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IN THE GRIP OF A VIRUS

EDITORIAL

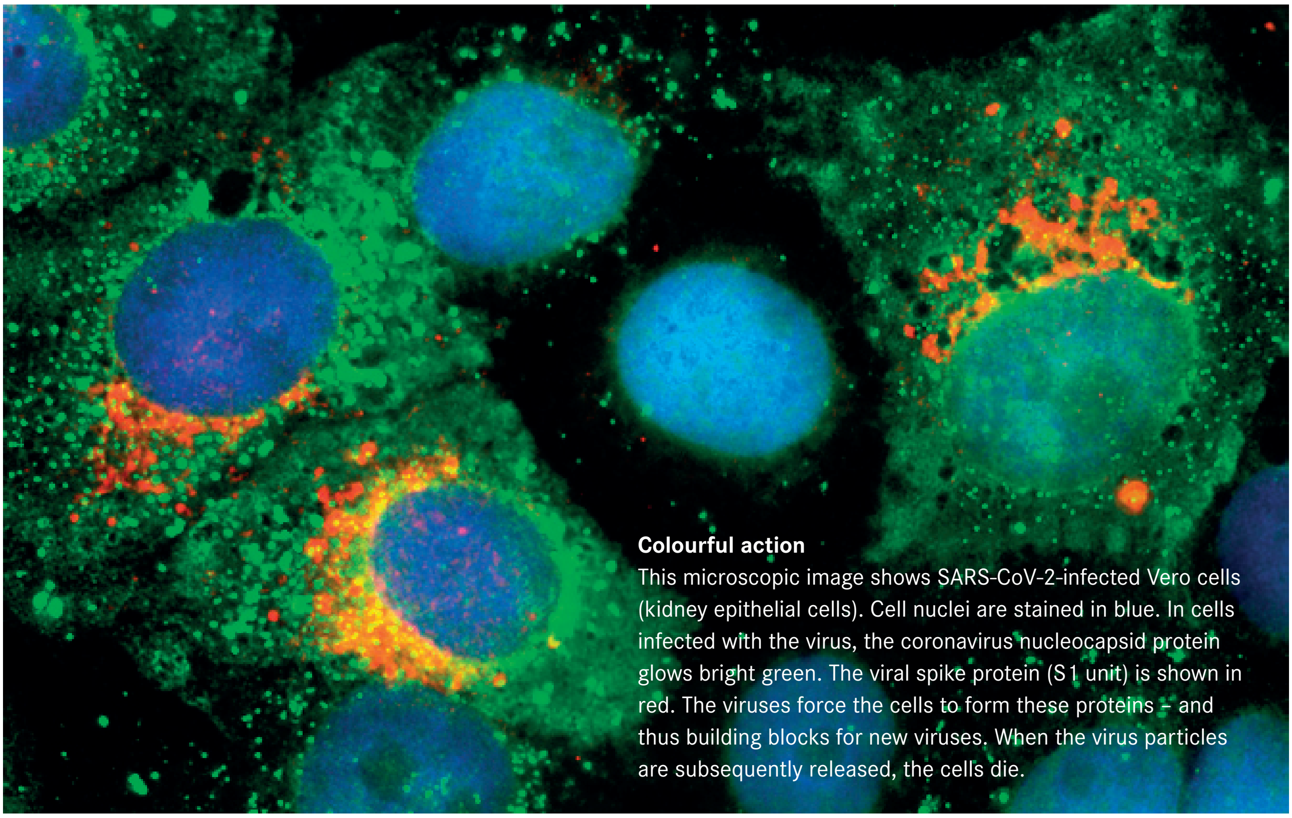
Dear readers,

After 2020, the year 2021 will also be dominated by the COVID-19 pandemic. We have adjusted our everyday life to a dangerous opponent that we cannot see with the naked eye, but which demonstrates its full power especially in intensive care units and nursing homes. In our cover story, we explain how newly emerging viruses such as SARS-CoV-2 repeatedly manage to conquer humans as hosts and which approaches there are to fend off such viral attacks in the future. With the outbreak of the pandemic, the HZI quickly established a large number of research projects to investigate SARS-CoV-2 in more detail and to contribute to its control. In our interview, the Scientific Director of the HZI, Dirk Heinz, reports on how this was possible and what he sees as the main focus at the HZI this year and in the years to come. We also asked some researchers how they simultaneously managed media appearances, childcare and household chores from home office during the first lockdown.

I wish you an informative read and take care!

***Andreas Fischer,** Editor-in-chief*

EYE-CATCHER



Colourful action
This microscopic image shows SARS-CoV-2-infected Vero cells (kidney epithelial cells). Cell nuclei are stained in blue. In cells infected with the virus, the coronavirus nucleocapsid protein glows bright green. The viral spike protein (S1 unit) is shown in red. The viruses force the cells to form these proteins – and thus building blocks for new viruses. When the virus particles are subsequently released, the cells die.

