HZI HELMHOLTZ Centre for Infection Research

# InFact

The magazine of the Helmholtz Centre for Infection Research | November 2019



# GERM TIME

## Safe protection against infections

## EDITORIAL

# Dear readers,

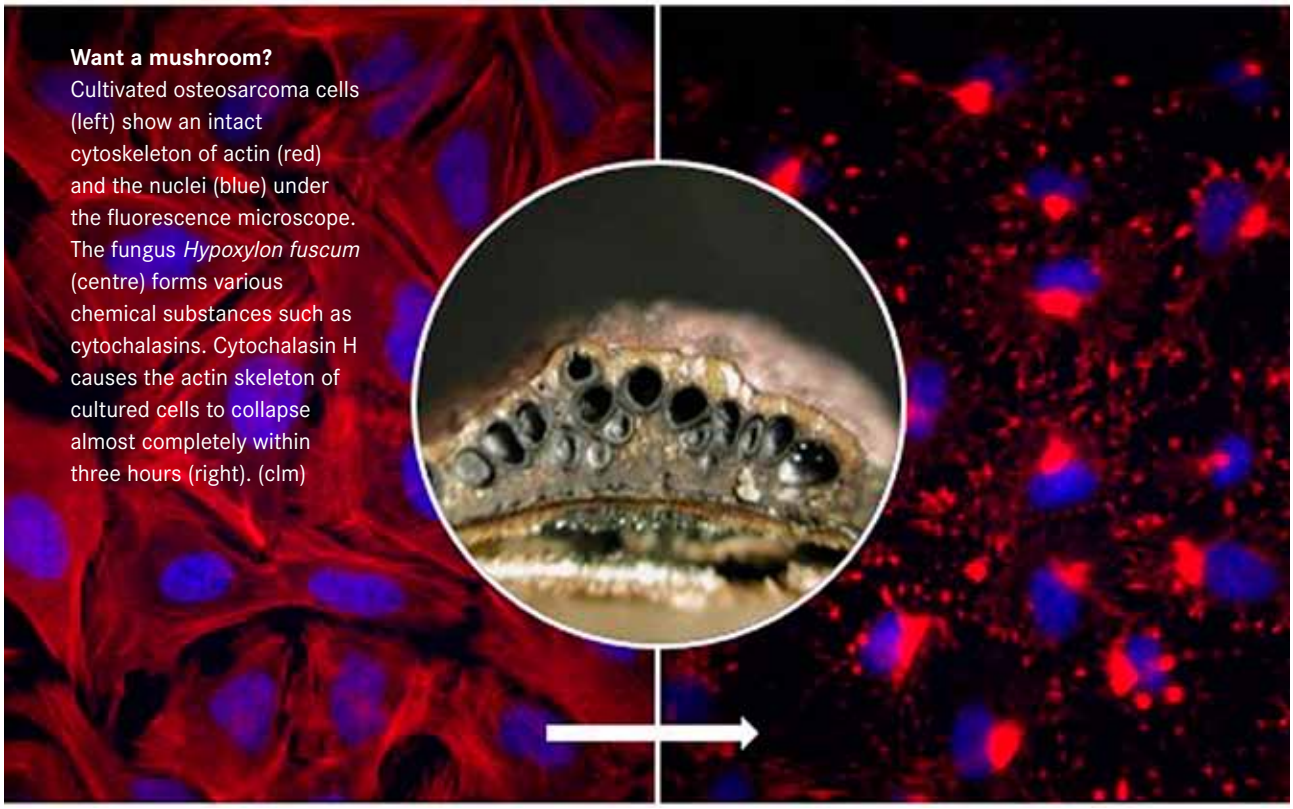
*Everywhere in us, on us and around us is teeming with bacteria, viruses and fungi. In fact, there is nothing wrong with that, because most microbes are completely harmless and, together with viruses, help to train our immune system, for example. Every now and then, however, an infection can occur. We have the most effective - and simplest - protective measures in our hands: Proper hygiene can already greatly reduce the risk of many infections, while the vaccinations recommended by the Standing Committee on Vaccination protect us against a number of aggressive pathogens. Read more about how to prevent infections in our cover story.*

*Pathogens are so tiny we cannot see them with the naked eye. An impressive technique for visualising the smallest structures is electron microscopy, which Manfred Rohde perfected at the HZI for research of infections. The topic article on page 8 presents his work to you. Furthermore, Ulrich Kalinke reports in an interview on the latest trends at TWINCORE in Hannover.*

*I look forward to your feedback and wish you pleasant reading!*

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

## EYE-CATCHER



**Want a mushroom?** Cultivated osteosarcoma cells (left) show an intact cytoskeleton of actin (red) and the nuclei (blue) under the fluorescence microscope. The fungus *Hypoxylon fuscum* (centre) forms various chemical substances such as cytochalasins. Cytochalasin H causes the actin skeleton of cultured cells to collapse almost completely within three hours (right). (clm)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Phone: +49 531 6181-1404
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**Editorial staff:** Susanne Thiele (V.i.S.d.P), Andreas Fischer (afi, Editor-in-chief), Yan Yan Beer (ydz), Christine Bentz, Jan Grabowski, Hansjörg Hauser, Christopher Lambert (clm), Minh Tam Nguyen, Jördis J. Ott, Carsten Peukert, Monike Schlüter, Nicole Silbermann

