isas Leibniz-Institut für Analytische Wissenschaften

ANNUAL REPORT 2021

advancing analytics

Leibniz Gemeinschaft

FOREWORD

Dear Readers

We are looking back on another year at ISAS – one in which we succeeded in expanding our networks and intensifying our interaction with clinics and universities, particularly our cooperation with the Essen University Hospital. In the coming years, ISAS will further the expansion of its translational disciplines in joint appointments with the University of Duisburg-Essen.

Junior researchers also play an important role in our goal of developing and optimising innovative and economical analytical methods for health research, and we are pleased to have been able to fill two new junior research groups for the next five years with the help of funding from the German Federal Ministry of Education and Research. I am particularly pleased that we were able to welcome Dr Jianxu Chen (AMBIOM – Analysis of Microscopic BIOMedical Images) and Dr Prasad Phapale (Spatial Metabolomics) to lead these groups. Another positive development is that we have two more junior groups ready to take off. We have laid the groundwork for them in the form of joint appointment procedures for junior professorships with the University of Bielefeld (Multidimensional Omics Analyses) and the University of Duisburg-Essen (Lipidomics).

In 2021, in addition to our DIGITAL LUNCH BREAK, we virtually opened our lab doors a bit more than before by creating a space on our website called ISAS Kompakt (www.isas.de/en/kompakt), where our scientists give the public clear insights into their research. In order to literally give a voice to the work of our institute, we have made preparations for our first podcast »NACHGEFORSCHT – Die Live-Schalte ins Labor«.

We hope the following pages will give you an idea of how eventful the past year was, highlight the research successes that we can look back on with satisfaction and, above all, show you what it was that drove and motivated our institute and its staff.

Enjoy your read!

Prof Dr Albert Sickmann

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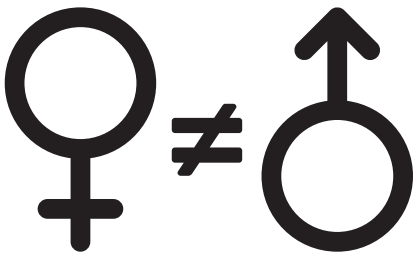
DIFFERENCES ARE CRITICAL



It is no longer a secret that women and men exhibit different symptoms during a heart attack. It is also clear that adverse drug reactions occur almost twice as often in women as in men.[1] However, the role of sex as a biological factor in the development of adverse drug reactions is poorly understood.[2] One thing is for sure — there is a significant difference between the sexes in the expression of a gene important for drug metabolism.[3] What do sex-specific differences generally mean for health research? What role do they play in applied basic research, for example in understanding the genesis of diseases or in the search for new therapeutic approaches? The editors asked five ISAS scientists to comment on sex-specific aspects in their fields of research.

1 Zucker I, Prendergast BJ. *Sex differences in pharmacokinetics predict adverse drug reactions in women*. Biol Sex Differ. 2020;11(1):32. Published 2020 Jun 5. https://doi.org/10.1186/S13293-020-00308-5.

2 Ibid

3 Guengerich FP, Waterman MR, Egli M. *Recent Structural Insights into Cytochrome P450 Function*. Trends Pharmacol Sci. 2016 Aug;37(8):625-640. https://doi.org/10.1016/j.tips.2016.05.006.

Prof Dr Kristina Lorenz, Director of Translational Research & Head of Cardiovascular Pharmacology

It is well-known that some medications work differently in women and men. This has to do, for example, with differences between the sexes in terms of drug intake, distribution, and effects. When transferring research results into practice, it is important to aim at including an equal number of male and female subjects or patients in the studies.

In my research group, we start at the very beginning, with the genesis of cardiovascular diseases. Once we have identified the disease mechanism, the first thing is to develop what is called a targeting strategy or therapeutic strategy. Depending on the question, we usually study them in one sex first before expanding the studies.

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Artificial intelligence (AI) might be able to detect a sex difference when evaluating microscopic biomedical images if such a difference exists, for instance, from a pathological perspective. For example, certain tissues from male donors might look different under the microscope than tissues from female donors. AI can compare the images and detect, for example, differences in the size of glands in tissues from females and males.

Dr Jianxu Chen, Head of AMBIOM – Analysis of Microscopic BIOMedical Images

Dr Andreas Hentschel,
Research Associate Translational Analytics

Sex-specific mass spectrometric analysis of proteins is important to our search for biomarkers for progression and therapy control (progression markers) in neuromuscular diseases (▸ p. 51). Despite many similarities between women and men at the biological level, there are some differences that may be critical in the search for biomarkers. For example, women and men differ not only in terms of their sex hormones, but also, for example, in the activity of their serotonergic systems, which are involved in the regulation of almost all brain functions, and in the level of the stress hormone, cortisol, in saliva.

Some neuromuscular diseases also exhibit differences between the sexes. For example, the hereditary disease Duchenne muscular dystrophy affects men almost exclusively. The reason for this is because women with the mutated gene on one X chromosome can compensate for this genetic defect with their second X chromosome. A gender-specific analysis is necessary when searching for biomarkers for some neuromuscular diseases, however, at the same time, it limits the sample size and especially in rare diseases, the small number of patients presents us with challenges.

Dr habil. Miloš Filipović,
Head of ERC-Sulfaging

It is true that sex affects the development of neurodegenerative diseases. One of the »simple« explanations to why women have a greater tendency to develop Alzheimer's disease (AD) lies in the fact that women live, in average, five years longer than men, and age is the main risk factor for the development of AD. In addition, women are more prone to autoimmune diseases and these inflammatory processes could be triggers

Prof Dr Anika Grüneboom, Head of Bioimaging

Rheumatoid arthritis (RA) primarily affects women, accounting for about 75 per cent of patients. Consequently, female sex hormones such as oestrogen and progesterone play a particularly important role in the development of this autoimmune disease. In most patients, RA occurs during menopause, when progesterone and oestrogen are deficient. Accordingly, several studies also demonstrate the positive effects of hormone replacement therapies in women with postmenopausal RA. However, as said, RA is not an exclusively female disease; about a quarter of those affected are male. Research has shown that RA in men is associated with low testosterone levels in the blood. Testosterone has immunoregulatory and anti-inflammatory functions, so male sex hormones also appear to have an important influence on the development of RA.

In our work, we take these sex differences into account and focus primarily on female mice to study RA in our animal models. To more closely evaluate the influence of sex-related differences in the development of the disease, we then additionally compare the findings of female mice with those of male animals. We also include both female and male patients in our studies when analysing human samples.

for plaque formation. As for Parkinson's Disease, while men do have a one and a half to twice fold bigger tendency to develop PD, women have a much worse and faster disease progression. The reasons for that remain unclear.

Taking both sexes into consideration when performing experiments is becoming increasingly appreciated, particularly among scientists studying aging and age-induced diseases. While this is not always easy to interpret and analyse due to inherent physiological differences among sexes, it may provide a key to understanding how these processes develop, on a molecular level, and maybe lead to some targeted drug design.

Early Testing for Endometriosis: Brenda Krishnacoumar Wants to Buy Women Time

Dr Brenda Krishnacoumar wants to replace the laparoscope, an instrument used to perform a laparoscopy, with a blood test. For her presentation at Postdoc Pitch Day, she recreated the instrument using a 3D printer, among other things.

Sharp pain, chronic inflammation and infertility – these are just a few examples of what endometriosis can do. It is a chronic disease in which tissue similar to the uterine lining attaches to organs outside the uterus. Endometriosis is insidious, because the symptoms are multifaceted and often ambiguous. As a result, the path to diagnosis is often an odyssey. According to the World Health Organisation (WHO), some 190 million women worldwide suffer from endometriosis, and it can take up to ten years to diagnose the disease. This is a long time during which the quality of life deteriorates, and it can also represent a valuable window of time that may be lost by women who wish to have children. Dr Brenda Krishnacoumar wants to change that. During the first Postdoc Pitch Day at ISAS in October 2021, she presented the approach by which she hopes to buy women time with her research into the incurable disease (▸ S. 54).

"Although endometriosis affects ten to 15 percent of all women of childbearing age in Germany, the research into the mechanisms of the disease have been insufficient up to now. And because the symptoms of endometriosis vary, it often goes undetected for a long time," says the 31-year-old. Krishnacoumar would like to do something about the emotional strain and the additional stress caused by uncertainty. What is currently lacking is a non-invasive method for early detection of endometriosis – before the disease breaks out. "This is exactly where I would like to start with my research and develop an early test," explains the biologist. For example, she plans to look for markers in blood and for biopsy testing that will allow screening for endometriosis even in young women.

> ***Even if symptoms improve, hormonal menopause still puts stress on family planning.***

Early testing should bring quality of life & facilitate family planning

At present, by the time women are diagnosed, endometriosis has often already caused irreparable damage. Examples: Ovaries can become adhered, endometrial cysts can limit ovarian function, or endometrial lesions in the pelvis can reduce fertility. According to Charité – Universitätsmedizin Berlin, 30 to 50 percent of women with endometriosis suffer from an unfulfilled desire to have children.

Although some women's fertility improves after the surgical removal of the misplaced tissue, others remain childless even after additional fertility treatment, and some sufferers are helped by artificially induced menopause. Krishnacoumar does not consider this to be an optimal solution: "Even if disease symptoms improve, hormonal menopause still puts stress on family planning." That said, surgery and hormone therapy are not a guaranteed cure-all; endometriosis can come back, she explains.

Early testing: understanding the unknown cause to facilitate a cure

Although there are several hypotheses on the genesis of endometriosis, they do not provide a valid explanation as to why the disease breaks out in some women and spares others. To help in her development of the early test, Krishnacoumar has been intensively studying what she calls the pathomechanism of endometriosis since Postdoc Pitch Day. To understand which processes in the body trigger the disease, the biologist first examines the uteri of mice and samples from endometriosis patients under light sheet fluorescence and confocal microscopes. Future analyses will also use spectral flow cytometry. If Krishnacoumar succeeds in finding out whether, for example, certain proteins or altered or special cell types can be used as biomarkers for her early test, this will also be an important step in the direction of a cure.

"We need sex-appropriate science"

Scientists like Krishnacoumar still have a lot of work to do before endometriosis can one day become a curable or even preventable disease. There is a lack of education about endometriosis and an even greater lack of research, Krishnacoumar laments. Diseases such as endometriosis which, although not fatal, are associated with severe physical and concomitant psychological suffering, should not be ignored. "For science to be sex-appropriate, we need more research for women," the biologist insists.

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SALIVA TEST VERSUS BLOOD TEST?

In February 2022, the French company Ziwig announced that it had developed a saliva test based on micro-RNA for the diagnosis of endometriosis. The test is based on 109 micro-RNAs which are associated with endometriosis. According to initial data, it is expected to be effective in patients who already have the disease. Once the saliva test is approved, it could significantly shorten the suffering of women with symptoms. However, it is unsuitable for early-detection screening. For this purpose, Krishnacoumar wants to find markers in the blood that can provide information about the risk of disease even before the onset of menstruation and in women without symptoms.

Clear the stage for new ideas at the first Postdoc Pitch Day

Krishnacoumar has been a postdoctoral fellow at ISAS since September 2021. The biologist attaches great importance to being able to pursue her own research questions. That is why she has been working on her research idea for the endometriosis early test for several months. “Postdoc Pitch Day was a great opportunity to find out if my project idea had any potential,” Krishnacoumar reports. The researcher was among those who presented their ideas to a panel made up of five research group leaders from various disciplines who served as mentors. After a five-minute pitch followed by a Q&A and discussion session, the mentors provided feedback to the postdocs. The postdocs and mentors also discussed opportunities for cooperation within and outside the institute. The presenters said the different perspectives and opinions were helpful in looking at their ideas from different angles. “I now have precise items that I can address, so I can apply for project funding later,” Krishnacoumar is pleased to say.

Laparoscope from the 3D printer

Krishnacoumar came up with something special to help the mentors understand the patients’ situation. She recreated a laparoscope using the 3D printers at ISAS and simple tools from the hardware store (see photo p. 08). The mentors at her presentation should be as surprised by this as Krishnacoumar was when she learned that minimally invasive surgery such as laparoscopy (abdominal endoscopy) is the gold standard for making a reliable diagnosis. Krishnacoumar would like to see the topic of endometriosis have more of a presence, not only in medical education and research, but also in the general public. “It’s not always about publishing papers that are only read by the professional community. You have to reach people,” she stresses. With her research idea for an early test, she hopes to contribute to exactly that.

(CMP/SR) ■

»NACHGEFORSCHT – DIE LIVESCHALTE INS LABOR« FOLGE 1 – Endometriose: Auf die Ursache kommt es an!

www.isas.de/kompakt/nachgeforscht-folge-1-endometriose

Cheyenne Peters (right) conducting the interview with Dr Brenda Krishnacoumar of the Bioimaging research group.

What's happening here, Cheyenne Peters?

This photo shows Dr Brenda Krishnacoumar and me in February 2022 recording our ISAS podcast »NACHGEFORSCHT – Die Liveschalte ins Labor«. Brenda is a post-doctoral researcher in the Bioimaging research group. She pitched her idea for research on endometriosis (▸ p. 08) at the first Postdoc Pitch Day (▸ p. 54) in October 2021. For me, it was exciting to see how much had happened with Brenda's idea within a few months. Her project is taking shape, and it's fascinating to hear how she's progressing. In our podcast episode, Brenda shares recent developments and explains how she plans to look for biomarkers in the blood to develop an early test for endometriosis. To this end, Brenda has already examined the uteri of mice under a confocal microscope. In addition to these initial measurements, the podcast looks ahead to future work, including a collaboration with a clinic. It's really fun to talk to someone who is so passionate about her research.

Cheyenne Peters,
Communications Associate

FOLGE 1 – Endometriose: Auf die Ursache kommt es an!

www.isas.de/kompakt/nachge-forscht-folge-1-endometriose

Cheyenne Moon Peters (23) is a science journalism student. Since 2021, she has been working in the Communications team at ISAS besides her studies at TU Dortmund University. Cheyenne Peters writes articles for ISAS Kompakt (www.isas.de/en/kompakt) and the institute's annual report. She also conducts interviews with ISAS' employees for the podcast »NACHGE-FORSCHT – Die Liveschalte ins Labor«.

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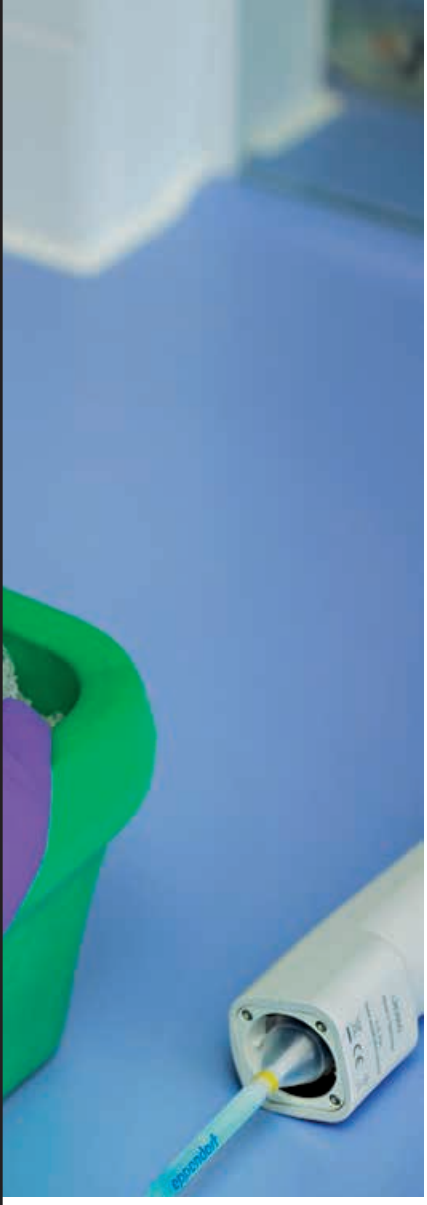
DISEASE MECHANISMS & TARGETS



One of the scientists preparing a real-time PCR plate for the regulation of specific genes.

This research programme focuses on the analysis of molecular mechanisms involved in the development of various diseases, such as cardiovascular diseases. The diseases have multi-factorial causes; genetic constellations play a role, as do environmental and nutritional influences. Because they progress differently in different patients, they respond differently to treatments. Researchers at ISAS are identifying potential target molecules in order to gain a comprehensive understanding of the pathomechanisms and facilitate earlier diagnosis of the diseases in the future, with fewer side effects and better individual therapy.

In their basic research, the scientists use methods that are by no means limited to the genome level, but also include proteomic and metabolomic parameters. The researchers use multi-omics techniques for this purpose and test and optimise them.

One focus in the »Disease Mechanisms & Targets« programme is on cardiovascular diseases. The institute can draw on many years of analytical expertise in this field, including extensive studies of the platelet proteome and the detailed elucidation of platelet dysfunction and molecular processes involved in heart failure (cardiac insufficiency).

Molecular mechanisms of heart failure

The molecular causes and the progression of the disease are still largely unknown for many diseases of the cardiovascular system. In the »Disease Mechanisms & Targets« research programme, the scientists are working on improving the diagnosis of heart failure and establishing new therapeutic approaches. They are combining classical methods of molecular genetics and biochemistry with high-throughput methods. The researchers at ISAS cover the entire spectrum of analysis, from the detailed investigation of individual components to the examination of entire cellular systems.

Characteristic disease progression & reduction of side effects

The scientists are developing new diagnostic and therapeutic tools for the differentiation of several heart diseases. To do this, they work with transgenic mice. The aim is to identify spectroscopic characteristics of different disease processes. The research group is also developing and optimising silicon-based nanocontainers that

enable the myocardial-cell-specific application of medications and thereby a reduction in side effects.

Healing processes in the heart through CAP

The researchers are investigating the mechanisms of cold atmospheric plasma (CAP) in the treatment of cardiovascular diseases. Up to now, plasmas such as these have been tested primarily in the fields of tissue repair, the treatment of infectious skin diseases, dentistry and cancer treatment. They could increase the concentration of nitrite in the blood and thus reduce a cardiovascular risk factor.

Imaging techniques

In 2021, the scientists strongly advanced biospectroscopic analyses using imaging vibrational microscopy and high-resolution microscopy. Using optical methods, they succeeded in investigating the various molecular mechanisms of heart failure and diagnosing the corresponding diseases in their early stages. In cooperation with the Julius-Maximilians-Universität of Würzburg and the University of Duisburg-Essen, the scientists investigated various mouse models with genetic diseases.

In 2021, in order to fully assess the potential of non-linear spectroscopic imaging instrument and various assays for the identification of cardiac involvement in metabolic disorders and genetic storage diseases such as Fabry disease, the researchers for the first time used the coherent anti-stokes raman scattering (CARS) microscopy to investigate a mouse model. The analysis method proved to be precise. Thanks to the high sensitivity of the spectral information obtained and computer-aided diagnosis, subtle changes in protein lipid changes in the protein-lipid content between heart tissue in Fabry disease and control tissue could be reliably detected by up to 96 percent. Diagnosis by means of CARS microscopy thus has the potential to support gold-standard histology and other diagnostic methods for detecting the involvement of specific organs in Fabry disease.

(SR) ■

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A Matter of the Heart: German-Chinese Collaboration

According to the Federal Statistical Office of Germany, cardiovascular diseases were the cause of more than one third of deaths in the country in 2020. One of these life-threatening cardiovascular diseases is chronic heart failure. If the disease remains untreated, it can progress further and damage the heart as well as other organs such as the lung in the long term. Since January 2020, the project »ChInValue – NRW–China Cooperations: Optimisation of GRK5 Inhibitors for the Therapy of Heart Failure and Heart Hypertrophy« is pursuing a new approach for the drug therapy of chronic heart failure and the abnormal enlargement of the heart's muscle cells that often goes along with it.

Miriam Kleindl, a PhD student in the Cardiovascular Pharmacology research group, analysing the activation and quantity of proteins of the in vivo GRK study in order to find out how the signalling pathways are regulated.

Chronic heart failure can have various causes, for example high blood pressure or a heart attack. In most cases, heart failure is only detected and treated when patients already display symptoms such as a reduced performance, shortness of breath and breast pain.

G-protein-coupled receptors (GPCRs) play an important role in the physiological heart function. They are located in the cell membrane and transmit signals to the inside of the cell, for example to regulate the strength and rate of the heartbeat. In cardiovascular diseases, GPCRs are often chronically stimulated. As a result, certain enzymes, the so-called G-protein-coupled receptor kinases (GRK), desensitise the receptors. "In the long run, the overstimulation can lead to a reduced heart function and ultimately to heart failure. That is why we want to develop an agent that specifically inhibits the key enzyme that is upregulated in heart failure: GRK5," says Miriam Kleindl, PhD student in the research group Cardiovascular Pharmacology at ISAS.

Preventive and therapeutic approaches show initial successes in the mouse model

In the ChInValue consortium, Kleindl conducts research together with scientists from the Lead Discovery Center GmbH (LDC) in Dortmund and the Chinese project partner Shanghai Jemincare Pharmaceutical Co. At the LDC and at Jemincare, the researchers optimise the inhibitors for the molecular target GRK5 multiparametrically, in medicinal chemistry cycles that consist of organic syntheses as well as tests of the new compounds in biochemical and cellular assays. “In the course of these optimisation cycles, we managed to develop potent, compatible and selective GRK5 inhibitors that meet the qualitative requirements to show activity in therapeutic animal experiments – an important step in the value chain on the path towards a new drug,” Dr Bert Klebl, chief scientific officer and managing director at LDC, reports delightedly.

> ***We do not only look at how well the inhibitors block GRK5, but also at whether they influence the progression of the disease.***

At ISAS, Kleindl and her colleagues study the agent’s effect in the case of an actual disease in vivo by means of different murine models that replicate heart hypertrophy (increase in the heart’s muscle mass and weight), high blood pressure and heart attacks. “We do not only look at how well the inhibitors block GRK5, but also at whether they influence the progression of the disease,” the human biologist explains. In a first study, Kleindl and her colleagues at ISAS treated some of the animals preventively in order to analyse the inhibitors’ effectiveness – before a heart attack or chronic high blood pressure occurred and caused heart failure. They treated the other animals immediately after the mice fell ill. Afterwards, the scientists studied the heart function in both groups and compared it to a healthy control group. “We discovered that a preventive treatment with one of the GRK5 inhibitors we developed had a positive effect on the animals’ heart function and life span,” Kleindl sums up. The GRK5 inhibitors also show effectiveness in already sick mice.

