought in their

expertise with imaging and flow cytometry techniques, I was responsible for the proteomic analyses using liquid chromatography-mass spectrometry (LC-MS). Since the neutrophils' behaviour depends on their protein expression, we chose proteomic analysis to understand the neutrophils' behaviour after a stroke. From the brain of mice with stroke, we got only a handful of neutrophils, which is difficult for proteome analyses. Since I had already optimised the proteomics approach for low input samples in a previous study, it was easy to apply this method to investigate the gut microbiota's influence on neutrophils. ►

What exactly did your results reveal about gut microbiota and neutrophil activation?

Ghosh: I analysed the proteome of neutrophils isolated from the brains and blood of mice that had experienced a stroke. Using label-free quantitative proteomics, I identified the changes in protein expression between neutrophils upon microbiota depletion compared to the control sample in which microbiota was present. This enabled us to infer that neutrophils from mice with depleted microbiota were less activated and provided greater support for tissue repair in the brain following a stroke. This finding indicates that gut microbes positively influence neutrophil activation after stroke, causing more and worsening existing inflammation. We were able to validate my results with those from other experiments, using ELISA (enzyme-linked immunosorbent assay). This was important to us, as validating proteomic data is difficult and often missing in research papers.

How do your findings about the gut microbiota contribute to our understanding of its role after stroke, and what are the next steps in this line of research?

Ghosh: The gut microbiota is essential for our day-to-day life. However, our results suggest that healthy microbiota can have a negative influence on stroke outcomes due to activated neutrophils. But we still do

not know how this microbiota-neutrophil-interaction occurs. If we manage to identify any factor that activates the neutrophils, we could try to inhibit it to reduce tissue damage. However, we also do not yet know if our findings apply to human gut microbiota. This is an exciting area of research with many questions still to be answered.

(The interview was conducted by AB.) ■



EPISODE 12: Less Is More, at Least When It Comes to the Number of Cells



<https://www.isas.de/kompakt/podcast-nachgeforscht-die-liveschalte-ins-labor-folge-12-less-is-more-at-least-when-it-comes-to-the-number-of-cells>



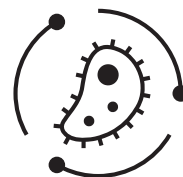
JUNIOR SCIENTISTS

To nurture talented minds, ISAS has established programmes covering all stages of an academic career. These include a graduate programme for PhD students and further training opportunities for postdocs. The programmes are aimed at bachelor's and master's students, including interns, and enable them to undertake work placements within the research groups. Students of science journalism also have the opportunity to complete an internship in the Communications team.

More information about the ISAS graduate programmes is available online.



Microbiome Research: EU Network METAMIC 3 for PhD Students



Whether in humans, animals or environmental ecosystems – microbiomes are a link, and crucial for health and ecological balance. A microbiome is the totality of all microorganisms that colonise living beings. Their role is the focus of the new network “Metaproteome-based leveraged microbiome management in the context of One Health” (METAMIC 3), which is dedicated to training young scientists in this field. The European Union is providing 4.4 million euros in funding to the Marie Skłodowska-Curie doctoral network until 2029. Fifteen students will have the opportunity to conduct doctoral research within this European network. Thirty-one research institutions, universities and companies are participating, including twelve partner organisations that are now recruiting doctoral students.

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Prof. Dr Robert Heyer is Head of the research group Multidimensional Omics Data Analysis at ISAS and coordinator of the METAMIC 3 network.

” In METAMIC 3, we are using metaproteomic analyses to gain insights, for the first time, into the dynamics and role of microbial molecules within the context of One Health.

The One Health concept regards animal and plant health, as well as environmental factors, as crucial for human health. Zoonoses, infectious diseases transmitted between humans and animals, can influence the human microbiome. Conversely, susceptibility to infection also depends on the human microbiome. Water and air pollutants, as well as the spread of antibiotic resistance among humans and animals, also have an impact. METAMIC 3 focuses on these interactions and the analysis of microbiomes using omics technologies. Omics refers to the holistic characterisation of, for example, genes (genomics), proteins (proteomics) or metabolites (metabolomics). A new research approach is metaproteomics.

