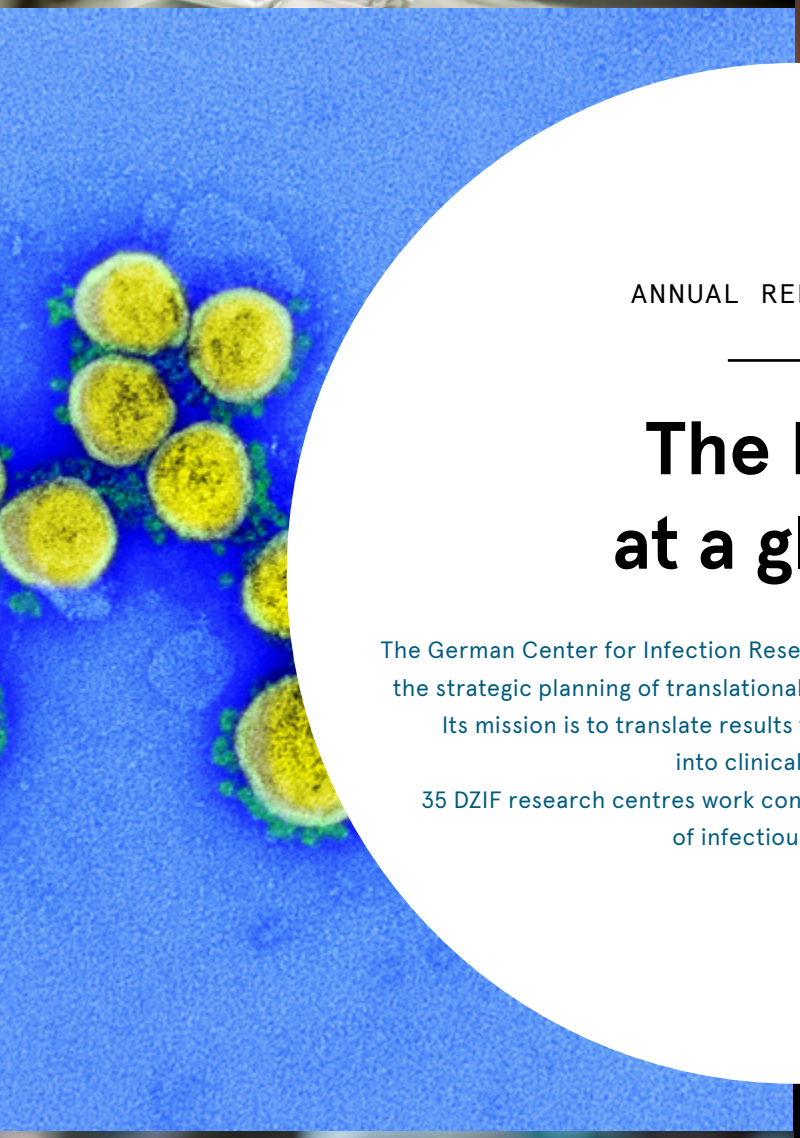
DZIF

DZG DEUTSCHE ZENTREN DER GESUNDHEITSFORSCHUNG

# GERMAN CENTER FOR INFECTION RESEARCH

## Annual Report 2020

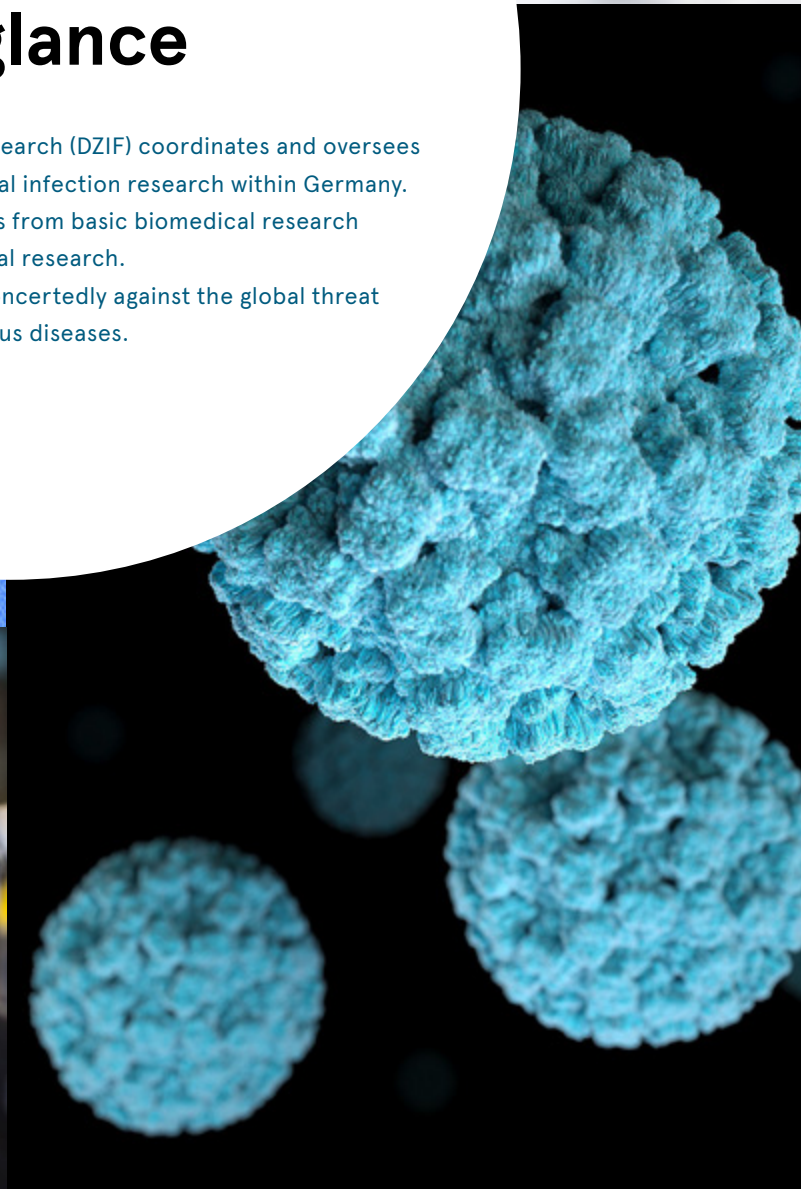
*Cover image: What in the past was only used in hospitals is symbolic of the „Corona Year 2020“: the surgical mask worn by a young patient at a clinic in St. Petersburg, Russia. She is being treated there not for corona, but for tuberculosis, which is still the most common fatal bacterial infection in the world. The DZIF focuses on new and old infectious diseases and is engaged in research to prevention, diagnosis and treatment of tuberculosis in Eastern Europe.*