Consortium strengthens international cooperation

The project partners' continuous exchange of information enables the researchers at LDC to further develop the inhibitors according to the results of the in vivo studies. Furthermore, data from in vivo compatibility studies (pharmacokinetic studies) feed into the optimisation. These take place at Jemincare, the Chinese project partner. Together, the consortium wants to develop the agent to a level where it can be nominated as a preclinical candidate after the project is finished. In a preclinical phase, the scientists check for possible side effects in order to ensure its safety before the first application in human studies.

About ChInValue

BIO.NRW and BIO Clustermanagement NRW GmbH designed ChInValue in the context of the internationalisation measure »NRW-China Cooperations: A Strategic Perspective for Innovative Life Science SME Value Chains« (NRW-China Kooperationen: Eine strategische Perspektive für innovative Life-Science-KMU Wertschöpfungsketten). The project lasts three years, until the end of 2022. The Federal Ministry of Education and Research funds the German partners with about one million euros. The funds come from the initiative »InterSpiN+: Internationalisation of Leading-Edge Clusters, Forward-Looking Projects and Comparable Networks«.

About the Lead Discovery Center

The Lead Discovery Center GmbH was established in Dortmund in 2008 by the technology transfer organisation Max Planck Innovation GmbH in order to tap into the potential of excellent basic research for the development of new, urgently needed drugs. The Lead Discovery Center takes in promising projects from academic research and typically develops them further up to pharmaceutical leads (proof of concept in model systems). In close cooperation with leading partners from academic research and the industry, the Lead Discovery Center develops an extensive portfolio of projects in the field of small molecule drugs as well as therapeutic antibodies with exceptionally high medicinal and commercial potential.

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GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

H_2S: Is this Foul Compound a Fountain of Youth?

How can a substance that is neurotoxic, i.e. has a damaging effect on the nerves, possibly play a positive role in the treatment of patients with Alzheimer's disease? Hydrogen sulfide is the name of the chemical compound we are talking about here. Chemical formula: H_2S. This is the gas that makes rotten eggs stink and is released by digested sludge.

The effects of sulfur-containing compounds on the human body are by no means harmful per se; some are even indispensable. Cysteine and methionine, two amino acids, serve as an example of this; the human body can only partially synthesise the former and cannot synthesise the latter at all. As amino acids, they are components of countless proteins. And with their sulfur atom, they are involved in other central metabolic processes whose importance for living cells has only recently become a subject of research.

Gasotransmitters – small molecules with a great impact

Hydrogen sulfide, for example, belongs to a group of gaseous compounds that can transmit signals within and between cells. In addition to H_2S, these »gasotransmitters« include carbon monoxide (CO), nitrogen oxide (NO) and nitrous oxide (N_2O) among others. The small inorganic molecules are endogenously produced through enzymatic processes in all organisms, and their production is regulated according to their physiological concentration and function. It is believed that this type of cellular communication originated very early in the phylogeny of living organisms.

Research results from previous years have highlighted the importance of gasotransmitters and their involvement in many regulatory processes; however, the specific functions they assume and to what extent they can generally take effect in cells and tissues is still unexplored in many cases.

Dr habil. Miloš Filipović's research on metabolic biochemistry provides important insights in order to improve for example the diagnosis and treatment of age-related diseases. Worms of the genus *Caenorhabditis elegans* are helping him and his team analyse the persulfidation in nematodes.

In the case of hydrogen sulfide, however, our scientific understanding has already advanced further, and the involvement of this gasotransmitter in a number of physiological and pathological processes has been proven in numerous studies – not least by the work of Dr habil. Miloš Filipović at ISAS.

"Evolutionary conservation offers potential protection against oxidative stress"

Filipović's research group in Dortmund is looking for answers to the question of the extent to which H_2S-mediated signals are involved in ageing processes. "In combination with the ERC funding, the multi-omics analysis established here at ISAS (► p. 48) gives us the opportunity to conduct a detailed investigation into the role of hydrogen sulfide in normal brain function and its impairment such as in Alzheimer's disease," explains Filipović.

The term sulfaging is an amalgamation of two words, sulfur and ageing, both representing a focal point of the ERC grant. They also indirectly hint to the type of reaction in which the amino acid cysteine plays a central role. The cysteine molecule contains two functional groups, an amino group (NH_2) and a thiol group (SH). Hydrogen sulfide is synthesised in the cells from L-cysteine by three enzymes: cystathionine gamma lyase (CSE), cysthationine beta synthase (CBE) and mercaptopyruvate sulfur transferase (MPST). All three are detectable in various types of tissues and in organs, including the brain.

The released H_2S readily and rapidly combines with the sulfur-containing thiol groups of amino acids in proteins from the environment. This leads to a conformational change of the protein molecules and is accompanied by an alteration of the biological activity. The post-translational modification of proteins induced by a transfer of a sulfur atom is known as sulfhydration or persulfidation. Persulfidated cysteines are more resilient to the oxidative damage. This basic regulatory principle is widely disseminated throughout all cells. "We think this is an evolutionarily conserved way of protecting against oxidative stress," the biochemist says.

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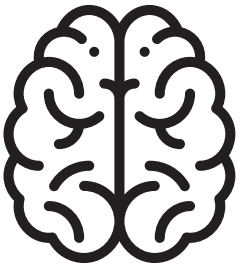
H_2S affects brain function

This assumption is also supported by the influence of H_2S on several essential physiological functions and processes in the body, such as blood pressure, the immune system, ageing processes and signal transmission in the brain. This can be demonstrated by disturbances in the normal processes of this regulation. In 2021, for example, the research group succeeded in identifying irregular protein persulfidation and H_2S metabolism as a hallmark of neurodegenerative diseases such as Parkinson's disease and Huntington's disease. During the course of these diseases, nerve cells in the brain gradually die for various reasons. Ageing processes and neuronal degradation are also accompanied by decreased persulfidation and cysteine synthesis.



Alzheimer's is by far the most common form of dementia and inevitably leads to massive memory loss, speech problems, severe limitations in motor and mental performance, and premature death. It has now been proven that protein persulfidation plays a central role in neurons, but this effect is weakened in Alzheimer's disease. The corresponding publication, in which Filipović's team took part, appeared in Proceedings of the National Academy of Sciences of the USA (PNAS) 2021 (► p. 21). Typical pathological changes in Alzheimer's disease are the extracellular deposition of amyloid plaques and neurofibrils (neurofibrillary tangles, NFTs), which form larger filaments in a helical structure (NFTs) in the cytoplasm of neurons. The central component of NFTs is the τ or tau protein. It regulates the stability of microtubules in cells and

PERSULFIDATION

As humans age, the proteins in their cells oxidise. The reason for this is their contact with hydrogen peroxide, a waste product in human metabolism. This is where hydrogen sulfide comes into play and protects the proteins from this very oxidation. This chemical reaction is called persulfidation. In order to slow down ageing processes in the future or to stop age-related diseases such as Alzheimer's or Parkinson's disease, Filipović's team is deciphering, among other things, the mechanisms of hydrogen sulfide actions in the cells. In their analyses of persulfidation, the researchers are supported by nematodes. *Caenorhabditis elegans*, a worm just one millimetre long that is popular in ageing research, also plays a major role in Filipović's laboratories.

is therefore essential for the development and stability of the cytoskeleton. In patients with Alzheimer's disease, on the other hand, the tau protein is altered by a mutation. As a result, it is insoluble, abnormally phosphorylated, and no longer able to bind to microtobules.

Impaired signal transmission in Alzheimer's disease

In their PNAS publication, the authors demonstrate that the regulation of H_2S metabolism and the associated signal transmission via persulfidation is impaired in age-related diseases such as Alzheimer's. In healthy neurons, the tau protein interacts with CSE and stimulates the enzyme to produce more H_2S. This, in turn, inhibits another enzyme, glycogen synthase kinase-3β (GSK3β), which is primarily responsible for the regulation of tau phosphorylation. Studies with a CSE mutant and an Alzheimer's mouse model support this finding: The measurably decreased CSE activity in the brain leads to increased kinase activity, a higher degree of tau phosphorylation, and a stronger aggregation of neurofibrils. The brains of deceased patients with Alzheimer's disease also exhibit significantly lower levels of CSE than those of individuals who are free of Alzheimer's disease.

Less calories, but more CSE & persulfidation

So, could the enzyme CSE or higher H_2S concentrations serve as a tuning instrument for slowing down, if not arresting, ageing processes in the brain? "After all, in experiments with Alzheimer's mice, we were able to increase mental abilities when we supplied H_2S from the outside through a donor," Filipović sums up. Meanwhile, he says, there are not yet any drugs that can increase CSE activity. However, the biochemist knows of several pharmaceutical companies working on developing such compounds. But this could possibly be achieved in a much easier way: through a reduced calorie intake, i.e. a lower food intake. Filipović: "We have already shown in a previous study that fewer calories result in more CSE and persulfidation." (Zivanovic et al, Cell Metabolism, 2019). In studies with various animal models, this has resulted in life extension.

(TK) ■

Giovinazzo D, Bursac B, Sbodio JI, Nalluru S, Vignane T, Snowman AM, Albacarys LM, Sedlak TW, Torregrossa R, Whiteman M, Filipović MR, Snyder SH, Paul BD

Hydrogen sulfide is neuroprotective in Alzmeimer's disease by sulfhydrating GSK3ß and inhibiting hyperphosphorylation

Proceedings of the National Academy of Sciences of the USA, Vol. 118, No. 4

https://doi.org/10.1073/pnas.2017225118

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No. 864921).

Fascinating Insights into Platelet Research

In the video, Dr Yvonne Reinders is showing at the mass spectrometer how ISAS works within the Transregio 240.

In the collaborative research centre Transregio 240 (TRR 240), scientists from Würzburg, Tübingen, Greifswald and Dortmund are investigating the complex and as yet little understood functions of thrombocytes (blood platelets). Their aim is to help doctors treat diseases such as heart attacks, strokes, acute lung failure and cancer better in the future.

In order to gain a deeper insight into the molecular mechanisms of platelets, ISAS contributes modern (phospho-)proteomics approaches, among other things. The researchers use mass spectrometry to investigate the (phospho-)proteome of platelets, meaning the totality of all proteins at a certain point in time. In this way, they gain information about changes in the amount, the interactions and the so-called post-translational modifications of the proteins. The latter process refers to the chemical modifications of proteins that have already been formed, meaning after complete translation. Many of these post-translational modifications control the function of the proteins. The findings obtained at TRR 240 can help to gain a deeper understanding of the physiology of platelets and their signal transmission.

(CMP) ■

WHAT IS PHOSPHOPROTEOMICS?

Phosphoproteomics is a branch of proteomics. Researchers investigate proteins that contain a phosphate group as a post-translational modification. In other words, after complete translation and protein synthesis, a phosphate group binds to the protein. These processes, also called phosphorylations, lead to a structural change of the molecules and their function. Because they control so many essential processes and changes in biological cells, these proteins are also referred to as molecular switches. With the help of phosphoproteome analyses, researchers can observe the entirety of phosphorylations and their changes.

INSIGHT INTO THE RESEARCH

https://www.youtube.com/watch?v=U6BWvhbE6M4

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DFG

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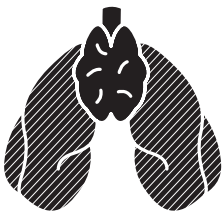
The spheroid/organoid in the glass incubator is so tiny that Mohammad I. AlWahsh can barely see it with his eye.

Novel NMR Technique Using 3D Models Simplifies the Quest for Cancer Drugs

It has been five years since Mohammad Ibrahim AlWahsh came to Germany as an exchange student. Back then, he was doing his Master's in pharmaceutical science at Al Zaytoonah University of Jordan. Impressed by the quality of the research in Germany, he decided to stay for his doctorate. Since 2018, the 27-year-old has been working on methods of analytical toxicology to improve the treatment of a rare form of cancer in the thymus gland. With success – AlWahsh and his colleagues at ISAS and Heidelberg University recently succeeded in using their method to measure the live reaction to chemotherapeutic agents in 3D models for the first time. Moreover, they were able to highlight possible therapeutic options for patients with thymoma and thymic carcinoma.



Thymoma and thymic carcinoma are both tumours in the thymus gland, a central organ of the lymphatic system and thus of the immune defence system in humans. Both are so-called thymic epithelial tumours (TETs). According to information published by the American Society of Clinical Oncology (ASCO) in 2021, about

400 people in the US are diagnosed with thymoma every year. Accordingly, thymic carcinoma is even more rare and makes up about 20 percent of thymic tumours. Rare diseases like these often present researchers with a huge problem: “Thymoma and thymic carcinoma are so rare that it is hard to find human tissue samples,” AlWahsh explains. That is why he cultivates the cancer cells in the laboratory.

> ***The tricky thing about cancer therapy is the physiologically different conditions deep inside a tumour, which cause tumour cells to behave differently there than they do on its surface.***

The 27-year-old reproduces the tumours as spherical 3D structures, so-called spheroids or organoids. “The tricky thing about cancer therapy is the physiologically different conditions deep inside a tumour, which cause tumour cells to behave differently there than they do on its surface,” he points out. 3D models can imitate this process – and are thus more realistic and persistent in terms of reaction to medication than common two-dimensional models. According to AlWahsh, it is therefore better to test new therapies for TETs in the laboratory (in vitro) not only on 2D but also on 3D models before moving on to animals or humans (in vivo). The pharmacist uses a nuclear magnetic resonance (NMR) spectrometer he developed and patented at ISAS while working in the Bioresponsive Materials group during his doctorate.

Hourly updates on a drug’s effect thanks to NMR spectroscopy

Until now, there has been a lack of methods to conduct a live analysis of 3D models to see how they react to drugs such as chemotherapeutic agents. AlWahsh’s analytical technique enables him to observe the metabolites of a living 3D tumour model over a long period of time after applying the medication: He can inject chemotherapeutic drugs into the spheroids via a probe and observe live how the cells react. Over two days, the NMR spectrometer measures the metabolic activity of the cells every hour so that

the researcher can see how the drug affects them. Particularly exciting and new: The scientist can link the metabolites to specific areas within the tumour. This allows him to adjust the medication accordingly to ensure that it not only attacks the outer cells of the tumour, but also the persistent, possibly dormant ones inside.

“One of the strengths of our method is that the spheroids remain undestroyed”

AlWahsh’s project is an interdisciplinary one, which was only possible through cross-group collaboration in the first place, he emphasises: “Teamwork was really the key to success in this project. Besides me as a pharmacist, the project involved physicians, engineers, chemists and physicists.” To ensure that the tumour can survive the two-day measurements and stay viable, the researchers had to come up with a complex solution. Outside the NMR spectrometer, they placed an incubator-like device that guarantees the optimal temperature and oxygen saturation for the growth of the tumour cells during the analyses. A microchip supplies the tumour with nutrients and the drug to be tested. In this way, the scientists recreate the situation in the human body in the best possible way. "One of the strengths of our method is that the spheroids remain undestroyed during the measurement," AlWahsh adds. After the analyses, the 3D models can continue to grow in an incubator outside the NMR spectrometer until the researchers perform new tests.

Including optical parameters in future analyses

At the end of 2021, shortly after his son was born, AlWahsh also celebrated the submission of his dissertation. However, that is no reason for the young father to rest on his laurels. He is currently working on validating the obtained therapeutic options. AlWahsh also wants to establish a new technique that integrates imaging techniques such as fluorescence microscopy into his method. This way, he would like to include optical parameters in his future analyses. A scholarship from Al Zaytoonah University of Jordan for his dissertation brought AlWahsh to ISAS and him to realise: Wherever his future path will take him, even far from home, far from his relatives and friends, he can flourish as a scientist.

(CMP) ■

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Dr Martín Hugo (right) talking to Radio 91.2's Malte Harzem – both are vaccinated.

"We age because our metabolism makes mistakes"

The research group ERC-Sulfaging does not associate hydrogen sulfide with the smell of rotten eggs, but rather with the secret of youth. More precisely, the researchers led by Dr habil. Miloš Filipović found out that the gas protects our cells from ageing. Talking to Malte Harzem from Radio 91.2, Dr Martín Hugo explained whether we can stop the ageing process and how the so-called persulfidation is involved in this.

The biochemist and research associate talks about ERC-Sulfaging's research work (► p. 18) in the podcast »Research from the Ruhr Area« (Ruhrpott, deine Forschung). In addition, he points out what the findings within this new research field imply for age-related diseases like Alzheimer's or Parkinson's.

(SR) ■

The research project Sulfaging has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No. 864921).

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RUHRPOTT, DEINE FORSCHUNG: STOP AGEING, INFINITE LIFE?

www.radio912.de/artikel/ruhrpott-deine-forschung-altern-stoppen-unendliches-leben-1125483.html

“I see the future of analytics in 3D printing”

Scientists have a variety of modern analytical methods at their disposal for analysing substances and identifying unknown constituents. This includes ion mobility spectrometry (IMS). An IMS can be used to characterise charged, gaseous molecules based on their individual velocities in an electric field. Compared to other analytical methods, IMS features high sensitivity and short measuring times with a low instrumentation requirement. It detects individual analyte molecules ten billion gas molecules with a measurement duration of less than one second. Researchers at ISAS succeeded in producing a fully functional IMS using 3D printing for the first time in 2021. They published their results in the renowned journal Materials Today. In an interview, Dr Sebastian Brandt, a physicist in the Miniaturisation research group and corresponding author of the publication, answers questions about the advantages and background of the development.

Dr Sebastian Brandt showing the first IMS from the 3D printer in the lab. In 2021, the physicist and his colleagues succeeded in printing an entire IMS (ion mobility spectrometer) for the first time.

How did the idea to produce an IMS exclusively using 3D printers come about?

Brandt: Our research group has been toying with the idea of printing a complex technical device using our 3D printers for some time. The idea for printing the entire IMS came to us at some point, as we had already printed small individual parts to customise conventional IMS according to our needs. However, these subsequent changes are difficult and time-consuming, just like the construction of an entire IMS itself. Here at ISAS, both are usually done by the workshop which has to make a new sketch for each new model.

That's why we initially only wanted to use the 3D printer to produce and optimise a prototype, which would facilitate subsequent production by our colleagues in the workshop. But that worked out so well, that we worked intensively on taking it beyond that point.

What is the advantage of an IMS from the 3D printer?

Brandt: A significant advantage is definitely the low material consumption. As a rule, an IMS is manufactured subtractively. That means that you start out with a block of material and remove some of it until you have the desired shape. The rest ends up in the trash. In contrast, the 3D printing process is quick and additive. With the 3D IMS, we only consume the material that we actually need. This makes the 3D printed IMS cheaper, faster and more environmentally friendly overall than a conventionally produced IMS. Compared to the subtractive manufacturing method, we can now almost halve the production time with 3D IMS. The costs of the materials also drops to a quarter. And current developments show that it is possible to optimise the IMS for an even shorter printing time. In addition, the 3D printer works almost completely autonomously. Only a small amount of post-processing by humans is needed, so we can also significantly reduce the operator's working time.

"With the 3D IMS, we only consume the material that we actually need."

Another point in its favour is flexibility. We have built in a magnetic click system into our 3D IMS, so we can change the parts very easily using modules. For example, not only can we quickly vary the Bradbury Nielsen Gate or the length of the drift tube depending on the sample or analyte by means of 3D printing, but we only have to shut the device down for a short time to replace it. This allows us to study samples of various textures including both liquid samples, such as blood or urine, and gaseous samples, such as breath. It also makes it easy for us to try out new modules. The path from the idea to the application is thus shortened many times over and is considerably less expensive.

Drees C, Höving S, Vautz W, Franzke J, Brandt S
3D-printing of a complete modular ion mobility spectrometer
Materials Today, Vol. 44, pp. 58–68

https://doi.org/10.1016/j.mattod.2020.10.033

What is a 3D IMS suitable for?

Brandt: In the past, the handy IMS were used almost exclusively for detecting drugs or hazardous substances. However, they are now also attracting interest in biomedical and forensic research. Doctors can use them, for example, to test patients' breath for certain bacterial or viral pathogens, such as in pneumonia. The IMS can also detect drugs, such as the anaesthetic propofol, in exhaled air, making it easier to monitor anaesthesia.

Despite the versatility of its application possibilities, however, an IMS is not yet a technology suitable for mass production.

The initial costs for a simple 3D printer are lower, given the production time and costs, and its handling can be quickly learned.

What role do other measuring instruments from the 3D printer play?

Brandt: I see the future of analytics in the use of additive manufacturing methods like 3D printing; at least I dream about it. However, I am also realistic and aware of its current limitations. One current hurdle, for example, is the right materials. Most commercially available 3D printing materials are designed to look good and have a nice colour, for example. Optics are not important to us in analytics; we need the material to be highly durable and compatible with the chemicals used. That's why our research group is currently working on our own materials that meet our requirements for measuring instruments from the 3D printer.

(The interview was conducted by CMP.) ■

Tools for New Cancer Medicines

Prof Dr Steven Verhelst, a project manager in the Proteomics research group, and Dr Daniel Krahn still have plenty of tricks in their bags. They want to combine knowledge from chemistry and biology at ISAS in order to combat cancer more efficiently and with fewer side effects than before. The focus of their work in the Proteomics research group is on active pharmaceutical substances whose targets they hope to adjust with new chemical tools for cancer therapy.

Prof Dr Steven Verhelst (photo above) is a project manager in the Proteomics research group, where Dr Daniel Krahn also conducts research.

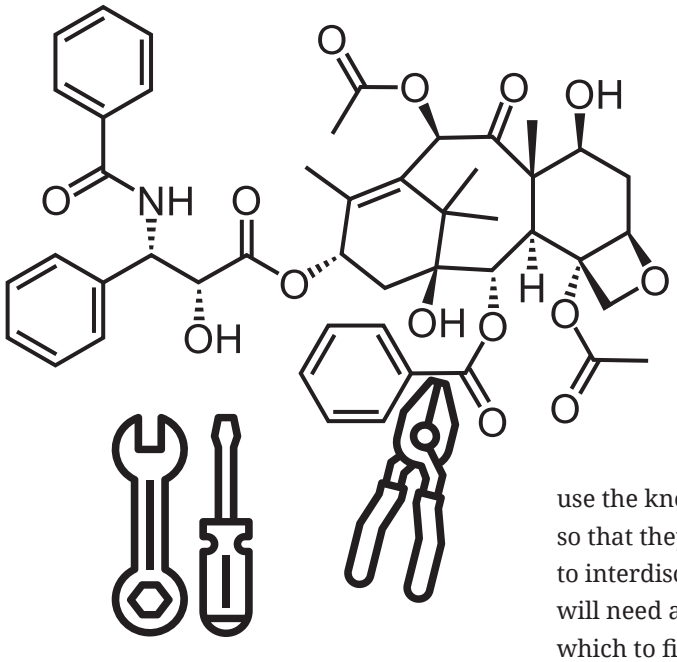
Cancer medicine has undergone tremendous development in the past decade, but some areas still require action or remain in the dark. For example, metastases are still the main cause of death in cancer patients. And while sufferers are fighting for their lives, other health complaints often come along, including side effects triggered by the drugs that are supposed to help. In some cases, they even hinder therapy or lead to concomitant diseases. The cardiovascular system suffers from the stress to which it is subjected in old age. In addition, cancer patients have a significantly elevated risk of stroke or heart failure, depending on the medication.

