isas Leibniz-Institut für Analytische Wissenschaften

ANNUAL REPORT 2020

advancing analytics

Leibniz Gemeinschaft

FOREWORD

Dear Readers

2020 will always be a memorable year for our institute, and not just because of the pandemic. It actually brought some positive innovations, so we can look back on a highly diverse year. In 2020, we pushed ahead with the expansion of preclinical research and entered into new collaborations with clinics, universities and partners from industry. We are delighted that we, along with the University of Duisburg-Essen, have been able to appoint Prof. Dr. Anika Grüneboom, an expert in novel imaging techniques, as professor. At the end of the year, ISAS advertised two junior professorships together with the University of Bielefeld (multidimensional omics analyses) and the University of Duisburg-Essen (lipidomics). In 2020, the institute set the course for further cooperation with universities in the region and for new research groups and junior research groups.

Despite travel restrictions, we were able to welcome new employees, including some from abroad, last year. Among these is ERC grantee, Dr. habil. Milos Filipović. I am very pleased that we have been able to recruit a top-class scientist such as him for our Translational Research department. His Sulfaging group conducts research on metabolic biochemistry and provides important insights that will ultimately help to improve the diagnosis and treatment of age-related diseases. His expertise fits our profile perfectly.

In the meantime, we have colleagues from 20 different nations working at ISAS. They form the core of our research institution and, as chemists, biologists, pharmacologists, physicists and computer scientists, they pursue the common goal of developing and optimising new, economical analytical methods for medical research. Together, we aim to improve the prevention, early diagnosis and treatment of various diseases. In the following pages, we introduce some of our research projects and staff members and not only present our findings, but also give you an insight into how many of us at the institute have experienced these turbulent times dealing with not only research but also, for example, home-schooling.

I hope you have an enjoyable read.
Stay healthy!

Prof. Dr. Albert Sickmann

CONTENTS

COVID-19

LUNCH BREAK Conveys Facts 04

"Our desire for excessive security during a pandemic is irrational" 08

Early Pandemic Phases: Virus Microscope Aims to Provide a Quick Overview 12

How ISAS Works Remotely 15

Virtual Exchange Provides Young Academics with Practical Knowledge 18

DISEASE MECHANISMS & TARGETS

Programme Portrait 2020 22

Searching for Proteases with Molecular Tools 25

LipidCreator Software Supports the Diagnosis & Prognosis of Diseases 27

Flipping Molecular 'Switches' for Heart Attacks 28

Physicist Elen Tolstik Conducts Research for the Heart 30

Deciphering the Effect of Thyroid Hormones in Brain, Liver & Heart 31

Molecular Phenotyping of Mice – MS Assays Successfully Replace Previous Immunoassays 32

Protein Sequence Provides Insights for the Therapy of Heart Failure & Cancer 34

PARTICULARS

ISAS & UDE Appoint Anika Grüneboom Professor 35

ERC Grantee Milos Filipović Joins ISAS 36

Announcement of a Joint Professorship in Bioinformatics 37

BIOMARKERS

Programme Portrait 2020 38

Blood Test for Drug Allergies Increases Patient Safety 40

Deciphering the Penmanship of Neuromuscular Diseases: Improved Diagnosis through Gene & Protein Signatures 41

Against the Current: A Way Back to Basic Research 44

Optimisation of Anaemia Therapy for Patients with Chronic Kidney Disease 47

Doctoral Students Are on the Trail of Thrombo-Inflammation 48

PROMOTION OF YOUNG SCIENTISTS

"I'd like to help induce the hibernation of the human body" 50

PhD Workshops: Elevating Science 52

What's Happening Here, Dr. Brandt? 54

Adriana Schneider Aims to Make Proteome Analyses More Efficient 56

What's Your Task as an Intern, Christopher? 57

Intern to Postdoc – Early Career Support for Young Academics 58

BIO-IMAGING

Programme Portrait 2020 59

ISAS Joins INFECTIONS 62

BIOINTERFACES

Programme Portrait 2020 63

OUR YEAR IN FIGURES

Staff Members 66

Scientific Degrees, Funding 67

Publications, Impact Factor 68

Poster Presentations, Colloquia 69

ORGANISATION

Organisation Chart 71

Boards 72

ACTIVITIES (see German part)

Publications 75

Lectures 84

Events 86

Third-Party-Funded Projects 89

Industrial Property Rights 92

Graduates 94

Scholarships 96

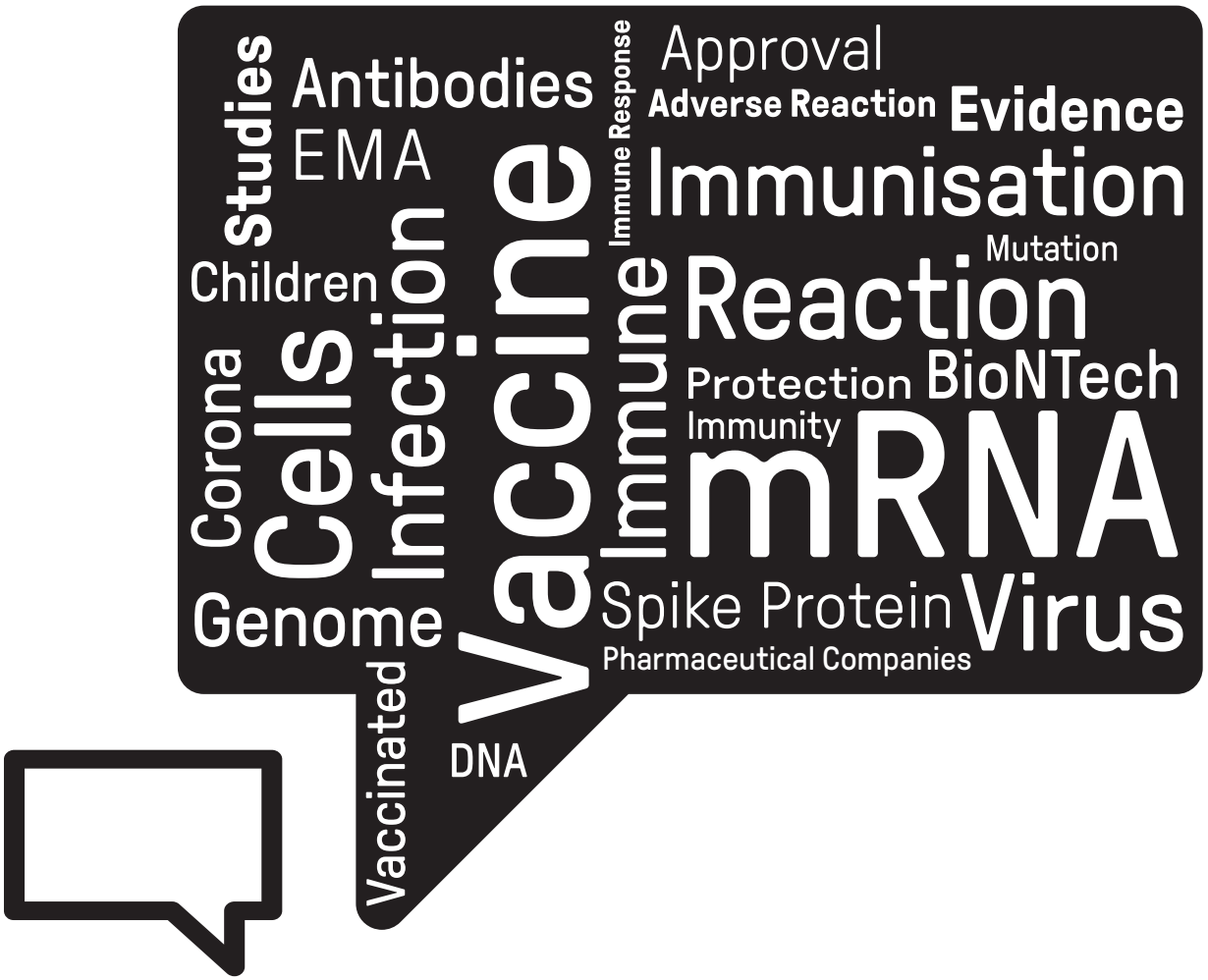
Awards 96

ISAS Memberships in Scientific Associations 97

Funding Sources 98

Imprint 99

COVID-19



LUNCH BREAK Conveys Facts

While the prospect of coronavirus vaccines inspired confidence despite the high number of infected people in December 2020, at the same time, sceptical voices and fears around future mRNA vaccines were growing louder in the public sphere.

No human mRNA vaccines had hitherto been licensed in Germany. But advanced clinical trials had already been underway for some therapeutic cancer vaccines of this type. It was time for ISAS to dispel the myths surrounding vaccination against the coronavirus and provide the facts. To that end, the institute invited the general public to the online event, DIGITAL LUNCH BREAK, “Covid-19: On the Road to Vaccination” with Prof. Dr. Matthias Gunzer on two days at the end of the year.

60 questions in 197 minutes

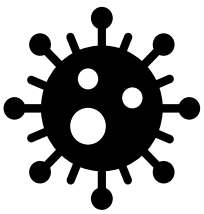
There was great interest in both events – a total of around three hundred people, including students, took part in the exchange with the immunologist. Gunzer talked about the development of the new vaccines and how they function and took a brief look at the history of vaccination before answering numerous questions. Among them: How safe is the new coronavirus vaccine? Can the mRNA vaccines alter our genetic make-up? Is there a health risk associated with immunisation?

Work & Personal Life

I take advantage of the opportunity to work from home and at flexible hours, so that my wife and I can look after our two-year-old regardless of reduced daycare hours or daycare cancellation. Our coordination at home works great, we take turns after our daughter’s midday nap: One of us works, the other takes care of the little one. At the moment, only the weekends leave room for a joint family life. Something I’d like to maintain in the future is virtual meetings. They’re ideal for certain topics, save time and are often more efficient than in-person appointments. It’ll still take some time until the pandemic is over. However, I’m already proud of how well our daughter’s coping with the change in everyday life.

Dr. Julian Heitkötter, Knowledge & Information Manager

More than 60 questions were asked at the two events, and Gunzer answered them in a sound and entertaining manner. He spent a total of 197 minutes answering the participants' questions. His conclusion: "As an immunologist, I feel it's my responsibility to raise awareness, particularly in times like these. The more information we provide about the coronavirus, vaccines and Covid-19, the better each individual will be able to make an informed vaccination decision."



mRNA
VACCINE MECHANISM

MYTH
GENETIC MANIPULATION

POTENTIAL INFECTION
VERSUS SIDE EFFECTS

With mRNA vaccination, the body receives only the genetic information that its own cells need to produce a characteristic of the coronavirus – the antigen – that triggers the desired immune response. The mRNA vaccines from BioNTech/Pfizer and Moderna contain a blueprint for the coronavirus spike protein in the form of messenger ribonucleic acid (mRNA) which is packaged in fat globules (liposomes). Unlike the fully intact coronavirus, the spike proteins are harmless to the human body. The mRNA from the vaccine enters the human cells, and the body uses the mRNA to manufacture the spike proteins. The immune system registers the spike proteins as foreign bodies and reacts to them by producing antibodies and immune cells, among other things. Once immunisation is complete, the immune response protects against infection with the actual coronavirus by recognising and inactivating its spike proteins, thereby preventing infection.

There is no scientific evidence that mRNA vaccination can alter human DNA and thus interfere with the human genome. Integration of RNA into DNA is impossible because of the different chemical structure. In addition, human cells degrade mRNA within a short period of time.

Vaccination protects not only individual vaccinated persons, but also infants, children or adults who cannot be vaccinated for health reasons. It is an indispensable tool for eventually overcoming the pandemic completely. Covid-19 can have serious consequences, but a reaction to the vaccine usually lasts a few days at most. Side effects such as fatigue, headache or flu-like symptoms are a sign that the immune system is reacting to the vaccination, and antibodies and immune cells are being produced.

(SR) ■

“Our desire for excessive security during a pandemic is irrational”

At the time that the December 2020 digital LUNCH BREAK was taking place, approval of the first mRNA vaccine against SARS-CoV-2 in the EU was imminent. There was a great deal of scepticism about mRNA vaccines. Half a year later, there is little, if any, sign of this initial reticence in Germany. We talked to Prof. Dr. Matthias Gunzer about how this came about and what type of protection vaccinated people can expect. He is an immunologist and the scientific director of the Biospectroscopy department.

Many people consider the preparations from BioNTech/Pfizer and Moderna to be first-class vaccines. What do you think is behind this development?

Gunzer: It’s fascinating to see that, at first, this new mRNA vaccine caused a great deal of anxiety. Many lay people feared that it would genetically reprogram us. But then several countries, led by Israel, went all in on BioNTech/Pfizer’s vaccine. The vaccination campaign there went off without a hitch. More to the point, the Israelis were able to replicate the pivotal trial in the field.

The data are nearly congruent in terms of efficiency and protection. The German media also reported on this success, and public confidence in the mRNA vaccine grew. AstraZeneca’s vaccine, on the other hand, has struggled from the beginning. The pivotal trial was bumpy and halted several times. Shortly after it was authorised, reports of serious side effects followed. And these have been so prominent in the media, that the issue has dominated all coverage of the vaccine. As a result, the incredibly high efficiency of this vaccine in itself has completely fallen by the wayside. The fact that the mRNA vaccines are now more popular with many people than the vector vaccines probably also has to do with the fact that reports of severe side effects for the former have failed to materialise.

In the meantime, due to reported cases of cerebral venous thrombosis, the vector-based vaccines are only regularly used in people aged 60 and over. At the same time, the German Federal Ministry of Health has also approved AstraZeneca’s vaccine for younger adults as well. How do you assess the use of this vaccine in view of the current data?

Gunzer: Every individual case of cerebral venous thrombosis reported in connection with the vaccine is terrible and tragic for those affected. However, what we can’t ignore at all in a pandemic is the overall balance of evidence. The risk of cerebral venous thrombosis after vaccination with AstraZeneca is extremely low.

»What we don’t yet understand from an immunological perspective is why immunological memory varies, and why some people have longer or shorter protection against recurrence.«

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 the Essen University Hospital.

To date, more than 33 million people worldwide have been vaccinated with this vaccine and are thus protected against a severe progression of the disease. Except for moderate side effects such as fatigue, they had no problems at all. So we have to put it all in perspective. There's no medication that has no side effects.

Vaccinations began picking up steam in this country in mid-May of 2021. However, we are making slow progress compared to other countries. For example, in Israel, around 59 percent of the population had been fully immunised by May 15, 2021, compared with only about eleven percent in Germany by May 14, 2021. In your opinion, what was the initial hold-up in the German vaccination campaign?

Gunzer: The desire for excessive safety that we, in our society, display for a vaccine during a volatile situation like this pandemic is irrational. To put it simply, it's like when a house is on fire, but the owners are still outside arguing with the fire brigade about whether the extinguishing water might leave stains.

»I appeal to people to remain rational and not forget the situation we've recently found ourselves in, both in Germany and throughout the world.«

Work & Personal Life

Some people are demanding a level of safety for the SARS-CoV-2 vaccines that no one can meet in a pandemic. The coronavirus costs human lives, so vaccine development has been and continues to be under high pressure.

What factors play a role in how long vaccinated individuals remain immune to SARS-CoV-2?