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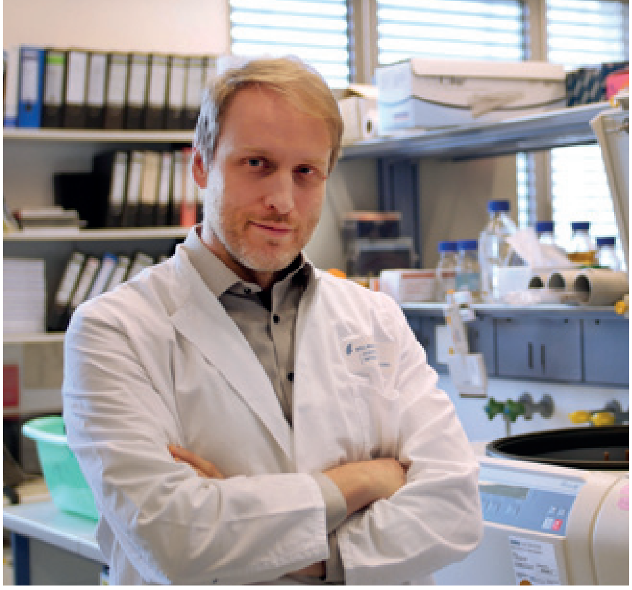
NEW VIRUSES, NEW CHALLENGES

by Charlotte Wermser

There are many thousands of viruses circulating in the animal world that could spread to humans. SARS-CoV-2 has shown how quickly new viruses can spread worldwide

Viruses have coexisted with mankind for a long time. The oldest genetic evidence of a viral disease shows that people already suffered from liver inflammation caused by hepatitis B viruses about 7,000 years ago. The genetic material of these viruses was found in teeth from this period, which were discovered in Saxony-Anhalt. Since then, many different viral diseases have appeared – and others, like smallpox, have disappeared forever. Newly emerging viruses, which have previously only spread in the animal kingdom, have been able to cross the species barrier and adapt to humans as new hosts. Since the end of 2019, the coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) has shown that nowadays such a virus can take over the whole world in a very short time. Virus particles are tiny – 20 to 300 nanometres in diameter and thus about 1000 times smaller than a human cell. They consist of little more than their genetic material and a protective protein shell. They even save their own metabolism and use their host's instead. Once they have invaded a host cell, they reprogram it. The cell reads the viral genome, multiplies it and produces viral proteins. Thus, the host cell produces more and more viral particles until it dies, thereby releasing the viruses.

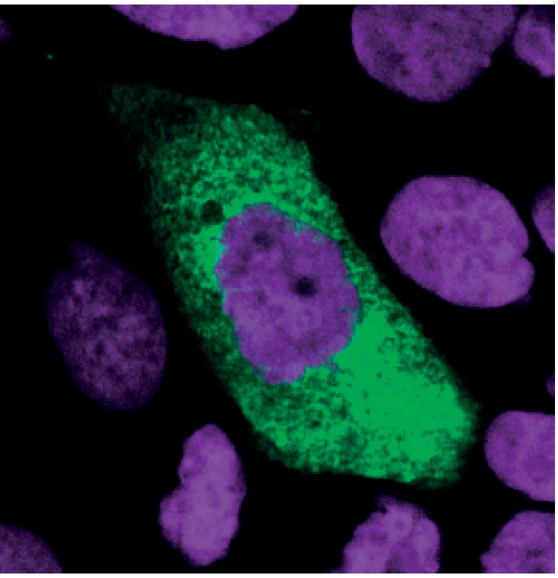
▽ SARS-CoV-2 virus particles bind to ACE2 receptors on the surface of a human cell



◁ Luka Cicin-Sain and his research group are currently investigating antibodies and active substances that prevent the proliferation of SARS-CoV-2

INTO THE HOST – AND OUT AGAIN

However, viruses cannot simply invade a new host such as humans. They need a "key" to enter its cells. "To do this, viruses use proteins on our cell surface. They can only infect us if these proteins match the proteins on the virus surface," says Prof Luka Cicin-Sain, head of the research group "Immune Aging and Chronic Infections" at the Helmholtz Centre for Infection Research (HZI). But not all host cells have the right "lock" on their surface: Viruses can only multiply in a tissue whose cells produce receptors that match the virus. This results in the migration of viruses into individual organs – influenza viruses multiply in the lungs and bronchial tubes, hepatitis viruses live in the liver and the human immune deficiency (HI) virus prefers cells of the immune system. In SARS-CoV-2, a surface protein, which scientists call the spike protein, plays the role of the "key". According to Cicin-Sain, the virus' key step in changing host to humans was a mutation of the spike protein that now enables SARS-CoV-2 to bind to the ACE2 receptor on human cells.



△ A lung cell infected with SARS-CoV-2 forms new virus particles (green) in its cytoplasm (purple: cell nuclei)

The place where a virus shelters is also crucial for its further spread.

"Getting into the body and multiplying there is one thing – but in order to spread further, viruses must also get out of the host,"

says Cicin-Sain.

Viruses that multiply in the airways or the digestive tract have it easier than those that occur in internal organs or the bloodstream.

"When a new, unknown virus appears, it is obvious to check whether it belongs to one of the virus families from which new viruses have emerged in the past. These are usually viruses whose genetic material consists of RNA," says Luka Cicin-Sain. Depending on the structure of their genetic material, viruses have different prerequisites for changing hosts. RNA viruses change faster genetically than viruses with a DNA genome. This is because the protein that multiplies the RNA often incorporates small defects. The mutations in the genetic material result in different virus variants, which differ slightly. Therefore, RNA viruses adapt to a host faster than DNA viruses.

USING MOSQUITOES TO GET TO THE HOST

Some viruses use assistants to move from person to person. For example, bloodsucking animals such as mosquitoes or ticks can absorb viruses whilst feeding. These multiply in the animals and are transferred back to a human host with another bite. This is why mosquitoes were involved in an epidemic in which a virus did not have to newly cross the species barrier, the Zika epidemic. This virus has been known since the 1950s. However, mass illness did not occur until the Zika virus was introduced to Central and South America in 2015 and conquered a new continent thanks to mosquitoes. "A prerequisite for the transmission of the Zika virus is that it can multiply in both humans and mosquitoes – two completely different species. This is an enormously complex system where the transition between two species must take place again and again," says Luka Cicin-Sain. A completely new virus that spreads to another species with the help of mosquitoes could then spread to humans instead. The West Nile virus is an observed example of this. The virus, which is transmitted by mosquitoes, normally circulates between mosquitoes and birds, but it can also infect humans and other mammals.