“At METAMIC 3, we will apply metaproteomics analyses to gain initial insights into the dynamics and role of microbial molecules in the context of One Health. Based on these findings, we will develop strategies for a better microbiome management,” says Prof. Dr Robert Heyer, Head of the research group Multidimensional Omics Data Analysis at ISAS and coordinator of the network.

Interdisciplinary doctoral programme with rotating placements in Europe

To train young scientists in this field of research, the network takes an interdisciplinary approach. As part of the three-year doctoral programme, each candidate will conduct research at several European institutions. In addition to ISAS, the following institutions are partners of METAMIC 3: Leibniz-Institut für Analytische Wissenschaften – ISAS (Germany), Hochschule Anhalt (Germany), Università degli Studi di Sassari (Italy), Universität Hohenheim (Germany), Commissariat à l'Énergie Atomique et aux Énergies Alternatives (France), Technische Universiteit Delft (Netherlands), Universiteit Gent (Belgium), Université du Luxembourg (Luxembourg), Helmholtz-Zentrum für Umweltforschung (Germany), Max-Planck-Institut für terrestrische Mikrobiologie (Germany), Università di Pisa (Italy), Consejo Superior de Investigaciones Científicas (Spain). More information about the network: <https://metamic3.isas.de/>.

(SR) ■

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union. Neither the European Union nor the granting authority can be held responsible for them.



Finanziert von der
Europäischen Union



In Prof. Dr Christian Janfelt's laboratory, Felix Hormann works as a visiting researcher for several hours a day on the mass spectrometer – until it's time for the obligatory break with his Danish colleagues.

Copenhagen: Different Molecules, New Perspectives?

Felix Hormann is a PhD student in the Lipidomics research group at ISAS, and he conducts research on the spatial quantification of lipids. Since November 2025, he has been in Copenhagen for a three-month research stay. In this interview, the 27-year-old chemist talks about his experiences at the University of Copenhagen and shares his impressions of life inside and outside the laboratory.

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Why did you decide to undertake a research stay in Copenhagen?

Hormann: Originally, I wanted to spend a semester abroad during my master's studies, but unfortunately that coincided with the COVID-19 pandemic. It's important to me to experience other working cultures and to live outside Germany for a while. From a professional perspective, the prospect of receiving valuable feedback to complement my research at ISAS with Prof. Dr Sven Heiles was decisive. Prof. Dr Christian Janfelt's research group here in Copenhagen can offer me insights that are not available in this form in Germany. I am currently working at the Department of Pharmacy at the University of Copenhagen, where the focus is on analysing drugs, their interactions, and their distribution within tissue. Various mass spectrometry imaging methods are employed, similar to those we use in Dortmund. Therefore, the methods I'm learning here can easily be transferred to our target molecules, such as lipids and metabolites, which we are investigating in Dortmund.

“The group led by Prof. Dr Christian Janfelt in Copenhagen offers me insights into research that simply aren't available in Germany.”

What do you think of the Danish capital so far?

Hormann: I really like Copenhagen. The city is very bicycle-friendly, and you can get almost anywhere by bike. At first, it was a new experience to find myself in a real bicycle traffic jam in the mornings, together with so many other people, in front of the university. Of course, there are traffic rules, but you also have to go with the flow a bit. Copenhagen is especially beautiful during the Christmas season. There are many Christmas markets

offering gløgg and ice rinks for skating. The harbour is filled with illuminated canoes during the Santa Lucia Festival of Lights. And, of course, there's the traditional julefrokost in the research groups – Christmas parties that already begin at lunchtime and go on well into the evening. However, I was repeatedly told that I should definitely come back in the summer, when Copenhagen is said to be even more beautiful.

What are you researching during your time in Copenhagen?

Hormann: In general, it involves the spatial quantification of analytes within a tissue, that means determining the absolute concentration of a substance in specific areas – for instance, in the brain. Unlike my work at ISAS, which focuses on measuring lipids, Prof. Dr Janfelt's research group examines the distribution of drugs in the body. The spatial quantification of these molecules is somewhat easier as it involves the targeted analysis of a few defined molecules. My long-term research goal in Germany is to use these experiments as a basis for quantifying large numbers of lipids with spatial resolution. In Copenhagen, I'm learning the most important basics for this purpose, so that I can then improve our measurement strategies at ISAS in the Lipidomics research group.