Gunzer: We develop two reactions as an immunological response to a vaccination or infection. First, we produce antibodies that prevent the virus from infecting us in the first place. In the second response, our body reacts with immune cells called cytotoxic T cells which destroy the cells that have been infected despite antibodies and therefore replenish the virus particles in the body. Every human being has an immunological memory. Behind this are so-called memory cells that remain in the bone marrow and other parts of the body after an infection or a vaccination. They store all the information about the pathogen that has been staved off and can therefore protect against a new infection. From an immunological point of view, we don't yet understand why the immunological memory differs from person

My husband and I can take turns working from home, as our employers both make sure that our offices aren't too crowded. We coordinate in order to look after our sons at home. Right now, their vaccinated grandma usually fills in once a week. Before the pandemic, I worked at ISAS four days a week, now it's usually only three. All works quite well because I can enter orders or publications electronically, for example. Thanks to a very good internet connection, that runs smoothly at home. That's why I want to keep working from home at least one day per week after the pandemic. Without the 90 minutes of commute and traffic jams, I save time that benefits my work and family. The biggest challenge at the moment is keeping our seven- and 15-year-old children happy when the weather's bad. Apart from going for a walk or cycling, hardly any activities are possible. That's why I'm very proud that my sons are still motivated to study, even though they receive less feedback from the teachers.

Stefanie Güssgen,
Staff Member Technical Service Bioanalytics

Work & Personal Life

My daughter started going to the emergency daycare two weeks ago so that I can work at the institute a few days a week. Before that, we tried more home office and more homeschooling, but that didn't work for us. At the moment, I work from home once a week and that's going smoothly, so I'd like to keep that going in the future. My daughter and I've already been through a coronavirus infection and luckily a few people in our family have been vaccinated in the meantime. Therefore, the contact with other family members has become closer again. Nevertheless, we miss other social contacts, our friends and leisure activities. We've organised ourselves, but I can't get used to the situation! My biggest challenge is to make the best of it for my six-year-old despite everything. All in all, I'm relieved and happy that I can continue to work despite the pandemic and that we're not affected by short-time work or unemployment.

Sonja Hinterthan, HR Administrator

to person or why some people have a longer or shorter protection against recurrence of the disease.

For some vaccines, such as the smallpox vaccine, a single immunisation is enough for life. And then, there are vaccinations that need a booster after several years. For the BioNTech/Pfizer vaccine, there are data showing that both antibody and cytotoxic T cell protection last for several months after vaccination. We don't know any more details, because we haven't yet been able to study Covid-19 over a longer period of time.

Which vaccination myth would you like to dispel?

Gunzer: AstraZeneca's vaccine, which by the way is far more effective than the annual flu shot, has unfortunately fallen into disrepute, unjustifiably so in view of the data. I appeal to people to remain rational and not forget the situation we've recently found ourselves in, both in Germany and throughout the world. The fact that we now have several approved vaccines against Covid-19 in this country is a groundbreaking scientific achievement.

(SR) ■

Early Pandemic Phases: Virus Microscope Aims to Provide a Quick Overview

In order to be able to test a lot of people for viruses at the same time and, above all, quickly during a pandemic, precise analysis methods with a high throughput are needed. Researchers at ISAS and the TU Dortmund University have developed a virus microscope that is – under laboratory conditions – just as reliable as conventional antigen tests, but faster and more economical. Ideally, the device will make it possible to find out whether someone has been infected with a virus and help determine the viral load with just a few drops of liquid like saliva. For this purpose, the virus microscope combines three fundamental components: It has a gold surface for immobilised antibodies against the viruses that are being identified. To make the virus' signal visible, the device uses modified Surface Plasmon Resonance Spectroscopy (SPR-Spectroscopy). Artificial intelligence helps to identify the individual virus. The goal is to make the virus microscope fully automated, so that it requires low maintenance and can function without laboratory staff. The virus microscope is already small and mobile in the current development stage. Thus, it could be set up anywhere. In the future, it could help gain insights into the infection process at train stations or other critical spots quickly – especially in early phases of a pandemic, before broad testing is available. The Dortmund researchers want to further develop the virus microscope so that the process between sample collection and test result will only take a few minutes.

(SR) ■

Working group
Bioresponsive Materials
Dr. Roland Hergenröder
T: +49 (0)231 1392-178
E: roland.hergenroeder@isas.de

Work & Personal Life

We're in the luxurious situation that our son was able to go to kindergarten almost the entire time. As a family, we're handling the current situation very carefully and cautiously to ensure that we can send our son to kindergarten with a relatively clear conscience. My girlfriend has been working from home since the beginning of the pandemic and we've live with in the same house as

Work & Personal Life

It's challenging to balance your job and childcare. My husband and I both work full time and are happy when our four-and-a-half-year-old can go to daycare for at least a few hours a day. In the meantime, we've involved my parents and parents-in-law in the care of our little one. They fill in when we need to work – whether that is in the office or from home. Luckily, my sister and her family live in the same house as us, so my nephew and daughter have each other as playmates. Our employers both offered home office long before the regulation entered into force.

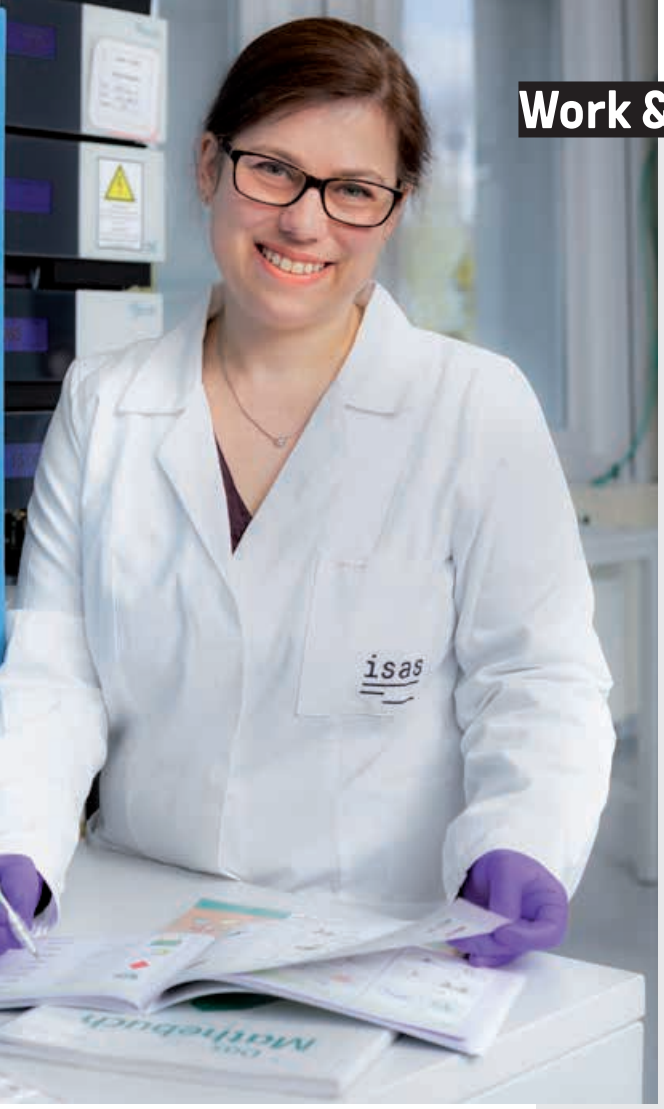
Before, I'd never have thought that working from home could be for me. But I was proven wrong because the communication in our team also works very well in a digital format. When I'm at home, I get up very early and use the time to work before my daughter wakes up. At the beginning of the pandemic, I'd sit at the kitchen table with my laptop. Not long after, I got a desk and set up a real work-station. I want to maintain this even after the pandemic.

The biggest challenge for our family life at the moment is monotony. We simply lack the variety and freedom to go on a trip to the zoo or meet friends. That makes me all the more grateful for my family and for the fact that we all support each other so well in times like these.

Dr. Christina Sengstock,
Research Funding Officer

my in-laws. This helps us in our everyday life. With my job, working from home is not an option, as my work is closely linked to the lab. But the flexible working hours give me the freedom to help out at home spontaneously and without any problems. Needless to say, the situation demands a lot from all of us. During the phases when our six-year-old hardly had any contact with his peers, I was able to take care of him intensively thanks to an early end of the working day and days off. As adults, we try to strengthen each other and bolster our resilience by recharging our batteries in the garden, through sports and video calls with friends, or on trips into nature.

Hannes Raschke,
Engineer Bioresponsive Materials



Work & Personal Life

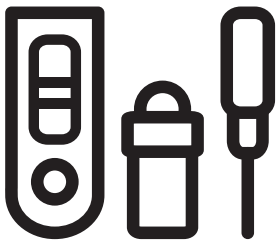
The pandemic demands a high level of compromise on both sides. I've been dividing my working hours more flexibly than before and sometimes I use the school's emergency care so that I can work in the lab. Nonetheless, I pick up my son and daughter as early as possible and try to spend the rest of the day helping with their homework and playing with them. Most evenings, when the children are in bed, I continue working. When I work from home and my ten-year-old and six-year-old are studying at home, my seminars and meetings require mutual understanding. This means that my children have to learn that I can't always be approachable, which can be difficult for a first-grader. My coworkers and superiors understand that the volume is different when working from home, that my concentration might not be the same and that my children might occasionally join me in front of the camera.

The lack of time is the biggest challenge at the moment. Additional time that, without the pandemic, I'd be spending in the lab, and time at home, during which I can't have fun with my children because distance learning challenges all of us. For the time after the pandemic, I wish to maintain my flexibility in terms of working hours and locations – especially when childcare falls through unexpectedly. I'm proud of my children, who have made it through this unique time happily and healthily so far. I'm also very proud of my students and technical assistants, who are always willing to discuss things over the phone and are motivated to carry out their tasks with guidance from afar.

Dr. Yvonne Reinders, Research Associate
Proteomics / Translational Analytics

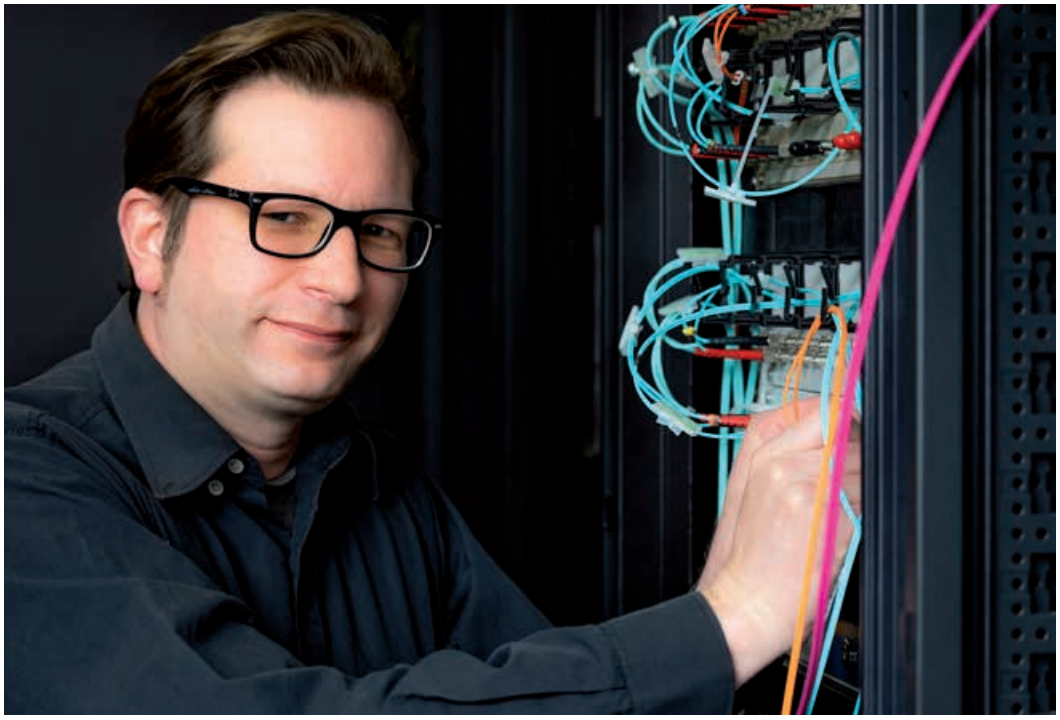
9,100

rapid tests for the antigen detection of SARS-CoV-2 were obtained and performed by the staff members at the institute.



Information as of June 10, 2021

How ISAS Works Remotely



To advance the institute's digitalisation in 2020, Jens Hinrichs relied, among other things, on additional servers.

Research in the home office – what was unthinkable for some scientists before the pandemic became reality for many employees at ISAS in 2020. In order to protect research and infrastructure staff against an infection with SARS-CoV-2, the institute worked out the conditions for mobile working for all employees within just two weeks. This, combined with other safety measures such as shift work in the laboratories, made it possible to limit the number of employees in each office to one person. In this interview, Jens Hinrichs, head of IT at ISAS, reports on the opportunities and challenges of digitalisation during the extraordinary time.

How did you and your team manage to equip the staff to work from home in such a short time?

Hinrichs: We worked hard to make it technically possible for as many colleagues as possible to work from home. We were fortunate that we had prepared our VPN (Virtual Private Network) for intensive use long before the Corona crisis, since under regular circumstances, everyone whose job allows it, can work remotely at least one day a week. Thus, at the beginning of the pandemic, we could quickly enable many staff members to access the internal ISAS services from outside via VPN connection. Since we also have many laptops for training purposes, we were able to equip many colleagues with notebooks for use at home in spring 2020, despite supply shortages at PC manufacturers.

Have more colleagues contacted the IT Helpdesk since the beginning of the pandemic than before?

Hinrichs: Yes, the number of requests we receive by e-mail alone has tripled in 2020. Often, this channel is the fastest way for employees working from home to get in touch with us. We provide support in the event of technical difficulties with video conferencing platforms or advice on problems with accessing the institute digitally.

What defines a good working environment in a home office in your opinion?

Hinrichs: A quiet room with a desk, a comfortable chair and a separate monitor make work much easier. That's why we've provided monitors, for example, so that our colleagues' workplaces also meet ergonomic requirements in the home office. Of course, the technical requirements are also crucial for trouble-free work. A bandwidth internet connection of at least 25 Mbit/s download and 5 Mbit/s upload is ideal. In addition, it's important for video conferences that the response times remain low. Unfortunately, this is often not the case. Despite high connection bandwidth, poor connections may occur because the partner is working from home at the same time or the children are taking part in online lessons. The wrong tariff from the internet provider can also lead to unstable VPN access despite sufficient guaranteed broadband. The reason for this is that some network providers have started to offer so-called DSLite connections, in which several participants share one internet address. This is noticeable through frequent disconnections in the VPN. Some of our colleagues who live in rural regions unfortunately have problems because the broadband expansion in their place of residence is progressing slowly.

»One of the biggest challenges is IT security. Since 2020, we've had a significant increase in attack attempts.«

What purchases has the IT department made since the beginning of the pandemic to digitally upgrade the institute?

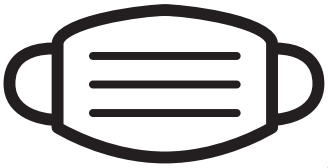
Hinrichs: In addition to laptops and monitors, we've purchased licences for video conferencing platforms and additional servers. We've also added a video conferencing module to our own cloud solution to complement existing services. In addition to the rollout and coordination of the laptops, we permanently have to expand our virtualisation environment in order to be able to provide colleagues with access to scientific evaluation systems, our intranet or to platforms for collaboration in the home office.

What challenges do you see in terms of digitalisation for research institutions the size of ISAS?

Hinrichs: The pandemic has speeded up digitalisation in some areas. For example, meetings via video conference, virtual lab tours or the exchange of scientific data via cloud are now the norm at ISAS. Basically, the challenges lie in the fact that in many areas, digital transformation can only be achieved with a special software, which is often based on expensive and confusing licensing models, burdens staff and tends to be designed for large institutions with several hundred employees. Simple tools that are easy to use and fit the institution are often lacking.

One of the biggest challenges is and remains IT security. Since 2020, we have seen a significant increase in attempted attacks on our IT infrastructure, which we have to prevent and investigate. Regardless of the pandemic, we will need more bandwidth in the near future because of new research projects.