Concentrating on certain host species is a typical characteristic of viruses – but this varies in severity depending on the virus family. "We know of both generalists and specialists among the viruses. The specialists are confined to a single host, whereas generalist viruses can change hosts more easily," says Cicin-Sain. With his team, he is conducting research on the cytomegalovirus (CMV), a virus that is highly specialised in humans. CMV, which belongs to the herpes virus family, has completely adapted its lifestyle to humans. Such highly specialised viruses carry the blueprint for many proteins that interact with the human immune system in their genome. With the help of these proteins, they can switch off the immune defence and prevent infected cells from being destroyed. Thus, CMV can survive unnoticed by the immune system for many decades in human cells. In up to 90 percent of the population, this virus lies dormant in the body without causing symptoms. The immune system keeps the pathogen in check to such an extent that no active infection breaks out. “However, such an interplay does not arise out of nowhere, but is the result of a very long adaptation to a host. In contrast, generalist and new viruses cannot permanently hide from the immune system,” says Luka Cicin-Sain. This would make it easier to develop a vaccine against such viruses.

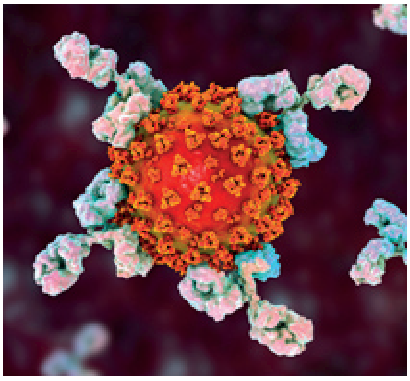
◁ Carlos A. Guzmán researches how vaccinations trigger an immune response and protect against a pathogen

NO SINGLE SOLUTION FOR VACCINATIONS

What can we do in future to stop new viruses that have already made the leap to humans? An important element is the rapid development of a vaccine. Vaccination trains the immune system to deal with a pathogen without a previous disease. An infection is imitated, so to speak. In case of a later encounter with the pathogen, the immune system can quickly recall the experience and prevent infection. While broad-spectrum antibiotics are available to fight bacterial infections and research for an equivalent against viruses – i.e. broadly effective antiviral drugs – is also being conducted, there is no such thing as a universal vaccination. “Our immune system is a master in triggering highly precise immune reactions specifically directed against a pathogen. This is why known vaccines cannot be converted so easily,” says Prof Carlos A. Guzmán, head of the department “Vaccinology and Applied Microbiology” at HZI.

> ***“Fortunately, with SARS-CoV-2 we did not have to start from scratch. There has already been intensive research into vaccination against SARS and MERS coronaviruses,”***
>
> says Guzmán.

So scientists already knew that the spike protein was a good target for vaccine development. If a vaccination uses this protein as an antigen, it stimulates the immune system to produce antibodies against it. On contact with the virus, the antibodies make the spike protein, the virus key, inaccessible and thus block its way into the cells.



△ Antibodies attack a SARS-CoV-2 virus particle

However, not every virus emerging in the future will be as closely related to already known pathogens as in the current case of SARS-CoV-2. Moreover, as it is impossible to predict which virus will be transmitted to humans next, vaccine research focuses on technical development: “Reverse vaccinology has literally turned the research process upside down,” says Carlos Guzmán. Traditionally, pathogens were characterised in lengthy fundamental research. For example, scientists investigate which mechanisms a pathogen uses to trigger a disease or which of its structures are particularly well recognised by the immune system. Vaccine development then builds on this knowledge. In contrast, reverse vaccinology is based on the genetic code of a pathogen, which can be determined very quickly using modern sequencing technology. In the case of SARS-CoV-2, the genetic code was already decoded and available in a database in mid-January 2020 – at a time when only a few dozen infections were known. “Having this dataset meant that vaccine research could start immediately without having to grow the virus in the laboratory or examine it in any other way,” says Guzmán. In such cases, computer-based approaches help to select the best antigen for a vaccine.

Vaccines must then go through a long development and optimisation process. “Normally it takes about ten years to develop and approve a vaccine,” says Carlos Guzmán. “With the SARS-CoV-2 vaccination, science is exploring the limits of how much the process can be accelerated. However, safety must under no circumstances fall by the wayside.” Eventually the vaccination against SARS-CoV-2 would be administered to a large proportion of the population. Even rare serious side effects would then affect a large number of people.

NEVER-ENDING CYCLE

Even in the Stone Age, viruses were our companions – and they will remain so in the future. “The reservoir of viruses in the animal kingdom is almost infinite. Sooner or later, it is inevitable that a new virus will spread to humans,” says Luka Cicin-Sain. The challenge will be to get the next wave of disease caused by a new virus under control before it develops into a major epidemic.

△ Dirk Heinz welcomed Federal Research Minister Anja Karliczek during her visit to the HZI in May 2020

"THE GREAT STRENGTHS OF THE HZI ARE ITS SOLIDARITY AND TEAM SPIRIT"

by Susanne Thiele

With the outbreak of the COVID-19 pandemic, the HZI quickly moved into the public spotlight. Scientific Director Prof Dirk Heinz talks about one year of pandemic, the fast establishment of corona research and new challenges

Professor Heinz, how do you remember the beginning of the pandemic?

I remember the last major face-to-face meeting in mid-March 2020 in Berlin very well: a kick-off meeting for the foundation of our new Helmholtz Institute in Greifswald. Even then, everything revolved around corona and the importance of infections caused by pathogens originating from animals. And shortly afterwards, the first meeting of the crisis unit took place at the HZI. We further developed the pandemic plan and took special measures to protect the staff, from increased hygiene measures to flexible home office solutions.

Looking back, how do you evaluate the year 2020 for the HZI?

