HZI HELMHOLTZ Centre for Infection Research

InFact

The magazine of the Helmholtz Centre for Infection Research | November 2018

RACING AGAINST PATHOGENS

EDITORIAL

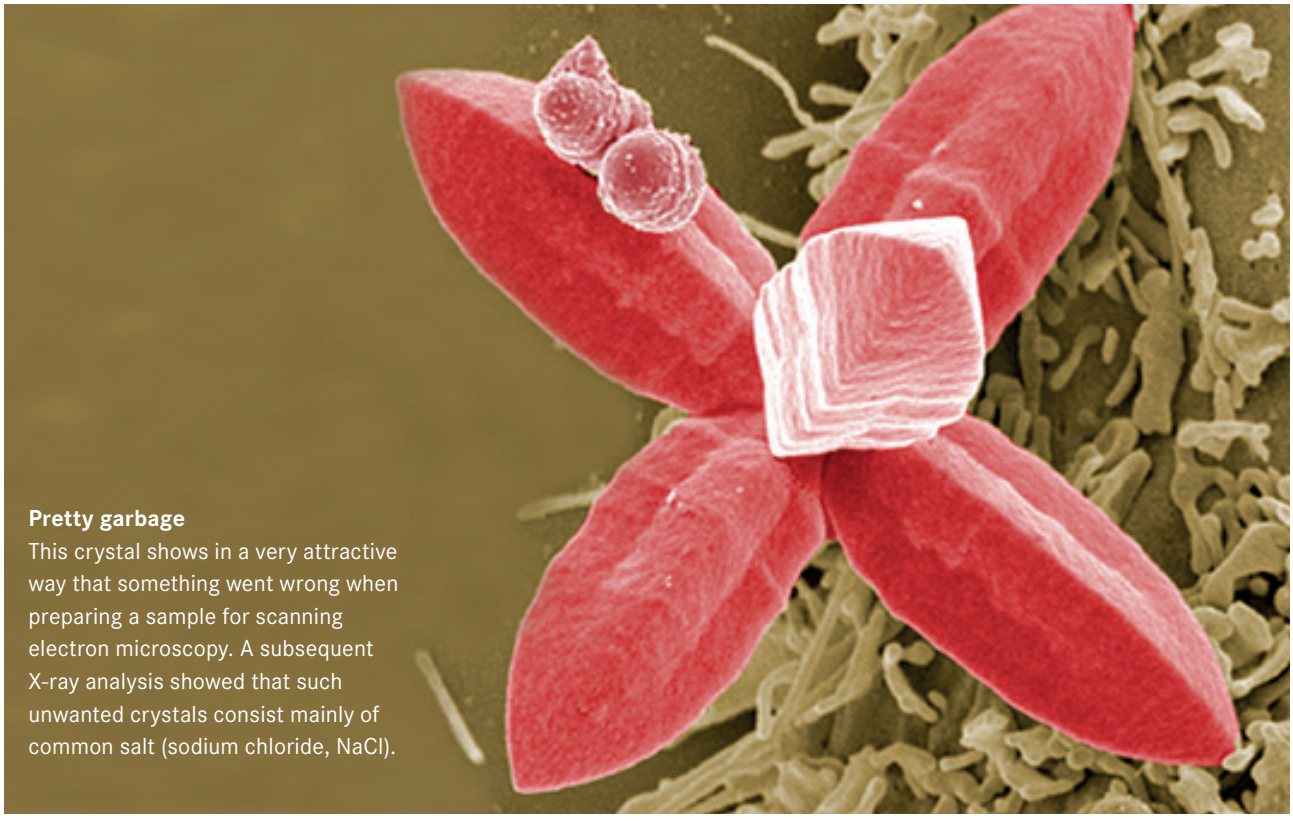
Dear readers,

pathogens that have become resistant to various antibiotics have been very present in the media lately and always cause great anxiety. The treatment of these pathogens is becoming increasingly difficult due to the lack of effective medications. This means that even harmless infections, for example small wounds, may soon turn harmful again. To make sure that this scenario does not come true, there is an urgent need for new classes of antibiotics – and alternative agents that do not force the development of resistance. Our cover story examines up-to-date research approaches and the present status of the race against resistant pathogens.
Searching for new agents against infections, scientists in Saarland are asking the populace for help: In the scope of a citizen science project, they are distributing sets for the collection of soil samples, which they then check for new species of soil bacteria. These microorganisms produce substances with an antibacterial and antiviral effect. Read about the project from page 8.

I look forward to your suggestions and I wish you pleasant reading!

Andreas Fischer, Editor-in-chief

EYE-CATCHER



Pretty garbage
This crystal shows in a very attractive way that something went wrong when preparing a sample for scanning electron microscopy. A subsequent X-ray analysis showed that such unwanted crystals consist mainly of common salt (sodium chloride, NaCl).

IMPRINT

Publisher:
Helmholtz Centre for Infection Research GmbH
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Photo credits: Title: Fotolia; p. 2: János Krüger, Manfred Rohde; p. 3: TWINCORE/Jo Schilling; p. 4-6: TWINCORE/Janne Thöming, Manfred Rohde, Heinrich Lünsdorf, János Krüger; p. 7: Sarah Meinicke; p. 8-9: HIPS, HIPS/Ronald Garcia, https://hips.saarland/sample, HIPS/Oliver Dietze; p. 10: Verena Meier; p. 12: Hilde Merkert; p. 13: Photo Professional, Frank Bierstedt; p. 14: Marie Wieczorek
Editorial staff: Susanne Thiele (V.i.S.d.P), Andreas Fischer (afi, Editor-in-chief), Tatyana Dubich, Yvonne Kemmling, Tobias Kerrinnes, Daniel Krug, Nina-Vanessa Littwin, Jo Schilling
Design: Britta Freise
Print: MAUL-DRUCK GmbH & Co. KG