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# 10 YEARS OF HIPS

*by Hansjörg Hauser*

The HIPS is one of the very first Helmholtz Institutes. This summer, it celebrated its 10th anniversary with a large symposium and a barbecue

In 2008, the German government initiated a programme to establish so-called "Helmholtz Institutes", collaborative institutions connecting Helmholtz Centres and universities. In the first Call for Proposals, the new institutes had to be set up in federal states without a Helmholtz Centre. One of the potential federal states was Saarland, and Rudi Balling, at that time Scientific Director of the Helmholtz Centre for Infection Research (HZI), immediately seized the opportunity: He contacted Rolf Müller, a former Junior Research Group Leader at the HZI, who at the time was successfully heading the Institute for Pharmaceutical Biotechnology at Saarland University. The idea to get Rolf Müller back to HZI had been discussed before. Suddenly, through this call, the opportunity emerged to tie Müller's capacity to the HZI and combine the outstanding expertise in pharmaceutical research in Saarbrücken with infection research being carried out in Braunschweig.

Rolf Müller then suggested building the new institute with three departments led by himself and two colleague professors from Saarland University, Rolf Hartmann and Claus-Michael Lehr. Finally, an international review panel – set up by then Helmholtz president Jürgen Mlynek – recommended the establishment of the institute resulting in the foundation of the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS) ten years ago on 24 August 2009.

Today, HIPS still consists of the three original departments but with a number of associated research groups. "The collaboration with Saarland University emerged as a fruitful cooperation from early on, something that cannot be taken for granted," says Rolf Müller. "Thanks to the former president Volker Linneweber and the current president Manfred Schmidt, this partnership is a great win-win situation for both sides and is characterised by an open culture of exchange and support."

△ At this year's HIPS Symposium about 300 participants celebrated the anniversary of HIPS

Over the past ten years, HIPS has succeeded in attracting outstanding young scientists and has offered many a springboard for their careers. A brief review of the scientific activities of HIPS shows enormous achievements: Hundreds of new natural compounds have been discovered with dozens of new anti-infectives and a remarkable array of lead compounds with fancy names have moved forward along the value chain. Examples are cystobactamide, chlorotonil, chelocardin, griselimycin, corrallopyronine and pathoblockers targeting bacterial communication. Additionally, HIPS researchers have made significant contributions towards better drug and vaccine delivery. Twelve of 39 infection-related patent families of the HZI are the work of HIPS scientists. More than 800 publications were released, many of them featured in highly ranked journals. Third party funding accounts for almost half of the HIPS budget, including funds from the Federal Ministry of Education and Research (BMBF), European Union, Helmholtz Association, German Center for Infection Research, Bill & Melinda Gates Foundation, Innovative Medicine Initiative as well as GARDP and Carb-X. Last but not least, the HIPS is engaged in numerous national and international collaborations including industrial partners – the prospects for new drugs and therapies against infectious diseases are therefore quite promising.

# HOW WE PROTECT OURSELVES FROM INFECTIONS

*by Andreas Fischer*

We live our everyday lives together with countless microbes and viruses that could also infect us. The immune system prevents many attacks, but it needs our cooperation: Proper hygiene and regular vaccinations effectively protect against infections

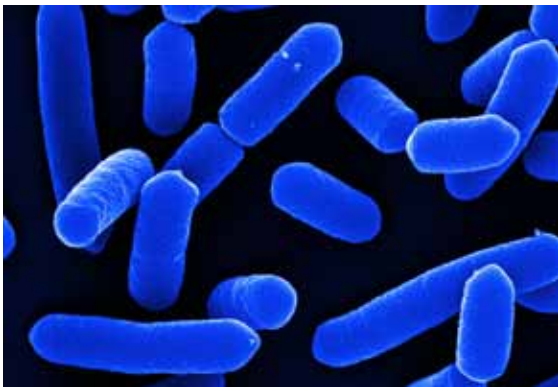
Viruses, bacteria, fungi and yeasts are lurking everywhere. Whether at home or work, in the hospital or even on or in human bodies – they can be found on every centimetre of every surface on Earth. The vast majority of microorganisms and viruses, which are not counted as living creatures, cannot harm us. Quite the opposite: Microbes are extremely useful in breaking down waste and toxic substances or, as intestinal flora, supporting our digestion. However, a few species may also cause infections, specifically if they reach the body at the wrong place or in a too large number.

We are exposed to microorganisms anywhere in our environment, because they are omnipresent. Litter bins, cleaning rags or the refrigerator characterised by their combination of moisture and food leftovers are specifically preferred places for growth of microorganisms. Bacteria and fungi especially reside and grow in open-ended food, for example in juice bottles that have been opened but not kept refrigerated or on wooden chopping boards, where bacteria such as *Campylobacter* or *Salmonella*, the most common causes of gastrointestinal infections, can often be found after handling poultry.