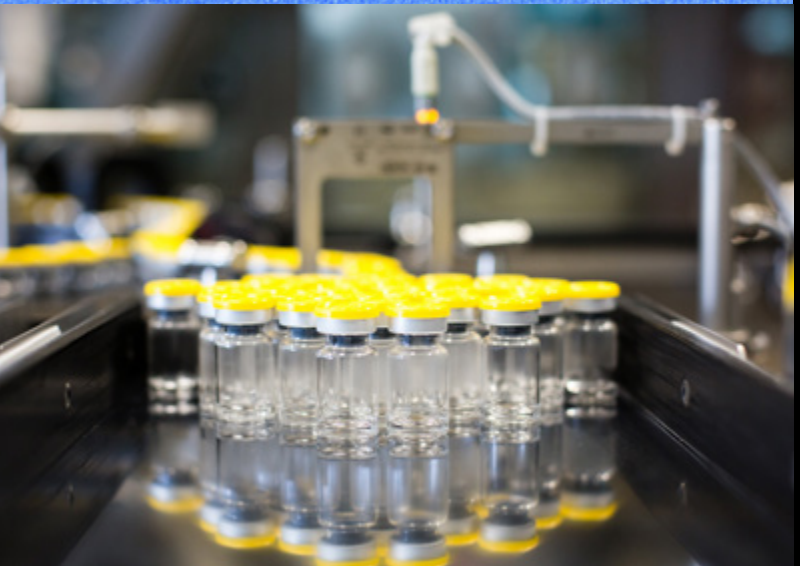


ANNUAL REPORT 2020

# The DZIF at a glance

The German Center for Infection Research (DZIF) coordinates and oversees the strategic planning of translational infection research within Germany. Its mission is to translate results from basic biomedical research into clinical research.
35 DZIF research centres work concertedly against the global threat of infectious diseases.





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# Editorial

The year 2020 will probably go down in history as the "Corona year". For infection researchers, it has been an extraordinary test. Numerous projects were set in motion within a short time, many scientists and physicians flexibly adapted to the need for research on SARS-CoV-2. And in addition to the current dangers posed by the new infectious diseases, it was also important not to lose sight of the old ones. Diseases such as tuberculosis, hepatitis or AIDS continue to constitute a global threat, and increasing antibiotic resistance is increasingly becoming apparent as the main risk of the coming years.

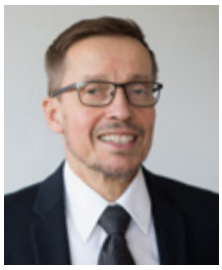
In order to ensure that the DZIF is well positioned and sets the right priorities, it underwent an evaluation by its Scientific Advisory Board and independent, external experts in 2020. All research areas and their plans for the coming years were examined in detail. Do they meet the standards of translation that the German Centers for Health Research have committed themselves to? Are the scientists able to get new drugs, vaccines and diagnostics off the ground faster than before? The result of the evaluation is worth seen: The successes so far were rated as „impressive", the plans for 2021 to 2024 as „outstanding" and „extraordinary". Not many countries, the reviewers concluded, have such a national network that pursues a common goal. All in all, it can be said: The DZIF is on the right track.