FSC www.fsc.org MIX Papier aus verantwortungsvollen Quellen FSC® C106855

Climate neutral
Print product
ClimatePartner.com/11022-1810-1004

10 YEARS OF TWINCORE

by Jo Schilling

Any tenth anniversary is quite special: It is a good opportunity to risk a look into the future, to look at the past and it is a wonderful occasion to gather friends and celebrate – and this is what the TWINCORE did during its tenth symposium on 30 August 2018

Naturally, the focus of this year's TWINCORE symposium, almost exactly ten years after the institute's founding ceremony, was on research – as the birthday child TWINCORE was not expected to suffer pre-adolescent excesses. But two days with 250 visitors at the symposium provided a scope for a little more than just science. But let's take one step at a time:

Firstly, there was the title of the symposium, "Frontiers in translational infection research", which directed the view to the future. In the past ten years, the TWINCORE – a joint institution of the Helmholtz Centre for Infection Research (HZI) and Hannover Medical School (MHH) – has combined basic research and clinical application in the field of infectious diseases and also developed into a crystallisation seed for the biomedical orientation of health research in this geographical region. In his welcoming address, Lower Saxony's Minister for Science and Culture, Björn Thümler, got right to the heart of it: "The anniversary celebration acknowledges the successes and the unique positioning of the facility in infection and translational research. Based on its focus on major infectious diseases and the networking with other European and extra-European facilities, the TWINCORE meets the expectations and demands of modern science policy."

How far the networking in research projects can go, what is technically feasible today and what should be possible in the future was illuminated in the 24 lectures by the cream of the crop of international infection research.

△ Ulrich Kalinke (Executive Director of the TWINCORE, left) and Dirk Heinz (Scientific Director of the HZI) planting the Balling plum tree

Then we had the retrospective. Starting with history and stories and charismatic people. Rudi Balling, the former Scientific Director of the HZI, and Dieter Bitter-Suermann, the former president of the MHH, got the TWINCORE off the ground. These two just had to be reunited at the TWINCORE on the occasion of the anniversary: Rudi Balling's Rhineland-sized laughter in full screen size via Skype from La Jolla, California, and Dieter Bitter-Suermann on the grounds. They reminisced together and wished the TWINCORE a happy birthday. Even this part of the anniversary appeared to reflect the symposium's "Frontiers" topic: Since the president of the MHH, Christopher Baum, could not hand over a bouquet of flowers via Skype – the current director of the TWINCORE, Ulrich Kalinke, accepted it on behalf of Rudi Balling. As a meeting point of the past and future, a Bitter-Suermann cherry tree and a Balling plum tree (representatively planted by Dirk Heinz, because – see above the "Frontiers" – Skype still fails at planting trees) have been standing in the garden of TWINCORE since that afternoon. Planted on behalf of the founding fathers to be harvested by those shaping the future of TWINCORE today: more than 100 young researchers from throughout the world.