First hit the right target

The research project on late stage functionalisation (LSF) in chemical proteomics is concerned with so-called target effects in the body. Every active pharmaceutical substance has a target for which it has been developed. These targets can be structures such as enzymes, ion channels or receptor proteins that are involved in the development of a disease – in Verhelst and Krahn's case, cancer cells – and should be destroyed. Although the molecules are very specific, there are structures (off-targets) to which they bind, even though they are not intended to do so at all. This off-target effect often manifests as an agonising side effect or concomitant disease for patients. "A better understanding of off-target effects could make cancer treatments safer and more tolerable than before. In this way, we could find targets for new drugs in future that stop or even prevent metastases," Verhelst explains.

A chemical toolbox

In 2021, scientists at ISAS began researching chemical tools that can be used to identify desirable and undesirable targets. They hope to



In the Proteomics research group, Prof Dr Steven Verhelst and Dr Daniel Krahn work on methods for optimising active substances (i.e. natural products such as Taxol) at the molecular level.

use the knowledge gained from this development to improve drugs so that they bind only the right targets. In the long term, in addition to interdisciplinary collaboration with other teams, the two chemists will need a whole range of new chemical components (probes) with which to fill their toolboxes.

Twofold increased risk of cardiovascular disease in adults who survived cancer as children or adolescents compared with those without childhood or adolescent cancer.[1]

Like toolmakers, the researchers in the Proteomics research group use raw materials from which they aim to produce precise, customised tools. But these materials are active substances, consisting of tiny complex molecules, instead of large amounts of metal or plastic. These specific chemical probes could be used to further explore and improve existing cancer medications (such as those based on Taxol or other natural products).

Fight against »deadly daughters«

Although cancer therapies are very advanced today, patients still face one great danger – the spreading of tumours, i.e. cancer cells that break away from the tumour and migrate to other areas of the body where they form daughter tumours, referred to in medicine as metastases. Metastases are the cause of 90 per cent of cancer-related deaths here.

1 Faber J et al., *Burden of cardiovascular risk factors and cardiovascular disease in childhood cancer survivors: data from the German CVSS-study*, European Heart Journal, Vol. 39, No. 17, 2018, pp. 1555–1562, https://doi.org/10.1093/eurheartj/ehy026z.

> ***Better understanding of off-target effects could make cancer therapy safer & more tolerable.***

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Verhelst and Krahn would like to use the chemical tools they have developed to further investigate the interaction between active substances and enzymes, for example. By doing so, they hope to uncover the hitherto little-studied networks within cancer cells. Communication in cancer cells plays a critical role in metastasis, and the two chemists suggest that metastases could be prevented once these networks are turned off or inhibited. If the Dortmund researchers, working with oncologists, succeed in better elucidating this interaction of tumour cells, it could result in a decisive advantage in the fight against cancer.

From old to new?

At this point, one might ask why this idea is needed. Why not design new drugs whose molecules bind the right targets and no off-targets? The answer is simple: On the one hand, according to Krahn, most of the off-targets are still unknown. And on the other hand, new molecules would again face unknown off-targets. Apart from that, the search for suitable active substances for new drugs takes several years. And the efforts do not promise success for a long time. “You may end up with dead ends by just excluding off-targets. And then, you might have a molecule that doesn’t dock to any off-targets but also doesn’t bind to the right targets,” Krahn says. The researcher calls such molecules »dead cows«. This comes from the saying, “You can’t milk a dead cow”.

The work on the chemical probes could help make the modification of an established active pharmaceutical substance easy, economical and, most importantly, quick. The chemical tools could be used to improve highly complex natural cancer therapy substances whose molecules currently bind unwanted off-targets or are unstable for the benefit of patients.

(CMP / SR) ■

Drug Discovery Hub – On the Way to Translation

For three years, the Drug Discovery Hub Dortmund (DDHD) has brought several cooperation partners together as a network for early drug discovery and development. TU Dortmund University coordinated the project which involved ISAS as well as the IfADo – Leibniz Research Centre for Working Environment and Human Factors, the Max Planck Institute of Molecular Physiology, the Biomedicine Centre (BioMedizinZentrum) and the following companies: Lead Discovery Center GmbH, Taros and PROvendis. The DDHD was an incubator for drug discovery projects from across North Rhine-Westphalia between April 2018 and September 2021. The goal of the interdisciplinary project was to close the critical innovation gap between pure academic and applied research and industrial application.

“We are looking back on a successful project in which our joint successes included developing new predictive in-vitro cardiotoxicity assays and gaining cooperation partners who bring our research results closer to translation into clinical application,” summs up Prof Dr Kristina Lorenz, head of the ISAS Translational research department at the end of the project period. One should also highlight the exchange between the doctoral students and the overall expansion of the regional active substance network with other externally funded research projects resulting from the inter-disciplinary collaboration.

(SR) ■

The State of North Rhine-Westphalia supported the project with funds from the 2014-2020 European Regional Development Fund (ERDF) “Investment for Growth and Jobs”, funding reference ERDF-0200474.

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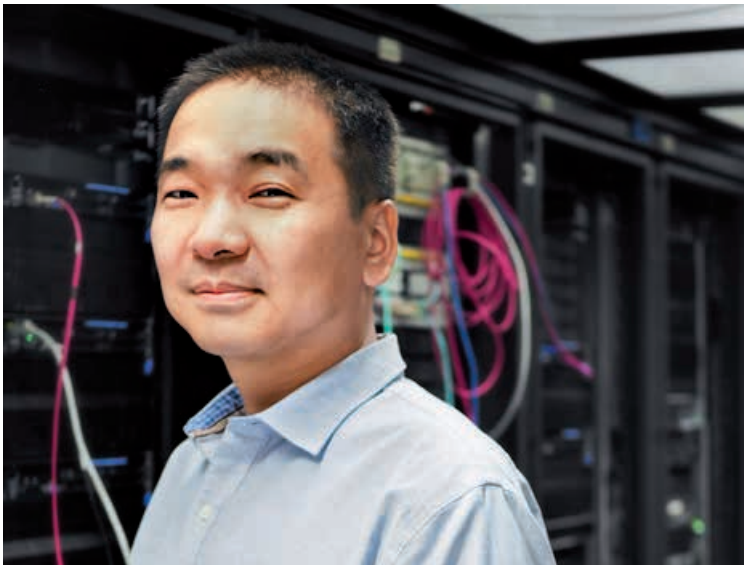
PARTICULARS

Jianxu Chen Wants to Develop "Eyes & Brains"



Dr Jianxu Chen started his work at ISAS in September 2021.

Medical imaging generates enormous amounts of data that can neither be managed efficiently nor evaluated thoroughly without artificial intelligence (AI). Therefore, ISAS has expanded its Biospectroscopy department with a new research group.

The junior research group AMBIOM – Analysis of Microscopic BIOMedical Images, which is funded by the Federal Ministry of Education and Research, aims to enable a high analytical throughput of microscope images. Led by Dr Jianxu Chen, a renowned expert in biomedical image analysis and deep learning, the research group plans to develop algorithms and methods (open source) by 2026 that will allow countless image data worldwide to be analysed automatically, quickly and economically. "My passion is to build eyes and brains for computers to understand image data in medical or biological studies," says Chen. In the future, for example, the work at AMBIOM should allow broad-based new studies on the development of diseases and their consequences at the level of entire organs and organ systems. Furthermore, the AI analysis methods developed at ISAS will support doctors in making diagnostic and therapeutic decisions.

Focus on large 3D microscopy image data

In his research, Chen has focused on developing scalable AI-based biomedical image analysis algorithms, especially for large 3D microscopy image data. Before joining ISAS, the 33-year-old had been working at the Allen Institute for Cell Science in Seattle for four years. For his new job in Dortmund, Chen moved to the neighbouring City of Bochum with his family of four.

(SR)

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The Junior research group AMBIOM – Analysis of Microscopic BIOMedical Images was funded by the Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung).

GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

Prasad Phapale Explores Space & Time of the Metabolome

Highly sensitive and precise analytical methods or their combination already allow quantitative investigations of the metabolome – i.e. all metabolic products of an organism – at the cellular level. What is currently lacking, however, are analytical methods with which the metabolome can also be completely mapped with its spatial and temporal details.

Dr Prasad Phapale came to Dortmund in October 2021.

This spatial and temporal information is important in order to be able to detect pathological changes in the cells, for example to analyse the cellular metabolic heterogeneity in heart disease or tumours in order to understand their early development. Such a molecular analysis of highly dynamic metabolic processes and changes in tissue areas poses a great challenge for research.

Development of a multi-method approach for precision medicine

For this reason, ISAS has established the junior research group Spatial Metabolomics under the leadership of Dr Prasad Phapale (41) in 2021. The research group, funded by the Federal Ministry of Education and Research (BMBF), will develop a multi-method approach over the next five years that will allow the parallel analysis of metabolic processes under spatial and temporal aspects. For this purpose, the team led by the analytical biochemist Phapale will combine two complementary analytical techniques such as mass spectrometry (MS) imaging and nuclear magnetic resonance (NMR) spectroscopy for multi-omics (▸ S. 48) analyses. The goal is to use future analytics to enable new and improved treatments in precision medicine for cardiovascular diseases and cancer.

(SR) ■

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The Federal Ministry of Education and Research is funding the MSCoreSys-associated junior research group Spatial Metabolomics under the funding code 161L0271.

GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

His unusual career path led doctoral student Suyuan Chen from China to Dortmund – and to application-oriented basic research. At ISAS, he develops chemical tools for analyses.

Glue for Cancer Patients: Suyuan Chen Wins Merck Innovation Cup 2021

Suyuan Chen, a doctoral student in the Proteomics research group, won the Merck Innovation Cup 2021 with his »drug discovery technologies« team. Together with six other junior scientists from Israel, Canada, London and Munich, he has worked out a plan on how molecular glue can be created and used even better in cancer treatment in the future.

These small molecules stabilise an interplay between proteins that normally hardly interact. In this way, researchers can glue disease-causing proteins to others, which the body then destroys. The doctoral students and postdocs from the disciplines of biochemistry, (structural) biology, chemical proteomics and medicinal and organic chemistry are not allowed to talk publicly about the details of their idea. Merck has taken up the winning idea in order to pursue it further within the group. “I am not only happy about the win, but especially that our idea could help advance drug development for cancer therapies,” says Chen.

Every year, young researchers can apply for a place at the summer camp and competition of the German science and technology company Merck KGaA. After a two-phase selection process in June 2021, based on CV and project ideas, the applicants were divided into six teams: oncology, immuno-oncology, immunology, drug discovery technologies, digitalisation and pandemic threat. Over the course of a week at the end of June, the teams not only had to develop their ideas but also prepare and present a complete business plan. For Chen and his teammates, the intensive work in the short amount of time was worth it: the team won first place and 20,000 euros, which they can use at their free disposal.

Change of perspective & more than just a competition

The »Innovation Cup Summer Camp« – which took place online due to the pandemic – offered participants more than just a competition. In lectures and discussion rounds, experts gave them the technical and economic perspective of a company on new research ideas. In addition, the young scientists learned how to successfully present projects to a corporate management. “It’s very exciting to learn how the industry thinks and what the business side looks like for them,” Chen concludes. Apart from the change of perspective, he especially liked the opportunity to meet so many like-minded people from all over the world: “In such a diverse group, you learn a lot about teamwork and how to deal with criticism.” In the future, the 30-year-old would like to keep in touch with his fellow participants through the alumni group and expand his network to include new international partners and friendships. The winners want to use the prize money to finally meet in person as soon as the pandemic allows.

(CMP) ■

Proteomics Research Group
(formerly named
Protein Dynamics)
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Kristina Lorenz Receives Award for Active Substance Against Heart Failure

Prof Dr Kristina Lorenz received the PHOENIX Pharmacy Science Award in the category »Pharmacology and Clinical Pharmacy«.

“The commendable feature of this research is that Professor Lorenz was able to override the pathological effect of a signalling protein with a peptide agent,” said Prof Dr Peter Ruth, jury member for the PHOENIX Pharmacy Science Prize, explaining the rationale for the award in November 2021.

Lorenz and her interdisciplinary team of scientists at the Julius-Maximilians-Universität of Würzburg and ISAS have succeeded in experimentally inhibiting the pathological growth of the heart to the point of cardiac insufficiency by means of a peptide substance. For this, the pharmacologist, who heads the Translational Research department at ISAS, received the 10,000 Euro prize in the »Pharmacology and Clinical Pharmacy« category. “We hope that the peptide compound will enable us to lay the foundation for a new therapy for heart failure with few side effects,” Lorenz said after the award ceremony. In addition, there are indications that the peptide may also be useful in the therapy of tumour diseases and genetic diseases in which this signalling pathway plays a role.

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First German-Serbian Knowledge Exchange at ISAS

In June, ISAS welcomed Dr Jasmina Živanović and her colleague Dr Marko Miler from the Serbian Institute for Biological Research »Sinisa Stankovic« as guests. Biologist Živanović took part in the »Serbian Science and Diaspora Collaboration Program«. The aim of the EU-funded project is to promote collaboration between Serbian scientists in their homeland and those living abroad. At ISAS, Živanović collaborated with Dr habil. Miloš Filipović, who has been leading the Sulfaging research group since 2020. They wanted to integrate his research findings on persulfidation into her project. Živanović's and Miler's goal for their stay in Dortmund was to integrate Filipović's results from his research on persulfidation (▸ p. 20) into their project.

Biologist Dr Jasmina Živanovic conducts research on the circadian rhythm.

Does the internal clock control cell functions?

In her work, Živanović analyses how the circadian rhythm, meaning the day-night rhythm, influences structural changes in proteins. In Dortmund, she therefore investigated redox modifications (e.g. oxidation) of the amino acid cysteine. "The redox modification is a very interesting approach that they could also use, for example, to find out what role ageing processes play in the day-night rhythm," said Filipović. For the time in Dortmund, Živanović had brought protein samples from different organs of rats. At ISAS, she used proteomic approaches to detect the location of various post-translational modifications – changes to the protein after translation has already taken place – of cysteine residues. Back in Belgrade, so the biologist hoped, they should be able to recognise from the data at which times of the day or night these redox changes occur and how they alter cell functions. Živanović's research could contribute to a better understanding and treatment of diseases such as sleep disorders in the future.

Old acquaintances in a young research field

The idea to come to Dortmund for the knowledge exchange was no coincidence. Back in 2016, project leader Živanović was part of Filipović's team for two and a half years. At the University of Bordeaux, they both conducted research on signal transmission through gasotransmitters such as H_2S and nitric oxide. During the summer of 2021, Živanović was very pleased that the Serbian government was supporting the country's science through a newly established fund more than before.

(CMP) ■

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An open high performance liquid chromatograph (HPLC) is not an uncommon sight for Ingo Feldmann. As head of the Technical Service Bioanalytics, he and his team are experienced with this highly sensitive equipment.

BIOMARKERS

Analytical methods that simultaneously map information on different classes of molecules and their spatial distribution patterns are needed in order to understand when and where in the body the biological decision between disease and health is made. The aim of the work in the research programme of the same name is to identify biomarkers for early diagnosis or personalised therapy using 4D analytics. Reliable markers expand the possibilities of evidence-based diagnostics in modern medicine, allowing for differentiated and individualised therapy. Marker-based diagnoses make it possible to classify diseases into subtypes and thus to specifically adapt treatments for individual patients.

Biological markers can be all sorts of molecules, large or small. For example, amino acids, lipids and metabolites can be used to make specific statements about metabolic changes and the modulation of protein functions. Proteins often serve as markers for the alteration of cellular structures, signalling pathways within a cell or in tissues. Researchers at ISAS are working to identify, investigate and validate biomarkers for various disease patterns and stages. The »Biomarkers« research programme focuses on markers for use in cardiovascular diseases, cardio-oncology and diseases such

as metabolic syndrome or type 2 diabetes, which increase the risk of cardiovascular diseases.

High-precision measurement techniques are a prerequisite

In addition to detecting and verifying biomarkers, the scientists are researching methods for improving the detection of the markers in complex biological matrices. Given the huge number of potential analytes in biological systems, high-precision measurements are required.

The research programme includes, for example, the »Targeted and Non-Targeted Metabolomics« project in which researchers are using nuclear magnetic resonance (NMR) spectroscopy to analyse the metabolome of three-dimensional cell cultures (organoids). Using NMR spectroscopy, the scientists are able to specifically observe defined metabolite sets for the early diagnosis of diseases or for monitoring the success of therapies. They also apply non-targeted analyses to the study of metabolic networks.

New BMBF junior research group Spatial Metabolomics

The term omics is used in research to describe molecular biological methods, such as genomics, lipidomics, metabolomics or proteomics, with which biomolecules from tissue samples or other biological samples can be examined on a global level. Omics technologies are an important starting point in precision medicine because they produce large amounts of data, which provide information about disease processes and potential therapeutic approaches. The research group established at ISAS in 2021 and funded by the Federal Ministry of Education and Research under the leadership of Dr Prasad Phapale is dedicated to the development of tools for the integration of omics data sets. To this end, the junior research group will use various analysis techniques such as MALDI (matrix assisted laser desorption/ionisation), mass spectrometry or light and fluorescence microscopy.

(SR) ■

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4D ANALYTICS

How much of which substance is in which place and when? The answer to this question is provided by 4D analytics. At ISAS, 4D analytics forms the technological basis for the comprehensive elucidation of pathological processes. The institute develops, refines and combines measurement procedures into »four-dimensional« analytical methods in order to simultaneously determine the quantities and types of various substances as well as their localisation within a sample at any time.

The samples that Dr Amol Fatangare uses for his research are being stored at minus 80 degrees Celsius.

Blood Test for a Safe Diagnosis of Drug Allergies

When a person's immune system reacts to a drug in an undesired and extreme way, doctors refer to this as a drug allergy. Although allergies only make up a small amount of the side effects of drugs, the symptoms go beyond just itchy rashes and fever. In the most serious cases, drug allergies can cause severe and potentially fatal reactions such as difficulties in breathing, organ failure and circulatory arrest. According to the World Allergy Organization (WAO), drugs are among the most common triggers of anaphylactic shocks, the most severe form of an allergic reaction. That is why it is important for doctors to be able to diagnose drug allergies without any risks for patients. In the project »Analysis of Differential Gene and Protein Expression for In-vitro Detection of Drug Allergies« (INA), scientists at ISAS are working together with the Federal Institute for Drugs and Medical Devices, the Clinic for Dermatology and Allergology of RWTH Aachen University Hospital and the biomedicine company Life & Brain GmbH in Bonn, in order to make a simple blood test for the diagnosis of drug allergies possible.

There are different ways to diagnose drug allergies. For example, doctors can conduct skin tests like prick- or intradermal tests. Furthermore, they can directly expose patients to a suspect drug via provocation tests. For the latter, patients take the relevant me-

dication, for example as a pill. This usually happens during a stay at the hospital. However, conducting allergy tests directly on humans (in vivo) can be dangerous. "Provocation tests and intradermal tests can cause reactions that range from uncomfortable to severe events. That is why patients often refuse to take these tests," states Dr Amol Fatangare, who conducts research for INA at ISAS. The lab tests (in vitro) that are available now, for example blood tests like a detection method for specific antibodies in cases of immediate hypersensitivity, are reportedly less dangerous than skin tests or provocation tests. However, they are currently only approved for few drugs or not suitable for routine diagnostics, according to BfArM.

> ***Allergy symptoms such as rashes, dizziness or fever can vary widely depending on the person and the drug.***

New blood test for a broad application

Fatangare and his colleagues are working on improving an existing blood test to make it suitable as a routine diagnostic for many different drugs and types of allergies. For this, the scientists examine the differential gene and protein expression of certain immune cells, the so-called peripheral blood mononuclear cells (PBMCs), of patients with known drug allergies. In other words, they analyse which genes and biomolecules change in the PBMCs during a reaction and, with regard to these drug allergies, look for characteristic biological commonalities, for biomarkers. "Allergy symptoms such as rashes, dizziness or fever can vary widely depending on the person and the drug," Fatangare explains. No matter what and how severe the allergy symptom is – the bodily mechanism that underlies the reaction is very similar in most patients. As soon as the researchers discover one or more biomarkers, they can identify them using a simple blood test and thus quickly spot a drug allergy; without exposing patients to health risks.

While their colleagues in Bonn deal with the gene expression, the scientists at ISAS concentrate on the protein expression. With the aid of mass spectrometry, they analyse the PBMCs' proteome, the entire set of proteins at a fixed point in time. This method, called proteomics, allows the researchers to examine the interactions between the proteins and their changes. They focus on several potential biomarkers such as interleukin 4 in particular. At the same time, they adopt a non-targeted approach: "One could say that we are deliberately blindfolded when searching for biomarkers, so that we do not only look at interleukins," Fatangare jokes. With this strategy, the biochemist wants to keep an open mind for all kinds of discoveries, even unexpected ones.

Searching for intra-individual differences

In order to find out what has changed after an allergic reaction, the scientists first divide the patients' blood samples. At BfArM, they treat one half with the proven allergenic drug, whereas the other half remains untreated. The researchers of Life & Brain GmbH and at ISAS look for intra-individual differences in the gene and protein expression, for instance differences in the same individual's blood cells upon allergenic drug ▸

treatment. This approach has two crucial advantages. First of all, the researchers can do with few samples, because all of the patients are at the same time in the treatment and control group. Second, the approach helps the scientists avoid individual differences: “If the samples were from different patients, it would be difficult to tell whether deviations in the protein expression were due to the drug or the different humans,” says Fatangare. In order to assign anomalies reliably to a single drug, the scientists would have to analyse samples from hundreds of patients. But with their method, samples from 20 people might be enough to gain meaningful data.