In fact, the human body is so attractive to microorganisms that the number of microbial inhabitants exceeds that of the human cells. For example, staphylococci are the most prevalent natural colonisers on the skin and in the nasopharyngeal cavity. However, staphylococci and specifically *Staphylococcus aureus* can also cause serious wound infections. MRSA (Methicillin-resistant *Staphylococcus aureus*) is resistant to common antibiotics and thus extremely difficult to treat. About 20 per cent of the human population carry *Staphylococcus aureus* in their nose, without being aware of it – but is

▽ Correct hand washing takes at least half a minute

△ Dietmar Pieper (centre) together with his HZI research group



△△ The bacterium *Staphylococcus aureus* can have several resistances at the same time

△ *Listeria* can lurk in contaminated food

that a reason for panic? Dietmar Pieper, head of the "Microbial Interactions and Processes" research group at the Helmholtz Centre for Infection Research (HZI), answers with a decisive 'no': "Bacteria are necessary for training the immune system, too. This is why we cannot and should not live in a sterile world." However, multi-resistant bacteria such as MRSA pose a threat, and require stricter hygiene measures – also to protect other humans.

## DAY-TO-DAY PROTECTION

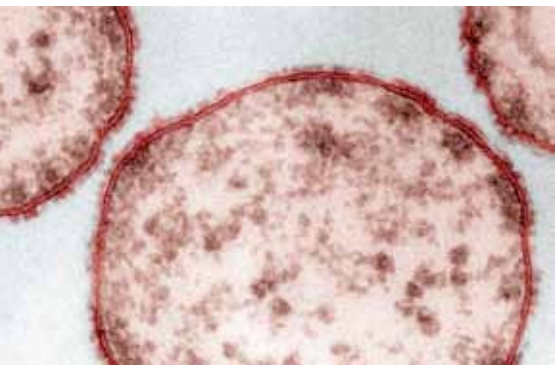
Our everyday lives confront us with many potential risks for infections, and often these cannot be avoided. "A shipment of food can sometimes be contaminated, for example with listeria," says Pieper. "Protection against it is difficult, because such a case is relatively rare and you cannot see it in the food." To minimise the risk, the microbiologist warns against eating any spoiled food in which both bacteria and fungi can grow and form toxins. In addition: "Foreign countries, foreign microbes. Therefore it is safer to prefer cooked food," says Pieper. A frequent path of infection is via the hands, as they may collect germs from different surfaces and transfer them to the mouth or nose. This contact infection can also transmit viruses including influenza or gastrointestinal bacteria such as *Escherichia coli*, but most environmental bacteria are harmless. The best protection is also the most simple: "In everyday life, regular hand washing with soap is more than sufficient; this is also better for the skin than disinfectants," says Pieper. However: Hand washing needs to be done properly. Quickly holding your fingers under the tap is not enough. The health authorities recommend holding your hands under running water, rubbing them with soap for 20 to 30 seconds, rinsing them again under running water, then drying them using paper towels or your own personal hand towel. In order to avoid infections, it is important to wash your hands every time you blow your nose, use the toilet, stroke an animal or handle raw meat.

## ARMING THE IMMUNE SYSTEM AGAINST TRICKSTERS

Viruses are particularly adept at taking over a human body. They change quickly and constantly surprise the immune system with new disguises. This means that the immune cells only register them as pathogenic once the infection is already underway. But the immune system can remember some pathogens for a lifetime; these include the rubella virus and the measles virus, which is responsible for the recent measles outbreaks. The immune system has a good memory that can be strengthened in these cases, without the need to first suffer through the sometimes life-threatening infections: "Vaccinations, along with hygiene and access to clean water, are one of the most important elements in preventing infections," says Berit Lange, medical doctor and epidemiologist at the HZI "Epidemiology" department. "A good vaccine can even eradicate a pathogen."

Vaccination has already achieved some major successes, such as the eradication of smallpox. The poliovirus, which causes infantile paralysis, has also largely disappeared. Thanks to consistent vaccination programmes, Germany has been polio-free since 1990 – with two last imported cases in 1992. Polio infections with the wild virus only occur in Pakistan and Afghanistan, from where the viruses could be spread to other countries, and therefore vaccination is still necessary. A prerequisite for the eradication of a pathogen with human-to-human transmission is herd immunity: This occurs when so many people are vaccinated or immune that individual cases of infection do not spread further. The level of coverage required depends on how effective the vaccine is, and how easy or complicated it is to transmit the pathogen required for infection. "In the case of measles, the necessary vaccination coverage is quite high at 95 per cent, even though the vaccine is very effective," says Berit Lange. "This is because one person with measles infects an average of 15 others."

△ Berit Lange is a medical doctor and epidemiologist



△△ Vaccinations are the safest protection against many infections

△ The measles virus could already be eradicated in Germany

## SHOULD VACCINATION BE COMPULSORY?

The Robert Koch Institute found that a decreasing number of children have been vaccinated recently: Since 2014, the rates of standard vaccinations against tetanus, diphtheria, whooping cough and polio have declined slightly. For measles, the vaccination rate has stagnated at a level that is too low, especially for the second vaccination, which means that there is still no herd immunity. Full protection can only be obtained after two vaccinations. This also applies to mumps, rubella and chickenpox. “The willingness to vaccinate and the vaccination coverage against measles in Germany is by no means bad, but it is still not high enough to eliminate measles,” says Lange. According to the World Health Organization (WHO), at least 95 per cent of the population must be vaccinated twice to eliminate measles. Germans have only achieved this figure for the first vaccination, with a total of 97.1 per cent, while the rate for the second vaccination has stagnated at 92.8 per cent (2016, 2017). So far, only two federal states have broken the 95 per cent mark for both vaccinations: Mecklenburg-Vorpommern and Brandenburg. Baden-Württemberg is the worst performer nationwide, with only 89.1 percent. The goal of eradicating measles cannot be achieved with these numbers, which, given the regional outbreaks of measles, has now led to the introduction of compulsory vaccination.