RACING AGAINST PATHOGENS

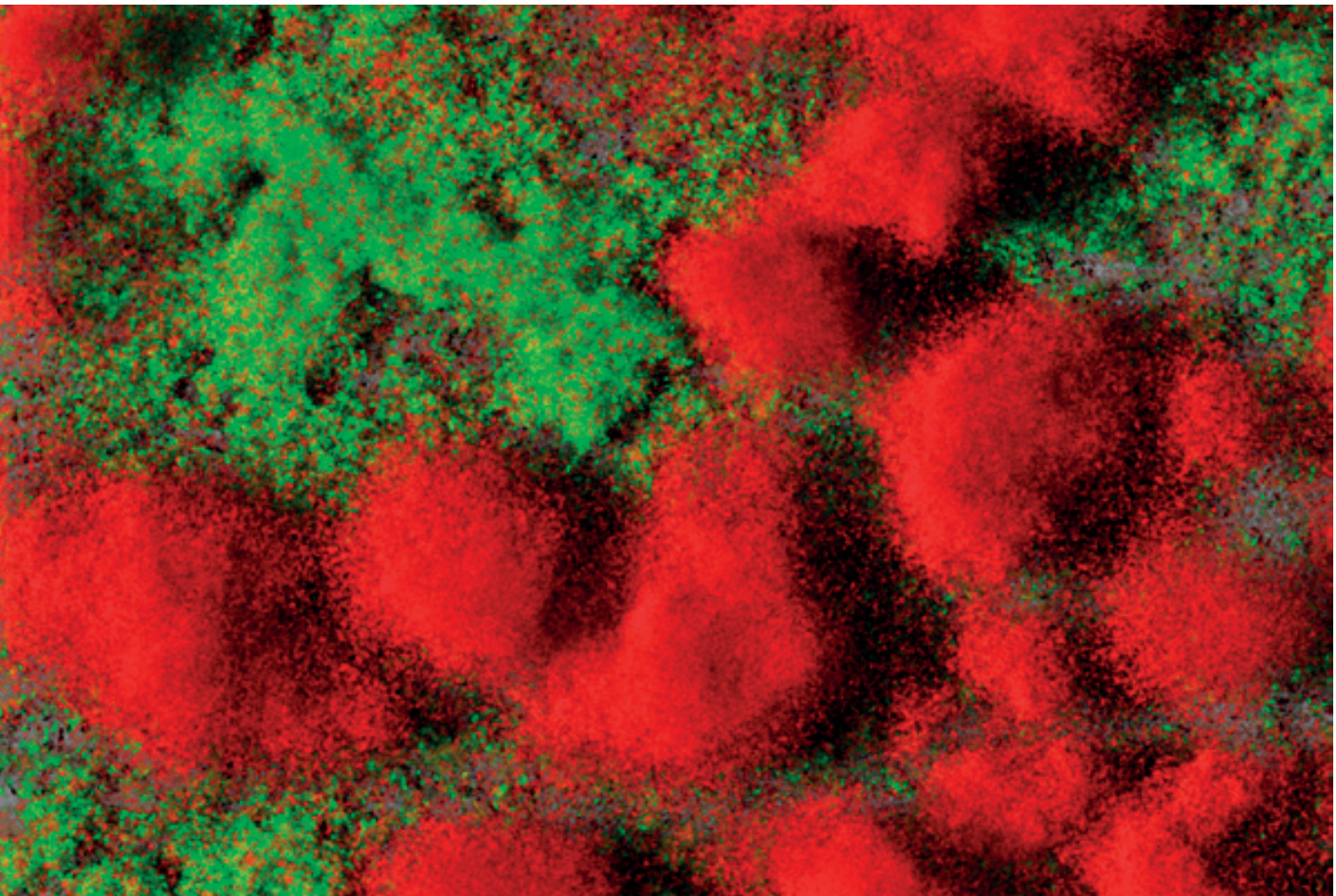
by Susanne Thiele

More and more resistant pathogens are spreading that cannot be harmed by traditional antibiotics. They are a great danger to the public health systems throughout the world. Without a major change in medical research and development, diseases that can be treated today may become incurable in just a few years

A small wound on a finger may suddenly turn life-threatening, since more and more bacteria become resistant to common antibiotics. The development of resistance is a natural effect of evolution. Resistance arises during the use of antibiotics as some bacteria that are immune to the medication due to genetic variance survive the treatment and then continue to proliferate. Meanwhile, the World Health Organization (WHO) considers antibiotic resistances to be one of the "major threats to global health and food safety". They cause longer stays in hospital and therefore increasing costs of therapy and higher mortality. The spreading of resistances can be explained by a number of reasons, for example overly eager administration of antibiotics in the treatment of the symptoms of common colds, the use of antibiotics for insufficient periods of time or the improper use in animal husbandry. But one fact is clear: Solutions must be found rapidly by innovative research.

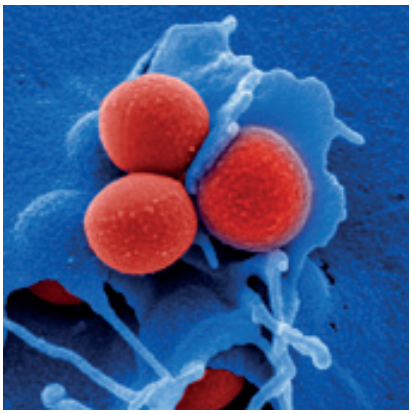
Prof Rolf Müller, who is the speaker of the research topic "Anti-infectives" at the Helmholtz Centre for Infection Research (HZI) and the Executive Director of the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS) in Saarbrücken, summarises the status quo as follows:

▽ The germ *Pseudomonas aeruginosa* can form dense constructs, so-called biofilms, in which the individual bacteria are protected from the immune system and medications such as antibiotics



"Antibiotic resistance is a global problem. According to estimates, more fatalities will be caused by antibiotics resistances than by cancer by the year 2050. Unfortunately, little has been done against the multi-resistant pathogens in the past ten years, and these are causing the greatest problems in our hospitals to date. Accordingly, there is an urgent need to develop new effective medications."

Hospitals in focus – backlog in diagnostics



△ *Staphylococcus aureus* bacteria can develop resistances to several antibiotics

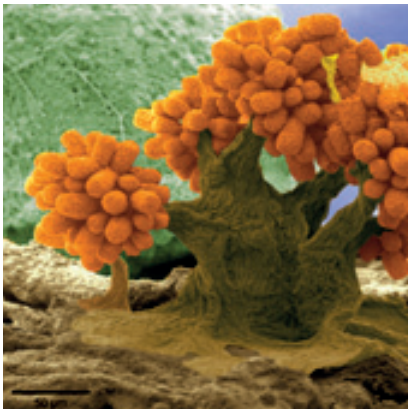
Prof Susanne Häußler, who is a medical doctor and the head of the "Molecular Bacteriology" department at the HZI, also considers the status quo to be very critical: "The number of multi-resistant pathogens in hospitals keeps growing, while the number of newly approved medications is dropping drastically." According to Häußler, medical microbiology still needs to do its homework, since the common resistance tests for bacteria in clinical settings are based exclusively on the growth in the presence of antibiotics. And this may take too long. Moreover, the researchers obtain no information concerning the resistance mechanisms and the clonal identity of the pathogens. "For this reason, we are working on molecular diagnostics: We isolate bacterial genetic material – RNA and DNA – and determine genetic markers of resistance. We also do accurate typing," says Häußler. "This allows us to monitor the spread of multi-resistant strains faster and more specifically. Medical doctors can then initiate the appropriate prophylactic and therapeutic measures."

Antibiotics research – unattractive to pharmaceutical companies

In most cases, only antibiotics that are not very commonly used yet can help against resistant pathogens. But these new medications are either very expensive or they don't even exist yet. Only a single new class of agents against Gram-negative pathogens has been developed since 1987 – and this class includes a single agent. In addition, pharmaceutical companies rarely invest in the development of new antibiotics anymore, because these products can be used only infrequently and only for a short period of time, which makes them not very profitable. As recently as in July 2018, the pharmaceutical company Novartis abandoned its antibiotics and infection research. "Without a major change in medical research and development, diseases that can be treated today may become incurable in just a few years," says Rolf Müller. "This gap in research must now be filled by extramural research facilities such as the HZI and other institutions that search for promising candidate agents and optimise the chemical compounds as much as possible for subsequent commercial development by pharmaceutical companies."