Find out more about this path in this annual report, covering a wide range of topics. In addition to corona-related research and the two outstanding projects – vaccine development and the search for antibodies (from page 6) – you can read on pages 8 and 9 about the more precise options for tuberculosis treatment that are being worked on at the Research Center Borstel. Malaria research investigates the ability of the pathogens to survive in the long dry season without their host mosquitoes (page 11). And in addition to the coronavirus, the hepatitis and HI viruses, noro- and cytomegaloviruses are also on the research agenda: At the University Hospital of Cologne, scientists and doctors are developing broad-neutralising antibodies against HIV (page 12) that could enable a cure for the first time. The Munich researchers who are developing TherVacB, a therapeutic vaccine against hepatitis B, are also confident (page 15). Or find out what is hidden behind a newly established stool bank and why it is urgently needed (page 19). These examples should suffice to arouse your curiosity about reading. In addition, you will find all important information on data and facts 2020 at a glance in the annual report.

Viruses, including emerging ones, will accompany us in the future same as the well-known pathogens – infection research faces major challenges. As a network with international cooperations, the DZIF can contribute to solving the problems. For both you and us, we hope that the work by scientists and physicians will continue to receive the required attention and appreciation.

Yours sincerely
The DZIF Executive Board





Prof. Hans-Georg Kräusslich | Prof. Dirk Busch | Prof. Andreas Peschel | Prof. Maura Dandri | Prof. Dirk Heinz

ABOUT THE DZIF

# Focus on new and old infectious diseases

The year 2020, that much is certain, will go down in the annals of research as the first corona year. At the German Center for Infection Research (DZIF), scientists from almost all fields have joined the fight against the coronavirus. Newly emerging and re-emerging viruses have been a focal point since the establishment of the DZIF, thus making it possible to react quickly. But the DZIF is not only facing up to this challenge, the problems are more diverse: chronic infections such as HIV or hepatitis, more and more immunocompromised people as well as the global increase in antibiotic resistance that is rolling towards us as a great danger. More than 500 scientists and physicians work together at the DZIF to solve these problems.

**2020: FOCUS ON SARS-COV-2**

Shortly after the SARS-CoV-2 virus had been identified, the scientists led by Prof. Christian Drosten at the Charité Berlin were able to develop and publish a diagnostic test that is still considered standard today. Previous experiences with coronaviruses, in particular with the MERS virus, were used as a blueprint for vaccine development at the DZIF, which the virologists initiated immediately after the outbreak. In the university hospitals in Frankfurt, Hamburg and München, the first corona patients were treated and important insights about the disease and its contagiousness collected. With LEOSS, the DZIF, together with the other German Centers for Health Research, established a European patient database that has become an important research base. Clinical studies as well as numerous studies on treatment options started. Without significant delay, corona projects in various DZIF research areas were set in motion, and additional funds were approved quickly and unbureaucratically via FlexFunds applications.

**TRANSLATION: FASTER TO THE PATIENT**

The importance of developing drugs and vaccines faster has been clearly demonstrated by the corona pandemic. However, the goal was already valid before, especially for common diseases. In order to achieve this goal, all German Centers for Health Research (DZG) have been committed to

*At the UKE in Hamburg, a SARS-CoV-2 vaccine went into clinical trials in 2020. In the picture: Prof. Marylyn Addo and her colleague Etienne Bartels.*

translation from the very beginning: the rapid implementation of research results into practice through close dovetailing of research and clinic. With the synergistic alliance of universities, clinics and research institutes, the DZIF has created a globally unique infrastructure.

**THE BIG CHALLENGES**

The DZIF focuses on four major infectiological challenges of our time that will determine research in the coming years:

- Tropical and emerging infectious diseases such as malaria, Ebola or COVID-19.
- Antimicrobial resistances (AMR): Many pathogens no longer respond to common antibiotics.
- Chronic infectious diseases such as HIV, hepatitis or tuberculosis.
- Immune prevention and therapy: Immunocompromised people are particularly at risk of infections.

**RESEARCH AREAS AND INFRASTRUCTURES**

In order to master these challenges, the scientists work together across institutions in nine research areas. On the one hand, these are dedicated to certain infectious diseases such as *Tuberculosis, Malaria and Neglected Tropical Diseases, HIV, Hepatitis* or *Gastrointestinal Infections*. On the other, the DZIF research areas also cover specific problem areas such as *Emerging Infections, Infections of the Immunocompromised Host, Healthcare-Associated and Antibiotic-Resistant Bacterial Infections* as well as *Novel Antibiotics*. The researchers are supported by overarching infrastructures, such as the *Clinical Trial Unit* or *Product Development Unit* that can accompany them on their way to application.

**YOUNG TALENTS FOR INFECTION RESEARCH**

Since its foundation, the DZIF has been working to ensure that young researchers and medical doctors can successfully embark on a career in infection research. The DZIF Academy was set up especially for this purpose. The Academy awards *Maternity Leave* as well as *Clinical Leave stipends* to young physicians, which allow them to reduce clinical practice in favour of research. These stipends are very popular. In addition to supporting medical students and doctors, the Academy has launched a stipend for *Advanced Clinician Scientists* in 2020 to start in 2021. This clears the way for research specialists in management positions.