It was a most unusual, exhausting and unique year in every respect. The COVID-19 pandemic, as you can see, has had far-reaching consequences on the way we work, but also on our private lives. For the HZI, its special role and responsibility in combating the pandemic became clear very quickly. This is also a great opportunity for our centre!

How was the HZI able to adapt so promptly to corona research?

In terms of research, the pandemic fortunately did not catch the HZI completely unprepared, although corona viruses had not been in our focus before. We were able to quickly bundle our competencies for research on SARS-CoV-2 and access appropriate infrastructures such as S3 laboratories. Within a very short time, more than 70 projects were established thanks to successful acquisition of third-party funding. We have benefited greatly from our priorities in research, the so-called “research foci”. It is remarkable how quickly our scientists have taken the initiative. I am also very proud of our experts, who immediately took on the important task of knowledge transfer - for example, in interviews, talk shows and background discussions - and support policy-makers in their difficult decision-making processes.

What are the HZI‘s most important scientific contributions to the fight against the pandemic?

Our scientists have, for example, developed computer-aided approaches that make it possible to model the course of the infection or that will relieve the health authorities of the burden of tracking cases and contacts in the future. In addition, epidemiological studies on the pandemic and numerous innovative research projects are underway to gain a deeper understanding of the infection process and develop solutions to combat the virus.

Has the public‘s perception of the HZI changed?

We are all pleased that the level of awareness has increased by leaps and bounds due to the media presence of our researchers during the corona crisis. As a feedback loop, we also notice this quite clearly in the enormous increase in third-party funding. It is outstanding what the HZI staff have achieved in a very short time. This of course includes Press and Communication, but also Administration and Technical Operations, who have been very supportive of the research efforts despite numerous restrictions and have thus contributed significantly to the success. Therefore, I would also like to express a very big compliment and many thanks to all of them at this point. The past year was certainly not an easy one, but the commitment and dedication have paid off. In my opinion, the HZI has never been in such a good position in its history as it is today.

So what happens next in 2021?

Many of our scientists remember the quite strenuous scientific and strategic reviews in 2018 and 2019, and the HZI scored outstandingly well both times. The year 2021 is a milestone in that it also marks the start of the Helmholtz Association‘s fourth period of programme-oriented funding. We have set ourselves ambitious goals for the next seven years in order to do even better justice to our translational mission. The concept must be adapted again against the backdrop of the corona pandemic, also because the pressure of expectations on the HZI from politics and society has grown significantly. We cannot and must not close our minds to this. We benefit from our flexible programme structure, which allows us to excellently integrate current topics such as respiratory infections into the overall strategy of the HZI. On the other hand, we can use our newly acquired Helmholtz Institute in Greifswald as well as the gratifying additional funding for our already existing Helmholtz Institute in Saarbrücken (HIPS) to do research on the topic of “Emerging Infections” with the necessary critical mass. Finally, some important new recruitments are planned for all sites.

What does this mean in detail for the sites?

At the new HZI site in Greifswald, we want to strengthen the “One Health” approach. This involves the epidemiology, pathogenesis and pathogen-host interactions of primarily zoonotic infections. As cooperation partners, we will work on site with the University of Greifswald, the University Medical Centre Greifswald and the Friedrich-Loeffler-Institut (Federal Research Institute for Animal Health). By the end of this year, the international review of the scientific concept and the foundation of the new institute will take place. At HIPS, the aim is to expand pharmaceutical research and add antiviral strategies. Substantial funds have been made permanently available for this expansion via the federal budget committee at the end of 2020. At HIRI in Würzburg, we will focus on investigating infection mechanisms at the single cell level in the coming years. RNA-based methods will be used to shed light on various host reactions in infections in order to understand their effects on the course of the disease and to intervene in a targeted manner.

Are there other key topics at the HZI?

An important topic in the Helmholtz Association is strengthening knowledge and technology transfer. We need to increase our efforts in this area in the coming years. This includes the establishment of successful innovation management. The topic of internationalisation must also be advanced. We are already in the process of establishing successful cooperations, for example with McGill University in Montreal. I am convinced that the corona crisis will contribute to strengthening infection research worldwide. Great opportunities also await us here. The key for the HZI will be to position itself optimally and to make good offers in order to be one of the guaranteed candidates for financial growth.

What is your wish - or your forecast - for 2021?

We certainly all wish that the COVID-19 pandemic will finally be overcome. But this means there are still exhausting months ahead. The vaccines now available will bring a significant improvement, while contact restrictions alone can at best lead to a stagnation in the number of cases, especially in the light of new mutations. Both patience and solidarity of all will continue to be called upon. For the HZI, I hope that after the review marathon, the financial consolidation, which was also successfully managed, and the restrictions associated with the COVID-19 pandemic, we will soon be able to focus again on our core topic, translational infection research, with all its opportunities. This should spur us all on not to let up. The great strengths of the HZI are its solidarity and team spirit, which is more important than ever in pandemic times - we should and can build on this for a good future.

COVID-19 RESEARCH AT HZI

by Andreas Fischer

With the outbreak of the pandemic, the HZI quickly established SARS-CoV-2 research as a new focus. Here we present some examples of new research projects

ANTIBODY STUDY ON THE SPREAD OF SARS-COV-2 INFECTIONS

The "Multilocal and Serial Prevalence Study on Antibodies against SARS-2 Coronavirus in Germany" (MuSPAD) is one of the most comprehensive and largest antibody studies in Germany and is coordinated by the HZI department "Epidemiology". The main objective is to determine the proportion of the population that has antibodies against SARS-CoV-2 in their blood and is therefore likely to have already been infected with the virus. Up to now, the infection counts have been based on reports to the health authorities; untested infected persons with an asymptomatic course are therefore not recorded. To better understand the temporal and geographical spread of the COVID-19 pandemic, since July 2020, up to 3000 people are being randomly selected in eight districts nationwide and their blood tested for antibodies. After three to four months, a second test cycle takes place in the districts so that the development of the antibody concentration in the blood of positively tested COVID-19 patients can also be monitored. This provides information on how long a person is immune to the virus.