(SR) ■



About 2,000

reusable mouth-nose-protections were organised by the institute in 2020.

Approx. 23,400

surgical masks have been made available for all employees since the end of January 2021; more are on their way.

Information as of June 10, 2021

Virtual Exchange Provides Young Academics with Practical Knowledge

Despite the pandemic, ISAS found a way to hold its traditional exchange with the German-Jordanian University (GJU) in 2020: For the first time, the organisers welcomed the Jordanian students digitally instead of face to face to Dortmund.

Dr. Ahmad Telfah, Dr. Roland Hergenröder and Lubaba Migdadi communicated digitally with the Jordanian students in 2020. One of the topics was the operation of the Halbach magnet – shown here – in combination with the pulse rate calculation developed at ISAS.

The interest in the nine-day 'DAAD German Jordanian (Virtual) School 2020' in December was so high that 35 young academics were admitted, more than twice as many as planned. "Our goal was to bring experiential learning and professional excellence to the students digitally, oriented towards the needs of the market and industry," explains Dr. Roland Hergenröder, head of the working group Bioresponsive Materials and member of the three-person organising team.

Multidisciplinary agenda & enough endurance

From December 9 to 17, 2020, lecturers from Germany and abroad gave talks in various disciplines, including physics, biology, chemistry, industrial engineering and computer science. "Particularly challenging, but at the same time exciting, was the intensive digital support of the participants with their different levels of knowledge, from bachelor to doctoral students," says Lubaba Migdadi from the organising team.

The participants came from the fields of physics, chemistry and chemical engineering, biology, nanotechnology, pharmacy and industrial engineering. They all brought not only a large portion of curiosity, but also enough endurance. Depending on the topic and the speaker, the knowledge was presented in 15 to 120 minutes.

More competitiveness & economic strength

The German Jordanian School is all about practical knowledge that can make a positive contribution to solving problems in Jordan. The young scientists are thus given the tools to strengthen Jordan's industrial and economic position in the future. This year, the focus was on initialising independent Jordanian research groups. The participants practised the systematic use of engineering concepts and methods to transform raw materials into useful products of commercial interest. They also learned new spectroscopic techniques.

Culture & Covid-19

Participants gave positive feedback for the first virtual event: many praised the multidisciplinary content and the integration of scientific, social and cultural topics. Some students expressed the wish to continue the online school at regular intervals, even after the end of the pandemic. "Despite the distance, the participants were able to establish personal contacts and exchange ideas," says Dr. Ahmad Telfah, who supervised the exchange with the GJU for the ▸

ABOUT THE GERMAN JORDANIAN SCHOOL

The German Jordanian School is a cooperation between ISAS and the German-Jordan University (GJU), funded by the German Academic Exchange Service (Deutscher Akademischer Austauschdienst, DAAD). Several joint projects have existed between ISAS and the GJU since 2015. Every year, ISAS welcomes students, graduates and professors in Dortmund for a two-month training programme. Scientists from other institutes and universities also take part every year.

second time. Even though they were not able to meet the participants in person, the team tried to encourage the students to share their thoughts, views and beliefs about their research as well as their cultural and social interests. The German culture was the topic at the end – during a virtual live tour through the city centre of Dortmund.

(PJ) ■

Work & Personal Life

At the weekend, my wife and I plan the coming week. Which appointments are important and not to be disturbed and when do I have to go to the lab? I split up my work. For experiments, I work ahead at home, do the calculations, plan the set-up and make CAD drawings in case I'll be needing parts from the 3D printer later. For the experiments, I go to the lab and then evaluate the data at home. It took me a while to adjust to working from home, but now it works very well. When I work at home, I'm also a primary school teacher for my children until lunchtime. My son is in third grade and usually does his homework on his own. I often sit with my six-year-old daughter to motivate her or answer her questions. Besides my job, I'm also a caregiver and playmate in the afternoons.

Switching between my job and other roles in a short time is a real challenge. Still, working from home makes childcare a lot easier. Fortunately, we also have grandparents who take over homeschooling once or twice a week and also play with the children. For the little ones, the situation is very difficult because the social structure of school is missing. Especially for my daughter, who has hardly had the opportunity to make new friends since she started school, it's not easy. Nevertheless, both children are holding up great – they master the challenges of school and are happy when we're there for them at home. I'm very proud of them. The pandemic also has positive sides: It's nice to be able to spend more time with the family and to experience this time with my children more intensively than would otherwise be the case. So it would be nice to keep one day a week of home office after the pandemic.

Daniel Foest,
PhD Student Miniaturisation

Work & Personal Life

Job and childcare can only work together because I'm able to work from home and arrange my hours flexibly. In between, my sister-in-law supports me by looking after my seven-year-old daughter for a few hours from time to time. When our daughter is doing her homework, we usually share a large desk so that I can quickly help with any questions. This has become a good arrangement and we can work side by side amicably. However, my daughter switches rooms in order for us not to distract each other when I have video conferences. As I was able to borrow a monitor and keyboard from the institute, my home office is well equipped.

The biggest challenge for our family life at the moment is the lack of structure and being together constantly. Where school, work and hobbies usually determine the daily routine, my daughter and I are now often together all day due to homeschooling, pausing hobbies and contact restrictions. For better or worse, I have to take on different roles and, in addition to being a mother, I also have to be a teacher, a playmate, a crisis manager and sometimes a partner in an argument. This is sometimes difficult for both sides. Despite all the obstacles, our daughter tries to make the best of the situation. Her ability to learn and adapt makes me proud.

After more than a year into the pandemic, I'm thankful that we can still enjoy being on the bright side despite all the limitations. I hope that we stay healthy and continue to get through this exceptional time so well. What would I like to take with me for the time after? A little less appointments in my private life. A certain amount of slowing down in everyday life is good. It's nice to be able to enjoy your free time together in the garden or forest without having to look at the clock because you have an appointment at a certain time.

Wiebke Bartels,
Personnel Development Officer

DISEASE MECHANISMS & TARGETS

For research on heart failure, Dr. Elen Tolstik examines tissue sections of mice under the confocal microscope.

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 (► p. 43) for this purpose and test and optimise them.

One focus in the 'Disease Mechanisms and 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 and 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 this 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 2020, 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.

A peptide called 'EDI'

In addition, the researchers have developed a peptide that protects against pressure-induced heart failure without negatively affecting cell survival. The selective inhibition of kinases used for this purpose may be of future interest not only for heart failure but also for cancer therapy, as it has no cardiotoxic effects and has a growth-inhibiting (antiproliferative) effect on cancer cells.

(PJ / SR) ■

Working group Cardiovascular Pharmacology
Prof. Dr. Kristina Lorenz
T: +49 (0)231 1392-103
E: kristina.lorenz@isas.de

Working group Miniaturisation
PD Dr. Joachim Franzke
T: +49 (0)231 1392-174/199
E: joachim.franzke@isas.de

Working group Proteomics
(formerly named Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

ERC group Sulfaging
Dr. habil. Milos Filipović
T: +49 (0)231 1392-4173
E: milos.filipovic@isas.de

Working group Translational Analytics
(formerly named Standardisation)
Dr. Dirk Janasek
T: +49 (0)231 1392-202
E: dirk.janasek@isas.de

Searching for Proteases with Molecular Tools

Enzymes control the majority of biochemical reactions in the human body. But although they are essential for humans, they can also be the cause of many diseases.

Dr. Steven Verhelst works at ISAS and the Institute of Cell and Molecular Medicine at KU Leuven – University of Leuven, Belgium. He conducts research on chemical biology and chemical proteomics.

Scientists in the 'Molecular tools for the investigation of intramembrane proteases' project at ISAS are studying a class of protein-cleaving enzymes, the proteases. Intramembrane proteases (proteases in the cell membrane), including rhomboid proteases, are the particular focus of the work. The researchers are using synthetic chemistry methods in order to study these proteases. "We're developing molecular tools, more specifically activity-based and affinity-based probes that can particularly track the enzymes," reports project leader, Dr. Steven Verhelst. This will give the project group some insight into the physiological and potentially pathological role of intramembrane proteases.

Better adaptation of medications to targets in the future

In 2020, Verhelst's team completed work on ketoamide inhibitors that inhibit rhomboid proteases. They were able to demonstrate that certain parts of the inhibitors, the "primed site" binding elements, are crucial for inhibition. The researchers use these findings together with their chemical toolbox to identify drug binding sites, or targets (▸ p. 26). Using mass spectrometric analyses, the scientists were also able to demonstrate that the probes they developed, for example based on pepstatin A, an aspartyl protease inhibitor, not only label their protease target but also identify other interaction partners such as substrates. In order to facilitate the quick adaptation of complex small molecules to target structures in the future, they studied the reagents for this "late stage functionalisation" during 2020 and have already started their synthesis.

Exchange via enzymes of the immune defence

Another class of enzymes that the research group has been studying in detail over the past year are the neutrophil serine proteases which influence whether the white blood cells (leukocytes) in the immune system perform a protective or pathological function. In an exchange with the Laboratory for Chemical Biology at the University of Leuven, the group developed probes for these enzymes based on phosphonate and phosphinate esters. They have begun to design a method for fluorescence microscopy in which they hope to visualise the activation process of certain leukocytes with the help of esters.

(CMP) ■

Working group Proteomics
(formerly named
Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

Project leader
Prof. Dr. Steven Verhelst
Working group Chemical
Proteomics
E: steven.verhelst@isas.de

TARGETS AND OFF-TARGETS

Every active pharmaceutical ingredient 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 and are to 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 can have an unexpectedly positive impact on a treatment, but often manifests itself as an agonising side effect or concomitant disease for patients.

LipidCreator Software Supports the Diagnosis & Prognosis of Diseases

Researchers are increasingly using the diverse functions of lipids in the human body to diagnose diseases earlier and better predict their progression.

In 2020, researchers at ISAS and the Institute of Analytical Chemistry at the University of Vienna developed the first software for the targeted mass spectrometric analyses of lipids. LipidCreator can be used, for example, to gain insights into blood clotting and the development of thromboses.

The software not only facilitates new studies in health research, but is also suitable for various laboratory environments. At the same time, it serves as a vast library of lipid knowledge. “Following the successes of omics technologies, we have a much broader picture that non-coding biomolecules such as lipids and metabolites influence the regulatory functions of the cell and are thus involved in the development of complex diseases. This is the case, for example, in cardiovascular diseases, neurodegenerative diseases, inflammatory processes or in the metabolic syndrome,” explains Dr. Albert Sickmann, Chairman of the ISAS Executive Committee. Therefore, a research group at ISAS is exclusively concerned with lipidomics and is studying new and continued development of methods that contribute to improved lipid analytics.

(SR)

LipidCreator was developed by the ‘de.NBI/LIFS Associated Partner Project’ and the ‘German Network for Bioinformatics Infrastructure (de.NBI)’. Both projects were funded by the Federal Ministry of Education and Research within the framework of the federal budget (funding number 031L0108A and 031A534B).

GEFÖRDERT VOM

de.NBI GERMAN NETWORK FOR BIOINFORMATICS INFRASTRUCTURE

Bundesministerium für Bildung und Forschung

Flipping Molecular ‘Switches’ for Heart Attacks

Coronary artery disease (CAD, also called cardiac ischemia) is the leading cause of death worldwide, according to the World Health Organisation. It occurs when the heart is not supplied with enough blood, and the heart muscle, or myocardium, can no longer be supplied with sufficient oxygen. This results in a sudden, severe blockage of the heart arteries, which can lead, for example, to cardiac arrhythmias or a heart attack.

The Special Research Field (SRF) 1116 ‘Master Switches in Cardiac Ischemia’ of the German Research Foundation (DFG), in which ISAS scientists are also involved, is studying the phase after an acute infarction on the basis of molecular mechanisms. The aim is to find new therapeutic approaches for reducing complications and late effects of heart attacks, such as permanent cardiac insufficiency. ISAS has belonged to the association of 15 research groups from Düsseldorf and Dortmund since November of 2018 (and thus from the beginning of the second four-year funding period).

Insight into the processes occurring after a heart attack

The researchers at ISAS hope to find new therapeutic targets, such as specific metabolic processes or cell functions. The eponymous ‘master switches’ play a crucial role in the recovery process after cardiac ischemia. “Despite numerous studies, the regulation of and mechanisms for various activation triggers of receptors in the heart are still unclear. We have identified a protein that can initiate its own activation mode,” reports Prof. Dr. Kristina Lorenz. Under her leadership, scientists in the Cardiovascular Pharmacology research group at ISAS are studying the Raf kinase inhibitor protein (RKIP) and its cardioprotective properties. They are investigating how RKIP activates beta-adrenoceptors, which are significantly involved in the muscle function of the heart. The findings from last year’s research can help in the optimisation of known drug target structures and the design of new therapeutic strategies. Consequently,

Funded by Deutsche Forschungsgemeinschaft (DFG) – Project number 236177352-SFB1116.

DFG

Working group
Cardiovascular Pharmacology
Prof. Dr. Kristina Lorenz
T: +49 (0)231 1392-103
E: kristina.lorenz@isas.de

Prof. Dr. Kristina Lorenz commutes between Dortmund and Würzburg, where she heads the Institute of Pharmacology and Toxicology at the Julius Maximilians University, to conduct her research.

for example, the cardiovascular system could be stabilised with medications after a heart attack in such a way that the contraction force of the heart can be increased despite fewer side effects.

ISAS provides multi-omics techniques

The ISAS Proteomics research group provides the experimental models as well as the mass spectrometry-based technologies for the analysis. For example, the institute is supporting the SFB 1116 project with multi-omics techniques for deciphering disease mechanisms. In 2020, the scientists worked with other researchers to analyse the tissue of mice that had lived under different feeding conditions. They were also able to develop a method for quantifying different forms of CD73, an enzyme that protects the heart from an uncontrolled inflammatory reaction after a heart attack, in human cells.

In the fall of 2020, a Liquid Extraction Surface Analysis (LESA™) was also installed at ISAS. This allows a more in-depth mass spectrometric analysis. The researchers hope to use this technique in future to examine tissue after an infarction in order to gain a deeper insight into the mechanisms of cardiac ischemia.

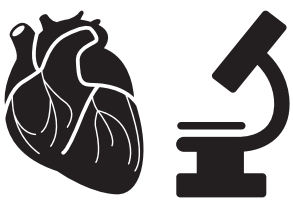
(CMP) ■

»The regulation of and mechanisms for various activation triggers of receptors in the heart are still unclear. We have identified a protein that can initiate its own activation mode.«

At ISAS, Dr. Elen Tolstik searches for the molecular fingerprint with which cardiovascular diseases can be treated more effectively in the future.

Physicist Elen Tolstik Conducts Research for the Heart

There are around 1,400 kilometres between Minsk, home of Elen Tolstik, postdoc at ISAS, and the institute's headquarters in Dortmund. Her way to the city in the Ruhr area led the mother of two young children first to Jena for her doctorate before she came to ISAS in 2018. Since then, the physicist has been working in the groups Cardiovascular Pharmacology and Translational Analytics.



Tolstik is researching biomarkers with which common diseases such as cardiovascular diseases can be detected earlier and better treated. To do this, she uses vibrational spectroscopic imaging and high-resolution microscopy. With these two instruments, the scientist examines lipids and proteins in cells and tissues of healthy and sick mice. How many of these fats and proteins are present when and where in a sample provide information about the cause and course of the disease – like a molecular fingerprint. The animals' therapy and the analysis of the local effects of the drugs in their body are also part of Tolstik's work.

The 36-year-old's research is not only important for the quality of life of people with cardiovascular diseases. Her scientific results help to better understand and treat other diseases with similar deposits of proteins and lipids in the future.