What does your day-to-day work as a visiting scientist involve?

Hormann: I have access to several mass spectrometry imaging systems that use different approaches to ionisation and imaging. My work involves characterising the performance parameters of these technologies. We compare them with one another to determine which methods are most effective for which molecules. Sensitivity plays a major role here, that is how reliably very small quantities can be measured.

Until now, I've worked with mass spectrometry imaging using matrix-assisted laser desorption/ionisation, or

MALDI for short. In this process, the molecules are ionised using a laser and an auxiliary substance called a matrix which is then analysed using a mass spectrometer. In Copenhagen, I've also received training in desorption electrospray ionisation, or DESI for short. With this technique, ionisation is carried out using a fine solvent spray. I also spend a large part of my time optimising various sample preparation steps so that they can be applied in Dortmund later on.

Are there any differences between the German and Danish research mindsets?

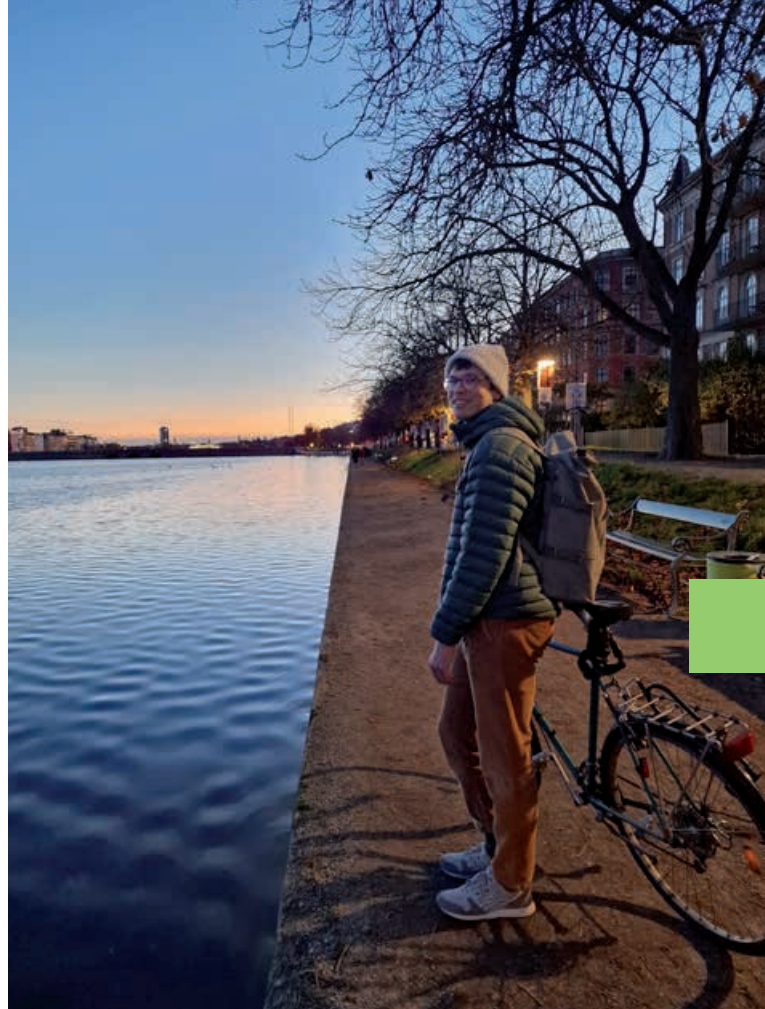
Hormann: The first few days at the institute felt quite different from those in Dortmund. Because it's winter and it gets dark in Copenhagen as early as 3 p.m., many people don't start work until 9 in the morning. This way, they can at least make use of a little daylight before the day begins. After eight hours of work, most researchers leave; only a few stay longer, for example to run one more experiment. The idea is to use the time on site as efficiently as possible and then find time to clear your head afterwards.