DIGITAL INFECTION MANAGEMENT WITH SORMAS

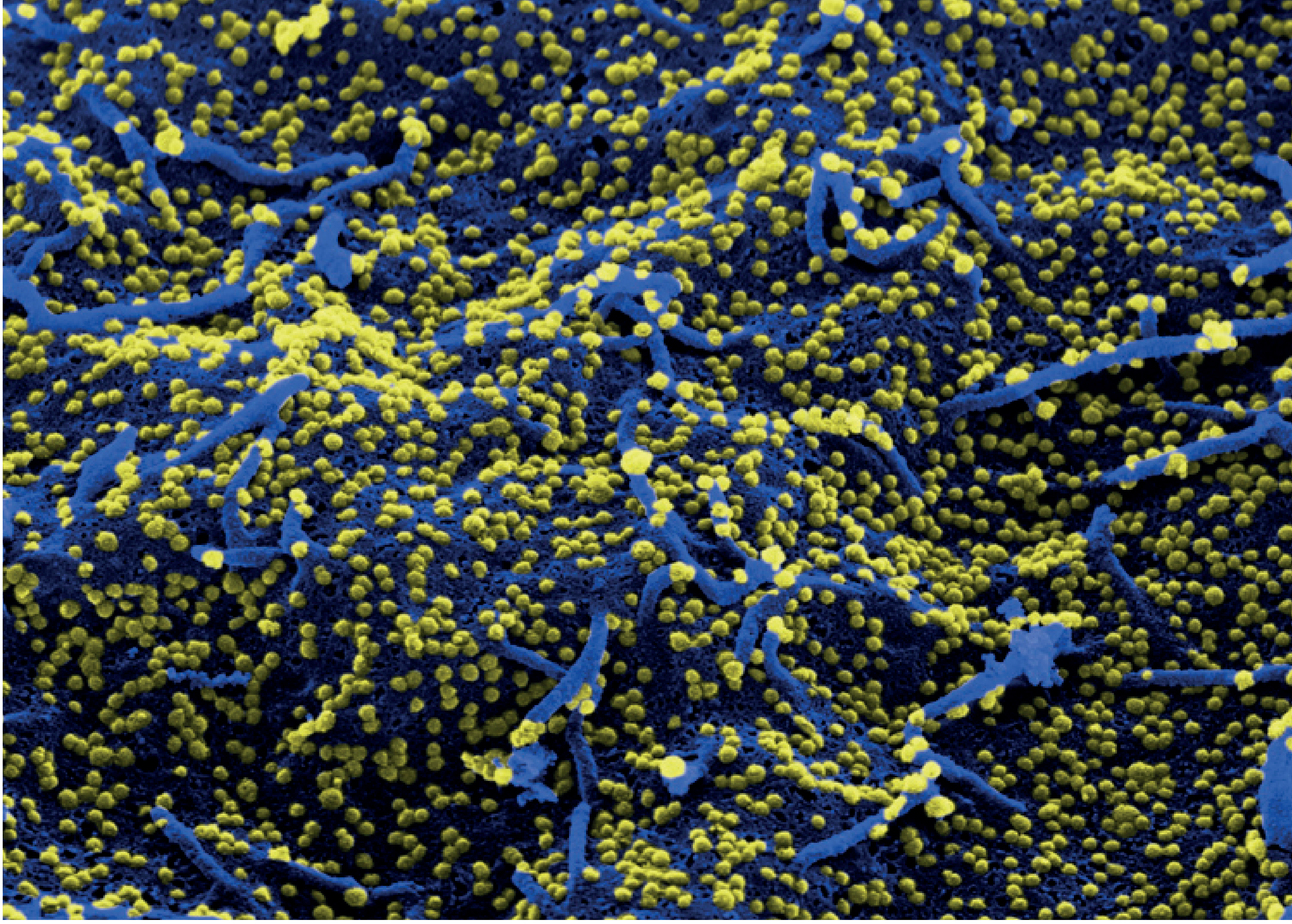
The name of the software SORMAS stands for "Surveillance Outbreak Response Management and Analysis System". Originally, the HZI department "Epidemiology", headed by Prof Gérard Krause, developed SORMAS together with its partners during the Ebola outbreak in West Africa in 2014-15 and has since continuously expanded it to include modules for other infectious diseases. SORMAS is available free of charge as open-source software and has been specially adapted to the needs of COVID-19 pandemic management since March 2020. SORMAS is now being used in Germany, Switzerland, France, Ghana, Nigeria and Fiji and covers a population of over 300 million people. The newly implemented COVID-19 module primarily improves the digital management of quarantine procedures and the tracking of infection chains across district and national borders. At the same time, SORMAS generates real-time data for ongoing risk assessment at national and international level.

MATHEMATICAL MODELLING OF THE PANDEMIC SCENARIO

Together with partners from Forschungszentrum Jülich, a research team led by Prof Michael Meyer-Hermann has developed a method that can simulate the effects of various infection control measures and the pandemic situation on a daily basis. The data obtained shall provide decision-makers in politics with a basis for assessing the current situation. A decisive variable in the description of the spread of an infectious pathogen is the reproduction number. The basic reproduction number indicates how many other people an infected person infects on average. It is an important indicator of how quickly an epidemic spreads. In addition, the research team has published a joint study with the ifo Institute calculating the health and economic scenarios for easing pandemic-related restrictions. Daily updated data for the SARS-CoV-2 reproduction number can be found at http://secir.theoretical-biology.de.