“As a doctor, I would rather convince people to get vaccinated than force them. From a healthcare perspective and as a researcher, I can understand the introduction of compulsory vaccination. But I find it disappointing that this step was felt to be necessary,” says Berit Lange. “I think that it is right, however, that only vaccinated children can be accepted into childcare centres – especially with children under the age of three – in order to protect the children who cannot be vaccinated.” It is also important that the centres know which of the registered children are vaccinated and which are not. “This documentation will certainly be improved by the new law.”

The “Epidemiology” department at the HZI is researching how to ensure that vaccines and vaccination campaigns remain safe and lead to the highest possible vaccination coverage. For example, a project team, led by Lange’s colleague Jördis Ott, has developed the “SafeVac” app as part of a study, and is now investigating how successfully it can be used to monitor symptoms after an influenza vaccination. Berit Lange and colleagues at the University Hospital in Freiburg are investigating how diseases that we could be protected against by vaccination can best be prevented in more susceptible population groups.

## HOSPITALS AS GERM FACTORIES

More and more pathogens are becoming resistant to antibiotics. This is specifically due to the excessive use of antibiotics, for example in animal breeding and in patients that do not need antibiotics such as in the case of colds caused by viruses. Antibiotics only fight bacteria and are completely ineffective against viruses. Used incorrectly, antibiotics only encourage the development of resistance. “Bacteria can mutate or take up foreign DNA, resulting in the natural development of antibiotic resistance,” says Dietmar Pieper. “That is why resistant bacteria are found everywhere and in each one of us.” Resistant bacteria may also develop in hospitals and can further spread through inadequate hygiene and also via wastewater. “Proper hygiene measures are critical when dealing with patients. Thorough hand washing and disinfection after each patient contact must be routine,” says Pieper. But good hygiene also relies on properly trained medical personnel. “In the Netherlands, every patient in the hospital is tested for carriage of MRSA – with the result that hospital acquired infections with this pathogen are far less common there,” says Pieper.

In addition to the growing danger posed by multiresistant bacteria, strains of all bacteria on and in us are under unknown circumstances capable of triggering an infection, for example in severely immunocompromised people,” says Pieper. “However, no one should fear these microbes, as life without them is impossible.”

# SAFEVAC: STUDY ON APP-BASED REPORTING OF SYMPTOMS AFTER INFLUENZA VACCINATION

*by Monike Schlüter, Minh Tam Nguyen, Jördis J. Ott*

To ensure the safety of vaccines, they have to be continuously monitored even post licensure. Could a new mobile app help?

Adverse events occurring after vaccination can be reported through the spontaneous reporting system of the Paul-Ehrlich-Institut (PEI), the Federal Institute for Vaccines and Biomedicines. However, such reports are often incomplete and delayed; little is known about vaccinated persons without (reported) adverse events.

The influenza vaccine is one of the most frequently administered vaccinations in Germany, and its composition changes annually. As part of an epidemiological study, researchers of the Helmholtz Centre for Infection Research (HZI) and the PEI developed a mobile app to collect detailed data on the presence and absence of symptoms after vaccination and to evaluate the feasibility of an app-based reporting system. The study is also a doctoral project in the PhD programme "Epidemiology" of the HZI department by Gérard Krause and is funded by the Federal Ministry of Health. The newly designed app SafeVac is based on both the existing reporting system and the results of a preliminary study on user preferences, conducted by the HZI and PEI.

The app was implemented in three institutions, e.g. the University Hospital of Frankfurt, during the occupational influenza vaccination in 2018. In total, 337 study participants were recruited and installed SafeVac on their smartphones. The participants entered information on the presence and absence of symptoms for up to three months after vaccination. Preliminary results show that the majority of participants are between 18 and 30 years old (44.51 per cent, 150/337) and indicate 'Abitur' (general qualification for university entrance) as their highest school qualification (83.98 per cent, 283/337). Around two thirds (71.81 per cent, 242/337) of the study participants were vaccinated against influenza within the last five years. Gender, education level and age did not impact the duration of app usage and reporting adherence. Current analyses aim to identify determinants of app usage, for example the occurrence of adverse events or the subjective evaluation of the app's usability. In addition, the reported adverse events after vaccination are analysed with regard to their type and frequency – for example, to conclude on trends over time.


This epidemiologic study shows the feasibility and applicability of an app for active reporting of adverse events up to three months after vaccination. The department of Epidemiology and the PEI therefore aim to use these findings as a foundation for a possible expansion of the project. Future research can investigate to which extent this reporting system is applicable to other vaccines, if different groups of persons can be reached by using apps in addition to the existing reporting system and how generated data on adverse events can improve vaccine safety in general.