**SUCCESSFUL WITH COOPERATION PARTNERS**

In order to bring drugs, vaccines or diagnostics into use, the DZIF depends on cooperation partners in industry. Clinical trials with thousands of subjects cannot be conducted without support. The industry, on the other hand, depends on minimizing the risk of such a development until approval. The DZIF can close this gap. For example, it has already laid the foundations for the first clinical trials in vaccine development for Ebola, MERS and SARS-CoV-2 viruses. In 2020, together with IDT Biologika, a first clinical trial with a SARS-CoV-2 vaccine was able to begin.

**INFECTION RESEARCH IN WORLDWIDE EXCHANGE**

Bacteria and viruses do not care about national borders. Researchers must therefore think and act internationally. This is an essential aspect of the DZIF programme: close cooperation with partner institutions in Africa and Europe. The DZIF is also committed to the CEPI vaccine initiative and is one of ten partners in the CARB-X Global Accelerator network. CARB-X accelerates projects worldwide in the development of new drugs to fight against antibiotic-resistant pathogens.

The DZIF pools together its activities in research areas and interdisciplinary infrastructures - internally referred to as Thematic Translational Units (TTUs) and Translational Infrastructures (TIs) (as of 2020):

**Research fields**

- *Emerging Infections*
- *Tuberculosis*
- *Malaria*
- *HIV*
- *Hepatitis*
- *Gastrointestinal Infections*
- *Infections of the Immunocompromised Host*
- *Healthcare-Associated and Antibiotic-Resistant Bacterial Infections*
- *Novel Antibiotics*

**Infrastructures**

- *African Partner Institutions*
- *Biobanking*
- *Bioinformatics*
- *Clinical Trial Unit*
- *Epidemiology*
- *Novel Antivirals*
- *Pathogen Repository*
- *Product Development Unit*
- *DZIF Academy*

From January 2021, the *African Partner Institutions* will be integrated into the *Malaria and Neglected Tropical Diseases* research area and the *Novel Antivirals* will be transferred to the research area *Infections of the Immunocompromised Host*. The *Biobanking, Bioinformatics, Epidemiology* and *the Pathogen Repository* will be brought together into a large infrastructure of *Bioresources, Biodata and Digital Health*.

EMERGING INFECTIONS

# With expertise against the pandemic

2020 was dominated by the SARS-CoV-2 pandemic. Infection researchers worked at full speed to control the pandemic. DZIF scientists participated in research on two new vaccines and antibodies against COVID-19.

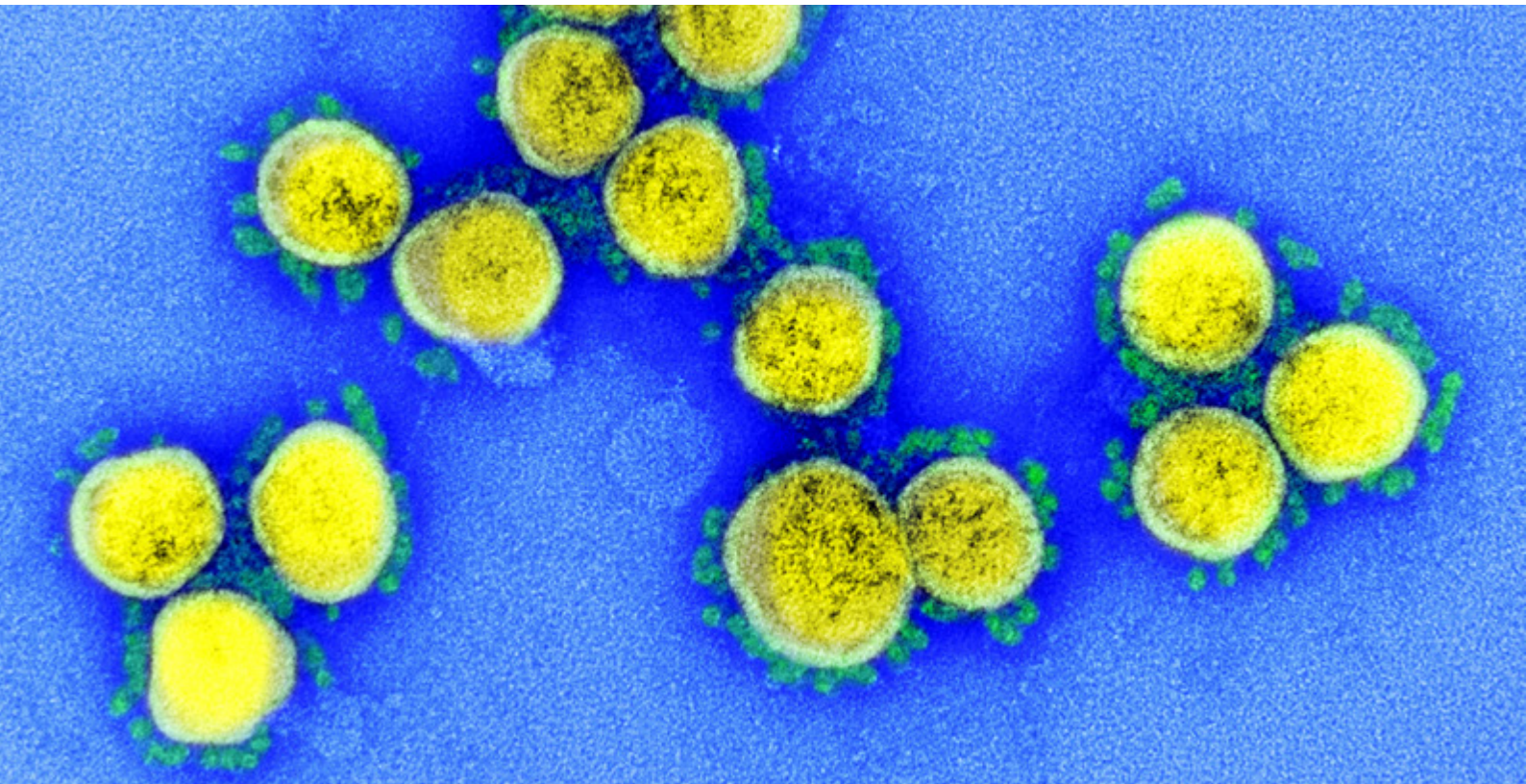
Besides, Prof. Christian Drosten from the Charité Hospital, who co-discovered the SARS virus in 2003, developed the world's first PCR test against SARS-CoV-2 in the course of his work with the DZIF.