TESTING KNOWN DRUGS FOR ACTIVITY AGAINST SARS-COV-2

An international research network is investigating already approved drugs for a possible effect against SARS-CoV-2. The studies taking place in Germany are led by Prof Thomas Pietschmann, a researcher at the HZI and TWINCORE. In a first step, the scientists in Hannover use high-throughput processes to search for active ingredients inhibiting the replication of viruses. For these candidates, the mode of action, the effect on lung cells and the optimal dose are analysed. The "ReFrame" drug database from Scripps Research (USA), which contains around 14,000 approved drugs and active compounds, is used for this purpose. Promising drug candidates are to be rapidly transferred into clinical trials. This so-called repurposing - i.e. the use of an already proven active compound for new indications - shortens the development phase of a drug, as safety data on its use and tolerance are already available. The HZI is also involved in the EU project "SCORE". The aim of this project is the development of antivirals against SARS-CoV-2 and future coronavirus outbreaks. SCORE focuses both on the repurposing of already known substances and on new active compounds. Under the leadership



△ A research team led by Prof Andrea Kröger infected Vero6 cells with SARS-CoV-2, which Dr Mathias Müsken used for this electron micrograph. It shows the viruses (yellow) on the cell surface at a magnification of 16,000 times

of Dr Katharina Rox, pharmacological characterisation and pharmacokinetic studies are carried out at the HZI to identify suitable candidates.

SINGLE-CELL ANALYSES EXPLAIN VARYING DEGREES OF COVID-19 COURSE

The differences in the course of the disease when infected with SARS-CoV-2 are considerable. In addition to the mostly mild courses, ten to 20 percent of infected persons develop pneumonia, which can be life-threatening. A nationwide research network has succeeded in identifying differences in the immune response between patients with mild and severe courses. The research teams of Prof Yang Li (CiiM) and Dr Antoine-Emmanuel Saliba (HIRI) as well as the HZI Genome Analytics of Dr Robert Geffers were involved. In the study, blood samples from a total of 53 COVID-19 patients were examined simultaneously at two different locations using single-cell-based methods. This allowed the individual immune defence mechanisms to be broken down in time. The results revealed that severe courses are associated with profound changes in immune cells: They showed an increased number of neutrophil precursor cells as well as dysfunctional neutrophil cells (certain white blood cells) with altered morphology. This is in contrast to the previous assumption that severe COVID-19 courses are associated with an excessive immune response. Instead, neutrophil cells appear to be trapped in a continuous loop of activation and inhibition, which may contribute to an ineffective immune response. The study thus provides crucial information for the identification of suitable biomarkers and therapeutic targets for the treatment of COVID-19.

NEUTRALISING ANTIBODIES AGAINST SARS-COV-2

Entry of SARS-CoV-2 into a host cell is mediated via the host cellular receptor ACE2 and the viral spike protein. In previous epidemics caused by SARS and MERS coronaviruses, it was shown that monoclonal neutralising antibodies are suitable for therapies because they can prevent the virus from binding to the receptor and thus from entering the cell. Based on these findings, a research team from the HZI led by Prof Luka Cicin-Sain and the Technische Universität Braunschweig identified 17 human antibodies that neutralised infection with SARS-CoV-2 in human cell lines. Four of these antibodies showed a high binding affinity in the subnanomolar range. In contrast to previously known approaches, which obtain human neutralising antibodies from recovered patients, the research team was able to identify promising antibody candidates from samples of healthy donors in this work. A cooperation partner in the search for antibodies is YUMAB GmbH on the Science Campus Braunschweig-Süd.

ABOUT HOME OFFICE, VIDEO CONFERENCES AND A WASHING MACHINE

HZI scientists also "enjoyed" home office – reports from the first lockdown

PROF MELANIE BRINKMANN
Research group leader at the HZI
Married; three children

How did you manage scientific work, childcare and numerous media events for the HZI during the first lockdown?

I was fortunate because my children were eligible for emergency childcare. Otherwise, I would have been desperate and wouldn't have been able to do much media work. Even so, our family pretty much reached its limits. This is because not only did the school stop, but also the kids' leisure activities such as gymnastics, handball and soccer were no longer available. Contact with grandparents was also considerably reduced. In any case, we are now all significantly better at playing table tennis - our table tennis table proved to be a lifeline. However, I struggled since I had no administrative assistance at that time. I received tons of e-mails after each media event. Responding to all of them took a lot of time and organising all the invitations was also quite a challenge.

Which family experience will you remember from that time?

I remember one evening at the dinner table when we all discussed whether I should continue to be involved in public outreach activities such as talk shows and interviews. I was travelling a lot and even when I was at home, I was absent minded, thinking about the pandemic nearly the whole time and was quite stressed. My oldest son then said: "Mom, you're doing great, and what you're doing is so important. I think you should carry on." That was our final decision, then.

How did you manage the supervision of your research group?

We were lucky because three of my PhD students were about to write their papers. So the timing was perfect, and we achieved a lot. However, it was and still is a difficult time in terms of the team spirit. Personal exchange is just so important. And we haven't been able to celebrate any of our papers properly. We have a lot to catch up on! ■

DR VIVIEN NAGY
Funding Management for the German Center for Infection Research (DZIF) at the HZI

PROF TILL STROWIG
Research department head at the HZI
Two children, 8 and 5 years old

How did you organise your home office time as an "HZI double-career couple", and how did it work out with your children?