(SR) ■

Deciphering the Effect of Thyroid Hormones in Brain, Liver & Heart

As the central endocrine organ, the thyroid gland produces hormones that are of fundamental importance for the development and function of the human organism.

Working group
Cardiovascular Pharmacology
Prof. Dr. Kristina Lorenz
T: +49 (0)231 1392-103
E: kristina.lorenz@isas.de

Funded by Deutsche Forschungsgemeinschaft (DFG) – project number 424957847-TRR 296.

The special research programme 'Local Control of Thyroid Hormone Action – LocoTACT', led by the University Hospital Essen, is investigating the local control of the effects of thyroid hormones in a joint research network with the University of Lübeck and the Charité – Universitätsmedizin Berlin in cooperation with the Helmholtz Zentrum Munich, the University of Leipzig and ISAS. From 2020 to 2024, the project will focus on how these control mechanisms function, particularly in the brain, heart and liver. During this period, the Deutsche Forschungsgemeinschaft (DFG) is going to fund the special research programme with a total of 13.7 million euros.

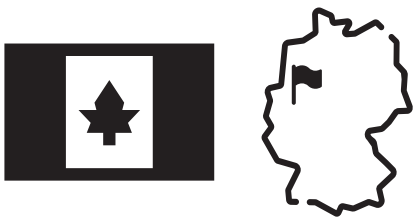
Thyroid hormones and ischemic heart diseases

Brain, heart and liver are starting points for many common diseases such as stroke, heart failure (cardiac insufficiency) or liver diseases (hepatopathy). The scientists at LocoTACT aim to find new therapeutic approaches by deciphering how the transport, metabolism and mechanism of action of thyroid hormones are controlled in the organs. The researchers also explore what effects a disruption would have on these processes. Thereby, they want to find out to what extent a changed local thyroid hormone status in the organs can have a positive effect on common diseases such as "fatty liver". For this, they would like to develop strategies for a therapeutic modification of the tissue- and cell-specific thyroid hormone status and evaluate where thyroid hormones have beneficial effects in disease processes. "The goal is to use the local modulation of the thyroid hormone effect organ-specifically for the prevention and therapy of rare and common diseases. At ISAS, for instance, we're investigating the influence of thyroid hormones in ischemic heart disease. To do so, we'd like to further explore the underlying mechanisms and assess the signal transduction pathways," explains Prof. Dr. Kristina Lorenz, head of the Translational Research department (formerly Biomedical Research) at ISAS.

(PJ) ■

Molecular Phenotyping of Mice – MS Assays Successfully Replace Previous Immunoassays

Mice are the most widely used mammals in health research due to their physiological proximity to humans, ease of breeding, and availability of molecular tools for genetic manipulation.



Models need to be validated and characterised in order to gain new insights into health and disease, new treatment approaches and drug development. In science, this is usually done by determining the concentration of a variety of proteins in the biofluids and tissues of mice. Immunoassays are normally used for this purpose, but they only allow limited statements to be made about individual proteins in a sample. Researchers at ISAS, the University of Victoria and McGill University in Canada have succeeded in replacing laboratory and clinical immunoassays with mass spectrometry (MS) assays in the project entitled, 'Qualitative Proteome Analysis in the Mouse Model'.

New MS assays & proteomic kits

Unlike conventional protein phenotyping techniques, MRM mass spectrometry can be highly parallelised without sacrificing specificity or quantitative precision. The aim of this project was to develop MS assays for 3,000 proteins in 20 mouse tissues in order to increase our knowledge of regular protein concentrations in mouse tissues. The scientists also developed easy-to-use quantitative proteomic kits for 20 different mouse tissues, which they now offer worldwide, plus interpretive aids for the results. "We hope this will increase the scientific reach to eventually achieve in-depth molecular phenotyping of mice, as well as a detailed and complete picture of the full range of proteins in the genome," explains Prof. Dr. Christoph Borchers from the Faculty of Medicine at McGill University.

Project target exceeded

Scientists involved in the project, which ran from July 2016 to the end of 2019, analysed samples of 20 tissues from six male and six female animals from three strains. They performed a total of 5,182 measurements in all tissues, corresponding to 1,691 unique proteins found only in the mouse species. In the first step, they identified 9,601 unique proteins in 42 tissues. Researchers at ISAS synthesised standards for 3,932 peptides corresponding to 1,199 proteins. In the second step, they developed 2,838 assays, corresponding to

1,023 unique proteins for platelets, heart, white fat, serum and mitochondrial proteins. The scientists in Dortmund and Montreal have collectively exceeded the project target of developing 3,000 protein assays with a total of 9,765 assays.

Free knowledge base & kits developed for ongoing research

The scientists have developed a special database for storing and displaying the large amount of data generated during this project. The Quantitative Mouse Proteomics Knowledge Base contains the measured concentration values and related information. The knowledge base is designed to be easily supplemented as results on new proteins, tissues or strains are added from subsequent

Prof. Dr. Christoph Borchers is dedicated to the improvement, development and application of proteomics technologies. His research focuses on techniques for quantitative targeted proteomics for clinical diagnostics.

»The measured protein concentrations are a valuable resource for international researchers who want to use our mouse models to understand complex biological processes.«

analyses. Users can filter all data to focus on, for example, a specific group of proteins, a specific mouse strain, or a gender. Most recently, the scientists have developed a kit that can be used to characterise mouse models in a fundamentally better way than is currently possible with conventional assays, and the results of the analyses help to improve our understanding of diseases and identify a large number of potential targets for drug therapy.

Working group Proteomics
(formerly named
Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

McGill University
Prof. Dr. Christoph Borchers
E: christoph.borchers@mcgill.ca

In co-operation with:
Working group
Translational Analytics
(formerly named
Standardisation)

Exchange & better understanding of diseases

The project enabled the participants to stimulate interdisciplinary exchange between researchers throughout the world by publishing their results in a freely accessible database and the assays as a molecular phenotyping service. “The protein concentrations measured in three mouse strains commonly used in research are a valuable resource for international researchers who want to use our mouse models to understand complex biological processes,” said Borchers.

(PJ) ■

Protein Sequence Provides Insights for the Therapy of Heart Failure & Cancer

In the project ‘Cardio Save Targeting of ERK (ERK-CASTing)’, ISAS, in collaboration with TU Dortmund University and the Lead Discovery Center, is validating a possible drug target for the use in heart failure.

In 2020, the interdisciplinary team led by Prof. Dr. Kristina Lorenz, scientific director of the Translational Research department (formerly Biomedical Research), investigated the role of extracellular regulated kinases (ERK) in pathological cardiac growth. The scientists managed to identify an important protein sequence for the first time. Knowledge gained in this research project could not only help people with heart failure but also benefit cancer patients in the future.

■

This project was funded by the Federal Ministry for Education and Research (Bundesministerium für Bildung und Forschung, BMBF) as part of the “Health Research” programme (funding number 16GW0262K).

GEFÖRDERT VOM

Bundesministerium
für Bildung
und Forschung

PARTICULARS

ISAS & UDE Appoint Anika Grüneboom Professor

Cinnamon? It has nothing to do with baking for Prof. Dr. Anika Grüneboom. The immunologist came to ISAS from the University of Erlangen-Nuremberg during the holiday season. However, she uses cinnamic acid ethyl ester to make bones and tissue transparent all year round.

'Experimental Medical Imaging' is the title of the professorship Anika Grüneboom has been holding at the University of Duisburg-Essen since November 2020.

With her transfer to the institute Grüneboom was concurrently appointed professor at the University of Duisburg-Essen. At ISAS, the 34-year-old has been leading the Bioimaging working group since December. Her research is focused on using 4D analytics to determine biomarkers for early diagnosis or personalised therapy. For this purpose, the Essen native works, for example, with the light sheet fluorescence microscope to simultaneously map information on different classes of molecules and their three-dimensional distribution patterns. "With the usual bioanalytical laboratory methods, cells or biomolecules are isolated from tissue samples in order to examine them. However, this means that all information about their spatial location is lost," Grüneboom explains. How relevant the location is, can be seen, for example, in cardiovascular diseases. In the case of a heart attack, the molecular and cellular composition of the affected tissue areas of the heart change massively compared to healthy areas.

Working group Bioimaging
Prof. Dr. Anika Grüneboom
T: +49 (0)231 1392-239
E: anika.grueneboom@isas.de

ERC Grantee Milos Filipović Joins ISAS

Dr. habil. Milos Filipović's associations with hydrogen sulfide are far beyond the smell of rotten eggs. For him, the gasotransmitter is a core subject of his research.

With Dr. habil. Milos Filipović joining ISAS in October, the institute gained a top researcher for Germany as a science location. The biochemist arrived here from Bordeaux, and not only did he bring tissue samples and model organisms with him, but also an EU grant of two million euros for his excellent research on ageing processes.

Filipović conducts research in the fields of biochemistry and neuroscience. He has already received several awards for his work – most recently the European Research Council (ERC) Consolidator Grant. At ISAS, the 39-year-old heads the Sulfaging group in the Translational Research department. With his team, he investigates the connection between ageing processes and so-called gasotransmitter signalling. In this context, the biochemist focuses on signal transmission in cells using hydrogen sulfide. Working in this young research area, the ERC grantee aims to decipher the precise mechanisms of hydrogen sulfide actions, for example with the help of transgenic worms. Filipović's research on metabolic biochemistry provides important insights that will enable a better diagnosis and treatment of age-related diseases in the future.

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).

ERC group Sulfaging
Dr. habil. Milos Filipović
T: +49 (0)231 1392-4173
E: milos.filipovic@isas.de

GASOTRANSMITTERS

Gasotransmitters include the gases hydrogen sulfide, nitric oxide and carbon monoxide. They act as signaling substances within and between cells and play an important role in the human body, for example in controlling the heartbeat or nerve activity.

Announcement of a Joint Professorship in Bioinformatics

Bielefeld University and ISAS are expanding their cooperation in research and teaching and aim to strategically complement each other in bioinformatics, bioanalytics and biomedicine. The common goal is to contribute to personalised medicine.

Setting the seal on a new cooperation in 2020: Prof. Dr. Markus Nebel and Prof. Dr. Ing. Gerhard Sagerer of Bielefeld University along with ISAS' Prof. Dr. Albert Sickmann (in the middle).

As a first step, the partners announced a joint junior professorship for multidimensional omics analyses in December 2020. It is based in bioinformatics and the future junior professor will work on methods for analysing and visualising measurement data that provide insights into the human body at the genomic level. In conjunction with the professorship, a research group at ISAS will be established.

■

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 developing and validating 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.

Studies on thymomas successfully completed

In 2020, the scientists successfully completed studies on the chemosusceptibility of thymomas (tumours of the thymus gland), i.e. the susceptibility of tumour cells to specific chemotherapy. For this purpose, they generated various spheroids on the basis of patient samples and combined NMR and fluorescence measurements to obtain information on the toxicity of different chemotherapeutic agents on 2D and 3D cell cultures. Only a quarter of all thymomas are malignant. Thymic carcinoma is a rare cancer, and the number of available patient samples is small. Therefore, techniques that do not consume the biopsy material are important, and NMR spectroscopy has the advantage of being non-invasive. The researchers were able to complete a combined expression and NMR metabolome study on thymomas and thymic carcinomas, respectively, thereby contributing to a better classification of malignant thymomas and an improved understanding of the differences. The combined measurements helped to draw a consistent picture of the different groups of tumours.

Platform for faster development of techniques

In order to simplify specific methods for the analysis of a large number of proteins in metabolism and signal transduction using mass spectrometry-based proteomics, the scientists developed the 'STAMPS' (Simple Targeted Assays for Metabolic Pathways and Signalling) platform in 2020.

This speeds up the development of a targeted assay, because the information for it can be evaluated in real time using the software.

(SR) ■

Working group
Bioresponsive Materials
Dr. Roland Hergenröder
T: +49 (0)231 1392-178
E: roland.hergenroeder@isas.de

Working group Proteomics
(formerly named
Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

Working group
Translational Analytics
(formerly named
Standardisation)
Dr. Dirk Janasek
T: +49 (0)231 1392-202
E: dirk.janasek@isas.de

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, it 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.

Blood Test for Drug Allergies Increases Patient Safety

How can we detect drug allergies better? Current diagnostic methods such as skin tests are time consuming and often suitable only for a few active ingredients. Moreover, in some rare cases, severe allergic reactions can occur.

Unlike these tests, in vitro methods (laboratory tests) are harmless, as patients only need to have some blood taken. In the project 'INA' (In-Vitro-Nachweis Arzneimittelallergien) for the in vitro detection of drug allergies, ISAS, the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM), RWTH Aachen University Hospital and Life & Brain GmbH Bonn are developing a new blood test for the detection of allergies that is safe for patients and fast at the same time.

(SR) ■

Working group Proteomics
(formerly named
Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

This project was supported by funds from the European Regional Development Fund (ERDF), funding reference EFRE-0801772.

EUROPÄISCHE UNION
Europäischer Fonds für
Regionale Entwicklung

EFRE.NRW
Investitionen in Wachstum
und Beschäftigung

Deciphering the Penmanship of Neuromuscular Diseases: Improved Diagnosis through Gene & Protein Signatures

The term neuromuscular diseases (NMD), commonly known as muscular atrophy, encompasses all diseases that affect the interaction of nerves and muscles. They can be of a genetic or idiopathic (without an identifiable cause) nature and are very rare and incurable. These diseases, which include polyneuropathies, spinal muscular atrophies, and Duchenne muscular dystrophy, are characterised by a progressive weakness of the skeletal muscles and, frequently, of the cardiac or respiratory muscles.

Dr. Andreas Hentschel is investigating patterns of gene and protein co-regulation in order to narrow down the genetic defect in neuromuscular diseases more precisely than was previously possible.

The diagnosis often comes late, which delays or even prevents treatment. This limits the quality of life of those affected and increases their mortality. A more precise understanding of the molecular causes of these NMDs is needed in order to improve the treatment options, which are currently limited. Gene and protein signatures can revolutionise the diagnosis of NMD patients and improve genetic counselling. Several research groups (Proteomics and Translational Analytics) at ISAS are therefore collaborating intensively on NMD research.

Prediction of genetic defects & new classification

The researchers are making use of muscle biopsies from patients to generate new proteomic and morphological data by applying omics technologies (▸ p. 43). In the first step, they quantify the causative (i.e. pathogenic) proteins, and in the second step, they compare the results of the measurement with the results of the DNA analysis. The data from ISAS then becomes part of an algorithm. “This algorithm has made it possible, for the first time, to identify patterns

of gene and protein co-regulation in NMDs, allowing the pathogenic genetic defect to be narrowed down much more precisely, if not predicted exactly," explains Dr. Andreas Hentschel, a member of the Translational Analytics research group.

In conjunction with histological-biochemical characterisation by means of biospectroscopy, this allows a new classification of hereditary and acquired NMD disorders. This facilitates the tracing of the underlying pathomechanism, the causal chain of bodily processes leading to disease. This is particularly important for the testing of new therapies.

Established procedure & increased efficiency

In 2020, the researchers processed approximately 300 samples from patients with different genetic neuromuscular diseases and subsequently examined 100 of them using global proteomics. "We achieved our annual goal of completing the analyses using global proteomics. We also mastered the challenge of quickly tailoring the purification of the samples, as they originate from many different hospitals," summarises Hentschel. The mass spectrometric measurements were performed in 'data independent acquisition' (DIA) mode. The scientists evaluated the results using the spectra library they had previously created. In this way, they were able to increase the efficiency of the analysis by approx. 10 to 40 percent compared to the previously common procedure, data dependent acquisition (DDA). In addition, scientists began to further their research into idiopathic NMD disorders. By the end of the year, the inventory already included 140 samples.