Time between allergy and blood sampling

“In 2021, we found out that the samples of some patients showed a very severe reaction to the drugs, while others hardly reacted at all. We wanted to determine whether that could be a result of the different periods of time between the allergy and the later blood sampling,” Fatangare sums up. The researchers’ aim is to analyse more patients’ samples for biomarkers in the PBMCs, before they optimise the test for a wider use.

(CMP) ■

HOW DO SKIN TESTS FOR DRUG ALLERGIES WORK?

Allergic reactions to drugs mostly arise within the first hour after administration. In order to diagnose these immediate hypersensitivities quickly, doctors often use skin tests. For the so-called skin prick test, they drip a solution with the suspect allergen onto the forearm and lighty scratch the skin on that spot. Reddened and itchy welts show whether the immune system is overreacting – and the patient thus having an allergic reaction. The intradermal test is an example of a sensitive skin test. Instead of only testing on the surface, doctors inject the solution with the allergen directly underneath patients’ skin and watch whether a reaction occurs. This test is also suitable for the detection of a late reaction which can arise even days and weeks after taking a drug.

The project »Analysis of Differential Gene and Protein Expression for In-vitro Detection of Drug Allergies« is funded by the European Fund for Regional Development (EFRE).

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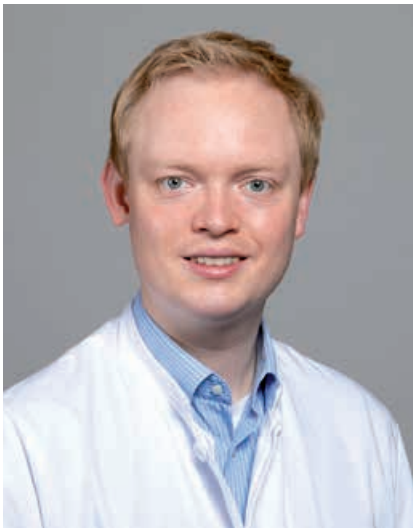
A Step on the Way to Harmless Immunotherapies

Significant advances have been made in cancer therapy over the previous decade, and several new methods are now available to physicians. Among these are a number of therapies that activate the body's immune system against cancer cells, including a treatment known as immune checkpoint inhibitor therapy. The downside of this form of cancer treatment is that, like other modern cancer therapies, it is often accompanied by serious adverse reactions that can affect various organs. The heart is often damaged and affected in such a way that even the death of the patient is not excluded.



Dr Lars Michel is a resident physician (Department of Cardiology and Angiology at Essen University Hospital) and a researcher at the Faculty of Medicine at the University of Duisburg-Essen.
© Essen University Hospital

The research results of a team led by Prof Dr Tienush Rassaf at the Angiology and Cardiology Clinic at the Essen University Hospital and scientists at ISAS provide initial insights into the changes underlying cardiac damage as an adverse reaction of immune checkpoint inhibitor therapy at the cellular and biochemical levels – and how it might be avoided. More than 20 scientists from various institutes and facilities in Germany and abroad are involved in the translational research project. The results from 2021 appeared in the prestigious European Heart Journal under the title *Targeting early stages of cardiotoxicity from anti-PD1 immune checkpoint inhibitor therapy* in January 2022.

T lymphocytes or T cells play a central role in immune checkpoint inhibitor therapy. Like B lymphocytes, they are important actors in the immune system. T cells move through the body, seeking out cells with pathologically altered cell membranes, for example after a viral infection. Depending on the type of T cell, it can destroy the altered body cell directly, sound the alarm via soluble messenger substances such as cytokines, or request reinforcement, so to speak, in the form of additional immune cells.

Cancer cells on the run

The above-mentioned immune checkpoints (ICs) are located on the membranes of T lymphocytes. They consist of proteins or protein complexes and trigger the immune response mediated by T cells; depending on the type of cell, they can either increase or diminish it. The inhibiting or co-inhibitory ICs decrease the activation and effector function of T cells, in contrast to the pro-inflammatory co-stimulatory immune checkpoints. They are therefore important factors in the immune system and play a major role in preventing autoimmune reactions as well as diseases. The surface receptors use ligands (molecules that bind to a target protein, such as a receptor) to prevent the body's own tissues from being attacked by auto-aggression.

Unfortunately, cancer cells can evade the immune system. This is known as immune escape or immune evasion and is a phenomenon that is still poorly understood. The degenerated cells achieve this by switching off the organism's defence system, so to speak, via the inhibitory immune checkpoints, and are therefore not recognised or eliminated by it. In addition, it is known that in malignant tumours, the co-inhibitory receptors on the T cells are upregulated which, in addition to other regulation steps, leads to a suppressed immune response.

If the inhibitory immune checkpoints are inhibited in turn, it should be possible to reactivate the immune system. This is precisely the concept underlying the development of checkpoint inhibitors. These molecules, usually monoclonal antibodies, abolish the receptor-ligand binding on the T cell and thus enable the immune system to once again identify and fight tumour cells. They do this by targeting either the IC receptor (example: PD-1) or its ligands (PD-L1).

> ***In tumour therapy, we achieve a significant increase in immune response by blocking immune checkpoints.***

Many modern immunotherapies are based on this knowledge and the checkpoint inhibitors derived from it. The development was a quantum leap, so to speak, for oncology. It enabled the first treatment options for metastatic tumours such as metastatic melanoma, which until then had been inoperable and difficult to treat. "In tumour therapy, we achieve a significant increase in immune response by blocking immune checkpoints," says Dr Lars Michel, explaining the benefits of the new immunotherapy from his own experience. He also said that drug-based tumour therapy can be applied to several types of cancer. The resident physician (Cardiology and Angiology Clinic at Essen University Hospital) is a researcher at the Faculty of Medicine at the University of Duisburg-Essen and first author of the publication mentioned.

While immune checkpoint inhibitors (ICIs) have produced significant treatment results in numerous clinical trials, they are associated with "immune-mediated adverse reactions," as Michel calls the sometimes significant impairment of various organs during therapies, as mentioned at the

outset. These reactions could be explained by excessive autoimmune reactions of the body tissue. “Almost all patients exhibit cardiac involvement during therapy,” states the physician, adding that one to two percent of them even suffer severe to very severe cardiac damage. This had a negative effect on cardiac function as well as metabolism and immunity.

On the trail of new biomarkers with omics analyses

Among the approaches the researchers used for their physiological and biochemical studies were combined analytical methods. “In our multi-omics analyses, we have been able to temporally analyse the total inventory of lipids, proteins and metabolites within a sample,” explains co-author Prof Dr Albert Sickmann, chairman of the board at ISAS. He adds that time savings and reduced error rates are additional advantages of omics analyses, because the individual operations do not have to be performed separately as they did previously, but can be combined.

> ***Our mid-term goal is to turn factors that are detectable in blood plasma into new biomarkers that are released when an organ or tissue is damaged under immune checkpoint inhibitor therapy.***

The omics method promises to their developers, such as Sickmann, numerous new and better insights that should advance translational medicine, the transfer of findings from the laboratory to the sickbed, for example, as regards our understanding of the adverse reactions of active substances. “Our mid-term goal is to turn factors that are detectable in blood plasma into new biomarkers that are released when an organ or tissue is damaged under immune checkpoint inhibitor therapy,” says Sickmann.

Prof Dr Albert Sickmann’s team carried out the multi-omics analyses for the study.

Inhibition of tumour necrosis factor-α by an antibody demonstrates initial successes

To further investigate the effects of a therapy against the primary inhibitor PD-1 on the heart, the scientists at the Essen University Hospital and ISAS chose a dual experimental approach. One provided the necessary biochemical data via omics analysis, and the other provided in vivo results using melanoma mice with stimulated T cells.

Under inhibition of PD-1 in the mouse experiment, there was significant impairment of the left ventricular function and metabolism. An analysis of a parallel group of melanoma patients with anti-PD-1 treatment resulted in a similar functional decline in

the left side of the heart. At the end of their studies, the researchers succeeded in largely avoiding this type of heart damage in animal experiments, if they first blocked the tumour necrosis factor-α (TNF-α) with an antibody while retaining the effectiveness of the anti-PD1 therapy. TNF is a cytokine, a signalling substance, involved in inflammation.

How to explain the TNF effect? “We suspect that it is related to lymphocyte activity and modulation,” explains Michel. Will this one day lead to a new form of therapy? He says that it is too early to judge this, and certainly more studies are needed.

(TK) ■

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WHAT ARE OMICS TECHNOLOGIES?

The term omics is used by researchers to describe molecular biological methods, for example genomics, lipidomics, metabolomics or proteomics, with which biomolecules from tissue samples or other biological samples can be studied on a global level. Omics technologies are an important starting point in personalised medicine (precision medicine), as they produce large amounts of data that provide information about disease processes and potential therapeutic approaches.

Michel L, Helfrich I, Hendgen-Cotta UB, Mincu R-I, Korste S, Mrotzek SM, Spomer A, Odersky A, Rischpler C, Herrmann K, Umutlu L, Coman C, Ahrends R, Sickmann A, Löffek S, Livingstone E, Ugurel S, Zimmer L, Gunzer M, Schadendorf D, Totzeck M, Rassaf T
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“The aim is to prolong the lives of cancer patients without additional damage”

In this interview, Prof Dr Tienush Rassaf, Director of the Angiology and Cardiology Clinic at Essen University Hospital, speaks about the background of the research into immune checkpoint inhibitors (ICIs) and their effect on the heart.

Prof Dr Tienush Rassaf is Director of the Clinic for Angiology and Cardiology at Essen University Hospital.
© Essen University Hospital

As a cardiologist, you diagnose and treat people with various heart conditions. At the same time, you have also been working for several years on cancer therapies based on the use of ICIs. What is the relationship between cancer therapy and heart disease?

Rassaf: Cancer patients treated with ICI often have to deal with more or less severe adverse reactions that can affect various organs, not infrequently the heart. We want to understand the exact cause of this.

How often do these adverse reactions occur?

Rassaf: In the first year of their treatment, up to ten percent of cancer patients exhibit severe immune-mediated adverse reactions.

“Up to ten percent of cancer patients exhibit severe immune-mediated side effects in the first year of treatment.”

In the 2021 paper published in the European Heart Journal, you and your co-authors were able to show that heart damage can be avoided if tumour necrosis factor-α, or TNF-α, is inhibited beforehand. How did you come to explore this connection?

Rassaf: In previous studies, there was evidence of TNF-α involvement in the intestinal tract and experiments that yielded similar results. This is the approach we have taken with hearts over the past four years. Our goal continues to be, first and foremost, to develop a therapeutic approach with which we can both treat the cancer effectively, with new drugs for example, and exclude the negative sides of the treatment such as adverse reactions and consequential damage. The aim is to prolong the lives of cancer patients without causing additional damage through immunotherapy.

Do you have other »candidate« drugs in mind besides TNF to prevent damage to the heart or ▸

other organs during tumour therapy?

Rassaf: Yes, there are already others under consideration. We want to conduct new studies on them in the preclinical area, for example in animal models or cell cultures, during 2022, so the results are naturally not yet available. We are working closely with ISAS on this research. The institute's multi-omics analyses provide us with important biochemical and physiological data, for example for understanding adverse reactions. In the coming years, we would like to devote ourselves to the question of exactly how immunotherapies work.

Are there any other research partners in this regard?

Rassaf: Yes, in addition to ISAS, we cooperate here on site with the Tumour Clinic and Nuclear Medicine or Radiology. We also have an exchange with Charité – Universitätsmedizin Berlin and the Cologne University Hospital.

What other projects are you currently researching?

Rassaf: We currently have two studies underway. The first addresses the question of how to prolong the lives of cancer patients with cardiac damage. The second study concerns exercise, or more specifically, exercise as a possible means of preventing premature heart damage.

How do you envisage your scientific work in the next few years?

Rassaf: We advertised two joint professorships in cooperation with ISAS in 2021. Both could be titled »Individualisation of Medicine«. One of these professorships is located entirely at ISAS in Dortmund. The task there will be to examine samples from patients in detail using multi-omics analyses in order to obtain new, detailed information on the metabolism of individual patients. The other professorship at the University Hospital will build on this. It should lead to the development of new treatment procedures in cardiology. Our common goal is ultimately a tailor-made therapy, individually adapted to each patient.

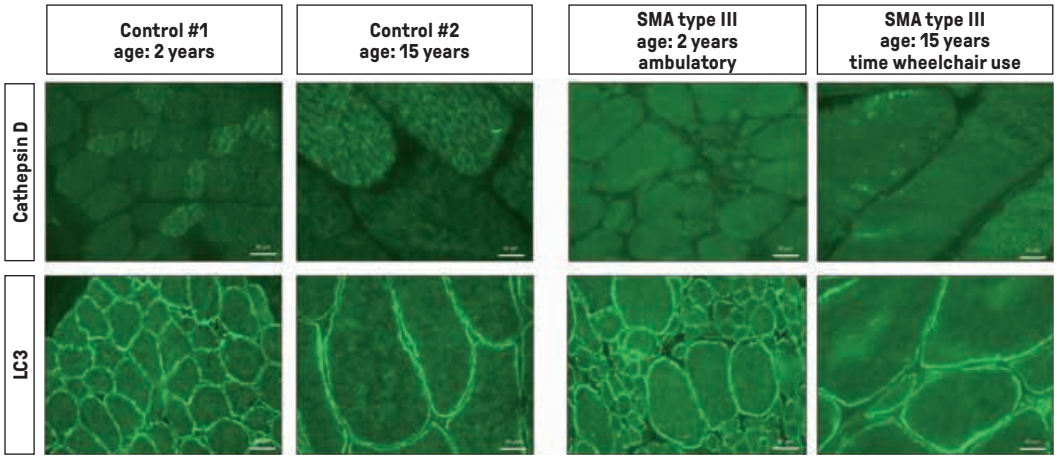
(The interview was conducted by TK.) ■

PROF DR TIENUSH RASSAF

has been Director of the Cardiology and Angiology Clinic at the West German Heart and Vascular Centre (University of Duisburg-Essen) since 2015. The range of treatments offered by his clinic includes all areas of cardiovascular medicine, including all therapies for coronary heart disease, cardiac arrhythmias, valvular heart disease, heart failure, aortic diseases and congenital heart defects, as well as emergency and intensive care medicine. Rassaf is one of the initiators of the nationwide Oncological Cardiology research group, which was established in 2018.

Biomarkers for Babies with Rare Diseases

Toddlers who can barely sit, let alone crawl or walk: Although the disease they suffer from, spinal muscular atrophy (SMA), is rare, patient cases have increased in media coverage during recent years. The reason for the media interest was and is the high cost of a drug approved in Europe in 2020 for SMA: One dose of Zolgensma® (onasemnogene abeparvovec) costs approximately two million euros, making it considerably more expensive than the alternative drug Spinraza® (nusinersen). Zolgensma® is intended to halt progressive muscle weakness after a single dose in patients under two years of age. To assess whether SMA therapies are working and how they are progressing, biomarkers known as progression markers come into play in clinical practice. During 2021, scientists at ISAS working on the project »Gene and protein signatures as GPS for patients with neuromuscular diseases« identified a protein that could help optimise SMA therapy.



The microscope images show stained muscle biopsies from seven SMA patients aged two and 15 years who had not received any drug therapy. Result: Compared to the control samples from healthy individuals, the protein cathepsin D was downregulated as a uniform pattern in all samples. As a control, the scientists carried out another immunostaining of another protein, LC3. This showed no changes in the muscle cells of SMA patients. © Department of Pediatric Neurology, Developmental Neurology and Social Pediatrics, Centre for Neuromuscular Disorders in Children and Adolescents, University of Duisburg-Essen

The hereditary disease SMA is a disease of the nerves of the spinal cord and the motor neurons. SMA is triggered by a mutation in the gene for surviving motor neuron 1 (SMN1). This gene is responsible for the production of the »Survival Motor Neuron« (SMN) protein which maintains the health and normal functioning of motor neurons which, in turn, regulate muscle activity by sending signals from the central nervous system – the part of the nervous system that includes the brain and spinal cord. Degeneration of motor neurons leads to a gradual decrease in muscle mass and strength. When neurons are damaged or die, as in SMA, the body releases structural proteins called neurofilaments into the bloodstream or into the cerebospinal fluid (CSF) (brain

and spinal cord). “In young SMA patients, the number of neurofilaments is elevated. During treatment with Spinraza® they decrease faster than in untreated patients. However, significant changes are primarily observed in children under one year of age,” says Dr Andreas Hentschel, a member of the Translational Analytics research group.

Dr Andreas Hentschel’s research includes looking for biomarkers with which to monitor therapy and disease progression in SMA patients.

Cathepsin D as a progression marker

How might a protein help optimise therapy in SMA? “We found that cathepsin D levels in CSF samples decreased in our cohort of SMA patients on Spinraza® therapy,” Hentschel explains. According to the researcher, this decrease appeared in all SMA subtypes and in all age categories of two months or older. In addition, the decrease was more pronounced in patients who exhibited a positive motor response to drug treatment.

“Although our cohort was too small to compare age groups and SMA subtypes within the therapy responder group, we believe these results are very promising. They suggest that the cathepsin D level is also suitable as a biomarker in older SMA patients – in combination with the analysis of the neurofilament light chain protein in adolescents or as a sole marker in adults,” Hentschel summarises. Further validation studies in larger cohorts and with serum samples are needed to assess the applicability of cathepsin D as a progression marker for the various SMA treatments.

(SR) ■

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The project entitled »Gene and protein signatures as GPS for patients with neuromuscular diseases« was funded by the State of North Rhine-Westphalia using resources from the 2014-2020 European Regional Development Fund (ERDF), »Investment for Growth and Jobs« (funding reference EFRE-0801301).

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JUNIOR SCIENTISTS

Intern to Postdoc – Early Career Support for Young Academics

In order to support junior researchers, ISAS has established programmes that encompass all stages of their scientific careers: The offer is directed at bachelor's and master's students, including a structured graduate programme for doctoral students as well as further educational opportunities for postdocs.

In the first three years of the doctoral phase, the curriculum of the structured doctoral training at ISAS includes ten workshops, an information event on career planning, an internal lab rotation and optionally a doctoral-related stay at a research institution abroad. In the final phase, the focus is on the completion of the work and the doctoral thesis. The duration of a PhD at ISAS depends on the department and averages three and a half to four and a half years.

Close exchange with collaborating universities

In addition, ISAS promotes the career opportunities of excellent young researchers by enabling them to lead projects through junior research groups. The early responsibility as a group leader aims to support particularly young researchers who wish to pursue a further career in science.

The junior scientists benefit from the institute's cooperation in research and training with the following universities: TU Dortmund University, Ruhr-Universität Bochum, University of Duisburg Essen and Bielefeld University.

(SR) ■

Postdoc Pitch Day

Postdoc Pitch Day is an internal event developed by the Grant Management and Communications teams. It is directed towards all postdocs at ISAS. The starting shot for Postdoc Pitch Day was fired in October 2021 at the ISAS Campus location.

The response of the participants after the first Postdoc Pitch Day was so positive, that the event is now established at the institute and is held regularly. “The goal is to provide postdocs with a casual but confidential forum to use as a career development tool for presenting initial research ideas and receiving feedback from experienced researchers,” explains Dr Maria Gies, Grant Management team leader. Postdoc Pitch Day aims to motivate postdocs to develop their own research ideas in a way that ideally leads to support measures, third-party funding applications or further career development activities (such as interdisciplinary collaboration projects with internal or external partners or patent applications).

(SR) ■

Dr Maria Gies heads the Grant Management team at ISAS.

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> ***The goal is to provide a casual but confidential forum for postdocs to use as a career development tool.***

INTRODUCTION

1 to 2 minutes – Postdocs introduce themselves and tell the audience why they are attending the event. Is it about financial support for a stay abroad? Or about overseeing a collaborative project? Or do they hope to attract funding to further their research career?

PITCH

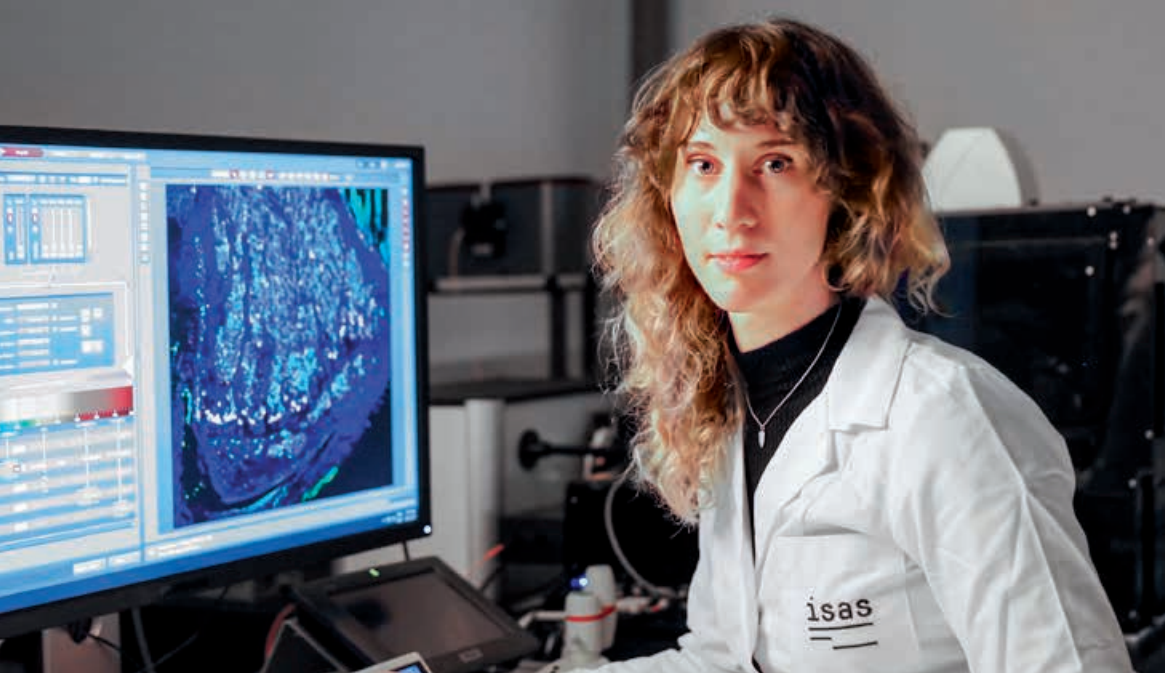
5 minutes – Participants can present their research ideas by drawing on a flip-board, bringing an object, telling a story, singing a song, or showing pictures. Almost anything is allowed! The only exception: Postdocs will have to do without a PowerPoint presentation. The important thing is not to go into too much scientific detail. This is because not all the mentors – senior scientists at ISAS – conduct research in the same field, nor are the representatives of potential funding sources always experts.