## Examples from research

**WITH ANTIBODIES AGAINST COVID-19**

SARS-CoV-2 neutralising antibodies can be used to protect against, and treat, COVID-19 and prevent severe courses of disease. The team led by Prof. Florian Klein at University Hospital Cologne developed such an antibody very early on in collaboration with the Philipps-Universität Marburg, the DZIF and the company Boehringer Ingelheim. "An initial challenge was to obtain blood samples very quickly from persons with or after SARS-CoV-2 infection. The close and good cooperation with colleagues from Frankfurt, Köln, München and the DZIF was of very great importance here." To develop highly potent SARS-CoV-2 antibodies, antigen-specific B-lymphocytes were first isolated from the blood of persons who had recovered from COVID-19 and the genetic sequence encoding the antibodies was decoded. This made it possible to express and further investigate SARS-CoV-2 neutralising antibodies in the laboratory. Thanks to the collaboration with Boehringer Ingelheim it was possible to produce individual antibodies of the highest quality for use in humans. Starting already in December 2020, the first two phase I/IIa clinical trials, in which the antibody was administered as an infusion or by inhalation, were initiated at University Hospital Cologne. This rapid translation to clinical trial was primarily due to the extensive prior experience of scientists in Köln and Marburg and the cooperation with the Clinical Infectiology Department at University Hospital Cologne.

*SARS-CoV-2 virus particle under the electron microscope.*



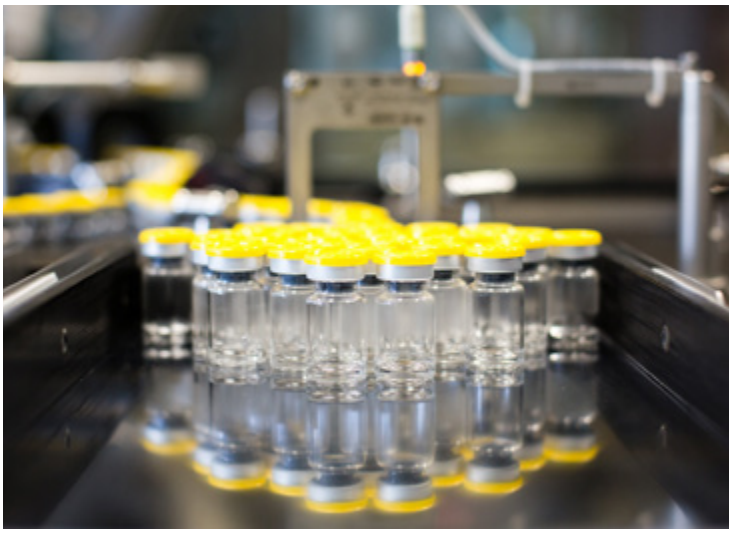
**LEARNING FROM EXPERIENCE**

The rapid development of a SARS-CoV-2 vaccine was the top priority for many researchers in 2020. Currently, there are 96 vaccines in clinical trials, of which 32 are already in phase III. The group led by Prof. Marylyn Addo at University Hospital Hamburg-Eppendorf is also working closely with DZIF scientists from Marburg and München on a potential vaccine. The infection researcher is responsible for clinical testing of a new vector vaccine based on the modified vaccinia virus Ankara (MVA). "MVA has been known for more than 30 years as a vaccine vector against smallpox," said Addo.