»We achieved our target for the year by completing the global proteomic analyses.«

Using CARS microscopy, ISAS researchers have examined more than 80 patient samples (160 muscle biopsy sections in total) from various disease entities since the project started in 2019. In the process, they made overview measurements and detailed measurements. The researchers recorded the muscle fibre calibres of 73 patient samples, evaluated the spectra of 40 samples and used computer-assisted methods for 34 samples. These include the description of intensity ratios between different wavelengths and non-linear unmixing according to Heylen et al. With this unmixing, "pure" spectra are unmixed from the raw spectra, which are usually mixtures of spectra from different substances, and the abundances based on these spectra are displayed in the image or recording.

Working group Proteomics
(formerly named Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

Working group Translational Analytics
(formerly named Standardisation)
Dr. Dirk Janasek
T: +49 (0)231 1392-202
E: dirk.janasek@isas.de

Targeted assays established

The researchers have succeeded in establishing a targeted assay, a standardised reaction procedure for the detection of gene and protein signatures, using LC-MS-MS (liquid chromatography in combination with mass spectrometry), which has a high degree of sensitivity and specificity. At the same time, the researchers developed another method that considerably shortens the measurement time. They have already used both assays on patient samples to detect the regulation of 74 neuromuscularly relevant proteins.

They also worked on an additional 110 proteins out of the total of 380 known proteins of neuromuscular relevance in 2020. The scientists have already completed the pre-selection and verification of the proteotypic peptides of these proteins and could start the synthesis of the isotopically labelled standard peptides in 2020.

(PJ)

OMICS TECHNOLOGIES

The term omics is used in research 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.

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 ERDF-0801301.

EUROPÄISCHE UNION
Europäischer Fonds für Regionale Entwicklung

EFRE.NRW
Investitionen in Wachstum und Beschäftigung

Against the Current: A Way Back to Basic Research

Suyuan Chen (30) is a chemical biologist specialising in chemical proteomics. After his graduation from the Chengdu Institute of Biology (Chinese Academy of Sciences) in organic chemistry and medicinal chemistry, he began his doctorate at ISAS in 2017. In the interview, the visiting scientist opens up about the characteristics of his work in Dortmund and what he currently longs for.

You're part of the Proteomics working group. What are you researching now?

Chen: In the Proteomics working group, we're developing chemical tools for protein post-translational modifications research, biomarker imaging as well as therapeutic targets profiling. The latter refers to disease-causing molecules to which drugs can dock. We also work on identifying off-targets. These are binding sites with which active pharmaceutical ingredients interact, although they are not actually intended for this. The information on off-targets can help avoid side effects and serious consequences for patients early in drug development. For example: I'm currently developing some multi-functional tools for breast cancer diagnosis.

Why did you choose to come to ISAS to obtain your PhD?

Chen: One of the interdisciplinary projects at ISAS, which deals with the mapping of drug binding sites and off-targets, fascinated me! That's why I applied to the Chinese government for a scholarship. Being part of an interdisciplinary project and working with biologists, chemists and bioinformaticians is one of the best aspects of my work at the institute.

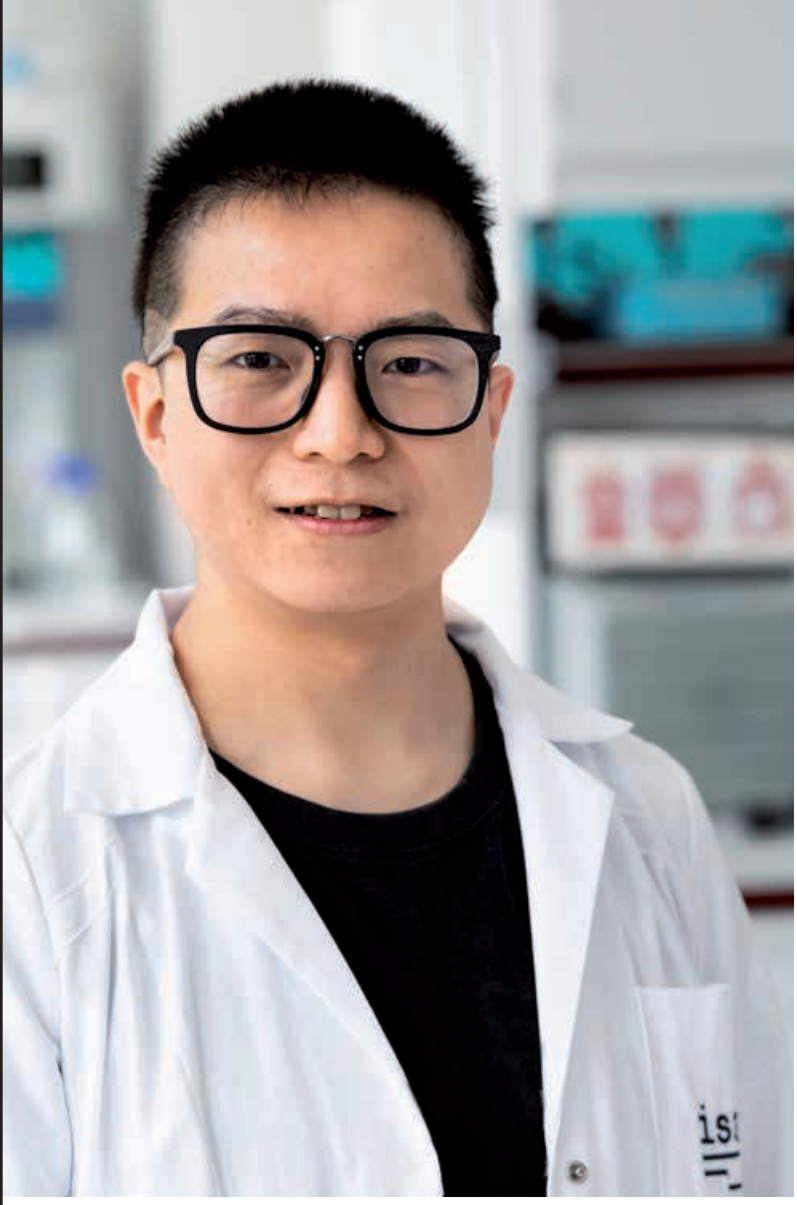
What does your typical day at ISAS Campus look like?

Chen: In the morning, I monitor the synthesis of chemical probes in the lab and in the afternoon, I measure biological samples with the mass spectrometer, more precisely with the Orbitrap™. In the evening, I have to analyse the profiling data. Working on such an interdisciplinary project challenges me. You have to function well in the team, have the courage to learn something new at any time and, above all, be open to other points of view. Of course, all of this is a challenge, but it is also lots of fun.

»I can't find the taste of my hometown anywhere else.«

Does the work that you do here differ from your research in China?

Chen: Before coming to the Chinese Academy of



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.

Suyuan Chen comes from Mianyang, a city in the province of Sichuan, which is famous for its spicy cuisine and variety of aromas. Since the beginning of the pandemic, he has not been able to visit his family and keeps in touch with them via video call instead.

Sciences, I studied Pharmaceutical Engineering. Afterwards, I was a medicinal chemist and worked in a joint department of the Chinese Academy of Sciences and a local pharmaceutical company (Chengdu Di'ao Pharmaceutical Group Co. Ltd.). There I mainly focused on clinical needs in China and developed cancer therapies. In Dortmund, I identify targets for cancer therapies. This application-oriented basic research is

Working group Proteomics
(formerly named
Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

the scientific preliminary stage of what I used to work on in China. You could say right now, I'm like a salmon swimming against the current, upstream. In my case, that's basic research. My experience in both areas allows me to see things from a different perspective. This knowledge is very helpful for my work here in Dortmund.

Is there anything particular that you miss about China?

Chen: Hot-Pot and Mianyang Rice Noodle! I was born in a spicy town. I can't find the taste of my hometown Mianyang anywhere else.

You're a member of the Chinese-German Chemical Association (CGCA). One of the CGCA's goals is to promote science communication amongst their members. How important is science communication for you personally?

Chen: Science communication is very important and I can hardly imagine my professional but also private everyday life without it. Because I'm into biomedical research, friends have been asking me for advice since the beginning of the pandemic. They've been asking me whether they should wear a mask or take chloroquine, an active ingredient from the group of antimalarial drugs, as a precautionary measure. The pandemic is unsettling people, and there's a great demand for scientifically sound answers. But even without the current exceptional situation: science communication can increase public appreciation and understanding of science. As researchers, we should therefore attach importance to a good communication of our work and to the dialogue with the public.

»As researchers, we should attach importance to the dialogue with the public.«

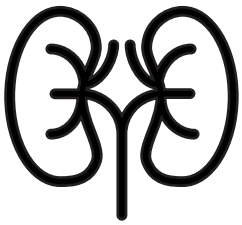
You're staying in Dortmund until September 2021 – what are your plans for the time after?

Chen: The European Proteomics Infrastructure Consortium providing access (EPIC-XS) has funded an idea from our research group, so I've planned a research stay in the Netherlands. I'd like to continue working as a postdoc in Germany or Europe after that, because I appreciate the conditions for scientists here.

(CPM / SR) ■

Optimisation of Anaemia Therapy for Patients with Chronic Kidney Disease

More and more people are suffering from chronic kidney disease (CKD). More than ten percent of the population in this country, around 8.3 million people, are affected by CKD.



Working group Proteomics
(formerly named
Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

Reduced kidney function leads to anaemia in many patients. The cause of this renal anaemia is a reduced production of the hormone erythropoietin (EPO), which is responsible for the formation of erythrocytes (red blood cells). Thus, CKD sufferers also experience inflammation and iron deficiency.

Up to now, patients have received EPO or other erythropoiesis stimulatory agents (ESA) for therapy. However, those with advanced CKD are at particularly high risk for thrombosis, heart attack or stroke with these medications. Individual patient factors play a major role in the success of the therapy. In order to improve treatment for anaemia, researchers involved in the project entitled, 'Model-based Optimisation of Anaemia Treatment for Individual Patients with Chronic Kidney Disease' (NephrESA) are developing a computer model that can be used to determine risks and prognoses for medication for each individual patient. The aim is to use this knowledge to enable personalised, and ultimately improved, treatment of anaemia for nephrology patients.

Results from analytics find their way into clinical application with the aid of a computer model

In order to optimise the application and dosage of drugs containing EPO and to improve their adaptation to individual patients in the future, scientists at ISAS are conducting an initial investigation into the complexity of interactions, inflammatory processes, changes in the regulation of iron metabolism and, for example, the risk of thrombosis in CKD patients. The findings will then be incorporated into mathematical models, so that doctors will be able to make reliable prognoses for therapies that are individually tailored to anaemia patients in the future.

NephrESA is funded by the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF) and coordinated by Dr. Timmer (University of Freiburg). The partners in the collaboration are the German Cancer Research Centre (Deutsches Krebsforschungszentrum, DKFZ) in Heidelberg with Dr. Ursula Klingmüller, the University Hospital Heidelberg with Dr. Martina Muckenthaler, the University Medical Centre Hamburg-Eppendorf (Universitätsklinikum Hamburg-Eppendorf, UKE) with Dr. Tobias Huber, and ISAS.

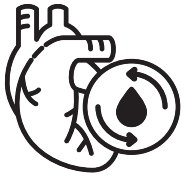
(SR)

GEFÖRDERT VOM

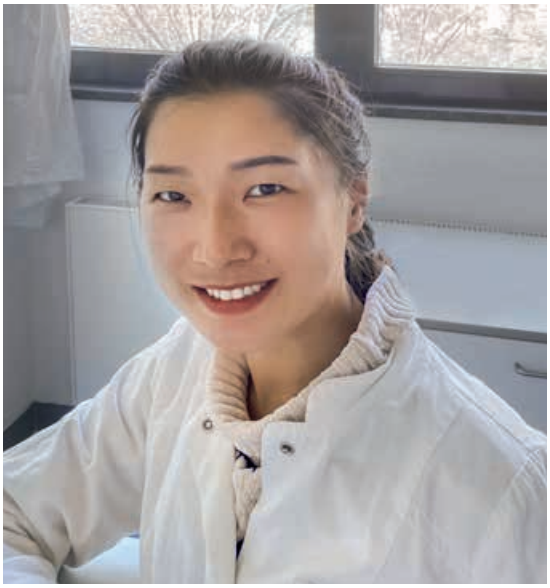
Bundesministerium für Bildung und Forschung

This project was funded by the Federal Ministry of Education and Research within the framework of the federal budget (funding number 031L0191D).

Doctoral Students Are on the Trail of Thrombo-Inflammation



Changes in demographics are a major challenge to healthcare systems worldwide. As we age, the risk of many health conditions increases, including one of the leading causes of death worldwide, according to the World Health Organisation: cardiovascular disease.



Pengyu Zhang is participating in 'TICARDIO' for her PhD. She is working on test methods that can be used to quantify the tyrosine-protein kinase SYK for ISAS.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement number 813409.

EUROPÄISCHE UNION
Europäischer Fonds für Regionale Entwicklung

If the finely tuned interaction of the cells in the vascular system is disturbed, this can promote inflammation and blood clots (thromboses). Since the end of 2019, the European-funded collaborative project 'TICARDIO' (Thrombo-inflammation in cardiovascular disease) has been investigating these two processes, which were previously studied independently of each other, together for the first time under the term 'thrombo-inflammation'. The approach taken in this project focuses on the key interactions between the vascular wall and the blood, which play a crucial role in pathological processes in cardiovascular diseases. In the long term, the researchers hope to find new targets for pharmaceutical substances and specific diagnostic markers. Under the direction of Dr. Albert Sickmann and the mentorship of Dr. Fiorella Solari, ISAS is supporting the research of two female doctoral students for three years with the Disease Mechanisms and Targets research programme.

Understanding platelet regulation in thrombosis

In healthy vessels, endothelial cells produce substances that are involved in the regulation of blood pressure and blood flow. In

order to better understand these processes and their role in the development of thrombosis, Pengyu Zhang is working at ISAS on the proteomic investigation of human blood platelets, the thrombocytes. “I focus on the endothelial-derived inhibitory and activating pathways of platelets in thrombosis,” Zhang explains. She aims to develop a phospho-targeted mass spectrometry (MS)-based assay to quantify key mediators of these pathways, such as the tyrosine-protein kinase SYK. In 2020, she was already able to detect the total SYK protein and three different phosphorylated sites. Optimised purification of the kinase for mass spectrometric analysis should further improve the work flow in future. Another goal of the scientist is to study the different variants of phosphorylation sites using ion-mobility spectrometryn.

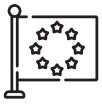
Development of a vessel-on-a-chip model

The second TICARDIO project in which ISAS is participating is dedicated to the development of an inflammatory vessel-on-a-chip model. The project aims to shed light on how endothelial cells affect thrombus formation and clotting. The scientists at the Cardiovascular Research Institute Maastricht (CARIM) at Maastricht University assume that the mutual reinforcement of dysfunctional platelets and endothelial cells contributes to thrombo-inflammatory diseases. In 2020, they were able to establish a reproducible model that facilitates the study of thrombus formation and clotting in the blood in the presence of endothelial cells. The researchers were able to mimic acute inflammatory situations and examine them using multicolour confocal microscopy. In future, they hope to have success in mild inflammatory settings such as atherosclerosis. To this end, they wish not only to simulate chronic vascular diseases, but also subsequently detect differences at the proteome level using liquid chromatography-mass spectrometry.