The hunt for new antibiotics

Nature is the best resource for new agents. "Approximately 80 per cent of all antibiotics are natural products. Fungi are a virtually inexhaustible source of new bioactive secondary metabolites. They produce antibiotics under natural conditions to prevail over bacteria and to survive their attacks," says Prof Marc Stadler, who is the head of the "Microbial Drugs" department at the HZI. Soil-dwelling myxobacteria are known to produce certain secondary metabolites, but have not yet been studied in much detail. To date, the collections of the HZI and the HIPS have accumulated more than 11,000 strains of myxobacteria. In their search for new anti-infective agents, the researchers analyse the genetic material of the microorganisms, which allows them to estimate whether or not there is any potential for the production of useful agents. If considerable amounts of the substance can be produced, the researchers use various assays to test for interesting effects against problematic



△ Myxobacteria such as *Chondromyces crocatus* are a rich source of new active agents

bacterial and fungal germs and cancer cell lines. In the end, all substances are gathered in a natural product library and can therefore be checked for further effects at any time. Aside from fungal and myxobacterial compounds, the library also contains numerous samples from the actinobacteria, i.e. the organism group from which historically the majority of antibiotics have been derived. Müller's team at the HZI and the HIPS already discovered new candidate antibiotics amongst these substances, for example the cystobactamides, which kill mainly Gram-negative pathogens that are particularly difficult to control. A proof of concept concerning the efficacy in infections in an animal model has already been documented. In collaboration with their colleagues from the HZI in Braunschweig and partners from the pharmaceutical industry, the researchers also optimised an agent called griselimycin, which is effective against the tuberculosis pathogen, and they even elucidated its mechanism of action. This agent showed excellent activity against the tuberculosis pathogen in an animal model and its activity is directed against all multi-resistant pathogens known at this time.

But substances that are very effective against bacteria are not automatically also well-suited for application in humans. It is often a long and rocky road in medicine – and only few candidates end up being successful. As if this was not difficult enough anyway, they must be amenable to being produced in sufficient quantities in biotechnological processes. In many cases, the biotechnology platform of the HZI has managed to provide

△ Prof Mark Brönstrup, head of the "Chemical Biology" department at HZI: "The chemical optimisation of new agents is a complex procedure, costs millions of Euros and takes years"

sustainable processes to access the desired molecules in multi-gram scale, but sometimes it is not feasible in a cost-efficient manner. This is where the synthetic biology and medical chemistry come into play, as they replace the often very complex structures of these natural products by simpler molecules that are easier to optimise. These can then be adapted further, for example in order to attain better tolerability, higher stability in circulating blood or higher effective levels at the site of infection.

Disarming pathogens instead of killing them

Besides the development of new antibiotics, alternative strategies to counteract antibiotic-resistant pathogens are currently being investigated. Among them, the anti-virulence approach has gained popularity in recent years: It aims at disarming pathogens rather than killing them. Dr Eva Medina, head of the "Infection Immunology" research group at the HZI, searches for agents that can specifically interfere with the activity of factors produced by pathogens to cause disease – so-called virulence factors. These include proteins used by pathogens to penetrate into host cells or to defend themselves against the immune system. "The major advantage of this approach is that the bacteria stay alive but disarmed and therefore they are more easily eliminated by the immune system. As a result, the development of resistance against anti-virulence agents will be minimised as selection pressure that favors the selection of resistant bacterial subpopulations is anticipated to be weaker than in the case of traditional antibiotics." This makes the development of anti-virulence agents more attractive for pharmaceutical industry since their effectiveness will not be lost and can therefore be used in the clinic for longer periods of time. One limitation of the anti-virulence therapies is that they are highly specific and only work against the target pathogen. This requires a rapid and very accurate diagnostic of the infecting agent – even in patients with a life-threatening disease – that can result in therapeutic delay. Furthermore, based on experimental infection models, the team of Eva Medina has recently reported that the expression of virulence factors by pathogens is strongly influenced by the genetic configuration and the immune system of the individual host. "Most probably, the anti-virulence strategy also needs to be tailored to individual patients," Medina says.

Innovative approach – programmable RNA antibiotics

Today's antibiotics usually are effective on a broad range: They attack either Gram-negative or Gram-positive bacteria and, doing so, destroy many harmless or useful microorganisms as well. But in certain infectious diseases, it may be necessary to eliminate one specific type of bacterium in the microbiome of the patient – e.g. in the intestinal flora. Prof Jörg Vogel, who is the director of the Helmholtz Institute for RNA-based Infection Research (HIRI) in Würzburg, pursues a novel research approach based on RNA molecules, which are copies of the genetic information. RNA molecules determine all kinds of processes in the cell and are also associated with many diseases. Vogel aims to drive back the pathogen and to better protect the host from the infection to the benefit of the patient. In both cases, RNA molecules play an important role, for example when pathogens check their surroundings to decide on the perfect moment for their attack on the host. "RNA molecules can be used to develop programmable drugs and to use them specifically against a certain type of bacterium, unlike traditional antibiotics. Other types of bacteria that are useful to humans stay unharmed," Vogel says. "Using a method we developed, we can monitor in detail, which genes of a pathogen are switched on or off during an infection and what happens in the host afterwards. These insights present us with novel approaches for therapies."

The major focus of the RNA researchers currently is on the pathogen called *Fusobacterium nucleatum*, which usually is present in the oral cavity, but also gets into the intestines when saliva is swallowed. Approximately seven years ago, it was found that fusobacteria attach themselves to precursor cells of intestinal cancer. "Although the bacteria do not seem to be a causative factor in the formation of intestinal cancer, they reduce the treatment opportunities drastically by inactivating the chemotherapeutic agents," Vogel says. "With a programmable antibiotic, we might be able to specifically eliminate just the fusobacteria." Currently, there are still many open questions concerning programmable antibiotics, but their efficacy has been confirmed on principle, and Vogel thinks they have great potential also in the correction of disease-related changes of the intestinal flora.