FEEDBACK

15 minutes – Mentors take time away from the audience to discuss the pitch and the round table. Afterwards, one of the mentors announces the collective feedback. This is always accompanied by tips on how to proceed. In addition to this verbal feedback, participants will receive written feedback after the event and, if they want, a video of their pitch. At the end of each pitch, two to three mentors agree to be available to each postdoc for further questions and support.

ROUND TABLE

25 minutes – After the pitch, the mentors ask their questions. Postdocs can also take the opportunity to ask questions.



By combining different imaging methods for the analysis of cells, Flora Weber, shown here with the confocal microscope, sees information about the larger contexts and specific details.

“In imaging, I must be willing to venture into something new”

When Flora Weber is looking at her samples under the microscope, the world around her fades away: A skill that the 25-year-old PhD student has learned while pursuing climbing as a hobby. Since July 1, 2021, she has been conducting research on the medication-induced death of the jaw bone in the Bioimaging research group. Before that, Weber studied biology and completed her master’s degree in the international programme »Integrated Immunology« at Friedrich-Alexander University Erlangen-Nuremberg. In the interview, the biologist explains why it is so important to concentrate on more than just the details in microscopy.

Why did you come to ISAS?

Weber: I already got to know Prof Dr Anika Grüneboom, who now leads a research group here at ISAS, during my master’s thesis in Erlangen. There, she introduced me to the imaging methods I use today, for example light sheet fluorescence microscopy. My thesis was about the bone structure of mice. I mainly dealt with bone cells, namely osteoblasts and osteoclasts. I liked this field of research a lot. That’s why I came to ISAS for my doctorate. Here, I get the chance to continue my research.

What is the aim of your research?

Weber: I study the medication-related osteonecrosis of the jaw (MRONJ). This is a disease during which parts of the jawbone die – caused, for example, by drugs for the treatment of osteoporosis. The drugs, mostly so-called bisphosphonates, are necessary to prevent bone resorption due to osteoporosis. However, we don’t know yet why they lead to the development of MRONJ. Cancer patients, who have a high risk of osteoporosis because of radiotherapy, also take this drug in high dosages. That’s why they also very often suffer from MRONJ.

In order to understand the mechanism of the disease better, I want to find out how the cells of the bone tissue interact with the cells of the blood supply. I concentrate on the connection of two processes: the forming of new bones (osteogenesis) and the development of blood vessels from pre-existing blood vessels (angiogenesis). I then compare this so-called osteogenic-angiogenic coupling in the jawbone with that in the shinbone, because the shinbone isn't affected by MRONJ. It isn't yet known why MRONJ only attacks the jawbone. If we manage to determine differences in the cell structures of the jawbone and other bones, like the shinbone, that would be our chance to prevent the development of MRONJ or to establish therapeutic approaches against osteoporosis that don't produce the described side-effects.

Which methods of analysis are relevant for your work, what is your approach?

Weber: To better understand the disease in humans, I look at the jaw- and shinbones of mice with MRONJ. I use different microscopes, for example the lightsheet fluorescence microscope or the confocal microscope. Depending on which microscope I use, I employ a clearing protocol devised by Anika Grüneboom, which makes bones transparent. That's necessary in order to reduce the light scattering during microscopy and to penetrate more deeply into the tissue visually.

Why do you work with different microscopes?

Weber: It's very important to examine not only the details, but also the larger context. For example, the lightsheet fluorescence microscope is suitable for depicting a whole organ or a complete bone. It takes a lot of single images of the respective layers, which I then combine into a 3D model. Thus, I get a complete overview and can see how the cells differ from each other, for example. After that, I look at specific details with the confocal microscope. In order to do so, I have to cut the bone into slim slices. That's why this method works without the clearing. By the way, this process is reversible – I can undo the clearing and look at the same sample under different microscopes. That's very important because I make a point of using resources in a sustainable way.

"It's very important to examine not only the details, but also the larger context."

How do you evaluate the images after that?

Weber: I use different programmes. My main programme is IMARIS, a software for image analysis. To distinguish the different cells, I colour characteristic proteins with fluorescent antibodies as a marker. With surface markers, I can see the cell's edges, whereas the focus is more on the inner structures in the case of intracellular markers. Depending on the marker, the signal is identified in different ranges of wavelength and displayed in a different colour on the computer. Using this method, I try to find differences in the spatial-temporal distribution of the cells. Ideally, I can see what the structures look like and whether the cells communicate with each other.

What fascinates you about imaging?

Weber: Imaging delights me, because it's virtually tangible. An image shows me all the important information at a glance. The spatial distribution of cells or their protein profiles are very hard to depict in a graph.

Moreover, I find bones fascinating, because they are very complex. At the beginning, I always thought the immune system only consisted of B cells and T cells – namely those cells that induce an immune response. However, osteoclasts and other cells associated with bones are also part of the immune system. Like other immune cells, they are developed in the bone marrow and react to inflammations and disturbances.

How do you like to spend your time outside the institute?

Weber: I like to meet friends and I do lots of sports. My favourite activity is to go bouldering – if the weather allows it, I love to climb outside. I need to overcome my fears and be ready to test my limits when I go climbing – just like in my research. When doing imaging work in the lab, I also need to tackle challenges and be willing to venture into something new.

(The interview was conducted by CMP.) ■

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New Partnership with the Università Cattolica del Sacro Cuore

In August 2021, for the first time, a pharmacy student from Italy was a guest at ISAS. Anna Percio was studying at the Catholic University of the Sacred Heart (Università Cattolica del Sacro Cuore) in Rome.

The 22-year-old spent two months of her lecture-free time in the ERC-Sulfaging to get to know the research work at ISAS. “We are very happy about this partnership and about being able to offer our students this exchange,” said Prof Andrea Urbani, Director of the Department of Basic Biotechnological Sciences, Intensivological and Perioperative Clinics, who visited Percio in Dortmund and got a first-hand impression of the exchange.

New insights into biochemistry at ISAS

Percio began the forth and therefore second last year of her studies in October. In the Italian capital, more than 250 km away from her hometown Avellino, she was following the example of her mother and grandmother, who are both pharmacists. Since the 22-year-old was not only interested in the health economic aspects of pharmacology, but also in the analytical methods from the field

> ***We are very happy about being able to offer our students this exchange.***

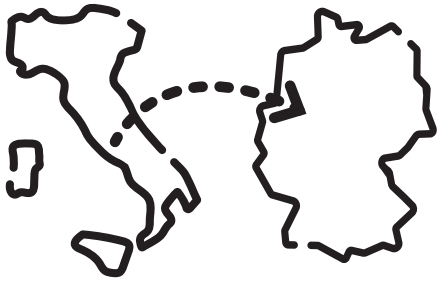
In August, Prof Albert Sickmann welcomed Anna Percio and Prof Andrea Urbani from the Università Cattolica del Sacro Cuore to ISAS.

of biochemistry, she decided to take part in the exchange at ISAS. “At the beginning, I had to learn a lot in Dortmund, because the work flows in a biochemical laboratory are very different from those in the laboratories at the university,” the student reported. In the research group ERC-Sulfaging, she was responsible for cultures of connective tissue cells (fibroblasts) and neuronal cells from mice. Using those, the Italian tested the extent to which hydrogen sulfide controls the cellular response to insulin signalling and thus influences the ageing process of cells.

Pandemic caused a later start than planned

Due to the pandemic, Percio was not able to leave Rome until a month later than originally planned. To ensure that she did not miss the start of the new semester in Italy in October, she stayed at ISAS for two months instead of the planned three. The student was glad that she was able to come to Germany at all: “Until now, there were few opportunities for pharmacy students to go abroad. I see it not only as a chance to get to know other cultures, but also to find out what kind of work I want to do after I graduate.” In addition to her interest in research, Percio shared a love of football with her colleagues in Dortmund: back home however, she did not support BVB, but her favourite club, Juventus Turin.

(CMP) ■



"They made me feel like I have a new family here"

In the middle of the pandemic, Susmita Ghosh decided to leave her home country for the first time in her life. For her dissertation, the 25-year-old moved from Kolkata to Dortmund, to ISAS. Since October 2021, the biologist has been actively involved with the doctoral students at the institute alongside her research project. In this interview, Ghosh reports on how she has settled in and what advice she has for other young researchers from abroad.

Susmita Ghosh uses the ultra-sensitive mass spectrometer to analyse her samples for her dissertation on »Unravelling the molecular makeup of neutrophils invading tumours and inflammatory tissues«. Outside the lab, the biologist writes short stories in her native language Bengali.

How did you first notice ISAS?

Ghosh: I've always been fascinated by immunology but didn't get many opportunities to work in this field in the past. Hence, I wanted to explore immunology more as a topic in my doctoral study. When I was looking for a PhD position in immunology, I found the job advertisement on the internet. I was fascinated by Prof Dr Matthias Gunzer's research as well as the scientific output at ISAS.

Why did you choose to leave India and come to ISAS for your PhD?

Ghosh: It was indeed a tough call for me to leave my parents and friends. However, I always believe that in order to achieve something great, you'll have to sacrifice something great. Today, I'm in Dortmund to achieve my goal. Here, I can undertake my doctoral studies and at the same time hone my knowledge and experience in immunology. All of this helps me get a step closer towards my goal of becoming an independent researcher. I can't thank myself enough for having made the right decision.

What was your job interview like?

Ghosh: I believe interviews always make any candidate nervous. I was additionally excited because I had just recovered from COVID-19. The interview was 15 days after I had a severe infection with breathing trouble including having to use an inhaler, and other complications. But the moment I saw Matthias Gunzer and one of his PhD students, I instantly felt more comfortable. My first interview with them was more like a scientific discussion rather than an interview. During my second interview, I had the opportunity to talk to Prof Dr Albert Sickmann. That's where I realised that I will get a ton to learn from the various scientific disciplines at ISAS.

What did it feel like to start a new chapter in your life during a pandemic?

Ghosh: It was very much a mix of emotions for me. Before I got here, a few other renowned research

institutes rejected my application because of the pandemic itself. In the mid of all negative things happening around me, the positive response from ISAS really made me happy and boosted my confidence, for which I am grateful. At the same time, it wasn't easy for me to leave my family during these difficult times.

How long did it take to settle in?

Ghosh: The first two months were very difficult; it took some time for me to settle in. In the second month of my stay here in Germany, I was diagnosed with back pain issues, but I managed those situations. I'm very thankful for my colleagues Fiorella, Ewelina, Amol and Laxmikanth, who helped me a lot whenever I needed their support. They made me feel like I have a new family here.

Congratulations on being elected as one of the two PhD student speakers. What do you and your co-speaker Flora Weber want to achieve, which topics would you like to address?

Ghosh: This is indeed a huge responsibility for us. The first thing we both felt is that we'd like to encourage the communication between the PhD students at the institute's City and Campus locations. There hasn't been much face-to- face contact lately. Of course, the pandemic is one of the major culprits for that. We'd like to engage our fellow PhD students more in social gatherings via various seminars, ISAS Summer School, workshops and excursions. We are currently preparing to bring in new ideas for our Summer School. Thanks to our former PhD representatives and their work, things are easier for us than we expected.

Before you came to ISAS – how much did you know about the institute's PhD programme?

Ghosh: I made myself familiar with ISAS' graduate programme before I made the decision to come. I'd like to thank my former PhD colleague Julia Lill (► p. 66) who is currently in Boston. She helped me a lot with information about the institute's work culture, its PhD programme and other necessities.

Was it easy to find an apartment in Dortmund? Did you have any help?

Ghosh: No, it was definitely not an easy job to find an apartment from India. At first, I booked an apartment via Airbnb for one month. My colleagues at ISAS were a huge help. It was through one of my fellow PhD students that I found the apartment where I'm currently living.

Do you have any tips for other PhD students coming from abroad?

Ghosh: I personally feel that most of the students I know have doubts whether they'll get used to a new country and culture. Even I felt the same when I was on the other side, back in India. However, what I've realised is that if you're passionate about your work, you should just follow your dream and go ahead and apply. The rest will eventually fall into place and you'll adjust to your new surroundings over time.

Is there anything in particular that you enjoy at ISAS?

Ghosh: Here, I really do enjoy the friendly working environment and work life balance. Moreover, I love the conversations with other scientists regarding my own or their research project. Frankly, who wouldn't be happy to have such friendly colleagues and a supervisor who encourages you to pursue new ideas?

(The interview was conducted by SR.) ■

Two ISAS Postdocs Accepted for Leibniz Mentoring

Dr Elen Tolstik (photo above) and Dr Fiorella Solari have been taking part in the Leibniz Mentoring programme in order to successfully pursue their careers in science.

Continuing to work in science after the doctorate, either at a university or non-university research institution – with their participation in the Leibniz Mentoring programme, Dr Fiorella Solari and Dr Elen Tolstik intend to make sure that their wish will become reality in the near future.

The two scientists from the research groups Proteomics (Solari) and Cardiovascular Pharmacology (Tolstik) applied for the 16-months programme in 2021. The Leibniz Association's selection criteria are excellent research achievements and the recognisably pursued goal of achieving a leading position in science and research. Since their acceptance, the two ISAS postdocs have been working on their path to a professorship or leadership position with the help of experienced mentors. They also participate in seminars to expand their leadership skills and to best develop their careers overall. Their participation in the mentoring programme also includes the development of discipline-specific networks.

"No matter how strong the support is within your own institute, it is always helpful to have an outside perspective. That's why I'm even more grateful that I can additionally advance my professional goals with the help of outside experts like Prof Dr Felix Meißner from the University of Bonn," says Solari. The 35-year-old biologist has been at ISAS since 2013 and conducts research in proteomics with particular focus on platelets biology. The mentoring programme is also an invaluable asset for Tolstik. The physicist, 37, has been researching biomarkers at ISAS since 2018, to detect cardiovascular diseases earlier and treat them better in the future. Her experience with the mentoring programme so far: "A career in the private sector was never an option for me. I'm doing everything I can to qualify myself so I'll have a real chance to take the next career step in science as soon as possible. The support I receive from my mentor, Prof Dr Raluca Niesner from Freie Universität Berlin, helps me a lot."

(SR) ■

Excellent Doctorate with Looping Plasma

Even as a student, Dr Sebastian Brandt found it difficult to decide on just one natural science. After studying physics at TU Dortmund University, he joined ISAS for his master's thesis. That was followed by his doctorate, which he completed in March 2021 with the distinction summa cum laude. As part of the Miniaturisation working group, the 31-year-old is using his research to build a bridge between physics, chemistry and bioanalytics.

The physicist optimises and miniaturises plasma-based ionisation sources. In analytical chemistry, they are commonly used to prepare samples, for example for the analysis with a mass spectrometer. When Brandt first encountered common ionisation methods and dielectrically impeded discharges used for ionisation, he immediately thought: "There has to be a better way!" During his doctorate at ISAS, Brandt worked on a new, powerful ionisation source. The result is the Flexible Microtube Plasma (FμTP), which, in combination with a nano-electrospray, initially combines sample delivery and ionisation in one setup. The FμTP, also known as looping plasma in the working group, is highly miniaturised, but robust and versatile. It is also compatible with various discharge gases such as argon, nitrogen or helium. Complex samples with numerous analytes like cholesterol can be analysed safely and efficiently with the FμTP.

The subject of Brandt's dissertation is not only the development of the FμTP, but also the particular manufacturing process. His doctoral supervisor, PD Dr Joachim Franzke, calls Brandt a 180 per cent guy: "His dedication reflects the quality and scope of his work, which goes far beyond the pure physical characterisation of the FμTP."

Dr Sebastian Brandt was awarded summa cum laude for his dissertation on the Flexible Microtube Plasma.

What's next?

After his doctorate, there is still plenty for Brandt to do at ISAS: he is currently working on integrating the FμTP onto a microchip to refine the technology. When he is not conducting research at the institute, Brandt is enthusiastic about 3D printing in his spare time. He has already been able to apply his knowledge in that area at ISAS: Brandt and his colleagues produced a complete ion mobility spectrometer (► p. 27) using 3D printing.

(CMP) ■

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What's your task as a PhD student, Kaja?

Kaja Reiffert (24) is a doctoral student in the Bioimaging research group. In her dissertation, she studies the effects of ultra-small silver nanoparticles on the human body. In order to learn more about her work in the lab, the editorial team asked Kaja to finish the following sentences.

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Bacteria such as *Escherichia coli* play an important role in Kaja Reiffert's research. The young scientist monitors the development of the bacterial strains she has cultivated and treated.

At ISAS I am working on...

investigating the influence of ultra-small metallic nanoparticles (1-2 nm small) on eukaryotic and prokaryotic cells. Eukaryotes are, for example, fungi, animals or plants. Bacteria are prokaryotes.

This research question is important because...

nanoparticles could potentially prevent bacterial infection in connection with implants in the clinic.

My theory is...

that ultra-small silver nanoparticles show an enhanced antimicrobial effect, but also cytotoxic activity. This means there is a chance that they kill bacteria, but damage our cells at the same time. I want to find out whether I can modulate this »toxic« activity through a combination of different metals and thus adjust it to eukaryotic and prokaryotic cells.

The equipment I use most in the lab is...

the confocal microscope for my analysis of fluorescence-marked nanoparticles.

My experiments are...

amongst others, so-called vitality assays, the cultivation of eukaryotic and prokaryotic cells as well as analyses with microscopes and a flow cytometer. I am always planning new experiments.

My highlight every day is...

to be able to look back on a productive and eventful day.

(NG accompanied the lab visit.)

Proteogenomics Method Enables Analyses for Cancer Medicine & Marine Research

From molecular biology to proteogenomics – an analytical approach that combines information on genomics, proteomics and transcriptomics: During his doctoral thesis, Dr Bernhard Blank-Landeshammer developed a peptide sequencing method at ISAS that can be applied in many ways. His proteogenomic method makes it possible to identify peptides in tissue samples using mass spectrometry.

The 31-year-old molecular biologist was able to contribute the analytical method to the initiative »Cancer Moonshot« to find and measure point mutations in tissue samples from colon cancer patients. The initiative, launched in 2016 by then Vice-President Joe Biden, aims at speeding up cancer research. For this purpose, ISAS collaborates with research institutions from North America on proteogenomic methods to improve research on the causes of cancer and to develop new therapies for precision medicine.

Method allows analyses for cancer & climate research

Blank-Landeshammer's method is not only suitable for cancer research, but also for climate research. In cooperation with the Leibniz Centre for Tropical Marine Research (Leibniz-Zentrum für Marine Tropenforschung, ZMT) in Bremen, he has used his method to study *foraminifera*, single-celled marine organisms. The organisms provide geoscientists with much information, for example on water temperature, salinity or the pH-value. "With the help of proteogenomic analysis, it is possible to measure the cellular stress response of the *foraminifera* to the increased ocean temperatures as a result of climate change," explains Blank-Landeshammer.

Dr Bernhard Blank-Landeshammer completed his doctorate in the research group Proteomics and developed a method to identify peptides in tissue samples using mass spectrometry.

What happened after the doctorate at ISAS?

Working on his doctorate, Blank-Landeshammer worked in the Proteomics research group from April 2015 to December 2019. After his time at ISAS, Blank-Landeshammer returned to his native home Austria in 2021. He is now working at the Centre of Excellence for Food Technology and Nutrition at the University of Applied Sciences Wels.

(BW) ■

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On The Trail of Deceptive Immune Cells

Our immune system is designed to protect us from diseases. But why is it that our own defence cells can even aggravate some diseases such as cancer? This question interests biologist Dr Julia Lill. In January 2020, she began researching specialised immune cells of the innate immune response, the neutrophil granulocytes (neutrophils), in the Bio-Fluorescence research group at ISAS. The scientist from Essen wants to understand what role these cells play in the microenvironment of a tumour and why they can sometimes even promote its growth.

Dr Julia Lill's research at ISAS dealt with the immune response by neutrophil granulocytes.

As a reaction to a tumour, the blood stem cells in the bone marrow produce more neutrophils, which then enter the tumour. Instead of fighting it, the immune cells often develop tumour-promoting properties. For example, they can produce substances that help the abnormal cells make other immune cells, such as the T cells of the adaptive immune system (see info box), »fall asleep«. The result: the tumour can grow almost entirely unhindered. In order to understand this mechanism including its causes, Lill has compiled a data set of 3,500 involved proteins from neutrophils from the bone marrow, blood or tumour of mice, in order to identify the critical molecules. “When I look at the proteome data, they tell me a story. I can see which proteins of the neutrophils in the tumour are regulated differently compared to normal tissue,” reports the 28-year-old. On the basis of her data, researchers can find out which proteins they should examine more closely in order to develop suitable drug targets in the future. A specific drug therapy could thereby block the tumour-promoting properties of the neutrophils.

Neutrophils are relevant in many ways

Lill already investigated the body’s immune response through neutrophils for her dissertation, which she completed in spring 2021 with the distinction summa cum laude. Her work at the University Hospital Essen focused on so-called enterohaemorrhagic *Escherichia coli*, better known as EHEC pathogens. They produce a cell-damaging protein (shigatoxin) that can cause severe inflammatory reactions in the body. Similar as in a tumour, the neutrophils can »overreact« and therefore harm the body more than protect it.

When I look at the proteome data, they tell me a story.

From ISAS to Harvard

Since July 2021, Lill has been working as a researcher at Harvard University. "Julia has quickly adapted to the proteome analysis technique, which was completely new to her. The first data are extremely interesting. Despite being here for just one and a half years, she built up a large network at ISAS. We will miss her, but we can now continue on her groundwork with new forces," says Prof Dr Matthias Gunzer, head of the Biospectroscopy department and Bio-Fluorescence research group at ISAS. In the US, Lill wants to combine her knowledge from her doctoral thesis and research at ISAS to better understand the immune response in the tumour microenvironment using microscopy on living animals (intravital microscopy).

(CMP) ■

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INNATE & ADAPTIVE IMMUNE RESPONSE

The immune system is the body's defence system. It consists of two parts that have different tasks: The innate (general) immune response, which includes the neutrophils, reacts quickly to foreign substances in the body. However, the involved immune cells hardly distinguish between individual pathogens and are often not sufficiently effective. The cells of the adaptive (specialised) immune response, such as the T cells, take considerably longer, but can specifically attack certain pathogens.

Dr Alexander Knodel modifying the previous model of the laser desorption technology.