We worked in shifts, and we worked a lot during the weekends. One of us was able to concentrate on work, and the other took care of the children. The person who had "kids' service" also took care of household chores such as cooking, laundry, etc. Just preparing three meals a day took up a lot of time. The number of dishes to clean afterwards was enormous! But it was nice to see that our children grew even closer together, out of necessity, and became wonderfully creative in games. They created huge miniature landscapes and great hideouts, and they cheered up their burned-out parents with funny dance performances and role-plays. After a few weeks, however, it became clear that our shift system was good for a sprint, but by no means for a marathon. The family life was neglected because one parent was always working. Besides the enormous double burden, we were also in a great internal conflict, because we weren't able to meet our own expectations with regards to professional challenges and childcare.

Would you have liked to receive more support?

Neither of us has family nearby that could help us with childcare. After about two months, our son went to emergency childcare for a few hours a day. Once contact restrictions were relaxed again, we were able to help each other out more with friends. Unfortunately, the HZI cancelled holiday childcare at the HZI during the summer holidays at short notice. We would have liked the planning to be more reliable. The core working time regulations have been waived in order to allow for flexible working hours. That definitely paved the way for our working model during the lockdown. That change, by the way, would also contribute to a better work-life balance regardless of COVID-19.

How did you organise the work with your research department?

Before the coronavirus pandemic, many scientists had already worked while travelling or from home. They were thus prepared to work from their home offices, using remote access and video conferences. Unfortunately, there are often technical problems, and the discussions often do not have the same dynamic as in person. When the institute gradually reopened, and the weather improved in the summer, we could hold many meetings outside. The time was particularly stressful for our international employees, who on the one hand had to experience the devastation the pandemic caused in their home countries, and on the other hand, often did not have a close social network nearby. ■

DR BERIT LANGE
Physician and epidemiologist at the HZI
Married; two children, 9 and 4 years old

Your primary residence is in Freiburg. How did you manage to combine science and home-schooling during the "hot phase"?

I am usually a weekly commuter. I work Mondays to Thursdays in Braunschweig, and Fridays from my home office at my family's house in Freiburg. For me, the first lockdown was demanding and exciting, but also exhausting. During that time, I significantly expanded my team to be able to tackle systematic reviews and impact assessment during the COVID-19 pandemic. At the same time, I monitored the planning for the MuSPAD antibody study. I also took on media communications and initiated various research applications. I was classified as systemically important, but my husband was not, and we were thus not entitled to emergency childcare. On the one hand, we had to equip our older kid with knowledge and equipment to master the various virtual and analogue school assignments. On the other hand, our little one often had to keep herself busy on her own, which is not always possible for a four-year-old. Video conferences with my child on my lap, who was playing, moaning, or screaming, were, therefore, the rule. And, of course, household chores always increase when everyone is at home the entire day. My husband, who heads a research group at a Fraunhofer Institute, took on more of that family work than I did.

What was your everyday life like?

I usually started working between 6 and 8 a.m. I then had a quick breakfast with my family around 8.30 or 9 a.m. The day was dominated by phone and video conferences. I could do the actual writing and calculations often only in the evening or on weekends. We had a quick lunch at about 12.30 p.m., a dinner between 6 and 8 p.m., and we then put the kids to bed. I often went back to work from 8 p.m. to 11 p.m. Of course, there were also the occasional night shifts. On weekends, I could take a break in the morning and only worked in the afternoon and evening.

What anecdote do you remember from that time?

I can best remember how I accidentally sent a washer-dryer to the wrong address (to Freiburg instead of Braunschweig) ... My husband, who knew nothing about that, was amazed when he was suddenly asked to accept a washing machine. He burst into a heated video conference with the sentence: "Tell me, Berit, did you order a washing machine?" I then had to explain that to my international partners during the video conference ... (sti, afi) ■

SHINING A SPOTLIGHT ON THE CELLULAR MECHANISM

by Nicole Silbermann

Antoine-Emmanuel Saliba researches the origin of infections

What exactly happens with infections in individual cells? How, where and when does the metabolism within infected cells change? "If we manage to gain a better understanding of this, we'll be able to find starting points for tailored and effective therapies," says Antoine-Emmanuel Saliba. He has been head of the Single-cell Analysis group at the Würzburg-based Helmholtz Institute for RNA-based Infection Research (HIRI), a branch of the Helmholtz Centre for Infection Research (HZI) headquartered in Braunschweig, Germany, for more than three years. To make the effects of an infection on cell metabolism visible, he compares healthy and infected cells in terms of their RNA (ribonucleic acid). RNA serves as a template for the production of proteins in the cell and indicates which genes have been activated in the cell. "By comparing the RNA profiles between healthy and infected cells, we can shine the spotlight on the cellular mechanism in detail and determine when and where it gets out of sync and where exactly pathogens throw a spanner into the works," explains Saliba.

His path towards infection research on a cellular level began with bioengineering studies in Toulouse. "Even back then, I had a keen interest in the microbiology and infection biology majors," says the 39-year-old with French-Lebanese roots. "What makes pathogens tick? At which points do they attack? How do they trick our cells? – Questions like these already fascinated me during my studies." During his doctorate at the Institut Curie in Paris, Saliba initially focused on a different topic and developed systems for cancer cell analysis. He then went to the European Molecular Biology Laboratory in Heidelberg, where he did research on methods to visualise protein-lipid interactions. "These are very important aspects in understanding how enzymes work in our body," says Saliba. "Biochemical research was exciting, but I wanted to research and work in an area that my heart beats for – infection research." Therefore, in 2013 he moved to the Institute for Molecular Infection Biology (IMIB) at the University of Würzburg, where he was involved in establishing RNA-based single cell analysis.