KEEPING ANTIBIOTICS EFFECTIVE IN THE FUTURE

by Tatyana Dubich

On average, every adult in Germany suffers from up to three respiratory infections per year. Although mostly caused by viruses, these infections are sometimes incorrectly treated with antibiotics. Dr Stefanie Castell, deputy head of the HZI Department of Epidemiology, talks about a training project called WASA ("Wirksamkeit von Antibiotika-Schulungen in der niedergelassenen Ärzteschaft" – effectiveness of trainings on antibiotic prescription in primary care) that should improve the handling of antibiotic prescriptions

Dr Castell, what is the focus of WASA?
Inappropriate treatment with antibiotics is one of the reasons for the development of antibiotic resistance, which has become a global problem. About 85 per cent of antibiotics are prescribed in ambulatory care – and not always according to medical guidelines. For this reason, the Hygiene Network of Southeast Lower Saxony together with partners has developed a guideline-based training for general practitioners. The WASA study investigates if the training would impact antibiotics prescriptions by doctors or at least their attitude. We evaluate the trainings scientifically.

How could the WASA training help doctors?
For many diseases, there are evidence-based clinical guidelines for diagnosis and treatment developed by professional societies to ensure a state-of-the-art treatment. For example, in 2017 new guidelines for urinary tract infections were released – with a volume of more than 200 pages! WASA offers standardised lectures that are a concise excerpt from the relevant guidelines. Every training is conducted in small groups to ensure lively discussions and better learning.

How do you evaluate WASA?
The effectiveness of the training is evaluated in two steps. We use a questionnaire to estimate whether participants intend to implement their insights in day-to-day clinical practice. Additionally, we use data from a large public health insurance to evaluate antibiotics prescriptions by general practitioners before and after the training and assess differences with practitioners who did not participate.

Lecturers with HZI scientists (from left): Dr Harald Junius, Prof Wilfried Bautsch, Dr Stefanie Castell (HZI), Dr Heike Raupach-Rosin, Dr Kirstin Haase, Dr Ole Scharmann, Dr Peter Hopp, Daniela Gornyk (HZI)

What are the challenges WASA is facing?
The project is complex and requires special expertise for the analysis of the insurance data. It took us about a year to coordinate all data flows with five participating institutions, to establish and standardise the presentations and to develop the questionnaire before we could start with the training. In addition, it is difficult to attract participating doctors, as there are many training opportunities on various medically burning topics.

When do you expect results of WASA?
The training will be completed by the beginning of 2019. In the further course of the project we will receive insurance data that accrue in the year after the trainings. The results will then facilitate the introduction of similar trainings in other regions and hopefully have a positive effect on antibiotic prescriptions in our region.

FURTHER INFORMATION:

Further partners in the government-funded project: AOK Niedersachsen, Klinikum Braunschweig, Niedersächsisches Landesgesundheitsamt, Stadt Braunschweig Gesundheitsamt und Gesundheitsplanung

“SAMPLE‘ DAS SAARLAND” – MICROBIAL TREASURES FROM SOIL

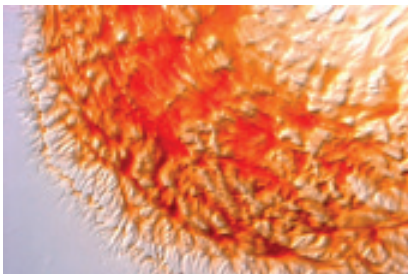
by Daniel Krug

Scientists in Saarbrücken are on a mission to discover natural products from soil bacteria in order to develop these into new medicines for the treatment of infectious diseases. They are asking the public to join their efforts and become part of an ongoing citizen science project launched recently to improve access to regional microbial biodiversity

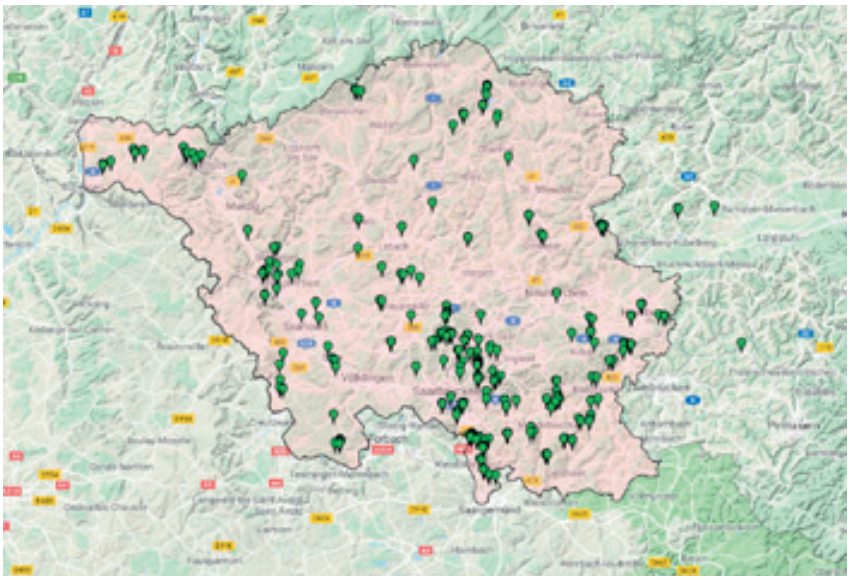
The increasing resistance of pathogens to known antibiotics is an alarming trend that has gained public awareness over the last couple of years, as more and more infections with multi-resistant germs are reported from the clinics where even treatment with reserve antibiotics fails. Scientists at HIPS – an institute jointly founded by HZI and Saarland University – are therefore investigating myxobacteria as a source of new anti-infective compounds. The soil-living myxobacteria, once regarded as exotic newcomers in natural products research, have in fact a long-standing tradition at HZI in Braunschweig where the scientists Hans Reichenbach and Gerhard Höfle worked for decades to establish a worldwide strain collection. Nowadays myxobacteria are well-known as a valuable source of natural products, whereas many of these so-called secondary metabolites show intriguing chemical structures and often exhibit potent biological activity. The myxobacteria collection has grown to contain more than 11,000 strains to date, and modern genomics- and metabolomics-based methods are applied at the HIPS-department “Microbial natural products”, which is led by Prof Rolf Müller, in order to uncover the chemical secrets from this microbial treasure chest. An exciting undertaking, as any novel chemical entity revealed raises hope that the new molecule could serve as the starting point for development towards a much-needed therapeutic agent.