*"The pandemic was the driver of all our work activities. I am very happy that within the space of a short time we were able to launch several projects to combat SARS-CoV-2."*

**Prof. Stephan Becker**, Marburg
Coordinator

"At DZIF we have already successfully developed a vaccine against the MERS coronavirus on this basis and are now drawing on that experience." The MERS virus is related to SARS-CoV-2. For the vaccine against SARS-CoV-2 the research team once again used the MVA vector and instead of a surface protein of the MERS virus incorporated the genetic information for the SARS-CoV-2 protein into the vaccine. The vaccinee's immune response to the spike protein is crucial for efficacy. This is because if a vaccine virus is inoculated into the body during vaccination and synthesises the spike protein, the immune system recognises this as foreign and generates an immune response. "The vaccine is well tolerated," said Addo. "However, its immunogenicity in the phase I trial has not yet been convincing." The DZIF team therefore developed an optimised vaccine. "We have just received regulatory approval for a new phase Ib trial and can now proceed with it." This would then be followed by the phase II trial. Once these data have been successfully collected efficacy testing studies can begin. The vaccine could be used as a booster vaccine but the precise way and time to approval are hard to predict due to the dynamic epidemiological situation and the possibility of changes to the approval requirements. Current developments have shown: "We now have a unique opportunity to gain a better understanding of vaccines and learn which vaccine is suitable for which population," said Addo. "All these insights will help us to be better prepared for the next pandemic."



*Clinical testing of the DZIF vector vaccine against coronaviruses and enteroviruses has been resumed.*

**GOALS FOR 2020: OUTCOMES**

- ● *Development of a murine model for SARS-CoV-2.*
- ● *Characterisation of cellular immunity following vaccination with MVA-SARS-CoV-2 S (for phase I).*
- ◐ *Further development of inhibitors of lipid metabolism and eIF4A-dependent translation as active substances against coronaviruses.*

◐ *Goal partially achieved/project is still ongoing*
● *Goal achieved*

**GOALS FOR 2021**

- ○ *Characterisation of optimised second generation measles virus (MeV) COVID-19 vaccine candidates.*
- ○ *Implementation of the CoRoPa project "Monitoring of Norway (brown) rats and house mice at sites in southern and northeastern Germany" and of the WBA-Zoo2 project "Phylogeographic analyses of West Nile virus infected birds from the 2020 season using next generation sequencing methods".*
- ○ *Optimisation of alpha-ketoamides as broad-spectrum inhibitors of coronavirus and enterovirus replication.*

*You can find more information at*

TUBERCULOSIS

# For precision treatment of tuberculosis

The clock is ticking – ever louder in the case of tuberculosis. Together with AIDS, this pulmonary disease is one of the deadliest infectious diseases in the world. Every day almost 4,000 people lose their life to this disease, also known as consumption. The World Health Organisation has set itself the goal of providing diagnostic and therapeutic access for all people.

DZIF scientists in the *Tuberculosis* (TB) research field are pursuing different avenues to defeat the disease. One of these avenues is the development of a precision medicine approach: Patients are to receive targeted treatments based on tests detecting possible resistances. In addition, scientists are developing biomarkers, to monitor and even predict the course of disease, as well as facilitating the development of novel, targeted drugs.

## Examples from research

**TARGETED PREVENTION OF TUBERCULOSIS**

250 million people worldwide are carriers of tuberculosis bacteria. Only one in 25 will actually fall ill. Until now, it has not been possible to predict exactly who that is. However, the PERISKOPE-TB software casts light on this: It is able to calculate the individual risk of TB-positive patients to develop active TB in the coming years – and thereby improves medical decision making for doctors. According to Prof. Christoph Lange, medical director of the Research Center Borstel "To date, there is no consensus among professional TB societies on who receives treatment after a positive tuberculosis test". Conventionally, people who had contact with a tuberculosis patient are tested. If the tested person is positive, doctors must assess whether to treat them preventatively with antibiotics. The risk of developing the disease depends on the age of the infected individual, where they come from and how long they have been in contact with the tuberculosis patient. Based on more than 80,000 datasets and on the individual risk profile, PERISKOPE-TB is able to calculate the probability of developing the active disease. DZIF researcher Lange contributed 7,000 of

*The close cooperation between researchers and doctors at the Research Center Borstel is a key to success.*

the datasets from people followed-up for up to five years after a positive TB test. “The program calculates in a few minutes the individual risk of developing the disease,” said Lange. According to him, the software denotes a milestone in the prevention of tuberculosis: “For the first time, we have an evidence-based method to make a patient-tailored recommendation following a positive tuberculosis test.”

**MORE RAPID DETECTION OF TB RESISTANCES**

Over half a million people worldwide are infected with multidrug-resistant mycobacteria strains. A team led by Prof. Stefan Niemann, head of the infection programme at the Research Center Borstel has now co-developed a method, the Deeplex-MycTB assay, for rapid detection of common types of mycobacteria resistance. Thus improving the chances of a cure. “In Germany to this date we have only been able to carry out a rapid resistance test for the most common drug rifampicin,“ said the deputy coordinator of the DZIF’s *Tuberculosis* research area. In case of a positive test for the resistance, additional culture media tests are conducted in the laboratory to determine which other antibiotics are effective. This can take up to eight weeks.