△ Electron microscopic image of the bacterium *Prosthecomicrobium hirschii*

# PATHS INTO THE UNKNOWN

*by Christine Bentz*

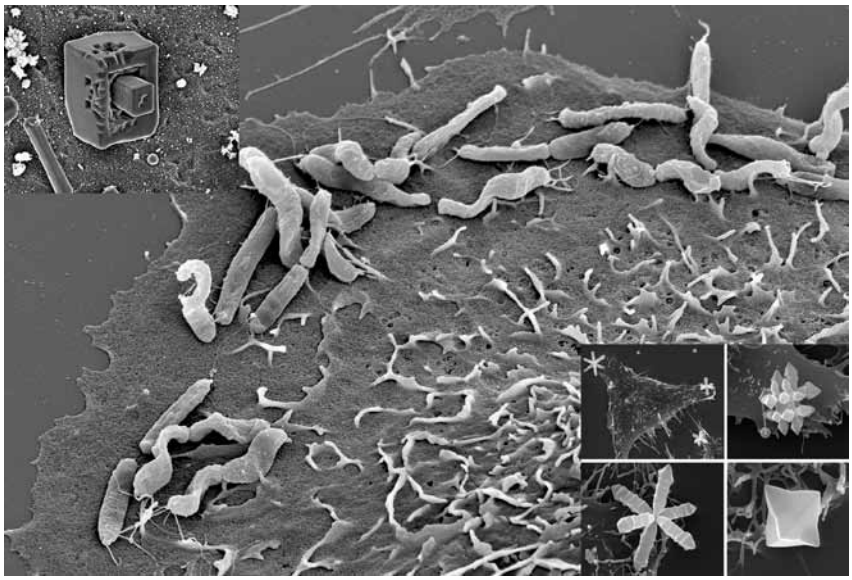
The Central Facility for Microscopy at the HZI works at the highest professional level, always discovering something new – even with the naked eye. We reveal how that works

◁ Manfred Rohde in action at the electron microscope in 1998 (top) and with visitors at today's device (bottom)

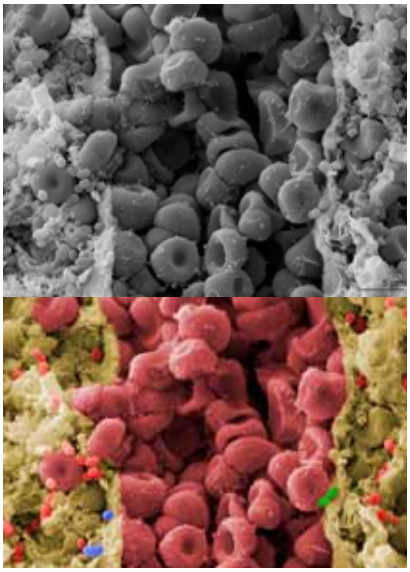
Electron microscopy (EM) is not some monotonous assembly-line job, because each assignment poses new challenges. A diverse range of things is magnified and examined, such as immune cells, algae or phages – the work is always different and always interesting. However, biological EM is only practiced by four specialists in Germany. One of these highly qualified experts is Manfred Rohde at the Helmholtz Centre for Infection Research (HZI).

EM started in 1982 at the former Gesellschaft für Biotechnologische Forschung (GBF) and in 1989 moved into a new building, which presented a major challenge in itself: The floors of the new building were covered with vibrating screed, which is not suitable for microscopes, as they are highly sensitive to vibrations. In addition, the floors were covered in linoleum. Carpet would have made more sense here, as linoleum quickly ruptures when it comes into contact with nitrogen. But all these obstacles were overcome and the employees continue to do this today. Even the prospect of a slipped disc, which is an occupational hazard for microscope operators, cannot keep this true enthusiast from his work. "I have found my ecological niche here," says Manfred Rohde. It is a passion that also requires talent. The human factor is still indispensable, because the eye sees far more than a comparison made by a computer programme, especially when that eye belongs to an experienced EM professional.

Good preparation is crucial for achieving good results, so manual work is required. The guiding principle here, pronounced with a wink, is "Crap



◁ In older preparation methods, salt crystals have often formed on the prepared cells (small pictures above left and below right), which hardly happens with today‘s standard method (background picture)



△ Streptococci in a mouse spleen: Without subsequent colouring of the image, the bacteria are difficult to recognise (small red, blue and green “balls”)

in, crap out”. Sometimes even the most knowledgeable expert has to try different things to find the right method for a specific preparation. The goal is to preserve the structure, but collapsed membranes or burst cell walls are typical mishaps that occur on the path to achieving this. Rapid freezing in cryo-EM is especially essential for samples with a high water content, explains Rohde. Slowly reducing the temperature would lead to crystallisation and damage or even destroy the preparation. In addition, crystals obstruct the view of the most important thing, i.e. the organic material. Rapid freezing without crystallisation can be achieved through either lowering the temperature to -196 degrees Celsius or by using high-pressure freezing in liquid nitrogen at a pressure of 2000 bar. Cryo-EM, which was made possible as early as the end of the 1950s, has the advantage that the preparations remain absolutely pure, since no chemical additives are used – ultimately, it is just a matter of freezing. A quote from the Spanish explorer Christopher Columbus can be applied to the motivation of the people who have found their vocation in microscopy: “When the old paths to the familiar are crowded and worn out, I will follow new paths into the unknown, overcome borders, expand my mind and return home with things that no one has ever seen before,” he said, according to legend. The unique insights that the microscopes, some of which are used at magnifications up to 200,000 times, offer are exactly that: images of the unknown and, in the moment of their discovery, reserved solely for the initiated. Over the years, the small departments at the GBF and later at the HZI typically consisted of just three scientists and a technical assistant, with two of the former TAs later even deciding to study biology out of enthusiasm for the subject.