My Danish colleagues find social factors very important. For example, we eat lunch together and set time aside for a coffee break between meetings. Overall, everything feels a bit more relaxed compared to Germany, but we are still very productive.

There are also many opportunities to try out the various devices in the laboratory. This may be partly because the institute is part of a university. Hierarchies are very flat, and you are free to look at other projects. This fosters many new ideas and joint experiments.

What are you learning from your time in Copenhagen?

Hormann: In Copenhagen, I've learnt more about the analysis of hormones and their influence on health than ever before. This was simply by being allowed to participate in the group seminars and lectures held by our



In Copenhagen, the chemist often travels by bicycle.

entire research department. To discover things beyond your own horizon, you have to keep asking yourself: What are others actually doing? Here in the Danish research group, the focus is on other molecules – hormones and drugs – and yet I still gained new insights into possible approaches to my own research. I came up with new ideas for topics to explore in my future research, too. Networking is very important. Having the phone numbers of other researchers outside your immediate environment is helpful, because you can ask them, “How would you do that?”

Is there anything that you would you like to contribute at ISAS after you return?

Hormann: In Copenhagen, I can build on existing guidelines and a substantial amount of preparatory work. My ►

goal is a transition from working with drugs to working with lipids. One major advantage is that the analytical equipment at ISAS is very similar to what we have here. This means that I can easily transfer the protocols I develop here to our research at ISAS. This will help us create a SOP, a standard operating procedure, for our research questions in Dortmund. Apart from that, I'd also welcome the obligatory coffee break during our group meetings – it's a nice tradition! (laughs)

What advice would you give to other doctoral students who are considering a research stay abroad?

Hormann: In any case, talking to people who have already conducted research abroad is helpful. Many people in academia are open about their experiences. It's also important to reflect on your own working methods and be open to new ideas. Building contacts, including the ones from abroad, is very valuable.

I applied for several scholarships and would advise against giving up if you don't succeed immediately. It may just be bad luck, and it doesn't necessarily mean that your research idea is flawed – often, there simply aren't enough places available. As doctoral students, we're enrolled at universities, which is how I ultimately obtained my ERASMUS+ grant. I'm also fortunate to have aid from ISAS.

(The interview was conducted by EA.) ■



MALDI & DESI

In matrix-assisted laser desorption/ionisation (MALDI), researchers embed the molecules from a sample in a matrix. The matrix molecules absorb the laser light, which leads to the ionisation of the target molecules (analytes).

Desorption electrospray ionisation (DESI), on the other hand, works with a fine solvent spray. The electrically charged mist hits the sample surface.

The applied solvent film extracts analytes from the sample surface.

The secondary solvent droplets from the solvent film then lead to the ionisation of the molecules.



What's going on here, Luisa Speicher?

This photo was taken during Girls' Day at ISAS. In 2025, our topic was 'Bacteria & Sweets: female pupils analyse their breath on Girls' Day'. For this experiment of exhaled air, my colleague Annika Fechner, the girls and I carried out the analyses with the ion mobility spectrometer (IMS). The volatile organic compounds – VOCs for short – in our exhaled air can help with the early detection of illnesses such as pneumonia. Because we never handle hazardous substances during Girls' Day, we used lollipops in various flavours for the demonstration. After that, we worked with the IMS to analyse the aromas in the girls' cherry or mint-flavoured exhaled air. The aromas acted as placeholders for the VOCs that come up as a result of diseases. The girls also prepared sweets solutions for a headspace analysis. By analysing the gases released from the sample, they were able to identify the sample's components. When the photo was taken, I was explaining to three young researchers how we first prepare the sweets samples for the upcoming headspace analysis. My hands, visible on the right side of the image, show how we vigorously mix the samples using a vortex mixer.

“



Dr Luisa Speicher is a medical physicist and postdoc in the Lipidomics research group.

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MS-BASED IMAGING

Most illnesses or medical conditions, including cardiovascular diseases or tumours, are associated with localised and heterogeneous changes of biochemical cascades within some cells. The reason is that cells often respond differently when triggered with external stimuli such as low oxygen levels, viruses, bacteria, or when genetic alteration occurs. This leads to a complex spatial assembly of diseased or infected cells surrounded by healthy tissue, which is responsible for the medically relevant phenotype (referring to the appearance, development, and behaviour of an organism). To fully understand these phenotypes on a molecular level, analytical methods need to be capable of mapping spatially confined molecular changes.