*“After five years of development work, the efficacy of a TB drug, BTZ-043, discovered in Germany has been demonstrated in a first study.”*

**Prof. Michael Hoelscher**, München
Coordinator

“Alternatively, molecular genetic methods are used to search for any changes pointing to resistance in the bacterium’s genome,” Niemann explained. However, because of the increasing incidence of resistances these tests have their limits. In contrast, the novel Deeplex-MycTB assay is a genome-sequencing method that amplifies and decodes only those regions of the genome directly associated to the resistance. The assay is able to predict resistance to up to 15 antibiotics. In a recent study, this method performed at least as well as conventional tests. Currently, the accuracy of the Deeplex-MycTB assay is evaluated in further studies. In parallel, scientists in three African countries are investigating the assay’s suitability for use in high incidence regions. Niemann views the Deeplex-MycTB assay as an ideal tool for rapid and comprehensive detection of resistances: “In the future we want to use the test for all tuberculosis patients in Germany, thus replacing the established resistance test methods.”

*A new molecular genetic test can predict resistance more rapidly and improve the chances for a cure.*

**GOALS FOR 2020: OUTCOMES**

- ● *Phase IIa for BTZ-043 will be initiated. Funding for phase IIb/c is assured.*
- ● *In vivo validation of p38 MAPK inhibitors for host-directed TB therapy.*
- ◐ *Creation of a clinical development plan to evaluate treatment success in TB patients using biomarkers.*

◐ *Goal partially achieved/project is still ongoing*
● *Goal achieved*

**GOALS FOR 2021**

- ○ *Validation of pathogen biomarkers to guide treatment of multidrug-resistant tuberculosis patients.*
- ○ *Identification of the mechanism of action of novel substances with antituberculous activity as well as ex vivo / in vivo activity.*
- ○ *Continuation of clinical evaluation of the DZIF’s RNA signature (TB22) and of other biomarkers to predict the end of TB therapy as well as TB outcome.*

*You can find more information at*

MALARIA

# How malaria parasites ensure their survival

The malaria parasite enters the human bloodstream through the bite of an infected Anopheles mosquito. *Plasmodium falciparum* causes some 200 million cases of malaria each year worldwide. In 2018 almost 400,000 people died from this – mostly children in Africa below the age of five years.

DZIF research teams are testing better diagnostic methods and alternative vaccination procedures, developing parasite inhibitors and analysing the human immune response to the parasites.

## Examples from research

**DETECTING RESISTANCE, FINDING TREATMENTS**

Malaria is widespread in Africa as well as in tropical regions of Asia and South America. In rural areas of sub-Saharan Africa, in particular, doctors often treat patients without a specific diagnosis because of limited resources: Anyone with fever is given antibiotics in most cases. And this is done despite not knowing whether the fever is caused by bacteraemia, i.e. the presence of bacteria in the bloodstream, malaria or another disease.

This empirical therapy often does not help patients, and it drives the development of antibiotic resistance. A team led by Prof. Jürgen May from the Bernhard Nocht Institute for Tropical Medicine (BNITM) in Hamburg therefore cultured blood, stool and urine samples from febrile patients in Burkina Faso, Gabon, Ghana and Tanzania over four years. For example, scientists investigated bacteria such as resistant, extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, ciprofloxacin-resistant Salmonella and other pathogenic bacteria for their sensitivity to various antibiotics. The results reveal different sensitivity patterns in each region. “Markedly high resistance levels were identified, for example, in Burkina Faso. Based on these data, specific and different treatment guidelines can be applied in the regional hospitals,” said Dr Denise Dekker from the BNITM’s Department of Infection Epidemiology. “It is important to collect such data in the long

*Good humour is the order of the day at the KCCR in Ghana, an African partner institution of the DZIF.*

term," Dekker stated. "Because they clearly demonstrate that the treatment and care of patients in rural hospitals can only be improved through continuous, long-term regional monitoring."

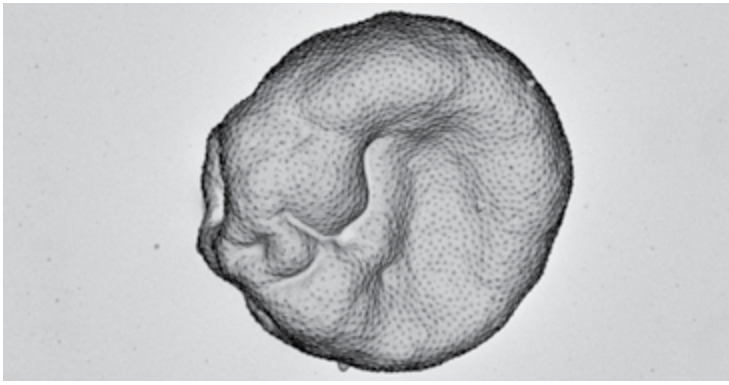
**MALARIA PARASITES HIDE OUT**

In malaria an infected Anopheles mosquito bites a person – the parasite *Plasmodium falciparum* enters the bloodstream where it multiplies inside the red blood cells. In dry seasons there are fewer mosquitos because their larvae need water to develop and survive. But how do malaria parasites survive a long dry season when there are fewer Anopheles mosquitos? Clues to this are provided by a study conducted by Dr Silvia Portugal from Heidelberg University Hospital. Her international team travelled to Mali several times in recent years and analysed the genetic differences, multiplication rates and survival strategies of parasites in the blood of around 600 malaria-infected persons, ranging in age from three months to 45 years, while also comparing these blood samples with those of uninfected individuals. What became clear: The parasites survive in the blood of infected people during the dry season.