Visitors approaching the new HIPS building on the Saarland University campus will catch sight of a large poster: “Sample’ das Saarland – Mikrobielle Schätze aus dem Boden” highlights the main research objective, followed by a call to help the HIPS scientists with soil sample collection. Are today’s scientists tired of adventurous expeditions to retrieve soil samples from remote locations around the

▽ Master student Julian Thimm collects a soil sample



△ Light microscope image of the edge of a swarming colony formed by a new myxobacterium. The strain was isolated from a soil sample collected by Hans (12 y.) in the Grumbachtal valley near Saarbrücken



△ A real-time map at https://hips.saarland/sample pinpoints the already sampled locations

△ PhD student Chantal Bader uses mass spectrometry to analyse the natural product profiles from myxobacteria belonging to newly discovered taxonomic groups

globe? Dr Ronald Garcia, microbiologist at HIPS, is eager to explain matters: “We do have agreements with a few countries for collecting soil samples. However, negotiating such contracts is always a lengthy process with uncertain outcome and generally comes with enormous judicial burden due to legal implications from the Nagoya protocol. In contrast, local sample collection is uncomplicated and we are confident that any ecological habitat accommodates a highly diverse microbial community.”

The idea of conducting a sample collection campaign in the Saarland region as a citizen science project originated from the planning of activities for a HIPS open day. Scientists then went on to manufacture sample collection kits (the most important part in these being a blue plastic spoon and a sterile barcoded plastic bag) and set up a website where collected samples can be registered on-the-spot. Sample kits also contain a leaflet with detailed instructions for sample-taking, a post-free reply envelope and a tiny magnifying glass. More than 600 of these sample kits have already been distributed, and they can be ordered via the website (http://hips.saarland/sample). A real-time map shows the current status of sample collection. When the first soil sample packages arrived by mail, the project initiators were happy: “At this point in time we realised that the concept could actually take off,” says Garcia.

Compared to soil samples collected by the researchers themselves, the samples sent by citizen scientists do not stand back in any way. “The methods used for isolation of new bacteria are key to success,” says Garcia. “We employ a highly selective procedure to favour the isolation of new myxobacteria, and due to the natural products they make these are very effective in defending themselves against other bacteria. Our prospects for the discovery of new myxobacterial species are therefore not troubled by contamination with germs commonly found in soil.” The “Sample’ das Saarland” campaign is now already running for the second year, and scientists are pleased with the outcome. Participants are highly motivated and some even contribute their own ideas, sending the project team emails and even hand-written letters with suggestions about special locations, such as slag-heaps grown over with wood or abandoned mining areas barred for public access. Others are concerned about the isolation methods and propose to pretreat samples in certain ways in order to increase chances for finding uncommon bacteria.

Until now, Garcia and his colleagues were already able to characterise more than 200 new myxobacteria from Saarland soil samples, and some of these turned out to be members of previously unknown genera as judged based on their low degree of genetic relatedness to the known myxobacterial species. “If we obtain a few hundred additional strains, that will enable us to perform statistics-based analysis of myxobacterial secondary metabolomes in order to find new natural product candidates with the help of mass spectrometry,” says Chantal Bader, PhD student at HIPS. “However, there is more to it than just a high number of samples – we really need to make sure to include new and rare taxonomic groups of myxobacteria in our analysis. These come with an increased likelihood for the production of novel bioactive compounds having a previously unseen molecular structure.”

More and more citizens living outside the Saarland region ask the HIPS scientists if samples from other German regions would be of interest. The answer is clearly “Yes”, and indeed preparations are already underway to develop the citizen science project into a nationwide campaign. “The financial effort necessary to extend the campaign is favourably little, but we need to further develop our infrastructure. Right now, we are finalising a mobile app that improves the sample registration process including precise recording of geo coordinates,” says Garcia and adds as an outlook: “Who knows – maybe sending soil samples in the future will become just as common as blood donation.”

△ Silke Tannapfel has been Administrative Director of the HZI since October 2018

"AIMING FOR ROUTINE PROCESSES"

by Andreas Fischer

One year can be quite long in times of important decision-making and budget constraints. But not in Silke Tannapfel's experience: Her first twelve months as the Administrative Director of the HZI passed by quickly – so let's take a closer look

Mrs Tannapfel, how was your first year at the HZI?
The year felt like just a single month, which is a good sign. Only unpleasant things tend to linger. The close and very good cooperation with Dirk Heinz and the office team support were and continue to be indispensable to me. We laugh easily together, which helps to overcome difficult situations. When I came to the HZI, I was looking to get closer to science and I enjoy very much getting to know the people who are behind it. Researchers are a special kind of people: They devote their life to one topic, rather than to making money. This really needs to be acknowledged and makes the cooperation so interesting.

What is your summary as the Administrative Director?
My experiences in this first year were ambivalent: Some things did not develop as hoped, while others clearly exceeded expectations. For example, the financial consolidation of the centre is proceeding really well. It is painful, but I see it as a necessary healing process. The

Federal government and the Federal State of Lower Saxony have supported us remarkably – which indicates that we managed to regain the confidence of our funding agencies. However, I underestimated the special challenges facing the HZI administration.