Anything but Average: Alexander Knodel Completes his Doctorate at 27 Years Old

His doctorate in physics took Dr Alexander Knodel only two and a half years. According to the federal record on young scientists 2021, he was not only about two years faster than usual in the natural sciences, but also exceptionally young. At 27 years old, the Dortmund native is three years younger than the average doctorate. At ISAS, the swift scientist is part of the Miniaturisation research group and is currently working on an optimised sample supply for mass spectrometry. Even before his dissertation, Knodel knew that he was no typical medical physicist.

As he is interested in medical modules and possible applications as well as classical physics, Knodel decided to study medical physics at the TU Dortmund in 2013. “To be able to help people in the clinic was a great

motivation at the beginning," the researcher states. Medical physicists often work in close collaboration with doctors, for example to draw up irradiation plans. In the course of his studies and during a research stay in the US, he discovered his interest for plasma physics in addition to medical physics.

> ***His method might be suitable for numerous biomedical applications, for example to find carcinogens in liver samples.***

Uncomplicated sample analysis for everyday laboratory work

For his dissertation, Knodel concentrated on the coupling of laser desorption and plasma ionisation in order to be able to examine analytical and biomedical samples. These samples might consist of cholesterol that has been dissolved in chloroform and then dried, for example. In laser desorption, a sample is irradiated with a diode laser on a specially made substrate. As a consequence, the molecules evaporate into gas. The neutral desorbed material that formed is then ionised with a flexible microtube plasma (FμTP) so that it can be analysed with a mass spectrometer. In addition to his coupled method, Knodel developed an imaging technique. He uses a uniquely designed copper-glass structure with pure copper spots onto which scientists can directly apply their biological samples and study them. That is not only quick and easy, but also allows analysing samples under ambient conditions and without a chemical matrix – leaving just the pure analytes.

An extraordinary doctorate in many respects

After his master, Knodel had been doubtful about a doctorate at first. However, when the leader of his research group and later PhD supervisor, PD Dr Joachim Franzke, invited him to ISAS and proposed a topic, the decision was ultimately easy. "Although he has not been here for very long, Alexander managed to achieve impressive results. His method might be suitable for numerous biomedical applications, for example to find carcinogens in liver samples," Franzke explains. The young age of the technophile scientist and his fast progress are not the only special feature of this doctorate: Of the eight doctoral theses written within the degree programme – which the TU Dortmund has been offering since 2011 – Knodel is the first male candidate.

(CMP) ■

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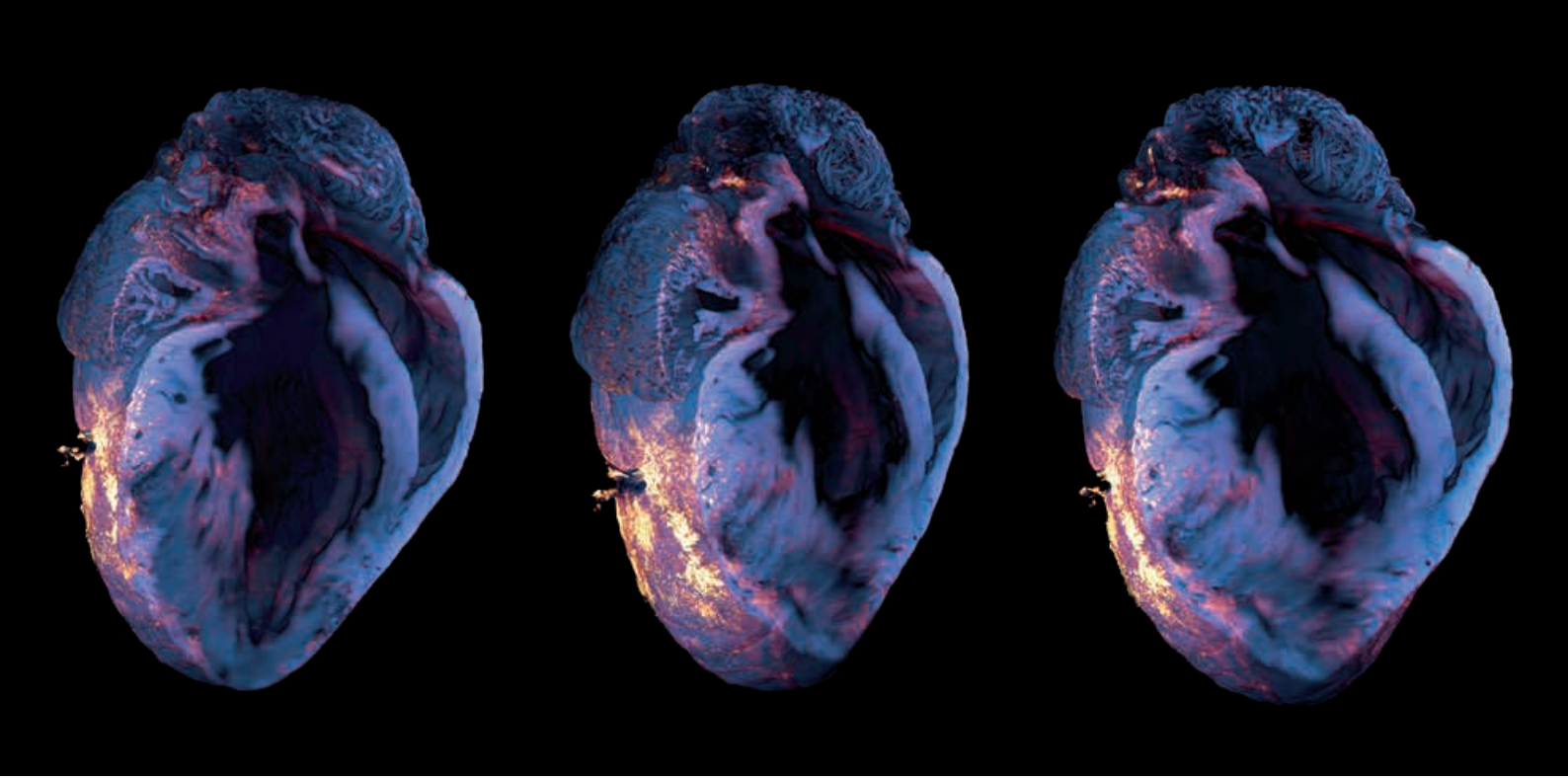

3D reconstruction of a light-sheet fluorescence microscopy-examined murine heart after myocardial infarction. Immune cells (here macrophages) that have invaded the tissue as an inflammatory response to the myocardial infarction, and regulate the tissue healing on site, light up in red-yellow.

BIO-IMAGING

Modern imaging techniques have long been regarded as a key technology for first-class medical research. At ISAS, the »Bio-Imaging« research programme focuses on the imaging of temporal and spatial molecular dynamics in organisms ranging from individual cells up to entire organs.

For example, the scientists are using light sheet fluorescence microscopy (LSFM), raman microscopy and coherent anti-stokes raman scattering (CARS) microscopy to validate biomarkers in order to accelerate the early detection of various diseases such as cardiovascular diseases or autoimmune diseases. Close cooperation with the Institute for Experimental Immunology and Imaging at the University Hospital in Essen, among other things, should ensure that the results of this basic research can later be translated into the clinic, i.e. transferred from the laboratory to patient care. ISAS

researchers also conduct both animal and human testing, take measurements on intact organs, and integrate artificial intelligence in their image analyses.

Combination with complementary analytical technologies

In order to augment the future advancement of the work in the »Bio-Imaging« research programme, ISAS established the Bio-imaging research group in 2020. In 2021, the focus was on further building up the research group. It aims to elucidate molecular and cellular processes underlying immunovascular interactions under inflammatory conditions.

The researchers study these cell interactions in acute inflammatory processes such as myocardial infarction and thrombo-inflammation, as well as in chronic autoimmune diseases such as rheumatoid arthritis. In addition to imaging methods such as LSFM, confocal laser scanning microscopy (CLSM) or two-photon laser scanning microscopy (TPLSM) are also used. These facilitate a three-dimensional analysis of biological samples from the cellular to the sub-cellular level. However, in order to characterise morphological and functional changes in inflammatory tissues over time with their underlying molecular mechanisms, scientists at ISAS combine LSFM, CLSM and TPLSM with complementary analytical technologies such as mass spectrometry (MS).

Non-destructive, integrative measurement strategies

Because not only the amount of a biomolecule in a system, but also its exact spatial location can be decisive for a disease mechanism, the combination of these optical methods with general and spatially resolved MS will open up completely new diagnostic possibilities in future. Many of the imaging techniques mentioned currently still require the destruction of the samples, which often reduces their analysis to a single technique. This is particularly problematic for rare samples, such as human tissue biopsies, as it makes comprehensive analyses impossible. For this reason, ISAS is working in the »Bio-Imaging« programme to coordinate complementary imaging and analytical methods and to combine them in such a way as to develop new, non-destructive, integrative measurement strategies. The

development of such a scale-independent multi-method concept, in the form of 4D analytics, should allow spatially and temporally resolved, quantitative, in-vivo analysis at cellular to molecular levels. These technical developments are crucial to comprehensive multi-modal and multi-dimensional analysis and thus for a holistic understanding of biomedically relevant processes. In the future, these new analytical technologies will be integrated into clinical diagnostics, thus facilitating improved prevention and early diagnosis as well as personalised approaches to therapy.

New BMBF junior research group AMBIOM

A single sample, depending on the microscope, leads to an average of 500 images. Without artificial intelligence (AI), one would neither be able to evaluate the information profoundly and quickly, nor manage it efficiently. Microscopy is just one of the many fields of application in medical imaging, where AI is continuously revolutionising the processing of enormous amounts of data. To meet the needs of current and future data volumes, ISAS established a junior research group entitled AMBIOM – Analysis of Microscopic BIOMedical Images in 2021. The Federal Ministry of Education and Research funds the junior research group which is led by Dr Jianxu Chen and which focuses on the evaluation and modeling of imaging data (▸ p. 34).

(SR) ■

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The Junior research group AMBIOM – Analysis of Microscopic BIOMedical Images was funded by the Federal Ministry for Education and Research (Bundesministerium für Bildung und Forschung).

GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

Leibniz HealthTech Lecture: Anika Grüneboom Opens the Toolbox of Fluorescence Microscopy

Imagine being able to observe the nervous or cardiovascular system from the outside, while it is working. A transparent human being would not only be incredibly exciting, but could certainly also clarify many medical questions about the genesis, early detection or therapy of diseases. After all, biological structures are incredibly complex. They consist of different tissues with various characteristics.

Prof Dr Anika Grüneboom has been head of the Bioimaging research group at ISAS since 2020, and has since held a professorship for »Experimental Biomedical Imaging« at the University of Duisburg-Essen.

Transparency is Prof Dr Anika Grüneboom's goal. "We need non-destructive and safe methods that allow us to look deep into the body," explained the immunologist and head of the Bioimaging research group at ISAS. The challenges and opportunities of these methods were the topic of the HealthTech Lecture »The Fluorescence Microscopy Toolbox – Building Bridges to Immunology« of the Leibniz Research Alliance »Leibniz Health Technologies« on November 22, 2021.

No »one size fits all« in microscopy

There is a lot to discover in Grüneboom's toolbox. To meet the diverse optical challenges of biological structures, the researcher and her team combine different microscopy techniques. "So far, there is no method that covers all scales in biological samples," said the biologist. For example, to understand an infection and the corresponding immune response, it is necessary to look at the process from different perspectives. One of the imaging techniques Grüneboom uses is fluorescence microscopy (see infobox, next page). This form of light microscopy includes light sheet fluorescence microscopy.

> **"In principle, my clearing can also be applied to human tissue samples.**

Here, a laser illuminates only one thin layer of the sample, for example tissue, at a time without destroying it. The many individual images are later used to create a 3D model of the entire sample on the computer. However, light sheet fluorescence microscopy alone does not provide a transparent result.

Grüneboom's patented clearing is used worldwide

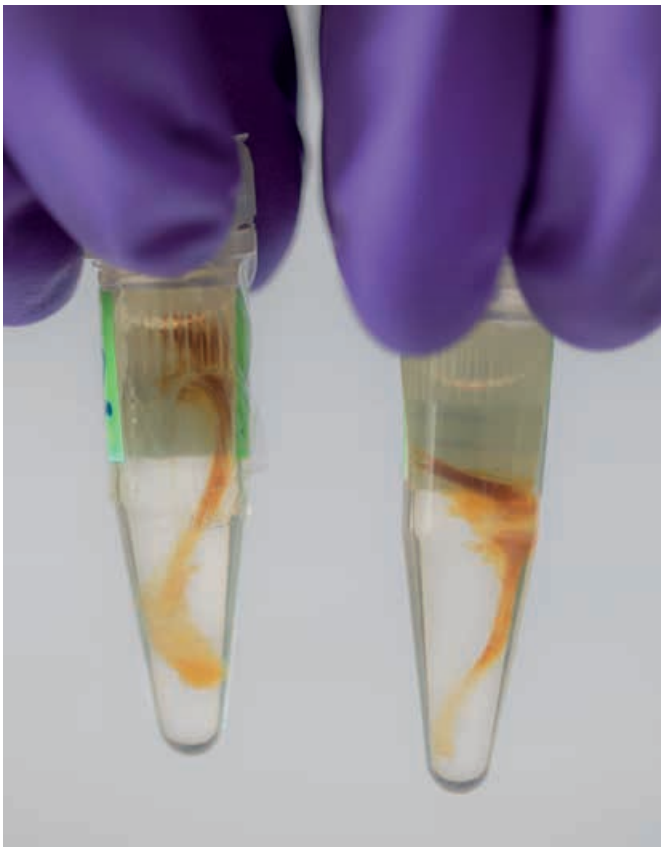
Since tissue, for example, can absorb, reflect or scatter light, it prevents a deeper insight beyond the surface without chemical treatment. That is why Grüneboom works with a clearing method she has developed. With the help of cinnamic acid ethyl ester, a naturally occurring aromatic substance, she makes her samples transparent before she analyses them under the microscope. Thus, in 2019, the biologist succeeded in discovering a previously unknown anatomical structure: blood vessels that run through the cortical bone of mice and serve as small »highways« for immune cells of the bone marrow. The unique feature of Grüneboom's technique, which is being used by researchers all over the world: The clearing can be reversed so that samples are not destroyed. In addition, her method is safe for everyday laboratory use, as it works without any toxic, carcinogenic or explosive chemicals.

Transparent human – no science fiction?

With the right »tools« – in this case, Grüneboom's clearing – light sheet fluorescence microscopy offers enormous opportunities as a method of analysis. In order to better understand immune diseases or thromboses and to be able to diagnose them more quickly in the future, the Bioimaging group is conducting research on samples from mice. In response to a participant's question about human samples, Grüneboom replied: "In principle, my clearing can also be applied to human tissue samples."

Artificial intelligence revolutionises the analysis

Grüneboom's method is not only relevant for application-oriented basic research. Fluorescence microscopy can also be used to optimise diagnostic procedures. For example, to detect changes in small vascular clusters (glomeruli) in the kidney. Instead of making histological sections of the kidney and



Cinnamic acid ethyl ester makes the bones of mice appear transparent, so that the inner structures can be seen with the bare eye.

HEALTHTECH LECTURE

www.youtube.com/watch?v=7-M6a8JR70g

measuring them manually, as is usually the case, an algorithm can recognise, count and analyse each of the approximately 15,000 glomeruli in a kidney from the fluorescence microscope images. “Artificial intelligence allows us to get much more precise statistics because we can not only see a section, but the whole organ,” Grüneboom said. She is facing the challenge of analysing the enormously large amounts of data that arise with the new ISAS research group AMBIOM (Analysis of Microscopic BIOMedical Images), headed by Dr Jianxu Chen, which specialises in artificial intelligence.

(CMP) ■

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HOW DOES FLUORESCENCE WORK?

Fluorescence describes the property of substances to absorb short-wave light and to emit it at a different wavelength. In the process, the electrons of the molecule are temporarily excited before they fall back to their original energy level. This releases energy that we perceive as light. In order to be able to recognise certain structures with a fluorescence microscope, researchers stain samples with fluorescent dyes that have the above-mentioned properties. Some substances have a natural fluorescence, they are autofluorescent.

Where the Human Brain Reaches its Limit

The cells in our blood vessels talk to each other. How they interact with each other, how far apart they are – all this provides us with important insights into inflammatory diseases. The cells of our immune system communicate with each other as well as with the endothelial cells that line the innermost layer of the blood vessels. This communication controls where immune cells attach to blood vessels, migrate through them, and then enter surrounding tissues to fight inflammation. In autoimmune diseases such as rheumatoid arthritis, however, the infiltration of immune cells into tissue does not lead to healing of the inflammation, but rather worsens it and ultimately causes the disease to become chronic. Therefore, we would like to identify criteria that will allow us, in the future, to detect these processes in the blood or tissue of each individual person before the actual onset of disease – that is, long before these inflammations become chronic.

For example, in my research group we examine the inner layer of blood vessels under the light sheet fluorescence microscope. We are studying which cells are involved in inflammatory processes, what the cell walls look like, how far apart the cells are from each other and how the cells communicate with each other. The light sheet fluorescence microscope expands the laser beam like a sheet of paper, and this thin disk of light that is created illuminates each individual plane of our samples and takes a picture of each plane. We later assemble the individual images into a 3D model on the computer. On average, we can produce well over 500 images from a single sample under the microscope, and we usually work with more than 20 samples per test series. The many images that the microscope creates pose a great challenge for us. Although there are computer programs available today, we researchers still spend a lot of time evaluating all the information from these images. Artificial intelligence can help us with this task much better than an individual computer program.

Prof Dr Anika Grüneboom,
Head of Bioimaging

Prof Dr Anika Grüneboom (left) and Dr Jianxu Chen talking about images of blood vessels in the murine mandible (lower jaw of the mouse), which were previously taken on the light sheet fluorescence microscope.

Communication is key – not only between the cells in our body, but also between our research groups. With artificial intelligence (AI), we can merge high amounts of data. There a mainly three important things machines can do that humans simply cannot. That is why there is a high potential for a deeper synergy between microscopic image analyses and AI.

First of all, AI lets us analyse far more images and thus gives us a higher throughput than ordinary computer programmes. We can have intelligent machines analysing a large amount of pictures with a precise outcome. Second, a big advantage is that AI can see things that are not visible for the human eye. AI is able to interpret every information in the images. For example: The human eye can look at the images and concentrate on the thickness of the blood vessels. AI can look at the same images, but evaluate more: not only the blood vessels' thickness, but also how rough their surface is, what is happening next to their walls, and even more. Third, our human brain is limited, whereas intelligent machines do not have that limitation. They are able to extract information and build knowledge that the human brain can hardly process. That is why my research group programs algorithms that serve as the eyes and brains for computers.

When we design our algorithms, we make sure that we are accurate and at the same time sustainable in terms of using power resources. What is also crucial is that we believe science should be transparent. Therefore, our analyses are fully reproducible, because my team's work is based on open source. It is important to us at ISAS that scientists all around the world have access to the AI methods that we develop here in Dortmund.

Dr Jianxu Chen,
Head of AMBIOM

COOPERATION BIOIMAGING & AMBIOM AT SCIENCE DAY 2021

www.isas.de/index.php/en/compact/where-the-human-brain-reaches-its-limit

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The Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung) provides funding for the junior research group AMBIOM – Analysis of Microscopic BIOMedical Images.

GEFÖRDERT VOM

Bundesministerium für Bildung und Forschung

“Microscopy has undergone a revolution over the past 20 years”

Prof Dr Matthias Gunzer heads the department of Biospectroscopy at ISAS and is Director of the Institute for Experimental Immunology and Imaging/Imaging Centre at Essen University Hospital.

Prof Dr Matthias Gunzer receives many e-mails every day. They are part of everyday life for the head of the Department of Biospectroscopy at ISAS and director of the Institute for Experimental Immunology and Imaging /Imaging Centre at the Essen University Hospital. But in February 2021, his mailbox had a surprise in store for him – an invitation for a review from a special addressee. The immunologist explains in an interview how this came about in the first place and what ultimately became of it.

How did you come to be invited to the review?

Gunzer: The invitation from Dr Ronald Germain of the National Institute of Allergy and Infectious Diseases (NIAID) in the USA came by e-mail and was completely unexpected for me. It is an honour to be asked for an opinion by such a well-known researcher. And Immunological Reviews is a renowned journal. That’s why my decision was a foregone conclusion from the very first. I also had some ideas in mind from the beginning and knew that I would like to collaborate on the review with Prof Dr Anika Grüneboom, who heads the Bioimaging research group in my department here at ISAS. We then agreed that it would be nice to involve our doctoral students in the review as well, so we divided the tasks amongst ourselves and regularly exchanged updates and came up with some exciting ideas and food for thought in the process. In the end, I think we were all able to learn something new whilst working for the review.

In your paper, you focus on the analysis of neutrophils and macrophages in sterile and infectious inflammation using imaging. What conclusions have you come to, or what is »state of the art« in this respect?

Gunzer: Around 150 years ago, physician Rudolf Virchow discovered that the cells of the immune system can move. We’ve come an incredibly long way since then. In the review, for example, we focused on recent findings in confocal microscopy and intravital two-photon microscopy. In combination with modern mouse models, such as the »catchup mouse« we developed, these methods contribute significantly to a better understanding of the innate immune response. Because intravital microscopy is excellent for observing individual cells, research has been able to break down exactly how and why neutrophils (► p. 70) and macrophages move. We can also measure and quantify them reliably. However, when it comes to examining larger areas, this

Grüneboom A, Aust O, Cibir Z, Weber F, Hermann DM & Gunzer M
Imaging innate immunity
Immunological Reviews, 2022; 306:293–303

https://doi.org/10.1111/imr.13048

method quickly reaches its limits. Therefore, imaging at the tissue level or »mesoscopic level« using light sheet fluorescence microscopy is required in order to fully understand innate immunity. This covers the range from one micrometre to several centimetres. It also makes light sheet fluorescence microscopy an essential tool in modern microscopy.

What is the future of imaging in terms of innate immune response?

Gunzer: When the development of the light microscope reached its technically feasible limit a few years ago, many people thought that research in this field had come to an end. Fortunately, a revolution has occurred in microscopy over the past 20 years with innovations that we once could barely have imagined, and so it is difficult for me to predict what technical possibilities the future may hold. However, there are two things that are of burning interest to me – one is to be able to observe the movement of neutrophils and macrophages in living humans. This type of microscopy, known as »intravital microscopy«, is already possible in smaller mammals, and from this, we've already learned that neutrophils increasingly migrate into tumours. Second, the question remains as to what we do with this newly gained knowledge. We do not yet have any use for it; at least, I'm not aware of any diagnostic method that examines the movement of these cells as a parameter. It also remains to be seen what happens if the neutrophils are prevented from moving, so there are still plenty of questions for the next years and decades *(laughs)*. One thing is certain however – as long as biomedical research exists, scientists will continue to study the movement of immune cells.