The images created by microscopy look as if they come from another world and evoke great fascination. The imaging possibilities have changed dramatically in recent decades, with the largest technical change that has had the most significant impact on everyday work being the invention of the “slow scan camera”. This means that images no longer have to be transferred to film plates as static single shots. The images are now digital and can be processed in any image-editing programme – and the pictures can be taken in daylight. The negatives that were previously used needed to be shot in the dark, and a darkroom was required. Two days a week had to be set aside for developing the images in the darkroom, meaning that this new technology also saves an enormous amount of time. “The digital scanning microscope has a screen, so it‘s similar to watching television,” says Manfred Rohde. But 20,000 old negatives are stored in the HZI archives and these are still usable for research purposes once they are magnified. One thing has not changed: Black-and-white images are subsequently coloured. “This not only makes them more visually appealing, it also makes it easier to identify crucial details,” says Rohde.

In the equipment pool at the HZI, you will find cutting-edge technology being used alongside 26-year-old devices that are still performing well. Also still in use are the dimmable neon lights on the ceilings, which have been performing their duty since 1993 and were quite the sensation at the time. Manfred Rohde is grateful for both progress as well as stability. And that his first supervisor, Ken Timmis, gave him the freedom from day one to choose his assignments according to his own interests. This has led to many different collaborations, which have resulted in numerous publications in high-ranking journals. The microscopy unit at the HZI operates at the highest level of quality and discovers something new every day. Sometimes even with the naked eye. Christopher Columbus would have liked it.

# "BIG DATA IS ONE OF THE BIG TOPICS OF THE FUTURE, ALSO FOR INFECTION RESEARCH"

*by Jan Grabowski*

A year after its 10th birthday, numerous changes are on the agenda at TWINCORE. Ulrich Kalinke, Scientific Director of the Centre for Experimental and Clinical Infection Research, speaks to us about clinician scientists, big data and new research topics

**Professor Kalinke, there are major changes being made at TWINCORE at the moment. Why is that?**
In recent months, several research group leaders have taken up new positions at other research institutes. We are proud that our people have been so successful in the selection procedures! And it also offers us the opportunity to explore new topics and redevelop research areas.

**One of these departures was Tim Sparwasser, who held the professorship of infection immunology. Will you reappoint this position?**
Most definitely, yes! Infection immunology is of key importance for TWINCORE, just as it is for the Hannover Medical School (MHH) and the HZI. The future focus of this position, however, will be more on human immunology.

**What other changes are on the agenda?**
One of the aims of TWINCORE was, and still is, to support clinician scientists, i.e. doctors who care for patients and are also actively involved in research, throughout all stages of their careers. In the past, we had not succeeded in establishing a sustainable model for clinician scientists, for example in the form of a research group leader position, but we have now achieved this goal. We have recruited Patrick Behrendt to head a clinician scientist junior research group in virology, which he has already started. He will invest about half of his time in patient care and the rest of the time will be available for research. We will soon announce a similar position in the area of immunology. Furthermore, we are also working on establishing a long-term collaboration with the Institute for Medical Microbiology and Hospital Epidemiology at the MHH. I am especially pleased that the joint establishment of a junior research group has been successful: Volker Winstel started his new position at TWINCORE on 1 September. He researches the hospital germ *Staphylococcus aureus*, and this will also lead to some new interactions with the HZI.

**What is the future of big data and personalisation at TWINCORE?**
We are currently enjoying a very good funding situation, which allows us to implement a whole series of measures. I would particularly like to highlight the two professorships in the area of data sciences in bacteriology and virology, both of which are funded by the RESIST cluster of excellence. In addition, TWINCORE is also participating in a total of five applications in the big data call from the Lower Saxony Ministry of Science and Culture. Three of these projects, in the areas of respiratory syncytial virus (RSV), noroviruses and immune monitoring, are being coordinated directly by TWINCORE. And of course, it is in our interest that the establishment of the new Centre for Individualised Infection Medicine (CiiM) is a success. This centre will open up new research perspectives for TWINCORE that we would otherwise never have been able to achieve alone. The CiiM will also help to improve the transfer of the latest findings to clinics, for the benefit of patients. That is why we are very happy to be accommodating the data scientists Yang Li and Cheng-Jian Xu, who have been appointed to the CiiM, at TWINCORE until the new CiiM building is completed. Through our close proximity, a wide range of collaborations has already been established with both of them. We

△ Ulrich Kalinke has been Managing Director of TWINCORE since 2008, where he heads the Institute for Experimental Infection Research

will also welcome Markus Cornberg as a clinician scientist at an advanced career level to TWINCORE. He will lead the CiiM together with Yang Li.

**How do all of these changes fit with the centre's strategy?**

The TWINCORE strategy is to align infection research topics to medical challenges and clinical observations. This means that establishing new positions for clinician scientists is very important to us and we also place great value on interdisciplinarity. Consequently, the situation with the RESIST professorships, the big data projects and the temporary residence of Yang Li and Cheng-Jian Xu at TWINCORE is very helpful for us. Without knowing that the conditions in the field of big data would develop so favourably at TWINCORE, we had already decided last year that the title of this year's TWINCORE symposium should be "Infection Research meets Big Data". Everyone who participated in the symposium was again able to experience for themselves the exciting new perspectives that data sciences open up for us. Big data is undoubtedly one of the big topics of the future, also for infection research.