He has been working at HIRI since 2017 and heads a six-member team. Together, they hope to track down the machinations of pathogens in the cell – especially at the beginning and in the further course of an infection. "There are bacterial pathogens that can survive undetected in different cell types and cause recurrent infections," says Saliba. "Paradoxically, this is even the case in macrophages, i.e. in the immune cells that are actually responsible for destroying pathogens." In order to find the dark hiding spots of the pathogens in the cells, RNA-based single cell analysis can, figuratively speaking, turn on the spotlights. "The changes in the RNA profiles give us important clues as to exactly how the pathogens affect the cells in order to remain undetected for a long time," says Saliba. "The single cell analysis provides us with a valuable and promising analysis tool to effectively tackle infections from a new angle in the future."

While Saliba focuses on small details in his research, he loves to see the big picture in his private life: "For me, nothing is more beautiful than flying. My dream is to get my pilot's licence soon." Saliba has been living and working in Germany for more than ten years now. Doesn't he miss the French way of life now and then? "In gastronomic terms, sometimes I do," laughs Saliba. "But that's basically the only thing. I live and experience the German-French friendship every day, and that's really great!"

NEW SURVEY ON MENTAL STRESS IN THE WORKPLACE

by Jennifer Fricke and Heike Kollmus

Absences due to mental illness continue to rise. Regular monitoring of stress in the workplace is intended to prevent this

In today's working environment, we are increasingly exposed to psychological stress. Frequent stress factors are tight deadlines, lack of communication, problems in hierarchical cooperation, increase in work intensity, unpredictable nature of working hours, and constant interruptions when executing actual tasks. Ultimately, this stress increases the number of sick days due to mental illness. The results of the current Psychoreport 2020 (psychological report) by the health insurance fund DAK-Gesundheit show that the number of sick days due to mental illness reached a new high in 2019. For every 100 policyholders, there were about 260 days of absence caused by mental illness. The number of these days of absence increased by 137 per cent between 2000 and 2019 (source: Ärzteblatt.de). Since the end of 2013, the law has stipulated that employers must carry out a risk assessment for psychological stress. This assessment is intended to identify and classify possible psychological risks in the context of work. In the next step, employers should derive occupational safety measures that would eliminate these risks or reduce them as far as possible. Regular recording of psychological stress should steadily improve working conditions.

At the Helmholtz Centre for Infection Research (HZI), a steering group deals with mental stress in the workplace. It consists of two persons delegated by the management and the works council and has the task of planning, initiating, and organising the risk assessment. Current members of the steering group are Jennifer Fricke (works concil), Heike Kollmus (quality management), Carsten Strömpl (occupational safety specialist), and Thomas Twardoch (works concil). The steering group works together with the head of the human resources department, the representative body for disabled employees, the equal opportunities commissioner, the head of the family office, the head of the addiction prevention working group, the company doctor, and representatives of the employees.

The next monitoring of psychological stress factors at the HZI is scheduled for the spring of 2021. For this purpose, an online survey will be conducted using the tool COPSOQ (Copenhagen Psychosocial Questionnaire) which allows a preliminary analysis to measure psychological stress. It contains questions from different categories: organisation of work, work content, work tools and environment, social relationships, and additional questions about how the working environment has changed due to the corona pandemic. The results obtained can be compared both internally at the HZI, as well as to 120,000 deposited data sets from commercial enterprises and other public institutions. Participation in the survey is voluntary for all employees. An external service provider analyses the questionnaires anonymously and provides all participants with their individual results online. Once the rough analysis has been evaluated, external consultants also provide support for detailed analysis if necessary, for example in the form of workshops or interviews. Based on the results obtained from those sources, the steering group will propose to the management possible implementation measures that should prevent, reduce or, in the best case, completely eliminate stress.

It is important that all employees of the HZI participate in order to obtain representative results and thus achieve the greatest possible improvement for all employees. Therefore, the steering group, the works council, and the management kindly asks you to participate in the survey. In spring 2021, HZI employees will receive an invitation from the steering group by email. The steering group is also happy to answer any questions.

NEWS

AWARD WINNING WORK

Rolf Müller, Managing Director of the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS) and head of the department "Microbial Natural Products", has received the Gottfried Wilhelm Leibniz Prize 2021. With this award, the Deutsche Forschungsgemeinschaft ("German Research Foundation") recognised Müller's outstanding achievements in natural products research and biomedical microbiology. With funding of up to 2.5 million euros over seven years, the Leibniz Prize is the highest endowed award regularly presented to scientists in Germany.

FLYING VISIT BY THE NOBEL PRIZE WINNER

"Finally," many will have said when **Emmanuelle Charpentier** received the 2020 Nobel Prize in Chemistry for her groundbreaking work on the genome editing tool CRISPR-Cas9. Just a few days after the announcement, Charpentier made a brief visit to the HZI, where she headed the "Regulation in Infection Biology" department from 2013 to 2015. "I am overwhelmed and deeply honoured to receive an award of such high distinction," she said. The HZI sincerely congratulates!

MY CORONA

The HZI Summer Party 2020 had to take place virtually as a video conference due to the COVID-19 pandemic. An integral part was the meanwhile traditional photo competition, for the current occasion this time under the motto "My Corona: Pictures From an Unusual Time". The employees voted these photos to the first places:

1ST PLACE: Berenike Henneberg (FC)

2ND PLACE: Diego Ortiz (MIKI)

3RD PLACE: Khadija Hassan (MWIS)

NEW PHD REPRESENTATIVES

In 2021, the HZI doctoral researchers will be represented by **Janyn Heisig** (VAC), **Marco Kirchenwitz** and **Christopher Lambert** (both MZBI). Kirchenwitz was already a spokesperson for the PhD initiative DO IT last year, Heisig and Lambert now succeed Carsten Peukert and Arne Bublitz. Together with the HZI Graduate School, DO IT represents the interests of doctoral researchers and promotes compliance with quality standards and continuous improvement of working conditions.

Janyn Heisig

Marco Kirchenwitz

Christopher Lambert