(The interview was conducted by CMP.) ■

INFECTIOUS & STERILE INFLAMMATION

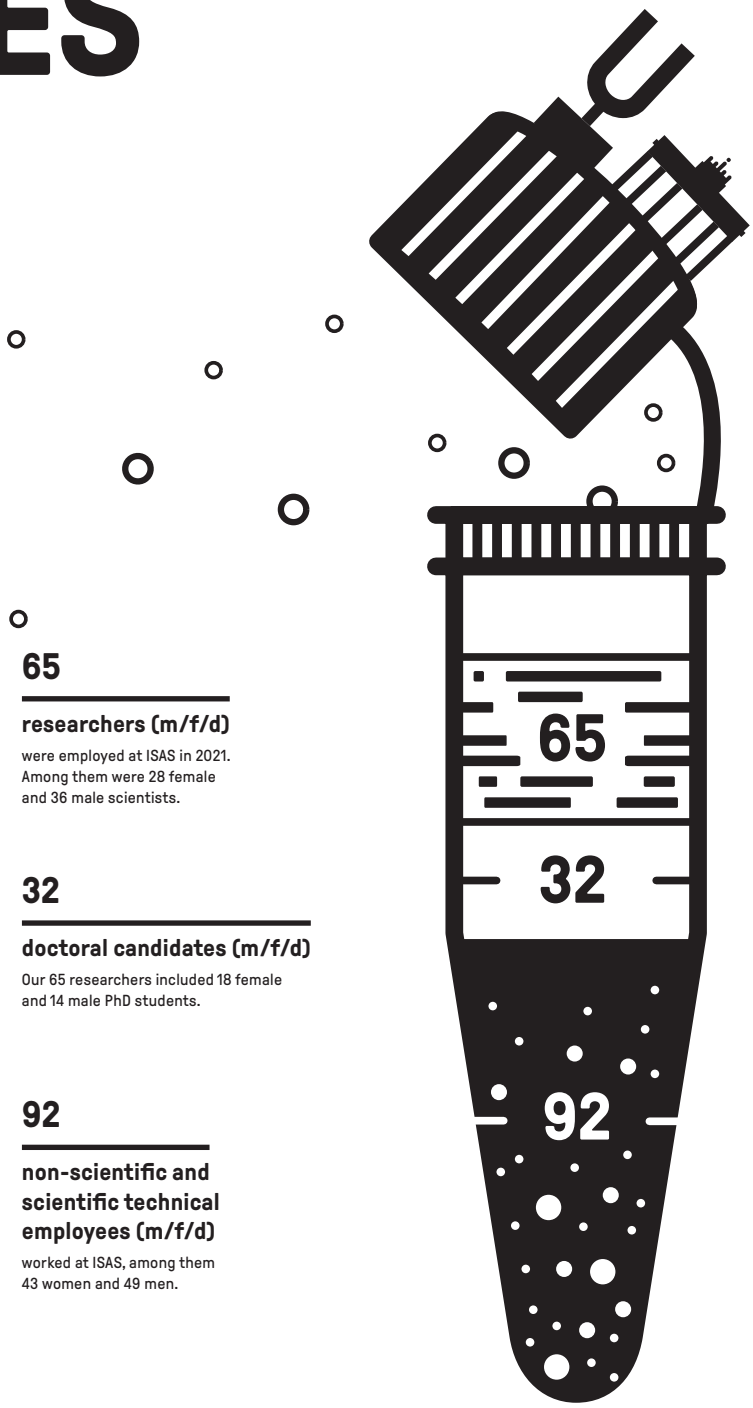
Every inflammation is the reaction of the body's own defence system, the immune system, to a stimulus. This can have various causes. Often pathogens like bacteria or viruses are responsible for the inflammation. But foreign elements, such as splinters, mechanical stimuli or a vascular blockage, as in a heart attack or stroke, can also cause an inflammatory reaction. Experts call the latter scenario sterile or aseptic inflammation, because no pathogens are involved in its development. One example for sterile infections is rheumatoid arthritis.

OUR YEAR IN FIGURES

157

staff members

worked at ISAS' locations in Dortmund and Berlin by December 31, 2021.



65

researchers (m/f/d)

were employed at ISAS in 2021. Among them were 28 female and 36 male scientists.

32

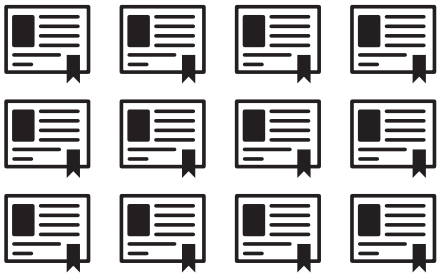
doctoral candidates (m/f/d)

Our 65 researchers included 18 female and 14 male PhD students.

92

non-scientific and scientific technical employees (m/f/d)

worked at ISAS, among them 43 women and 49 men.



27

scientific degrees

13 of them were final theses written at ISAS.*

16

doctorates

Nine of the 16 dissertations were produced at ISAS.*

15

B.Sc., M.Sc.

Of these degrees, two bachelor and six master students wrote their final theses at ISAS.*

* The other projects were external expert assessments.

99

publications

were published in peer-reviewed journals.

8.8

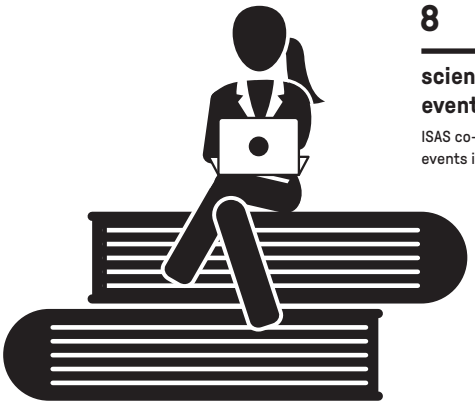
impact factor

The average impact factor of publications in peer-reviewed journals was 8.8.

49

papers

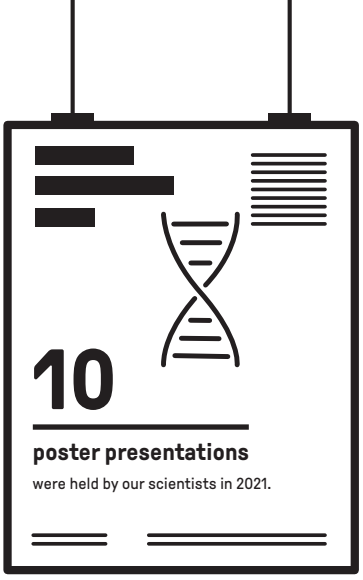
with first or corresponding ISAS authorships were published in 2021.



8

scientific events

ISAS co-organised 8 scientific events in 2021.



10

poster presentations

were held by our scientists in 2021.

32

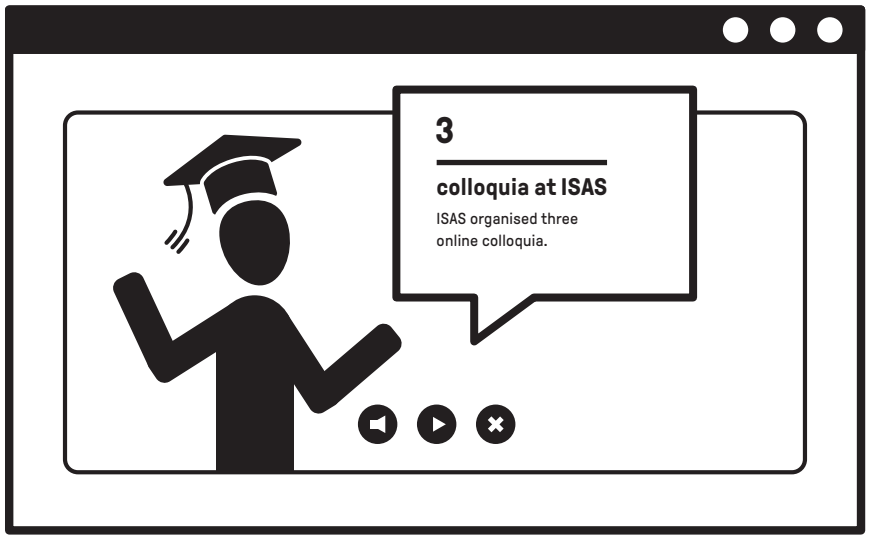
conferences

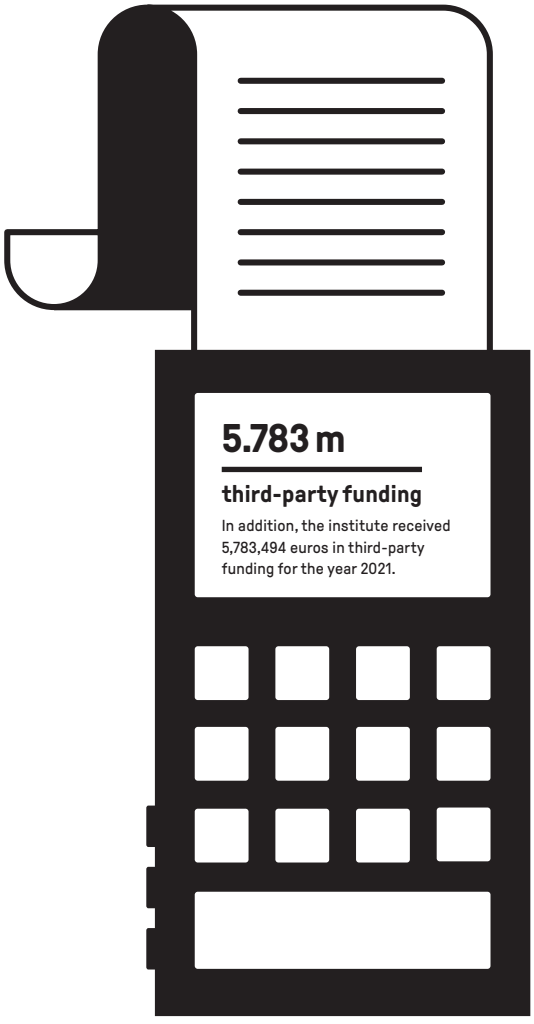
ISAS researchers participated in 32 conferences.

31

presentations

were held by ISAS researchers at conferences and other institutions.





13.538 m

funding for ISAS

The institute received 13,538,000 euros of institutional funding for its core budget from the federal government and the states.

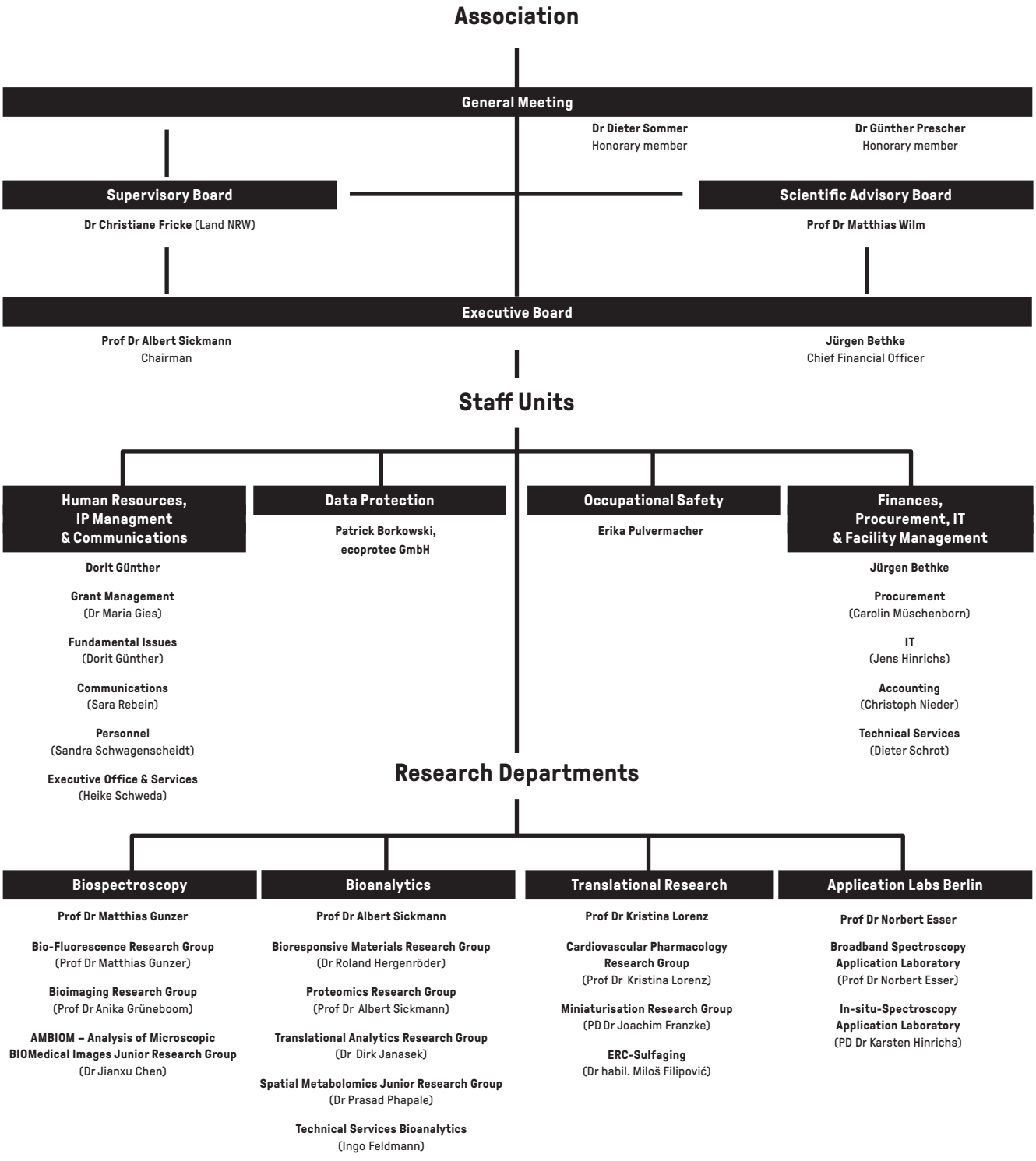
ORGANISATION

ISAS Executive Board

Prof Dr Albert Sickmann, Chairman (left)
Jürgen Bethke, Chief Financial Officer

Organisation Chart

Information as of December 31, 2021



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Information as of December 31, 2021

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AKTIVITÄTEN 2021

ACTIVITIES 2021

Publikationen
Publications

Publikationen in referierten Zeitschriften
Peer-reviewed Papers

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Evaluation of a novel controlled-atmosphere flexible microtube plasma soft ionization source for the determination of BTEX in olive oil by headspace-gas chromatography/mass spectrometry
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The Role of Protein Persulfidation in Brain Aging and Neurodegeneration
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Applikationslabore Berlin

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Andere Publikationen
Other Publications

Bioanalytik

Pagel O, Kollipara L & Sickmann A
Quantitative Proteome Data Analysis of Tandem Mass Tags Labeled Samples
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Bd. 2228, Methods in Molecular Biology,
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Pagel O, Kollipara L & Sickmann A
Tandem Mass Tags for Comparative and Discovery Proteomics
Quantitative Methods in Proteomics.
Bd. 2228, Methods in molecular biology
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Biospektroskopie

Hasenberg A, Otto L & Gunzer M
Intravital 2-Photon Microscopy of Diverse Cell Types in the Murine Tibia
Methods in Molecular Biology.
Bd. 2236, Methods in molecular biology
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https://doi.org/10.1007/978-1-0716-1060-2_15

Huang Y, Mill L, Stoll R, Kling L, Aust OP, Wagner F, Grüneboom A, Schett G, Christiansen S & Maier A
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Translationale Forschung

Tolstik E, Ali N, Saeidi T, Grahovac M, Guo S, Arias Loza PA, Nordbeck P, Debus J, Bocklitz T & Lorenz K
Nonlinear spectroscopy for Fabry Disease characterization based on cardiomyocytes
Proceedings of the Society of Photo-Optical Instrumentation Engineers (SPIE).
https://doi.org/10.1117/12.2614591

Applikationslabore Berlin

Hinrichs K, Shaykhutdinov T, Rappich J, Kratz C & Furchner A
IR laser polarimetry: breaking limits of FTIR polarimetry for thin film studies
Proceedings of the Society of Photo-Optical Instrumentation Engineers (SPIE).
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Vorträge
Lectures

Konferenzvorträge
Conference Talks

Bioanalytik

Yvonne Reinders
Translational Analytics
Online Symposium of the Leibniz Research Network Immune-Mediated Diseases
Online

Albert Sickmann
Platelet Phosphoproteomics
ISTH Masterclass
Online

Proteogenomics/Proteomics: Complementing Precision Medicine with Phenotypic Data
HUPO 2021 Reconnect
Online

Proteogenomics/Proteomics: Complementing Precision Medicine with Phenotypic Data
International Conference on Multi-omics technologies in Precious Medicine and the 10th Symposiums on Structural Proteomics at Skoltech

Proteomics Introduction & Application
TICARDIO Masterclass
Online

Proteomics-Strategien und deren Anwendung bei seltenen Erkrankungen
25. Kongress des Medizinisch-Wissenschaftlichen Beirats der Deutschen Gesellschaft für Muskelkranke e. V.
Online

Towards Highly Reprocible, Time- and Cost-efficient Proteomics Sample Preparation of Larger Sample Cohorts
37th MSB 2021 (International Symposium on Microscale Separations and Bioanalysis)
Online

Translationale Forschung

Theresa Brand, Kristina Lorenz
Defects in Ca2+ handling in phospholamban-R9C mice impact on excitation/contraction coupling but also on mitochondria and ER
ISHR 2021 – 36th Annual Meeting of the International Society for Heart Research European Section
Online

Sebastian Brandt
3D PRINTING FOR ION MOBILITY SPECTROMETRY
International Conference on Ion Mobility Spectrometry
Memphis, USA / Vereinigte Staaten

Annika Fechner
Sample Treatment And Analysis Using GC-Ion Mobility Spectrometry
International Caparica Christmas Conference on Sample Treatment 2021
Research, ISOFRR 2021
Lissabon, Portugal

Seamless analysis of liquid samples using TDC-FμTP-IMS
ISIMS International Conference on Ion Mobility Spectrometry
Memphis, USA / Vereinigte Staaten

Miloš Filipović
Does fontain of youth smells like sulfide: the role of protein persulfidation
Israel Society for Oxygen and Free Radical Research, ISOFRR 2021
Israel
Online

Protein persulfidation: the oldest solution for oxidative stress
SFRR-Europe Annual Meeting, Belgrade, Serbia
Serbia
Online

The role of protein persulfidation in brain aging and neurodegeneration
S-Bio & Glucosinate 2021 Meeting
Sevilla, Spain

Kristina Lorenz
Myokardiale Erkrankungen
87. Jahrestagung der Deutschen Gesellschaft für Kardiologie – Herz- und Kreislaufforschung e. V.
Online

Krebstherapie kann Herzprobleme fördern – welche Ansätze gibt es?
15. PharMSchool-Symposium
Online

Constanze Schanbacher
Interference with ERK-dimerization provides a cardio-safe strategy to protect from pathological ERK1/2 signaling
87. Jahrestagung der Deutschen Gesellschaft für Kardiologie – Herz- und Kreislaufforschung e. V.
Online

Elen Tolstik
Nonlinear spectroscopy for Fabry Disease characterization based on cardiomyocytes
European Conferences on Biomedical Optics
München, Deutschland

Spektroskopische Methoden für die Erforschung und Diagnostik von Herz-Kreislauf-Erkrankungen
CVD.NRW Mini-Symposium: Gesundheitsdaten für die Herz-Kreislauf-Forschung
Online

Applikationslabore Berlin

Karsten Hinrichs
IR laser polarimetry: breaking limits of FTIR polarimetry for thin film studies
SPIE Photonics West BIOS
Online

Ultrathin functionalization of silicon surfaces
ACS Fall 2021
Atlanta, USA / Vereinigte Staaten

Infrared spectroscopic polarimetry of anisotropic thin films and structured surfaces
SciX 2021
Providence, USA

Sonstige Vorträge
Other Lectures

Bioanalytik

Yvonne Reinders
Effects of cholinergic inflammation modulation on micro- and macrocirculation disorders in murine sepsis using high-resolution multi-organ sonography
Winterseminar Interdisziplinär Reloaded
Essen

Yvonne Reinders, Fiorella Solari
Functional, Metabolic and Multi-OMICS phenotyping in acute myocardial infarction
4. Retreat des SFB 1116/2
»Master Switches bei kardialer Ischämie«
Online

Biospektroskopie

Jianxu Chen
When AI meets biomedical imaging at scale
Graduate School of Biomedical Science, Universität Duisburg-Essen
Essen

Anika Grüneboom
Der Werkzeugkasten der Fluoreszenzmikroskopie – Brückenschlag in die Immunologie
Leibniz HealthTech-Lecture
22.11.2021
Online

Fluorescence microscopy in translational cancer research
Graduate School of Biomedical Science, Universität Duisburg-Essen
Essen

3D mapping of the vasculature using multimodal microscopy approaches
Graduate School of Biomedical Science, Universität Duisburg-Essen
Essen

From tissue clearing to cleared immunological processes
Miltenyi Biotec Cell Therapy Analytics Day 2021
Bergisch-Gladbach

Light sheet fluorescence microscopy in biomedical research
Imaging Facility CECAD Köln
Köln

A revised view on mononuclear phagocytes
Graduate School of Biomedical Science, Universität Duisburg-Essen
Essen

Matthias Gunzer
The impact of sterile inflammation on tissue infiltration and function of neutrophil granulocytes
Gastvortrag am Vanderbilt Institute for Infection, Immunology and Inflammation – Vanderbilt University Medical Center
Nashville, USA

Translationale Forschung

Sebastian Brandt
3D-Druck eines kompletten modularen Ionenmobilitätsspektrometers
IMS-Anwendertreffen
Potsdam

3D-printing of a complete modular ion mobility spectrometer – Design transformation, evaluation and prospective chances
Workshop on Plasma Science and Applications
Nikosia, Zypern

Annika Fechner
Analyse von flüssigen Proben mittels FμTP-TDC-IMS
IMS-Anwendertreffen
Potsdam