What are these challenges?
For example the complexity due to multiple locations, which all are in different stages of development. This is demanding in terms of administrative processes, but, in my experience, can be managed by an adaptive governance. At the same time, this status also is an opportunity to help each other in difficult phases, as long as there is no great performance gap between locations. I am very happy to note that the scientific evaluation in the course of the programme-oriented funding by Helmholtz concluded that all HZI research areas at all locations do outstanding work.

How do you envision the role of the administration at the HZI?
It is the task of the administration to support the science appropriately so that our talented researchers can develop and perform first class research at the HZI. This is the basic goal. We have to set guardrails between those we can navigate with a friendly "No" and an encouragement in the right place to visionary research. I want to see the gap between the scientific and the administrative departments get smaller. This also includes mutual appreciation. The conversational tone between these areas seems to be a little rougher than what I was used to at the University of Nürnberg-Erlangen or the Administrative Headquarters of the Max Planck Society.

Where do you see a need for improvement by the administration?
The process reliability needs to be improved. There are too many case-by-case agreements and not enough documented process knowledge. Individual solutions tend to stress the people involved and are unfair to those not involved. I am aiming for management to be an unagitated routine, i.e. with more standardisation. This might sound boring, but general rules are better than individual measures, since routine processes reduce stress and strengthen self-confidence.

Moreover, the administration is subject to an external evaluation. What are your expectations?
The evaluation is a decision made by the supervisory board. With the establishment of new locations, the HZI has changed, and, in turn, the administration must develop as well. Doing so, we can profit from the expertise of the external expert panel, which combines experience from the fields of science, business and ministerial administration. The aim is to optimally improve the processes such that the administration can best support the science while implementing the recommendations from the excellent scientific evaluation. This will require modernisation despite limited resources, because only thereby the HZI can stay competitive.

What steps are involved in the evaluation?
The first step is already completed: It included self-evaluation reports of the administrative department heads and a survey of the staff of the administrative departments in spring 2018. In a closed meeting with an external moderator, we analysed the results together with the department heads of the core administration. The assessment by the external expert panel is the second step and will take place on three days in March 2019. The heads of the administrative departments will then give presentations and have discussions in parallel sessions. In addition, the experts will have confidential talks with some of the administrative and scientific staff. In advance, we would like to get a view of the opinion of all staff members concerning the services of the administration in the scope of an anonymous online survey allowing us to develop the improvement processes in direct contact with the users. The final result of the evaluation will not involve a grade, but be a report that includes recommendations, so nobody needs to be afraid.

Which other projects are especially close to your heart besides the evaluation?
An administration of "short ways" is important to me. To this end, we combined most of the administrative departments under the same roof this year. I also want to establish effective committee work. The council of scientists is running really well already and the revival of the investment committee as well as the committee for spatial resources was another important step. Just as important to me is the direct exchange with all our staff, be it in the scope of open consulting hours or a talk at the summer party.

Besides all these active construction sites, what is your personal summary?
It definitely was a pleasant and smooth return to my homeland in Lower Saxony; there were no cultural misunderstandings unlike early on in Bavaria. Here, in the flat country I can see the wide horizon again, and after the hot summer I'm looking forward to northern German weather with its typical brisk breeze. I am happy to say that my favourite lounge chair now has its place in Wolfenbüttel.

THE GENE TINKERER

by Nina-Vanessa Littwin

Chase Beisel is dedicated to a research topic that is more emotional than almost any other: CRISPR-Cas. This new genetic tool can make the therapy of cancer, AIDS or hereditary diseases possible

△ Chase Beisel heads the HZI research group "RNA Synthetic Biology" at the Helmholtz Institute for RNA-based Infection Research (HIRI) in Würzburg

For researchers like Chase Beisel, the cryptic term CRISPR-Cas is much more than the sophisticated system used by bacteria to defend themselves against virus attacks: It is home to countless genetic engineering possibilities that Beisel hopes to exploit. His goal is to understand the diversity of CRISPR-Cas systems in order to be able to use them against genetic diseases or multi-resistant pathogens, for example. The social dimension of his research plays a decisive role for him: "CRISPR is a wonderful example of basic research that has already led to something that has enormous effects on society," he says. "However, we must never neglect social exchange about gene-editing technologies such as CRISPR, because in the end our work is useless if society is not prepared to accept it."

Since early 2018, the US-American has headed the "RNA Synthetic Biology" research group at the Helmholtz Institute for RNA-based Infection Research (HIRI) in Würzburg, a location of the HZI in cooperation with the Julius-Maximilians-Universität Würzburg. The chemical engineer and microbiologist works according to the principle of French researcher Louis Pasteur, a pioneer of basic translational research: "In line with Pasteur's approach, I work in problems that both grant fundamental knowledge but also tackle a societal issue."

A research career was not predetermined to Chase Beisel from the very beginning. As a teenager, his declared goal was to become a professional drummer. On his father's recommendation, however, he decided to concentrate on chemical engineering. A good choice, as he thinks today: "In chemistry I can fully contribute my personal inclinations. I can fiddle, develop novel solutions, be creative." After his studies, he obtained his doctorate in Christina Smolke's laboratory at CalTech (USA) on RNA engineering. RNA molecules are transcriptions of genetic information and perform a variety of tasks in each cell, including controlling regulatory processes. "Nature is able to use these RNAs for its own purposes, which engineers find very difficult – if not impossible." After his doctorate in 2009, Beisel studied the properties of regulatory RNAs in the laboratory of Gisela "Gigi" Storz at the National Institutes of Health in Maryland, USA, and finally came across the CRISPR-Cas system as one of many recently discovered functional RNAs.