(CPM) ■

Working group Proteomics
(formerly named
Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

About TICARDIO



TICARDIO is a European funded “Innovative Training Network” (ITN) for the collaborative training of doctoral students. The ITN offers 15 doctoral candidates in the sciences the opportunity to develop scientific and general competences within an international network. The aim of the EJD (European Joint Doctorate) variant is the awarding of a joint doctoral degree and multidisciplinary and inter-sectoral cooperation in doctoral training among the participating institutions. The network is coordinated by the Centre for Thrombosis and Haemostasis (CTH) at the University Medical Centre Mainz; in addition to ISAS, the academic partners include the Cardiovascular Research Institute Maastricht (CARIM) in the Netherlands, and the Aix-Marseille University in France. The European Commission is funding the ITN as a Marie Skłodowska-Curie action with four million euros over 48 months.

PROMOTION OF YOUNG SCIENTISTS

Vignane appreciates the interdisciplinary approach and access to the most modern research instruments and methods in Germany. Besides his interest in ageing processes, he loves drums and saxophone – he plays both instruments himself.

Thibaut Vignane did not yet get as close to the International Space station as he does in this photo. However, his research brings him closer to achieving his dream of putting humans into a state of hibernation.

“I’d like to help induce the hibernation of the human body”

ERC group Sulfaging
Dr. habil. Milos Filipović
T: +49 (0)231 1392-4173
E: milos.filipovic@isas.de

Thibaut Vignane (24) from Lyon in France has been working as a PhD student in the ERC group Sulfaging since October 2020. Before the biologist came to Dortmund, he studied at the University of Bordeaux. His dissertation deals with the role of the so-called protein persulfidation in ageing processes. Vignane's goal is to shed light on the molecular mechanisms by which persulfidation controls the ageing of human cells. In the interview, he explains what this has to do with space travel.

How did you first become interested in your research area?

Vignane: During my bachelor studies, I did an internship with Dr. Milos Filipović. That's how I discovered the hydrogen sulfide and persulfidation field. At the same time, I also got really interested in genetics. I was very happy when Dr. Filipović offered me an opportunity to combine my then newly discovered passion for genetics with the field of H2S, as we call hydrogen sulfide, and ageing. That's how I came to write my master's thesis on this topic.

What are you particularly keen on finding out?

Vignane: I'm generally interested in molecular biology and in understanding the mechanisms through which cells can regulate their functions. However, learning more about the specific mechanisms of ageing on the molecular level is something that interests me in particular. Since ageing is a mix of very complex and interconnected mechanisms, studying it is very challenging – but that's what additionally fuels my interest.

What is the topic of your work at ISAS?

Vignane: As the ageing field is very large, I'm focussing my research on two aspects right now: The first one is related to the change of persulfidation levels during ageing. Persulfidation is the posttranslational modification of the cysteine residue, which has been shown to play a role in ageing. The second aspect is to assess the role of the protein persulfidation on the telomere attrition process which occurs during ageing.

Are there animal experiments involved in your research?

Vignane: We work with rats and mice, albeit in collaboration with other working groups. We're currently studying changes in persulfidome in the ageing brains of mice. In addition to mice, I also work with Caenorhabditis elegans, a worm that is widely used to study ageing. Due to its relatively short life, it's the perfect model organism for our analyses.

What do you hope to accomplish with the results?

Vignane: The knowledge gained could lead to a huge advancement in many fields, because it could help cure some rare diseases. In my opinion, rare diseases are as important as common diseases for which more research is being conducted. Right now, our group is working on a very rare disease called Werner Syndrome (WS). WS is the most common of the premature ageing disorders. We believe that H2S might play an important role in the treatment of this accelerated ageing disease.

My greatest wish is that my research will enable a better understanding of how H2S controls the sleep-like state in our body. One day, I'd like to help induce the hibernation of the human body with my research and fulfil the dream of space travel for recreational purposes.

(RJ) ■

PhD Workshops: Elevating Science

With masks and a lot of fresh air, but in person. This is how the PhD workshops for 16 students could take place at ISAS from September 23 to 25, under the conditions of the Corona Protection Ordinance.

The event is part of the institute's own graduate programme. The aim of the curriculum, which spans three years, is to gain basic knowledge of interdisciplinary scientific work in an international context. In addition to ethical and legal principles such as the "rules of good scientific practice" or the protection of intellectual property, participants learn how to communicate their own research results and gain knowledge of intercultural cooperation. Each year, the doctoral students evaluate the workshops and external speakers: "This allows us to adapt the seminar content to our doctoral students' needs and to integrate current developments," explains Wiebke Bartels, Human Resources Development Advisor.

In 2020, the seminars for second-year doctoral students focused on scientific writing, project management as well as patent law and -research. The workshop 'Scientific Writing' was particularly useful for the young scientists. "In a short amount of time we received many tips on the use of language and on writing scientific texts in English that we practiced together. The course was not only informative, but also entertaining," Alexander Knodel sums up. Although group work was hardly possible due to the pandemic, Knodel draws a positive balance for the face-to-face event.

Especially popular: "Elevator Pitch"

For third-year doctoral students, ISAS offered courses on career development, "Proposal Writing" and "Elevator Pitch". This training for a presentation in the length of an elevator ride was the most popular among the participants. "We learned to put our research in a nutshell in a way that is also understandable for lay people," says Julia Lill. According to her, it was a bit unusual to be filmed during the pitch at first and then having to analyse the recording together, but the feedback from the trainer and the exchange in the group were very valuable.

Structured doctoral training at ISAS

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

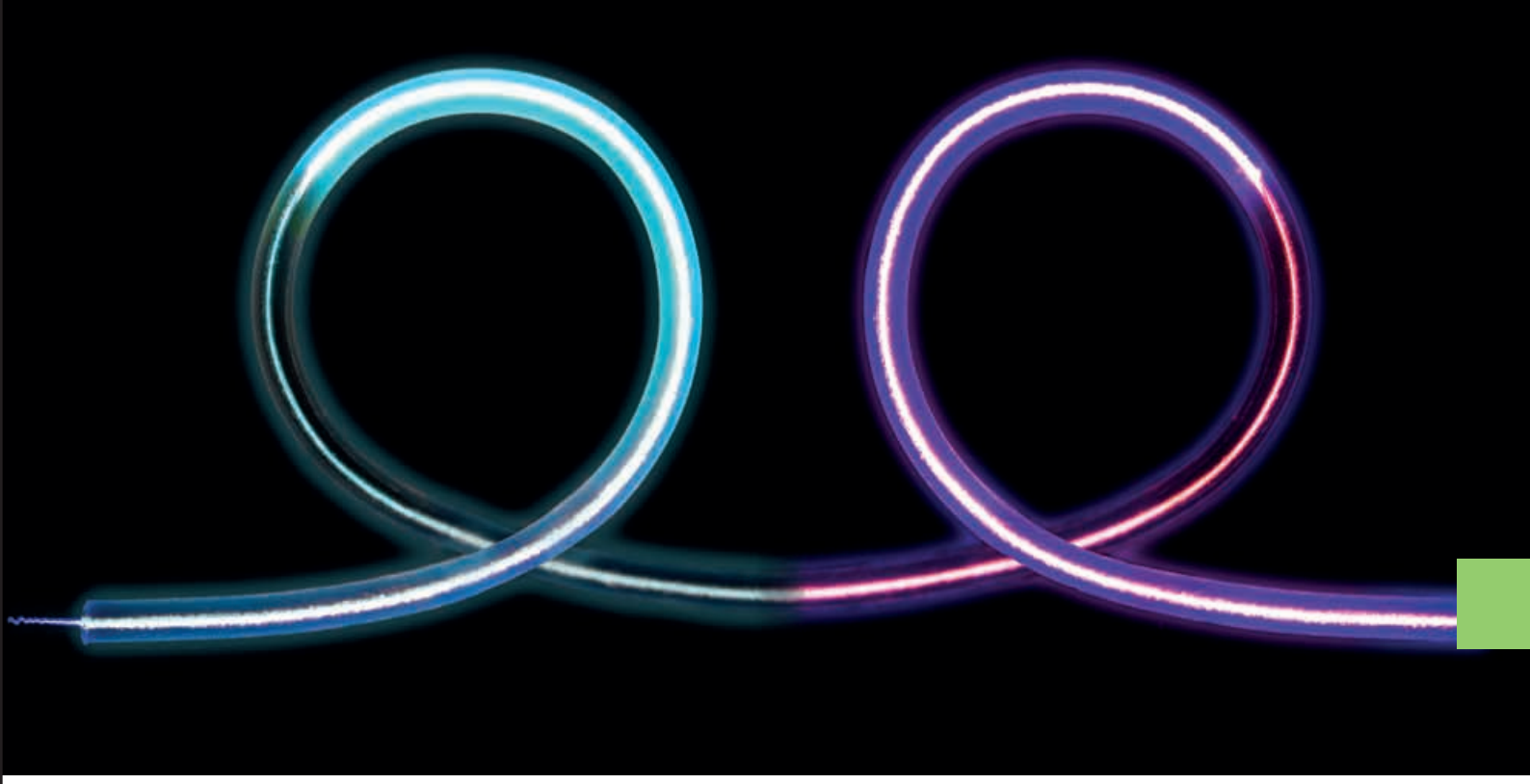
Keeping distance and wearing masks – but at least the 2020 PhD workshops could take place together and on-site.

Above: Wiebke Bartels, Personnel Development Officer.
Below: Julia Lill, PhD student in the Bio-Fluorescence working group.

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. However, progress in the work for a doctorate and the requirements of structured doctoral training do not always proceed in a linear manner. “As long as scientists complete the curriculum in the first three years of their doctoral phase, we are flexible, if only for organisational reasons. In 2020, for example, there were only three first-year PhD students, so they took the courses in the second year of the PhD. Next year, we’ll switch,” says Bartels.

(PJ) ■

»We learned to put our research in a nutshell in a way that is also understandable for lay people.«



The Flexible Microtube Plasma in use with the noble gases argon and helium.

What's Happening Here, Dr. Brandt?

This picture was taken in September in one of the labs at ISAS City. You can see my colleague, Daniel Foest, and me demonstrating the versatility of our highly miniaturised, flexible microtube plasma for the cover photo of my dissertation. For my doctorate, I researched new and efficient ionisation sources. The result of my work is the Flexible Microtube Plasma (FμTP) which, in combination with a nano-electrospray, combines sample delivery and ionisation in one setup for the first time. The FμTP, also known as looping plasma in our working group, is highly miniaturised, but robust as well as versatile and safe to use. It's also compatible with various discharge gases like argon, nitrogen or helium. Complex samples with numerous analytes like cholesterol can be analysed safely and efficiently with the FμTP. We've applied for a patent for this invention.

Dr. Sebastian Brandt,
Postdoc Miniaturisation

Working group Miniaturisation
PD Dr. Joachim Franzke
T: +49 (0)231 1392-174/199
E: joachim.franzke@isas.de

Adriana Schneider Aims to Make Proteome Analyses More Efficient

Adriana Schneider is regularly in the laboratory due to her master's thesis. There the 30-year-old knows every move.

Gaining more practical experience in science, that is Adriana Schneider's goal. When the master's student (bioengineering) learnt about ISAS in a lecture at TU Dortmund University, she decided to write her thesis here. Since November 2020, the japan-loving 30-year-old has been part of the Proteomics working group. She spends six to eight hours a day working in the laboratory.

Schneider is working on optimising the analyses of biological samples. For her master's thesis, she researches methods of proteome analyses based on the connection of liquid chromatography and mass spectrometry (LC-MS).

Fast analysis & high sample throughput

As high throughput is important for the analysis of clinical samples and in pharmaceutical research, Schneider wants to figure out which combination of LC-MS-methods and acquisition times provides the highest quality results with the shortest possible measurement times. For this, she considers all steps of the analysis: preparing the samples, handling and maintaining the LC-MS systems and evaluating the results are part of the junior researcher's everyday work. Finally, she examines the analytical depth, meaning the quality, of the data obtained and checks whether the results are reproducible. Through her work, she hopes to help increase sample throughput in

Working group Proteomics
(formerly named
Protein Dynamics)
Prof. Dr. Albert Sickmann
T: +49 (0)231 1392-100
E: albert.sickmann@isas.de

clinical and biomedical research. Schneider aims to submit her thesis in the summer of 2021. After that, the Dortmund researcher would not only like to broaden her Japanese language skills but also to continue working in the field of bioanalytics.

(CPM) ■

What's Your Task as an Intern, Christopher?

Christopher Borg liked his internship so much that he continued to work at ISAS as a student assistant.

Christopher Borg (24) studies Environmental Monitoring and Forensic Chemistry at the Hamm-Lippstadt University of Applied Sciences. During his internship at ISAS, he worked in the Miniaturisation group and investigated the influence of the inside diameter of an ionisation chamber developed for the Flexible Microtube Plasma (FμTP) on ion mobility spectrometry.

At ISAS I am working on... using a miniaturised plasma as an ion source for ion mobility spectrometry.

It has happened to me in the laboratory that... I wasn't careful enough and accidentally knocked a few things over. After that, I was really awake.

My highlight every day is... the cup of coffee in the morning, which is also the only constant – because every day, there are new things awaiting me in the lab.

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 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, the University of Duisburg Essen, Bielefeld University and Technische Universität Berlin.

The CARS microscope is one of the instruments used by scientists such as Prof. Dr. Anika Grüneboom in the Bio-Imaging research programme.

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 & 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.

CARS group successfully completes work

A junior research group founded by the Leibniz Research Cluster and funded by the Federal Ministry of Education and Research (BMBF) was also involved in the research programme from 2015 to 2020. The CARS microscopy group led by Dr. Erik Freier successfully completed its work last year. Its task was to develop methods for the measurement of complex metabolites and enzyme activities in minute amounts of liquid based on CARS microscopy. The principal focus of research was online analytics with non-destructive, or alternatively, slightly-destructive techniques such as the analytical methods with capillary electrophoresis (CE) and microfluidic free-flow electrophoresis mass spectrometry (µFFE-MS) that were developed. These are basic technologies that enable direct online analysis with minimal sample consumption and the simultaneous purification or separation of samples. With online analytics, errors in the process can be detected immediately and corrected if necessary, without having to destroy an entire product batch afterwards. The successes of the project also include nine degree theses, thereof two bachelor's theses, four master's theses and three doctoral dissertations written by students in cooperation with universities and universities of applied sciences on the development, application and transfer of the methods.

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. The new group headed by Prof. Dr. Anika Grüneboom aims to elucidate molecular and cellular processes underlying immunovascular interactions under inflammatory conditions.

The researchers will 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.