**What are these perspectives? What exactly will be researched in the new projects?**

The new approaches from the field of data sciences allow us to better understand extremely complex systems. For example, it enables us to analyse extensive data sets from patient cohorts with RSV or norovirus infections. At the same time, we can also merge very different data sets, and we are currently working on this in the immune classification of some individuals. In addition to information about individual types of immune cells, these new approaches can also take into account a diverse range of clinical parameters. The aim of this work is to obtain an improved understanding of how the human immune system functions. Lastly, the new approaches also enable the investigation of expression profiles of individual cells. We are currently investigating how human dendritic cells react to stimulation with the human cytomegalovirus (HCMV) on the single-cell level. We can expect many surprises in the course of these investigations.

**About RESIST**

*In the RESIST (Resolving Infection Susceptibility) excellence cluster, researchers from a total of 40 groups of TWINCORE, HZI, MHH and three other institutions aim to find out why certain patient groups are more susceptible to infections than others. The cluster finances two professorships at TWINCORE: the unfilled W1/W2 professorship "Integrative Virus-Host Bioinformatics" at the Institute for Experimental Virology and the W2 associate professorship "Systems Biology for Microbial Communities" at the Institute for Molecular Bacteriology, for which Marco Galardini from Boston University was appointed.*

# “EVERY DAY I FEEL THAT I AM DOING SOMETHING MEANINGFUL”

*by Nicole Silbermann*

Alice McHardy reveals how she came to bioinformatics and what fascinates her about her work with massive volumes of data

△ Alice McHardy heads the “Computational Biology of Infection Research” department at the Braunschweig Integrated Centre of Systems Biology, a joint facility of the HZI and the Technische Universität Braunschweig

She had never been afraid of numbers. Mathematics and science were her favourite subjects even back in her school days. But Alice McHardy never thought that she would end up working as a researcher in a field of information technology when she enrolled in biochemistry at Bielefeld University. “In the first few semesters I quickly discovered that working in a laboratory was not my thing,” remembers the 42-year-old. A career as a biochemist – working in a laboratory, day in, day out – did not seem to be the right choice for her. “So I started to look for other options that would mean I could work in research without a white lab coat,” says McHardy. “Because the theoretical underpinnings in science were still fascinating to me.” She stumbled across bioinformatics and, during her search for a topic for her thesis, met a group leader in the Genetics department who explained to her everything that can be read from the genetic code of a bacterium using bioinformatics. “I was extremely impressed by how powerful computer-aided analyses are as a tool for deriving information from huge amounts of data and generating new knowledge,” says McHardy. From then on, she was hooked and her decision was made: After her biochemistry studies were complete, she hung up her lab coat and completed a PhD in bioinformatics.

Since then, the researcher with Scottish roots has been plunging into a flood of data on a daily basis, to search for new patterns, unmask a hidden code or solve a mystery of science. For instance, she developed data-driven computational methods to predict the nature of new influenza virus strains as accurately as possible. After her PhD, Alice McHardy worked at the IBM research centre in the USA for two years. She then moved to the Max Planck Institute for Informatics in Saarbrücken and lectured in computer science at the Saarland University. She became a professor in 2010 and was appointed to the University of Düsseldorf. In 2014, McHardy then came to the Helmholtz Centre for Infection Research (HZI). Her research is focused on identifying new approaches for treatment options and advancing individualised medicine in infection research, so that patients can be more effectively treated in the future.

“It is wonderful that I can actively shape my own work and pursue my own research ideas,” says McHardy. “Every day I feel that I am doing something meaningful – and that is very fulfilling.” Planning and implementing projects and preparing scientific papers with partners based all around the world are the particular highlights of her job. “However, I do not have much time for hobbies, especially reading and dancing. My family and my work are my main priorities right now. And building with Lego is also quite relaxing,” says McHardy with a smile. When she is sitting with her four-year-old, surrounded by the colourful blocks, she is still completely in her element: deriving a meaningful structure from the chaos of a flood of individual building blocks and always keeping an eye on the bigger picture. And there will always be time for reading later. Her research is just as exciting as a detective story – or even more so!

# CLEAR ROADMAP FOR THE DOCTORATE

*by Carsten Peukert*

The Helmholtz Association, in conjunction with the Helmholtz Juniors and Dirk Heinz, has developed new doctoral guidelines. What developments do they reveal in light of the doctoral student survey in 2017?

Doctoral studies qualify candidates for positions in academia or in the private sector. This phase is usually associated with the rapid development of personal and professional skills under a high level of stress every day. The progression and success therefore does not depend solely on the commitment of the doctoral candidate: The individual research institution can also enhance the project by offering graduate schools with relevant soft-skills courses. The Helmholtz Association outlined the necessary conditions in its doctoral guidelines for the first time in 2015, and these particularly emphasised the importance of graduate schools for a structured doctoral programme with appropriate supervision.

△ The Helmholtz Juniors met in July at the Helmholtz head office in Berlin

Every two years, the Helmholtz Juniors, who represent the doctoral researchers in the Helmholtz Association, surveys the doctoral researchers on their satisfaction with these conditions – the last survey was completed in 2017. A key finding of this survey was the belief that the doctorate could be completed in three years decreased as the project progressed: The number of people who believed that they required more than three and a half years to complete their doctorate increased from 22 per cent in the first year to almost 80 per cent in the third year. Approximately half of respondents stated that they had begun their doctorate without having developed a project draft in advance and that they were aiming for a duration of more than four years.