More information about this research program is available online.



Endogenous Antioxidant Promotes Breast Cancer Cells in Lungs

In breast cancer, it is often not the original tumour that poses the greatest risk, but the spread of tumour cells to other organs like the lungs. In this environment, the cells initially encounter poor conditions for survival: a lack of nutrients, increased oxidative stress and the tissue's defence mechanisms make it difficult to survive. However, a small proportion of tumour cells manage to adapt to the new environment, grow and form metastases. A study published in the journal *Cancer Discovery*, involving researchers from ISAS, shows that the endogenous antioxidant glutathione plays a crucial role in this process.

The researchers from Rockefeller University, New York University, Memorial Sloan Kettering Cancer Center, University Hospital Essen, and ISAS compared breast cancer cells from primary tumours and lung metastases in vitro using cultured cancer cells from human and mice. They specifically analysed metabolic processes in the mitochondria. The metastatic cells exhibited significantly higher levels of mitochondrial glutathione.

Glutathione serves to protect cells from oxidative stress (► p. 42). However, in the context of cancer, this protective function can have adverse effects: tumour cells exploit this mechanism to become more resilient. They activate a metabolic adaptation programme that facilitates their survival in new organs and promotes the formation of metastases.

ATF4 activates a survival programme in tumour cells

“Using MALDI mass spectrometry imaging, we were able to detect glutathione in tumour tissue with spatial resolution and identify where it accumulates most within the metastasized organ,” explains Dr Karl Smith, Head of the Spatial Metabolomics junior research group. To this end, Smith and his team analysed lung tissue from mice with breast cancer metastases. Glutathione in the mitochondria acts as a signal for the protein ATF4. The latter regulates key genes involved in stress and metabolic responses, thereby activating the tumour cells’ survival mechanisms. The cells adapt their metabolism to the new environment,



At ISAS, Dr Karl Smith heads the Spatial Metabolomics junior research group.

“ We were able to detect glutathione in tumour tissue with spatial resolution and identify where it accumulates most within the metastasized organ.

enabling them to establish themselves in lung tissue – a crucial prerequisite for metastasis formation.

Transport protein as a key to new therapies?

The authors identified the protein SLC25A39 as a key component of the processes described. It is located in the mitochondrial membrane and acts as a transport protein for glutathione. The findings show that ►

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metastatic breast cancer cells produce increased levels of SLC25A39. They require this transport protein to adapt to new tissue. If SLC25A39 is switched off, less glutathione enters the mitochondria. Consequently, fewer metastases form. The growth of the primary tumour remains largely unaffected. This phenomenon is particularly pronounced in the early phase of metastasis, when tumour cells settle in the lungs and need to adapt to the new tissue environment.

The study reveals that tumor cells activate specific adaptation and survival mechanisms to successfully establish themselves in new tissues. The SLC25A39 protein is therefore emerging as a potential therapeutic target. If this transport protein could be specifically inhibited, it could regulate the import of glutathione into the mitochondria and prevent tumour cells from successfully establishing themselves in the new tissue. In the long term, this could lead to potential new therapeutic strategies specifically aimed at slowing down or preventing the spread of breast cancer in the body.

(SSL) ■

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GLUTATHIONE: CELLULAR PROTECTION AND METABOLIC BALANCE

Glutathione is a tripeptide produced naturally by the body, consisting of the amino acids glycine, cysteine and glutamic acid. It is one of the most important antioxidants within cells and protects them from oxidative stress. Oxidative stress refers to a metabolic imbalance in which too many free radicals (reactive oxygen molecules) encounter too few protective antioxidants. This can damage cells. Oxidative stress is linked to the development of various diseases, including cancer. Glutathione helps to maintain metabolic balance and stabilise key cellular functions.