(SR) ■

Working group
Bio-Fluorescence
Prof. Dr. Matthias Gunzer
T: +49 (0)231 1392-1403
E: matthias.gunzer@isas.de

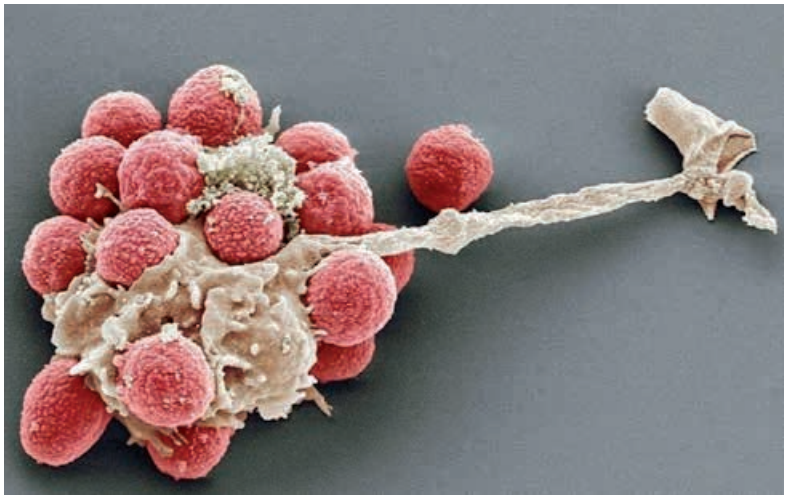
Working group Bioimaging
Prof. Dr. Anika Grüneboom
T: +49 (0)231 1392-239
E: anika.grueneboom@isas.de

Junior research group
CARS-Microscopy
(2015 to 2020)
Dr. Erik Freier

Working group
Cardiovascular Pharmacology
Prof. Dr. Kristina Lorenz
T: +49 (0)231 1392-103
E: kristina.lorenz@isas.de

Working group Miniaturisation
PD Dr. Joachim Franzke
T: +49 (0)231 1392-174/199
E: joachim.franzke@isas.de

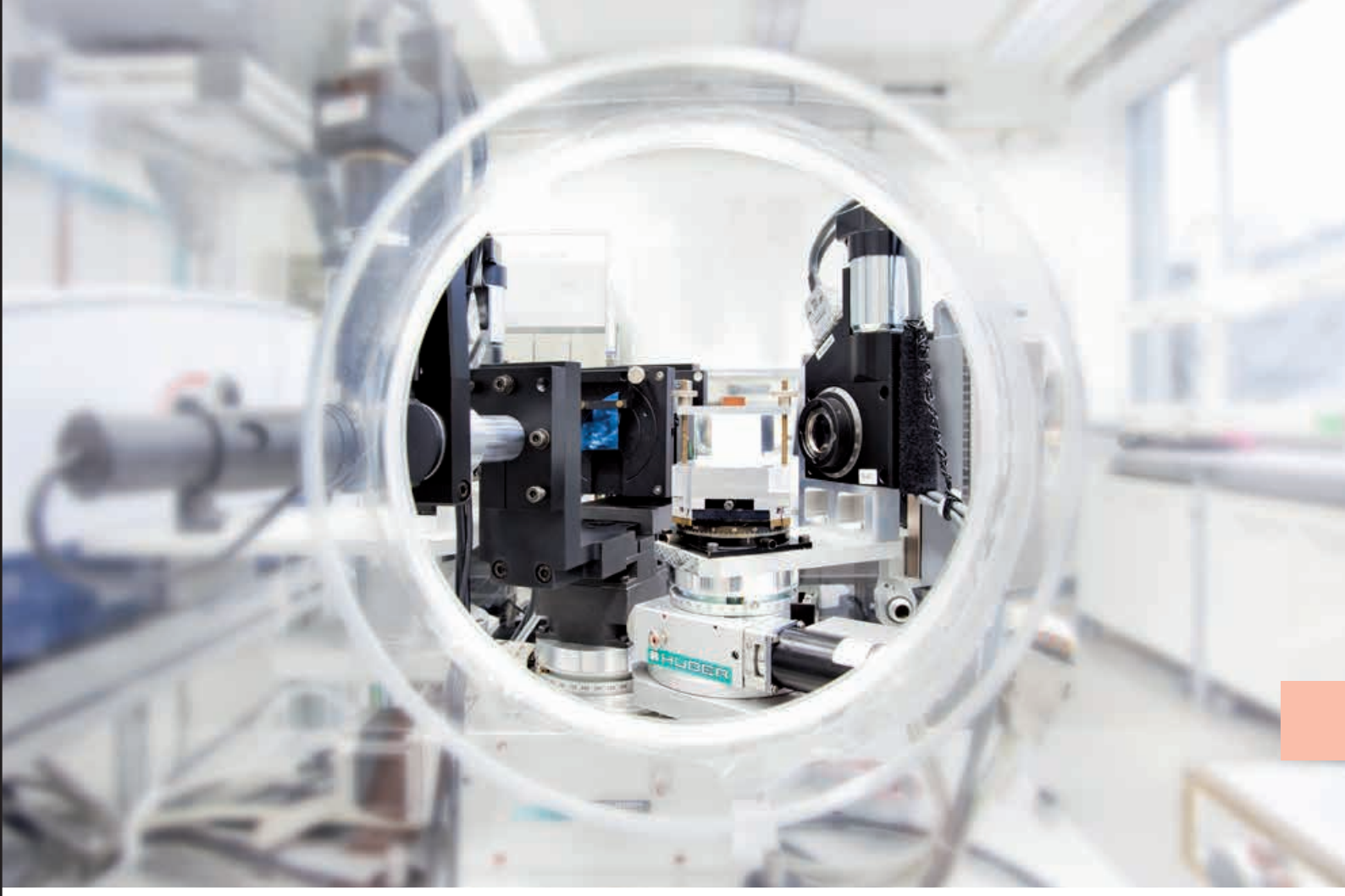
ISAS Joins INFECTIONS



Prof. Dr. Matthias Gunzer brings his expertise in human-pathogenic fungi like Aspergillus fumigatus (dyed red) to the Research Alliance INFECTIONS. The mould fungus poses a significant health threat to people with immune deficiencies.

SARS-CoV-2 made everyone aware how fast an unknown virus can spread worldwide and bring big parts of public life to a standstill.

The Leibniz Research Alliance 'INFECTIONS in an Urbanizing World – Humans, Animals, Environments' aims to understand how Covid-19 and other infectious diseases spread and which role biomedical, ecological, socio-economical and political aspects play in this. ISAS is one of the 18 partner institutes that are part of the alliance. Prof. Dr. Matthias Gunzer, immunologist and scientific director of the department Biospectroscopy, represents the institute.



The infrared ellipsometer facilitates the contactless, non-destructive, label-free analysis of the structure and composition of sample materials.

BIOINTERFACES

How can active substances, disease markers and biomolecules be reliably detected under variable environmental conditions, and how can their interaction with the environment be studied?

Scientists in the Biointerfaces research programme are working on techniques that can non-destructively record the structure, function and biochemical processes of bio-

molecules and surfaces, ideally under realistic conditions, without significantly affecting the functions of the target molecules. Due to structural changes, the research programme will be discontinued in the future. The following results are demonstrative of the work that the researchers did in 2020.

Functional surfaces for health research

The focus is on functional surfaces that can play a role in medical technology or biodiagnostics, for cell templates or in the development of novel sensor concepts. The projects cover both molecule-functionalised surfaces based on nitride and oxide semiconductors and on metal and metal oxides as well as biomimetic surfaces based on biomolecules or polymers. One focus is on the spectroscopic analysis of such interfaces and the biofunctionalisation of interfaces.

From stents to vaccines: Interfaces in material analytics

Interfaces constitute an important aspect in the development of new materials with specifically developed functionalities. Topics such as the biocompatibility of materials for implants, i.e. stents, new analytical sensors for the quality control of medical products, for example in the production of vaccines, as well as new diagnostic procedures or test methods for the biological activity of materials are concrete applications of this. They are supported by basic research-oriented studies of model systems using photoemission spectroscopy in order to study the desired functionalities of new materials under realistic conditions.

In 2020, the researchers continued to functionalise the metal surfaces with small biological molecules. The focus was on functionalisation with glutathione as a more complex amino acid, but still allowing thiol binding. The surfaces were functionalised via dip coating and ultra-high vacuum (UHV) evaporation. It turned out that functionalisation via evaporation is practically impossible in contrast to L-cysteine, a surprising result, as L-cysteine and glutathione are structurally very similar. To gain a better understanding of this result, DFT (density functional theory) calculations are currently running in parallel. Both molecules are interesting as a first step towards more complex functionalisations.

Optofluidic platform for IR & Raman spectroscopy

Optofluidics combines the advantages of microfluidics and optics. Applications of this technology include biosensors, lab-on-chip devices and procedures for molecular analysis in biochemistry. In particular, optofluidic systems can be used in pharmaceutical and biochemical research for in-situ applications as well as in quality control by means of on-chip detections or in the study and monitoring of molecular interactions or reactions.

A cross-institutional cooperation between the Interface Analytics and Bioanalytics departments is currently expanding the

microfluidic cell developed in the previous project. One focus is on the development, set-up and optimisation of a microfluidic platform with amplification substrates for the combinatorial application of Raman, CARS (Coherent Antistokes Raman Scattering) and infrared spectroscopy.

The new platform also enables the marker-free analysis of proteins, for example research into the kinetics of oxidative stress, structural analysis or the analysis and detection of interactions in protein complexes. As an important addition to the current range of techniques, it can help in the investigation of essential cellular processes that play a role in various disease patterns.

Working group
Bioresponsive Materials
Dr. Roland Hergenröder
T: +49 (0)231 1392-178
E: roland.hergenroeder@isas.de

Working group
In-Situ-Spectroscopy
PD Dr. Karsten Hinrichs
T: +49 (0)231 1392-3541
E: karsten.hinrichs@isas.de

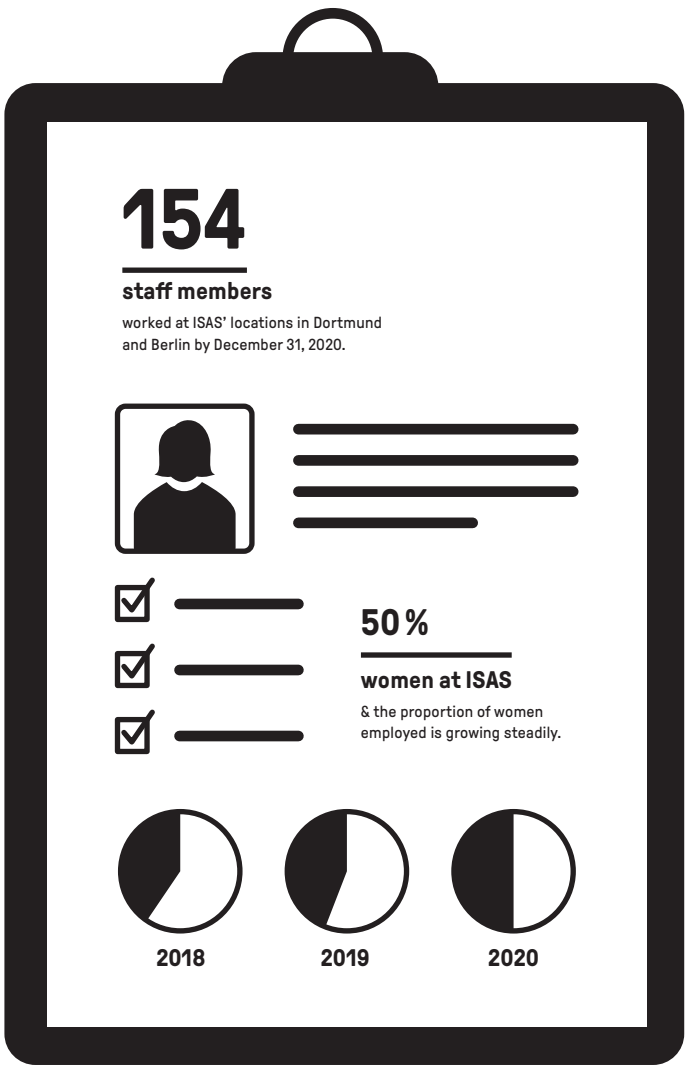
New insights into molecular & surface structures

How can concrete structural information on molecule-terminated interfaces be obtained from optical fingerprint spectra at an atomic or molecular scale? Using an approach that combines optical spectroscopy with quantum chemical numerical simulations, the scientists are studying hybrid model interfaces, i.e. ordered interfaces between organic molecules and semiconductors.

In 2020, the researchers were able to detect molecular and surface structures by comparing experimental and ab initio calculated Raman spectra. For example, the elucidation of the atomic structure of Au-modified Si(553) surfaces has resolved years of controversial debate, as the researchers were able to demonstrate that phonon modes localised at the surface can play an essential role in structure formation and structural phase transitions at surfaces through the electron charge transfer associated with the modification of atomic distances (bonds).

(CE) ■

OUR YEAR IN FIGURES



77

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

are currently working at ISAS, among them 40 women and 37 men.

77

researchers (m/f/d)

were employed at ISAS in 2020. Among them were 37 female and 40 male scientists.

32

doctoral candidates (m/f/d)

Our 77 researchers include 17 female and 13 male PhD students.

42

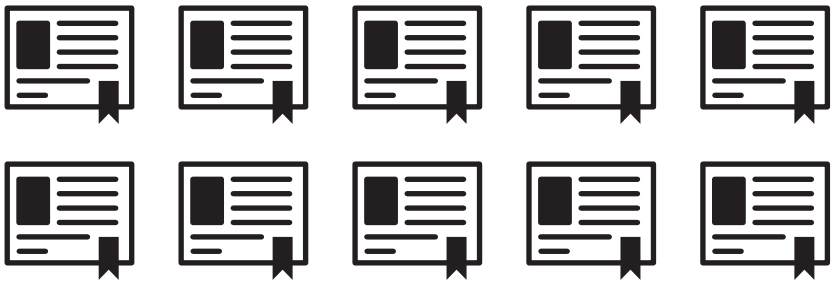
scientific degrees

Half of the 42 final theses were written at ISAS.*

26

doctorates

Eleven of the 26 dissertations were produced at ISAS.*



16

B.Sc., M.Sc., Dipl.

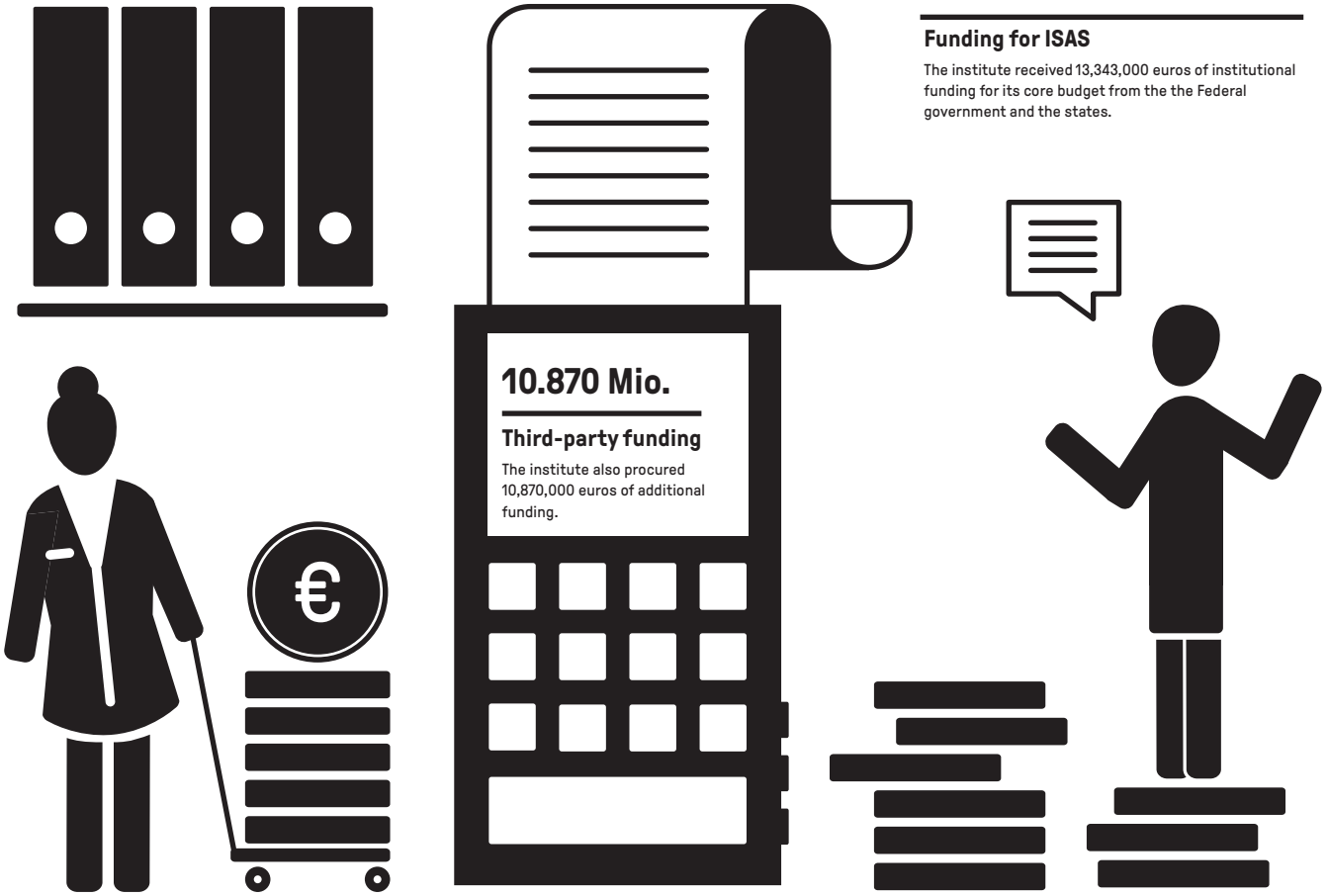
Of these degrees, four bachelor, five master and one diploma student wrote their final theses at ISAS.*

* The other projects were external expert assessments.