Currently, Beisel is involved in an international project that aims to genetically modify mosquitoes, the vectors of the malaria pathogen *Plasmodium*, in order to make them less susceptible to plasmodia infection or to prevent them from multiplying. "I see this as one of CRISPR's greatest opportunities to benefit society directly, because millions of people worldwide can benefit from it," says Beisel.

Even though his career as a drummer had to give way to research, Chase Beisel has not given up music. He always found ways to perform even while pursuing a scientific career, such as playing the djembe with his church, and is also finding ways to play here in Germany. At the beginning of 2018, when he, his wife and three daughters made the leap from the USA to Würzburg, he was still a little uneasy. But he has never regretted this step: "It was really easy to make new friends and build us a social network."

UPDATE FROM THE STUDY CENTRE IN HANNOVER

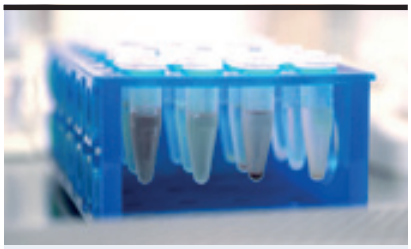
by Yvonne Kemmling and Tobias Kerrinnes

Germany‘s largest health study, the NAKO, is designed to run for 30 years and include 200,000 subjects. The aim of the study is to gain a better understanding of widespread diseases and the susceptibility to infections. But the recorded data will provide researchers with vastly more opportunities

Randomly selected citizens throughout Germany will be invited to participate in the NAKO health study. The planned total of 200,000 subjects between 20 and 69 years of age is expected to be recruited by next year. The NAKO involves a total of 18 study centres. The study centre in Hannover is operated by the HZI under the supervision of the head of the Department of Epidemiology, Prof Gérard Krause. Aiming for 10,000 subjects, the study centre in Hannover already recruited 9500 participants. Soon, the staff of the NAKO will start to re-invite previous participants who first have been recruited some 3.5 to five years ago. If these subjects agree to undergo the interviews again and to provide blood and urine samples, valuable long-term data will be obtained for analysis in combination with additional data on their progress.

The NAKO is a prospective cohort study investigating the causes and possible risk factors of common chronic diseases over the course of years and decades. Additionally, it records the influence of infectious diseases and immunity. Specifically for this purpose, an expert group has been set up in collaboration with the HZI Department of Epidemiology to advise the NAKO in all questions of infection research. During their first visits to the NAKO study centre, the subjects provide e.g. information on their medical history, lifestyle, nutrition, environmental influences, medication use during the previous seven days as well as on their susceptibility to infections. The visit also includes physical examinations and tests of the memory power. In addition, the subjects are asked to provide biological samples for later analysis.

The scientists expect to have the first intermediate data for analysis of the first 100,000 subjects of the NAKO health study in the next two years. Since the study centre is not a facility for NAKO purposes alone, but rather is an integral research infrastructure of the HZI, scientists can use the centre for future studies outside of the scope of the NAKO as well.



How can researchers utilise the data and samples?

Depending on the type of the biological sample, different amounts of the corresponding biomaterial are available. The blood samples, for example, result in the following materials: EDTA-buffy coat for genetic research, serum, EDTA-erythrocytes, EDTA-plasma, and RNA (PAXgene RNA-Vacutainer). The re-invitations of the first subjects getting started is an opportunity for recording acute infections in a NAKO sub-cohort by means of a mobile application that has been developed by the department in the scope of an additional project.

The HZI has facilitated access to the blood samples stored in Hannover. Scientists interested in data and biological samples can contact Gérard Krause. He will also provide advice on the regular application procedure for the utilisation of additional NAKO data and biomaterial from other participating study centres. An information event for interested scientists will take place in the first quarter of 2019.
www.nako.de

SUMMER PARTY 2018

This year's HZI Summer Party took place on 23 August 2018. In addition to the traditional HZI mile, which was again won by a TWINCORE relay team, the employees chose the most beautiful holiday photo for the first time:

1. Place: Zeljka Rupcic

2. Place: Kristin Kurch

3. Place: Thomas Twardoch

SCHEDULE

15 November: NoRDI VIII – North Regio Day on Infection: Symposium and Jürgen Wehland Award ceremony; HZI forum

22-23 November: Course "Good Scientific Practice", teachers: PD Dr Dr Gerlinde Sponholtz, Helga Nolte; registration via the Graduate School

28-30 November: Course "Coping with the challenges of a PhD", teacher: Dr Bärbel Tress; registration via the Graduate School

6 December: 11th International PhD Symposium of the HZI Graduate School; HZI forum

6 December: SharePoint update for all HZI secretariats; HZI forum, X1.04, 11 am

24-25 January 2019: Course "Scientific Writing", teacher: Dr Brian Cusack; registration via the Graduate School

NEW PERSONNEL

BRICS, Braunschweig: Leanne Evans, BIFO | Masoud Hoore, SIMM

HIPS, Saarbrücken: Eleonora Diamanti, DDOP | Katja Gerperlein, MINS

HIRI, Würzburg: Anne-Sophie Gribling, GARV | Chunyu Liao, RSYN | Victoria McParland, GARV | Sandy Pernitzsch, ADMIN | Daniel Ryan, HOPI

HZI, Braunschweig: Kirsten Emmert, GFW | Federica Fiorini, CBIO | Jana-Kristin Heise, EPID | Soleiman Helaly, MWIS | Sandra Koch, FMM | Sandra Lahr, FMM | Christopher Lambert, MWIS | Birgit Manno, WST | Jolanta Matys, DMC | Vivien Nagy, FMM | Monike Schlüter, EPID | Marina Steindorff, DZIF

TWINCORE, Hannover: Katharina Borst, EXPI | Ellen Ewald, AIVE | Davide Faggionato, TRAIN | Martina Thiele, EXPI