Yeh, H.W., DelGaudio, N.L., Uygur, B., Millet, A., Khan, A., Unlu, G., Xiao, M., Timson, R.C., Li, C., Ozcan, K., Smith, K.W., Martins Nascentes Melo, L., Allies, G., Basturk, O., Sickmann, A., Bayraktar, E.C., Possemato, R., Tasdogan, A., Birsoy, K.
 (2025) Mitochondrial Glutathione Import Enables Breast Cancer Metastasis via Integrated Stress Response Signaling.
Cancer Discovery, 15 (12), 2437–2449.

<https://doi.org/10.1158/2159-8290.cd-24-1556>

Effective Stress-coping Strategies Enable Tumour Cells to Survive in the Lung

How metastatic cancer cells adapt to new microenvironments is one of Prof. Dr Dr Alpaslan Tasdogan's areas of research. The oncologist is Head of the Institute for Tumour Metabolism at the Clinic for Dermatology at University Hospital Essen, and he heads the research group Preclinical Metabolomics at ISAS. In a study published in *Cancer Discovery* (► p. 42), he and his fellow researchers investigated metastatic breast cancer cells in the lung. In this interview, he explains why these tumour cells survive in the lung and what therapeutic prospects there are for patients.



Prof. Dr Dr Alpaslan Tasdogan is an oncologist and Head of the Institute for Tumour Metabolism at University Hospital Essen. Together with his research group there, he conducts research into metastases and the metabolism of malignant melanoma. At ISAS, the doctor and scientist has been leading a second research group since May 2024. Tasdogan has already received several awards for his research, including, for example, an ERC Starting Grant, an Emmy Noether Junior Research Group and the Peter Hans Hofschneider Endowed Professorship for Molecular Medicine.

Your publication shows that metastatic tumour cells utilise certain protective mechanisms against oxidative stress to successfully establish themselves in the lung. Why did you choose to investigate lung metastases specifically in the context of breast cancer?

Tasdogan: The lung is one of the first and most common target organs to which breast cancer cells metastasise. In many patients, the tumour cells spread further throughout the body from there. That is why we wanted to gain a better understanding of the mechanisms that help metastatic tumour cells to survive in the lung and successfully establish themselves there. By better understanding these early stages of metastasis, we can, in the long term, develop new ways to intervene specifically and prevent further spread.

What do your findings mean for the current and future treatment of lung metastases in different types of breast cancer?

Tasdogan: Our findings reveal new therapeutic targets for the early phase of metastasis. When tumour cells ►

migrate to the lung, they are exposed to particularly severe oxidative stress there. To survive and establish themselves, they activate protective mechanisms that counteract this stress. If we succeed in specifically blocking these mechanisms, the tumour cells would no longer be able to compensate for the oxidative stress and would undergo apoptosis – that is programmed cell death – even before a metastasis forms.

„Future therapies could aim to influence specific metabolic pathways in such a way that the tumour cells can no longer counteract the oxidative stress.“

Future therapies could aim to influence specific metabolic pathways in such a way that the tumour cells can no longer counteract the oxidative stress. Should effective compounds be identified in preclinical studies, these could open new treatment options for patients with metastatic breast cancer in long term.

What role might glutathione play in breast cancer, particularly regarding metastases in other organs – such as the liver, brain or bones?

Tasdogan: Glutathione helps the cell to counteract oxidative stress. Our findings suggest that tumour cells

utilise this protective function to overcome the stressful conditions of early metastasis. As the lung is one of the first and most common target organs for metastatic breast cancer cells, the stress adaptation acquired there could be crucial for further spread. We suspect that tumour cells which have already developed effective stress-defence strategies in the lung are also better able to cope with the stressful conditions in other organs. We therefore regard the lung as a kind of gatekeeper of metastasis – an intermediate site that can influence and facilitate the further spread of tumour cells.

Considering your findings, to what extent is it relevant where the primary tumour originated? Or to put it another way: Could one expect similar effects in colorectal cancer cells that have metastasised to the lungs?

Tasdogan: What matters is not so much where the primary tumour originated, but rather the challenges tumour cells face in a new organ. When tumour cells colonise the lungs, they must adapt to a hostile environment. We assume that metastasising tumour cells utilise, to some extent, similar adaptation mechanisms in this process. These fundamental processes of metastasis can be analysed using comparable technologies across different types of cancer. We are currently investigating this, for example, in melanoma and colorectal cancer. In this context, we aim to gain a better understanding of the common principles of metastasis and to identify the adaptive mechanisms tumour cells use to colonise new organs.