Satisfaction with remuneration and work-life balance varied wildly between the individual Helmholtz Centres. Only 40 per cent were satisfied with their conditions, with doctoral students in engineering and physics appearing significantly more satisfied due to the consistently higher remuneration. A total of 53 per cent of female doctoral researchers stated that they often or very often thought of abandoning their doctorate. For the male candidates, this figure was “only” 41 per cent. The main reasons for possible discontinuation included the supervision (43 per cent), project-related problems (36 per cent) and the workload (34 per cent).

The new doctoral guidelines for 2019, drafted with the participation of the Helmholtz Juniors and chaired by HZI Scientific Director Dirk Heinz, now paint a much clearer picture than in 2015. Among other things, they distinguish between a formal and a day-to-day supervisor and recommend a thesis committee for quality assurance. The committee would include two scientific experts from the institute as well as both supervisors. A project plan should be developed before the work actually begins, and it should be feasible to implement this work within three years.

For the first time, the guidelines include criteria for both doctoral researchers and their supervisors, and explicitly recommend the promotion of personal development, the presentation of one’s own project and career paths. Supervisors should also be offered further training. In the future, regular evaluations by Helmholtz and surveys by the Helmholtz Juniors will review the implementation of the guidelines and will be used to make adjustments. This makes the new doctoral guidelines an initial step towards recognising and promoting the individual potential of each doctoral researcher.

# NEWS

## AWARD WINNING WORK

As part of this year's HZI Summer Party on 5 September, a photo competition took place again - this time under the motto "Impressions of the Science Campus". The employees of the HZI voted for the best photos:

1ST PLACE: Alexander Seupt (MOBA)

2nd PLACE: Klaus Peter Conrad (MWIS)

3rd PLACE: Stephanie Schulz (MISG)

## NEW DEPUTY DIRECTOR

In August **Gerárd Krause**, head of the HZI department "Epidemiology", took over the position of deputy scientific director of the HZI with power of attorney. Krause succeeds Carlos A. Guzmán, head of the department "Vaccinology and Applied Microbiology", who held this position for five years but now wants to devote more time to his EU-funded vaccine projects.

## 30,000 PUPILS IN BIOS

Last August, the Biotechnologische Schülerlabor Braunschweig (BioS) broke through the 30,000 mark with a group of pupils. The BioS has been running since 2002 on the Science Campus Braunschweig-Süd in the premises of the HZI and offers laboratory courses for pupils in grades 10 to 12 (13). Through their own experiments in the laboratory, the participants gain an insight into biotechnological research. (afi)

## BUMBLEBEE PROTECTION AT THE HZI

In summer, dead bumblebees are amassing, especially under blossoming lime trees, as was the case this year on the Science Campus Braunschweig-Süd. The HZI is now planning activities to counteract the death of bumblebees. Usually, bumblebees do not die until autumn. However, the bumblebees that died in midsummer simply starved to death, as a study on the sugar reserves in bumblebees showed. Like honeybees, bumblebees feed on pollen and flower nectar, but hardly build up any stores. If the late-flowering lime trees no longer offer sufficient food for all insects, the less adaptable bumblebees usually lose out. This is remedied by additional plants that serve as sources of pollen and nectar for the bumblebees. In this context, the HZI is currently holding talks with a gardening and landscaping company to identify both suitable places on campus and suitable plants to expand the food supply for bumblebees. (ydz)

## SCHEDULE

**5 December:** 12th International PhD Symposium of the HZI Graduate School; HZI forum
**26. March 2020:** "Future Day" for girls and boys; HZI
**15 May 2020:** Visitor's Day for registered groups; HZI

## NEW PERSONNEL

**CSSB, Hamburg:** Jessica Schultz, STIB
**HIPS, Saarbrücken:** Lisa Marie Andre, DDOP | Sabine Backes, MINS | Alexander Kiefer, DDOP | Susanne Kirsch-Dahmen, MINS | Sangeun Lee, DDEL | Abhik Mallick, BION
**HIRI, Würzburg:** Christiane Albert-Weißenberger, ADMIN | Nina DiFabion, SIGA | Mathias Munschauer, LRIB | Sofiya Rachkevych, GARV | Gudrun Reinhard, ADMIN | Simone Werner, LRIB | Jiaqi Yu, RSYN
**HZI, Braunschweig:** Agata Bielecka, MIKI | Luiz Borges, MINP | Imke Dangelat, TEE | Hazel Fuchs, CBIO | Sara Haag, MOBA | Laura Jess, RPEX | Katjana Klages, MIKI/EXIM | Sarah Kramme, EM | Ivana Kutle, MSYS | Maria Lomeo, ORG | Hanna Meier, TEE | Maria Rinke, EM | Stefan Saretz, CBIO | Kumar Siddharth Singh, SFPR | Sara-Marie Soja, EPID | Nadine Wurzler, MWIS
**TWINCORE, Hannover:** Leonardo Araujo, BIOM | Luca Ghita, EXPI | Maurice Labuhn, EVIR | Inken Waltl, EXPI