13.343 Mio.

Funding for ISAS

The institute received 13,343,000 euros of institutional funding for its core budget from the the Federal government and the states.



93

publications

were published in peer-reviewed journals.

50

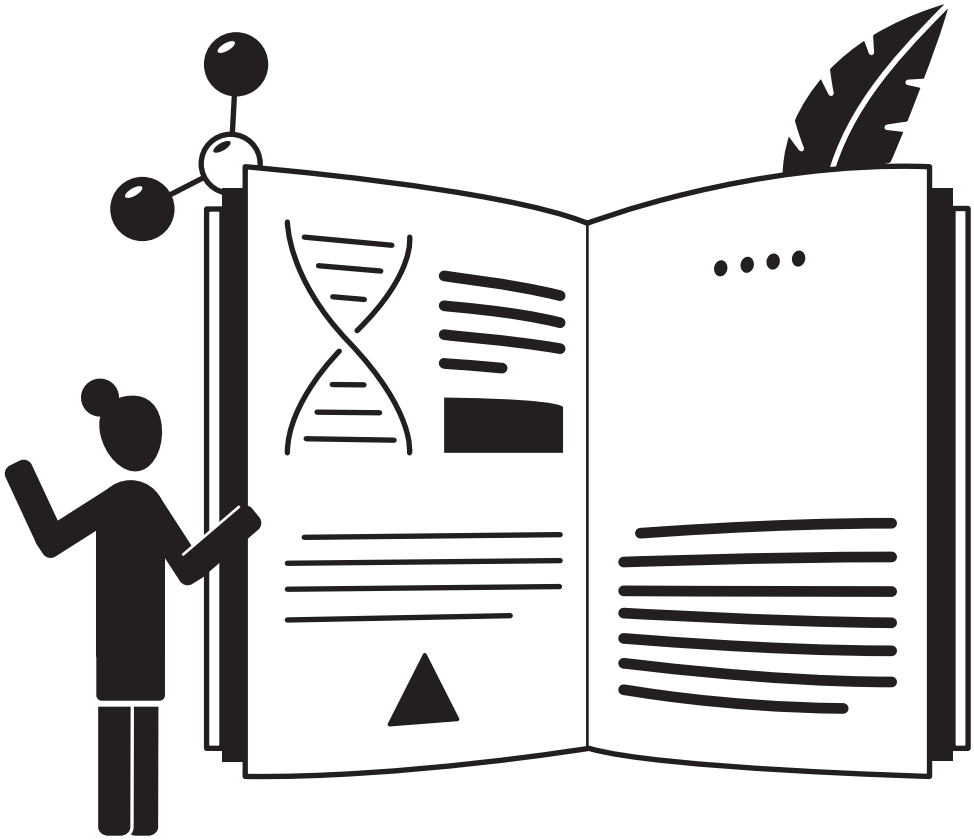
open access publications

Of the 93 publications, 50 were accessible free of charge.

7.22

impact factor

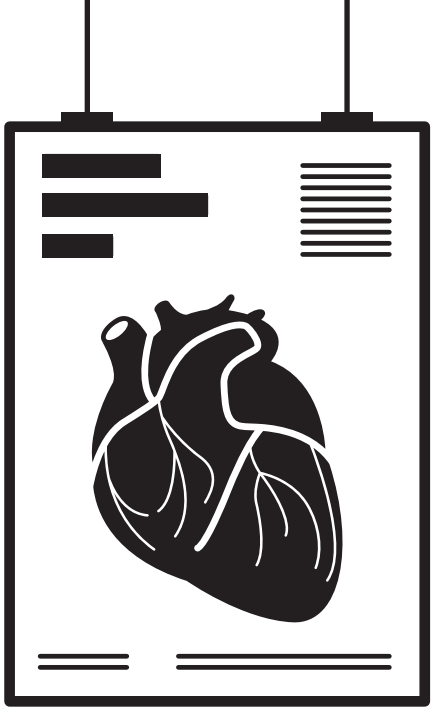
The average impact factor of publications in peer-reviewed journals was 7.22.



48

papers

with first or corresponding ISAS authorships were published in 2020.



12

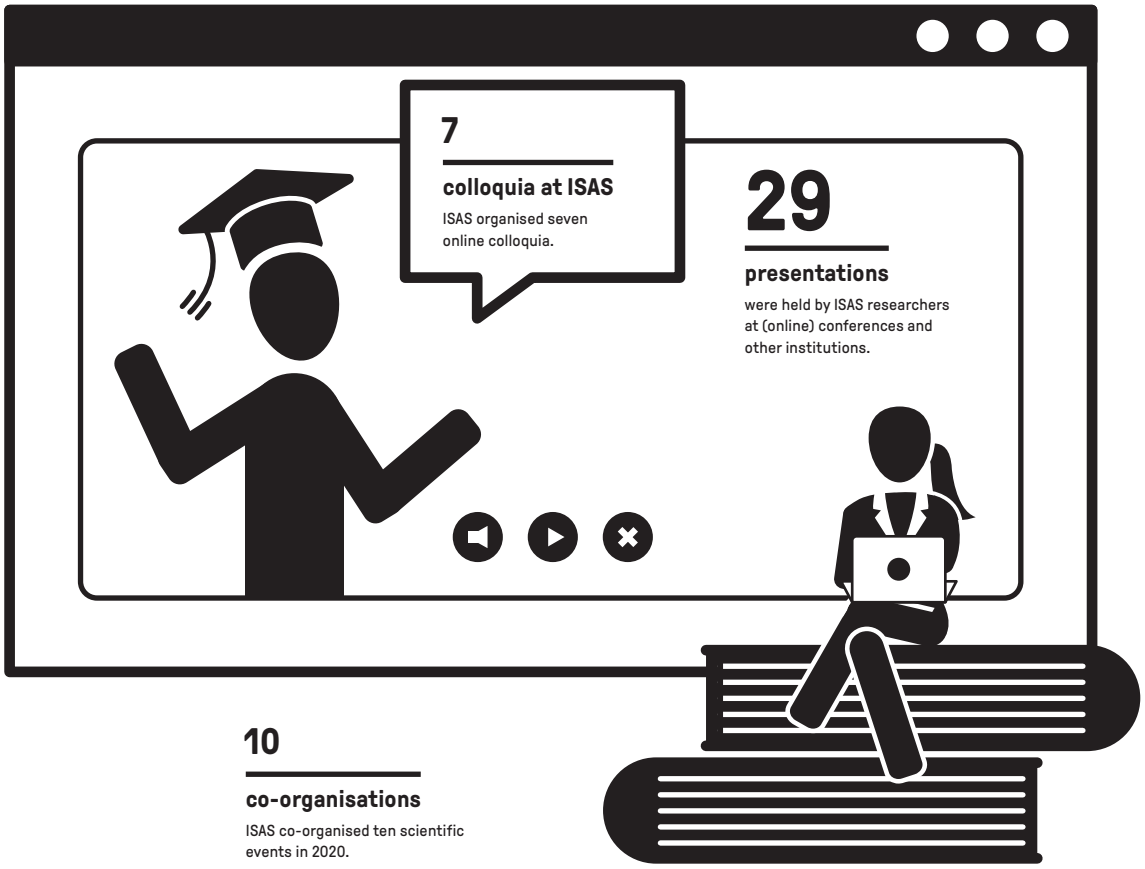
poster presentations

were held by our scientists in 2020.

41

conferences

ISAS researchers participated in 41 (online) conferences.



7

colloquia at ISAS

ISAS organised seven online colloquia.

29

presentations

were held by ISAS researchers at (online) conferences and other institutions.

10

co-organisations

ISAS co-organised ten scientific events in 2020.

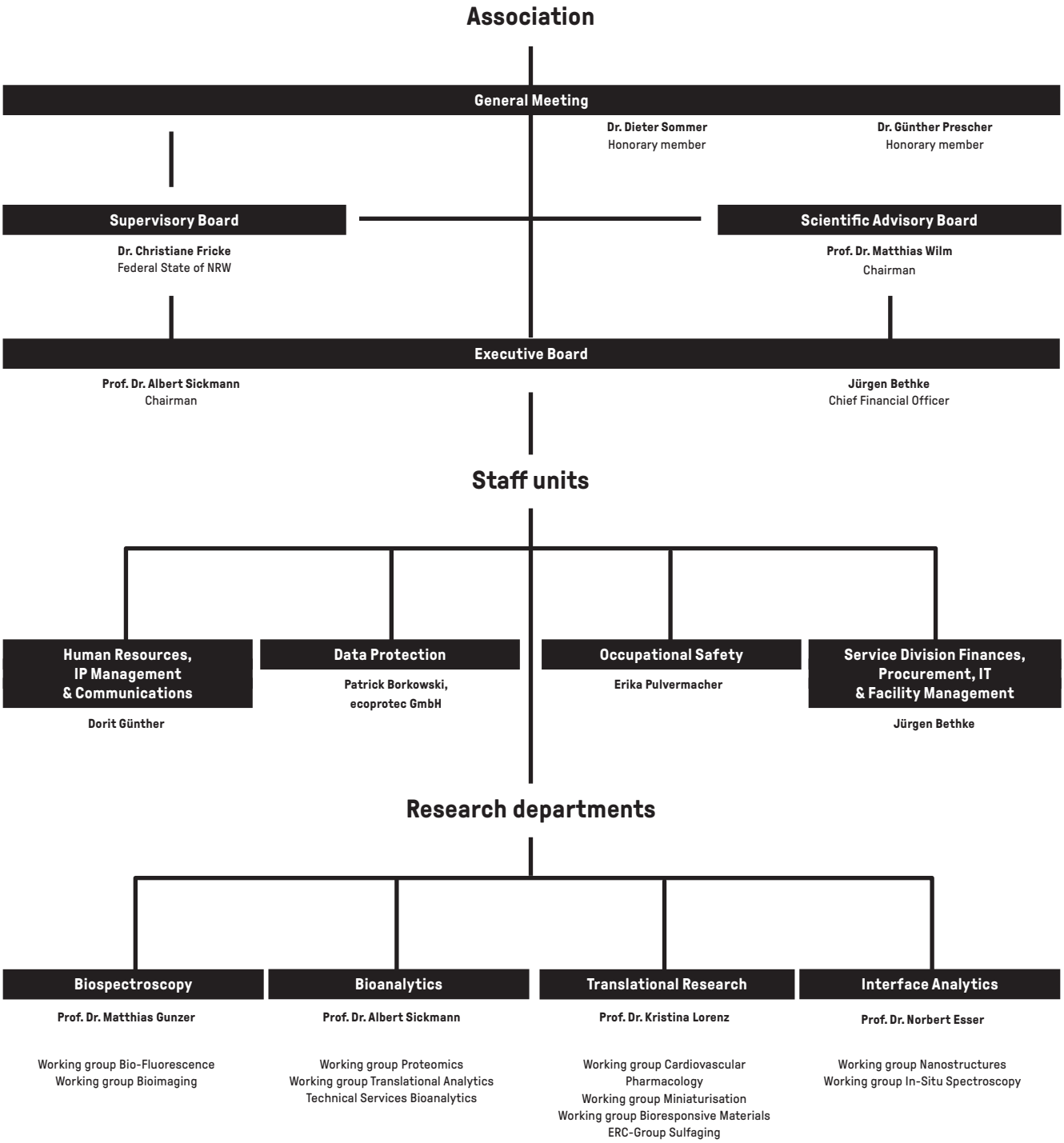
ORGANISATION

ISAS Executive Board

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

Information as of June 1, 2021

Organisation Chart



BOARDS

Executive Board

Prof. Dr. Albert Sickmann
Chairman

Jürgen Bethke
Chief Financial Officer

Scientific Advisory Board

Prof. Dr. Ronen Alon
Weizmann Institute of Science,
Department of Immunology
Israel

Dr. Anne K. Bendt
Singapore Lipidomics Incubator (SLING),
Life Sciences Institute (LSI),
National University of Singapore
Singapore

Prof. Dr. Britta Brügger
Biochemistry Center (BZH),
Heidelberg University
Heidelberg

Prof. Dr. Jörg Feldmann
Institute of Chemistry,
University of Graz
Austria

Prof. Dr. Ina Koch
Institute of Computer Sciences,
Department of Molecular Bioinformatics,
Goethe University
Frankfurt am Main

Prof. Dr. Markus Sauer
Department of Biotechnology and
Biophysics – Biozentrum,
Julius-Maximilians-Universität of Würzburg
Würzburg

Prof. Dr. Andrea Urbani
Faculty of Medicine and Surgery,
Università Cattolica del Sacro Cuore
Italy

Prof. Dr. Heike Walles
Core Facility Tissue Engineering,
Otto von Guericke University Magdeburg
Magdeburg

Prof. Dr. Matthias Wilm
Conway Institute,
University College Dublin (UCD)
Ireland

Board of Trustees

Appointed members

City of Dortmund
Wirtschaftsförderung Dortmund,
represented by Thomas Westphal
Dortmund

Federal Republic of Germany
Federal Ministry of Education and Research,
represented by Dr. Torsten Geißler
Berlin

Federal State of Berlin
The Governing Mayor of Berlin,
Senate Chancellery – Higher Education
and Research,
represented by Dr. Björn Maul
Berlin

Federal State of North Rhine-Westphalia
(Chair)
Ministry of Culture and Science,
represented by Dr. Christiane Fricke
Düsseldorf

Ruhr-Universität Bochum
represented by Prof. Dr. Andreas Ostendorf
Bochum

TU Berlin
represented by Prof. Dr. Christian Thomsen
Berlin

TU Dortmund University
(Deputy Chair)
represented by Prof. Dr. Gerhard Schembecker
Dortmund

Elected members

Guido Baranowski
TechnologieZentrumDortmund GmbH
Dortmund

Dr. Susanne Eickemeier
University of Design
Offenbach-on-Main

Prof. Dr. Dieter Häussinger
Heinrich Heine University
Düsseldorf

Dr. Jörg Schneider
Deutsche Forschungsgemeinschaft (DFG)
Bonn

Prof. Dr. Alfred Wittinghofer
Max Planck Institute of Molecular Physiology
Dortmund

Members of the Association

BASF SE

City of Dortmund

Federal Republic of Germany

Federal State of Berlin

Federal State of North Rhine-Westphalia

Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM)

Industrie- und Handelskammer zu Dortmund

Merck KGaA

OBLF Gesellschaft für Elektronik und Feinwerktechnik mbH

Ruhr-Universität Bochum

SENTECH Instruments GmbH

Shimadzu Europa GmbH

Siemens AG

TechnologieZentrumDortmund GmbH

Thermo Fisher Scientific GmbH (Bremen)

Thermo Fisher Scientific GmbH (Dreieich)

TU Dortmund University

University of Münster

ENGLISCHER TEIL