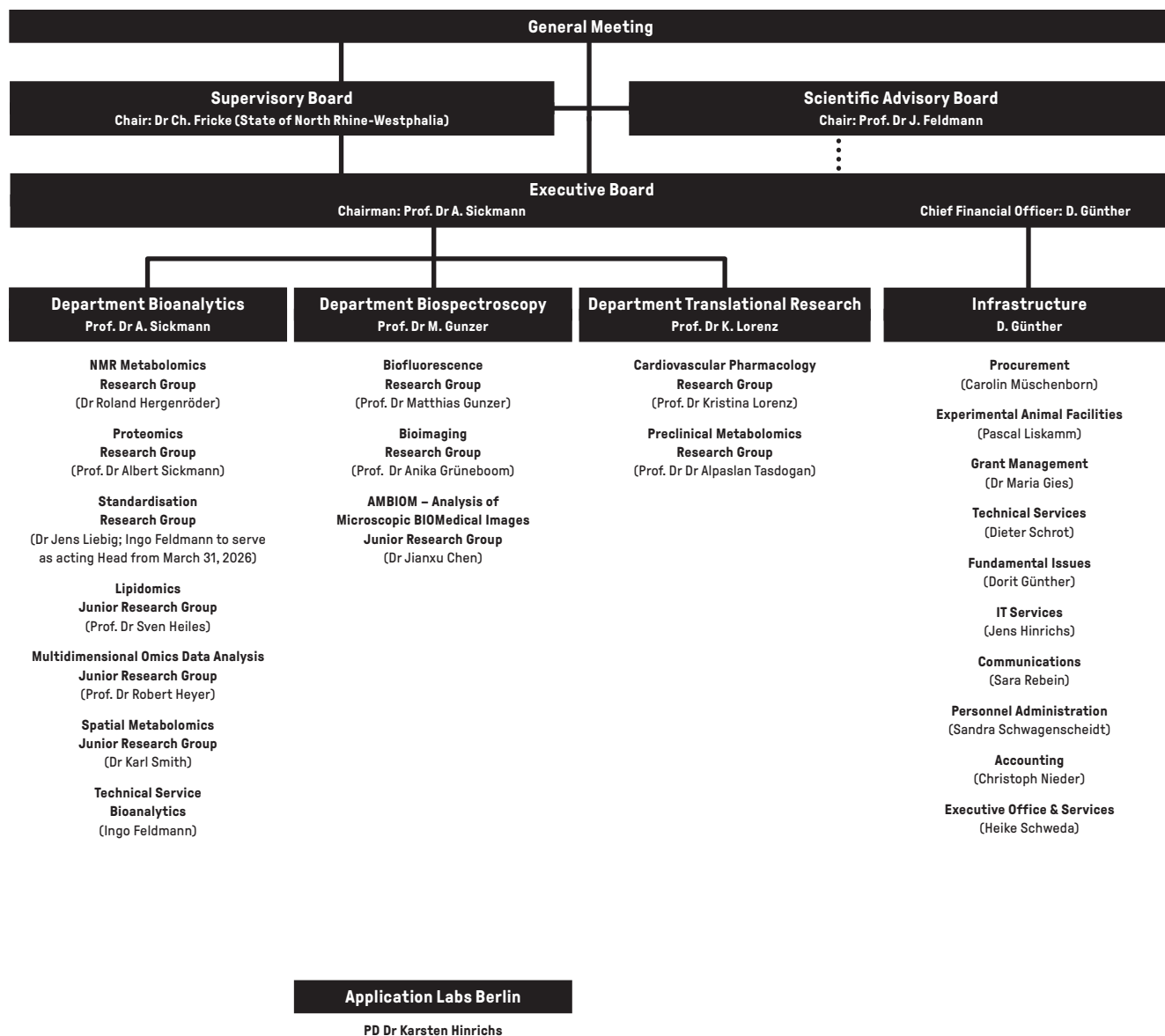
(The interview was conducted by SSL.) ■





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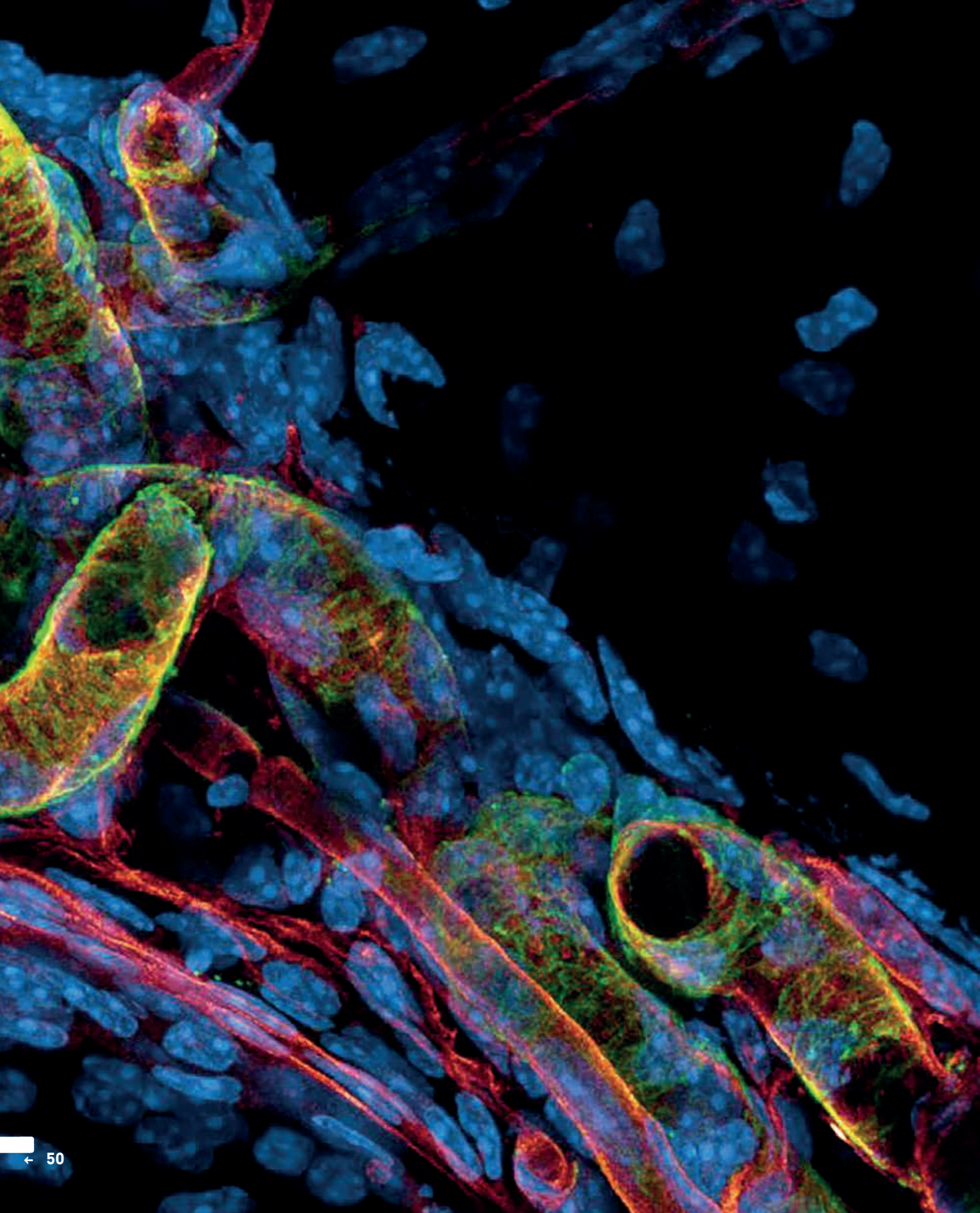
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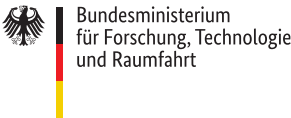
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