Miloš Filipović
Does fontain of youth smells like sulfide: the role of protein persulfidation
DFG RTG 2155 »ProMoAge«, Jena School of Molecular Medicine
Online

SULFAGING: living longer and healthier with H_2S
Gesellschaft fur Biochemie und Molecularbiologie e. V.
Online

Applikationslabore Berlin

Karsten Hinrichs
IR polarimetry of thin films and surfaces: Field manipulated bands and Berreman modes
11th Workshop Ellipsometry (WSE 11)
Steyr, Österreich

Veranstaltungen
Events

Mit-Organisation & Organisation wissenschaftlicher Veranstaltungen
Co-organisation & Organisation of Scientific Events

Bioanalytik

de.NBI LIFS Tools Training
26.01.21 – 27.01.21
Online

2021 micro Flow and Interfacial Phenomena Conference
07.06.21 – 09.06.21
Washington University St. Louis, USA

Online Symposium of the Leibniz Research Network Immune-Mediated Diseases
27.09.21 – 28.09.21
Online

de.NBI Summer School 2021 – Analysis and integration of Mass Spectrometry based omics data in Proteomics, Metabolomics and Lipidomics
27.09.21 – 30.09.21
Online

Translationale Forschung

Herztage 2021 – Deutsche Gesellschaft für Kardiologie – Herz- und Kreislaufforschung e. V.
30.09.21 – 02.10.21
Bonn

Wissenstransfer & Öffentlichkeitsarbeit
Knowledge Transfer & Public Relations

Personal, Technologietransfer & Kommunikation

Leibniz im Bundestag
20.05.21
Online

DIGITAL LUNCH BREAK
»Urlaub machen, aber sicher? (Bis) wann uns die Corona-Impfungen gegen neue Virusvarianten schützen«
28.07.21
Online

POSTDOC PITCH DAY
18.10.21
Dortmund

Leibniz im Landtag
03.12.21
Online

Lehrveranstaltungen
Teaching Activities

Bioanalytik

Dirk Janasek
Analytische Anwendungen von »Lab-on-a-Chip«-Systemen
Technische Universität Dortmund, Wintersemester 20/21

Physiologie & Anatomie
Fachhochschule Dortmund, Wintersemester 20/21

Biochemie
Fachhochschule Dortmund, Sommersemester 21

Analytische Anwendungen von »Lab-on-a-Chip«-Systemen
Technische Universität Dortmund, Wintersemester 21/22

Physiologie & Anatomie
Fachhochschule Dortmund, Wintersemester 21/22

Albert Sickmann
Biochemie I.
Ruhr-Universität Bochum, Wintersemester 20/21

Proteomik und Metabolomik
Hochschule Hamm-Lippstadt, Wintersemester 20/21

Biochemie II.
Ruhr-Universität Bochum, Sommersemester 21

Biochemie I.
Ruhr-Universität Bochum, Wintersemester 21/22

Proteomik und Metabolomik
Hochschule Hamm-Lippstadt, Wintersemester 21/22

Albert Sickmann, Dirk Janasek
Bioanalytik
Technische Universität Dortmund, Wintersemester 20/21

Chemische Analytik
Technische Universität Dortmund, Sommersemester 21

Bioanalytik
Technische Universität Dortmund, Wintersemester 21/22

Steven Verhelst
Skills in Biomedical Research 2: Information and Communication Skills 2
Katholieke Universiteit Leuven, Belgien, Sommersemester 21

Skills in Biomedical Research 3: Information and Communication Skills 3
Katholieke Universiteit Leuven, Belgien, Wintersemester 21/22

Skills in Biomedical Research 1: Information and Communication Skills 1
Katholieke Universiteit Leuven, Belgien, Wintersemester 21/22

Translationale Forschung

Joachim Franzke
Angewandte Laserspektroskopie
Technische Universität Dortmund, Wintersemester 20/21

Joachim Franzke, Sebastian Brandt
Grundlagen analytischer Methodik
South Westphalia University of Applied Sciences Iserlohn, Wintersemester 21/22

Angewandte Laserspektroskopie
Technische Universität Dortmund, Wintersemester 21/22

Applikationslabore Berlin

Andreas Furchner, Kasten Hinrichs
IR Ellipsometrie, Fortgeschrittenenpraktikum
Technische Universität Berlin, Wintersemester 20/21

Andreas Furchner, Kasten Hinrichs, Christoph Kratz
Hyperspektrale Infrarot Polarimetrie – Fortgeschrittenenpraktikum
Technische Universität Berlin, Wintersemester 20/21

Karsten Hinrichs
Ellipsometrie
Technische Universität Dresden, Wintersemester 20/21

Spektroskopische Ellipsometrie
Technische Universität Berlin, Sommersemester 21

Norbert Esser
Festkörperspektroskopie: Grundlagen und Methoden
Technische Universität Berlin, Wintersemester 20/21

Kolloquien
Colloquia

Dortmund

Dr. Cajetan Neubauer
Creating a super-targeted mass spectrometry
University of Colorado Boulder, Institute of Artic & Alpine Research (INSTAAR), USA
15.11.2021

Ali Zahraei
Mapping glucose uptake, transport, and metabolism in the bovine lens
University of Auckland, Faculty of Medical and Health Sciences, Neuseeland
23.11.2021

Karl Smith
Mass spectrometry imaging advances to aid exploration of biochemical processes
Florida State University, National High Magnetic Field Laboratory, USA
09.12.2021

Drittmittelprojekte
Third-Party-Funded Projects

Bioanalytik

A synaptoneurolipidomics view on neuronal plasticity in insulin resistance and Alzheimer's disease
Januar 2017 – Juni 2021
Leibniz Wettbewerb

Analyse differenzieller Gen- und Proteinexpression zum In-Vitro-Nachweis einer Arzneimittelallergie
INA
Januar 2020 – Dezember 2022
EFRE.NRW

Gen und Protein Signaturen als GPS für Patienten mit Neuromuskulären Erkrankungen
NME-GPS
Januar 2019 – Dezember 2021
EFRE.NRW

Modellbasierte Optimierung der Anämiebehandlung für den einzelnen Patienten mit chronischer Nierenerkrankung
NephrESA
Juni 2019 – November 2023
BMBF

Modernization and enabling advance research/higher education via transferring and implementing planar waveguide NMR spectroscopy for real-time investigation of living 3D cardiomyocyte stem cells
STEMCARDIONMR
Januar 2021 – Dezember 2022
DAAD

Modernization and transferring higher education, research and instrumentation in the field of nanoplasmonic optics and real-time remoting laboratory platform
Januar 2021 – Dezember 2022
DAAD

Nachwuchsgruppe Spatial Metabolomics
Oktober 2020 – März 2026
BMBF

Novel testing strategies for SARS-CoV-2 virus surveillance and determination of immunity
Januar 2021 – Juni 2022
Volkswagen Stiftung

Sonderforschungsbereich / Transregio 240: Platelets – Molecular, cellular and systemic functions in health and disease
Teilprojekt: Analyse von Signalmolekülen und Protein-Modifikationen von Thrombozyten mit Hilfe von Proteomik, Lipidomik und Bioinformatik
TRR 240
Juli 2018 – Juni 2022
DFG

Post-translational modifications of the synaptic scaffold controlling age-induced memory impairment
SyMetAge
Juli 2019 – Dezember 2023
Leibniz Wettbewerb

Raman-Sonden zur systematischen Bestimmung der Bioverfügbarkeit und Verteilung von Wirkstoffen in Pflanzen (»Lipinsky for Plants«)
Juli – Dezember 2021
Leibniz Forschungsverbund Wirkstoffe und Biotechnologie

»Service Center – Structural Bio- & Chemoinformatics«
Etablierungsphase – Leistungszentrum BioInfra-Prot im Rahmen des de.NBI Konsortium »BioInfraProt«
de.NBI SBCI
März 2015 – Dezember 2021
BMBF

Service Unit »Lipidomics Informatics for Life Sciences«
de.NBI LIFS
November 2016 – Dezember 2021
BMBF

Targeting Platelet Adhesion Receptors in Thrombosis
TAPAS
Januar 2018 – Juni 2022
EU

Thrombo-inflammation in cardiovascular disease
TICARDIO
April 2019 – März 2023
EU

Sonderforschungsbereich SFB 876: Verfügbarkeit von Information durch Analyse unter Ressourcenbeschränkung
Teilprojekt: Ressourcen-optimierte Echtzeitanalyse stark Artefakt-behafteter Bildsequenzen zur Detektion von Nanoobjekten
SFB 876
Januar 2011 – Dezember 2022
DFG

Bioanalytik + Translationale Forschung

Sonderforschungsbereich SFB 1116: Master switches bei kardialer Ischämie
Teilprojekt S01: Funktionelles, Metabolisches und Multi-Omics Phänotypisierung bei akutem Myokardinfarkt (A. Sickmann)
Teilprojekt A09: Kinasemodulator RKIP: Protektive Mechanismen bei Myokardinfarkt (K. Lorenz)
SFB 1116
Januar 2019 – Dezember 2022
DFG

Biospektroskopie

Nachwuchsgruppe Analysis of Microscopic BIOMedical Images / Analyse von mikroskopischen biomedizinischen Bildern
AMBIOM
Oktober 2020 – März 2026
BMBF

Synthese, Struktur und biologische Effekte von ultrakleinen (1-2 nm) bimetallischen Silber-Platin-Nanopartikeln
SE 2449/2-1
Dezember 2021 – November 2024
DFG

Translationale Forschung

Aufklärung von Dissoziationsmechanismen dielektrisch behinderter Entladungen für flüchtige Elementspezies
FR 1192/27-1
Juli 2016 – Juli 2021
DFG

Cardio Save Targeting of ERK
ERK-CASTing
August 2020 – Februar 2023
BMBF

Decoding protein persulfidation signaling
SULFAGING
Oktober 2020 – September 2025
EU ERC Consolidator Grant

Drug Discovery Hub Dortmund am ZIW – Translation akademischen Know-hows in die Anwendung
Teilprojekt: Kardiotoxizität
DDHD
April 2018 – September 2021
EFRE.NRW

Entwicklung eines Schnellnachweissystems für die Detektion von *Listeria monocythoenes* in Milch
QS-Listeria
Dezember 2017 – August 2021
BMWi

Früher adäquate Sepsis-Therapie mittels Ionenmobilitätsspektrometrie-basierter Diagnostik
Teilprojekt: Referenzanalytik für die Keimidentifikation und sterile Probenahme
FAST-IMS
September 2017 – Februar 2021
BMBF

Sonderforschungsbereich / Transregio 296: Lokale Kontrolle der Schilddrüsenhormonwirkung (LocoTact)
Teilprojekt P10: Lokale TH-Wirkung in der akuten und chronischen kardialen Ischämie
TRR 296
Juli 2020 – Juni 2024
DFG

Nicht-Radioaktive Ionisierung für Spektrometrie und Spektroskopie
NORISC
Juli 2020 – Juni 2023
BMBF VIP+

Optimierung von GRK5-Inhibitoren für die Therapie von Herzinsuffizienz und Herzhypertrophie
ChInValue
Januar 2020 – Dezember 2022
BMBF

The Role of Zinc Fingers in H2S Signaling
September 2020 – Juli 2024
University of Maryland

Twinning in atmospheric Plasma science and applications
TImPANI
November 2018 – April 2022
EU

Schutzrechte
Industrial Property Rights

Patente
Patents

Anordnung und Verfahren zur Wellenlängenkalibration bei einem Echelle-Spektrometer
EP-Patent: EP1472512 (validiert in Großbritannien, Schweden, Schweiz, Frankreich und Deutschland)
US-Patent: US7215422
AU-Patent: AU2003210190
CN-Patent: ZL03803518.9
JP-Patent: JP4534487B2

Anordnung zur Erfassung von Reflexions-Anisotropie
EP-Patent: EP3035034
(erteilt und validiert in Deutschland)

Spektrometer
DE-Patentanmeldung: DE102016110210

Detektor für die kernmagnetische Resonanzspektroskopie »Mehrfachresonanzkopf mit Hilfsinduktivität«
DE-Patent: DE102014115572

Probenkopf für die kernmagnetische Resonanzspektroskopie »Doppelresonanz-Probenkopf auf Mikrostreifenleiterbasis für die kernmagnetische Resonanzspektroskopie an massen- und volumenbegrenzten Proben«
DE-Patent: DE102014107296

Ionenbeweglichkeitsspektrometer
DE-Patent: DE102009008266

Echelle-Spektrometer mit verbesserter Detektorausnutzung »Aryelle«
EP-Patent: EP1754032 (erteilt und validiert in Großbritannien, Frankreich, Österreich und Deutschland)
US-Patent: US7804593
AU-Patent: AU2005252809
CN-Patent: CN101014841

Echelle-Spektrometeranordnung mit interner Vordispersion
EP-Patent: EP2384424 (validiert in Großbritanien, Österreich, Deutschland, Frankreich und Schweiz)
CN-Patent: CN102378904
US-Patent: US8681329
DE-Patent: DE102009003413

Ellipsometervorrichtung und Ellipsometrieverfahren zur Untersuchung einer Probe – »Einzelschussellipsometer«
DE-Patentanmeldung: DE102016202971

Verfahren zur Herstellung eines dreidimensionalen, einen elektrischen Widerstand bildenden Körpers »Filament«
DE-Patentanmeldung: DE102020109649.6

Verfahren und Vorrichtung zur Erzeugung von positiv und/oder negativ ionisierten Gasanalyten für die Gasanalyse
EP-Patent: EP2082221 (validiert in Großbritannien, Frankreich, Spanien und Deutschland)
US-Patent: US7973279
JP-Patent: JP5315248

Vorrichtung zur Detektion und Charakterisierung von organischen Molekülen in einem flüssigen Probenvolumen
DE-Patent: DE102016101001

Probenkopf für die kernmagnetische Resonanzspektroskopie »Mikrostreifenleiter Probenkopf mit dreiecksförmiger Einschnürung«
EP-Patent: EP3350610
(validiert in Deutschland)

Probenkopf für die kernmagnetische Resonanzspektroskopie »Mikrostreifenleiter-Probenkopf zur Erzeugung von Gradienten des äußeren Magnetfeldes in kernresonanzspektroskopischen Messungen«
DE-Patent: DE102015115996

Verfahren zur Detektion und Quantifizierung von einzelnen Analyten in flüssigen Analytgemischen »Pocket-NMR«
DE-Patentanmeldung: DE102016124177
US-Patent: US10782256

Verfahren zur optischen Erfassung einzelner Nanoobjekte »SPR-Blende«
DE-Patentanmeldung: DE102017116055

Verfahren zur hochaufgelösten Erfassung von Nanopartikeln auf zweidimensionalen Messflächen
DE-Patentanmeldung: DE102009003548
US-Patent: US8587786

Verfahren zur Messung der Thrombozytenfunktion »Blutplättchenmesssytem«
EP-Patent: EP2990787 (validiert in Frankreich, Spanien, Österreich, Großbritanien, Italien und Deutschland)
US-Patent: US9778248
JP-Patent: JP2016048236
CN-Patent: CN105388202

Vorrichtung zur Entnahme einer Probe und zur Zuführung in ein analytisches Auswertesystem
EP-Patent: 2977741 (validiert in Deutschland und Großbritanien)
US-Patent: US9874578

Spektrometeranordnung »SuZee«
EP-Patent: EP2516975 (validiert in Großbritannien, Frankreich und Deutschland)
US-Patent: US8873048
CN-Patent: CN102656431

Verfahren zur Anreicherung N-terminaler Peptide »ChaFRAtip«
DE-Patentanmeldung: DE102017104774

Verfahren zur Auswertung von Echelle-Spektren / Mike-Patent 1 »Binning«
DE-Patent: DE10055905
US-Patent: US7319519
EP-Patent: EP1783468 (validiert in Irland, Niederlande, Großbritannien, Frankreich und Deutschland)

Verfahren zur Auswertung von Echelle-Spektren / Mike-Patent 2 »Wellenlängenanbindung«
US-Patent: US7876435
EP-Patent: EP2068134 (validiert in Irland, Niederlande, Großbritannien, Frankreich und Deutschland)

Verfahren zur Auswertung von Echelle-Spektren / Mike-Patent 3 »Untergrund-Korrektur«
EP-Patent: EP2068134 (validiert in Großbritannien, Frankreich, Österreich, Schweiz und Deutschland)

Verfahren zur dielektrisch behinderten Elektrosprayionisierung von flüssigen Proben und zur nachfolgenden massenspektrometrischen Analyse der erzeugten Probenionen »Getaktetes DB-Elektrospray«
DE-Patent: DE102011015517
EP-Patent: EP2691974 (validiert in Deutschland, Spanien, Frankreich und Großbritanien)
JP-Patent: JP5814458

Verfahren zur Ionisierung von gasförmigen Proben mittels dielektrisch behinderter Entladung und zur nachfolgenden Analyse der erzeugten Probenionen in einem Analysegerät
DE-Patent: DE102016104852

Verfahren zur Ionisierung von gasförmigen Proben mittels dielektrisch behinderter Entladung und zur nachfolgenden Analyse der erzeugten Probenionen in einem Analysegerät »FµTP«
DE-Patentanmeldung: DE102017112726
EP-Patentanmeldung: EP187306501
US-Patent: US 16/615172

Verfahren zur Identifizierung von Markerproteinen zur Diagnose und Risikostratifizierung von Störungen der Blutgerinnung
EP-Patent: EP3295177 (validiert in Großbritannien, Frankreich, Schweiz, Österreich, Spanien, Italien und Deutschland)
US-Patentanmeldung: US15/572391
CN-Patent: CN202010371718.7
JP-Patentanmeldung: JP2018521306

Verfahren zur Analyse des Metaboloms dreidimensionaler lebender Zellkulturen mittels NMR-Spektroskopie »SLRO-NMR«
DE-Patentanmeldung: DE102021103574

Absolvent:innen
Graduates

Dissertationen
Dissertations

Bioanalytik

Bernhard Blank-Landeshammer
Studies on intracellular metabolism of pharmacological chaperones and the role of yeast as model organism
Fakultät Bio- und Chemieingenieurwesen, Technische Universität Dortmund

Eva Eilers
Mitochondrien als Signalplattformen: Funktionale Analyse linearer Ubiquitinketten an Mitochondrien
Fakultät für Chemie und Biochemie, Ruhr-Universität Bochum

Matthias Jender
Entwicklung eines mikrofluidischen Systems zur kontinuierlichen elektrophoretischen Auftrennung und Analyse von Enzymreaktionen
Fakultät Bio- und Chemieingenieurwesen, Technische Universität Dortmund

Biospektroskopie

Julia Lill
Renal macrophages promote Shiga toxin-induced Hemolytic Uremic Syndrome through TNFa and CXCR2- dependent neutrophil recruitment
Fakultät für Biologie, Universität Duisburg-Essen

Translationale Forschung

Bettina Baumgarten
Kardiotoxische Effekte von Chemotherapeutika – Evaluierung eines impedanzbasierten in vitro Testsystems und Bestimmung der Kardiotoxizität niedermolekularer Kinaseinhibitoren.
Fakultät für Biologie, Universität Duisburg-Essen

Sebastian Brandt
Entwicklungen und Kombinationen miniaturisierter Probenzufuhr- und Ionisierungssysteme
Fakultät Physik, Technische Universität Dortmund

Carolin Drees
Analyse mikrobiologischer Proben auf Basis der Ionenmobilitätsspektrometrie
Fakultät Physik, Technische Universität Dortmund

Alexander Knodel
Coupling diode laser desorption with plasmaionization in mass spectrometry for analyticaland biomedical applications.
Fakultät Physik, Technische Universität Dortmund

Applikationslabore Berlin

Timur Shaykhutdinov
Infrarot-Nanopolarimetrie: Anisotropie von strukturierten Biooberflächen, dünnen Polymerfilmen und Oxidschichten
Fakultät II – Mathematik und Naturwissenschaften, Technische Universität Berlin

Abschlussarbeiten
Degree Theses

Bioanalytik

Katharina Kaufmann, M. Sc.
Developing cell-carrying SPR sensor chip for the detection of individual extracellular vesicles and soluble proteins produced by HT29 cells.
Fakultät für Chemie und Chemische Biologie, Technische Universität Dortmund

Kudrat-E Khoda, M. Sc.
The development of a magnetometer for the NMR spectroscopy based on optical heterodyne detection and construction of a mechanical string oscillator in a magnetic field.
Fakultät für Elektrotechnik und Informationstechnik, Ruhr-Universität Bochum

Maedeh Nadertehrani, M. Sc.
Assessing Optimal Fluorescence Parameters for Staining of 3D Cell Culture in Confocal Fluorescence Microscopy
Fakultät für Elektrotechnik und Informationstechnik, Ruhr-Universität Bochum

Adriana Schneider, M. Sc.
Enhancing throughput in LC-MS-based proteomics
Fakultät Bio- und Chemieingenieurwesen, Technische Universität Dortmund

Maja Stahl, B. Sc.
Optimierung der Arbeitsabläufe zur Erstellung einer spektralen Bibliothek für die DIA-Bestimmung des Thrombozytenphosphoproteoms
Biotechnologie/Bioinformatik, Hochschule Emden/Leer

Rahat Talukder, M. Sc.
Analytical performance of the improved version of the PAMONO-sensor.
Fakultät für Elektrotechnik und Informationstechnik, Ruhr-Universität Bochum

Translationale Forschung

Christopher Borg, B. Sc.
Analytische Charakterisierung einer durch Sinus- und Rechteckspannung betriebenen, plasmabasierten Ionenquelle für die Ionenmobilitätsspektrometrie
Hochschule Hamm-Lippstadt

Moritz Pernecker, M. Sc.
Untersuchung der Kardiotoxizität verschiedener Chemotherapeutika an H9C2-Zellen mittels Fluoreszenzmikroskopie und konfokaler Ramanspektroskopie.
Hochschule Hamm-Lippstadt

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Auszeichnungen
Awards

Bioanalytik

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NTop Poster at the Society of Toxicology Annual Meeting 2021
15.03.2021

Suyuan Chen
1. Platz beim Merck Innovation Cup
02.07.2021

Translationale Forschung

Kristina Lorenz
Aufnahme in die Expertendatenbank SPRIND
11.03.2021

PHOENIX Pharmazie Wissenschaftspreises in der Kategorie Pharmakologie und Klinische Pharmazie
18.11.2021

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Rudi-Bussei-Young Investigator Award für experimentelle Herz- und Kreislaufforschung
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