*"Malaria parasites have developed an ingenious mechanism to survive the dry season when they cannot be transmitted by mosquitos."*

**Prof. Jürgen May**, Hamburg
Coordinator

One hallmark characteristic of the parasites is that – during the first 48 hours in which they multiply inside the red blood cells – they seemingly disappear from the blood circulation. They do so by adhering to the wall of blood vessels, thus avoiding clearance by the spleen. "The parasites in the red blood cells during the dry season differ genetically in many respects from those present during the rainy season," said the parasitologist. The most conspicuous finding is that they adhere less strongly to the vasculature wall and hence more infected blood cells float freely in the bloodstream. This stimulates the immune system's clearance mechanism: More old, damaged and longer-circulating human red blood cells are cleared in the spleen. "Through this genetic adaptation during the dry season the malaria parasites ensure both the survival of the human host and their own until the next mosquito season," explained the parasitologist, who has since moved to the Max Planck Institute for Infection Biology in Berlin, where she is continuing her projects.



*Electron microscope image of a red blood cell infected with malaria.*

**GOALS FOR 2020: OUTCOMES**

◐ *The clinical development of the malaria vaccine developed in Tübingen will be continued further. The tolerability and efficacy of the vaccine in children is currently being tested in a phase II trial in Gabon.*

● *We want to understand how the malaria parasites ensure their survival during the dry season as well as their transmission to mosquitos on resumption of the rainy season; and we want to conduct the first experiments on the development of a malaria vaccine with rodent parasites that can be transmitted by mosquitos and are in the blood stage.*

◐ *The existing birth cohorts will be expanded with new study participants and the recruited children will be closely followed up during the first months of life to obtain detailed information on the development of immunity to malaria parasites.*

◐ *Goal partially achieved/project is still ongoing*
● *Goal achieved*

**GOALS FOR 2021**

○ *The Antimicrobial Resistance (AMR) Surveillance System at the African partner institutions will be further expanded and AMR baseline data from patient samples will be entered into an electronic database.*

○ *Various methods for diagnosis of malaria, schistosomiasis and filariasis will be evaluated and compared in endemic areas.*

○ *Patients participate in clinical trials of multi-drug combination therapies against malaria to prevent the development of drug resistance.*

*You can find more information at*

HIV

# Learning from the rare in HIV

Human-immunodeficiency virus (HIV) is able to mutate rapidly and integrates itself into the cells and genome of humans. It also attacks important cells of the human immune system and can thus escape it. In particular, the virus is able to persist in a latent form inside cells. To date, there is neither a cure nor a preventive vaccine against HIV.

Broad-spectrum, neutralising antibodies, which are being researched by scientists at the DZIF, inter alia, could change all this. The goal of DZIF researchers is to apply various methods to reduce the viral load in the body to such an extent that the patient can live well also without expensive and long-term burdensome drugs. One focus is on early infections because the probability of remission or cure is greater when the virus has only been inside the body for a short time.

## Examples from research

**WHY A STEM CELL TRANSPLANT ALONE CANNOT CURE HIV**

So far, there have been reports in the literature on three patients who were considered to have been cured of HIV. All three had received stem cells from a healthy donor because of their underlying leukaemia. However, a cure was achieved only if the new stem cells were immune to HIV because of a rare genetic mutation in the CCR5 gene. A cure was not achieved when stem cells without this rare mutation were donated. In a study carried out in 2020 with 16 HIV patients, a German-French research team with the participation of DZIF scientists explored why a cure was not achieved for all patients – after all, the virus is largely suppressed by chemotherapy before stem cell donation. One thing is clear: In the first weeks after donation, immune cells belonging to the patient and the donor continue to live side by side. Scientists discovered that the CD4+ T-cells, which play a key role in HIV infection, were particularly activated during this stage. "Apparently there is a critical time window when the donor cells are especially susceptible to new infection by the viral material still harboured by the patient," said Prof. Julian Schulze zur Wiesch

*They identified a new, highly effective antibody against HIV (from left): Henning Grüll, Philipp Schommers and Florian Klein.*

from University Medical Center Hamburg-Eppendorf. "The activated CD4+ T-cells stimulate HIV so that the donor CD4+ T-cells also become infected." Hence, the immune system is not able to fully eliminate the HIV virus. "Other therapies, such as immune or gene therapy, are probably needed for long-term control of HIV infection in people following stem cell transplant from a donor," Schulze zur Wiesch said. "Only then would those infected be able to discontinue medication and be cured."

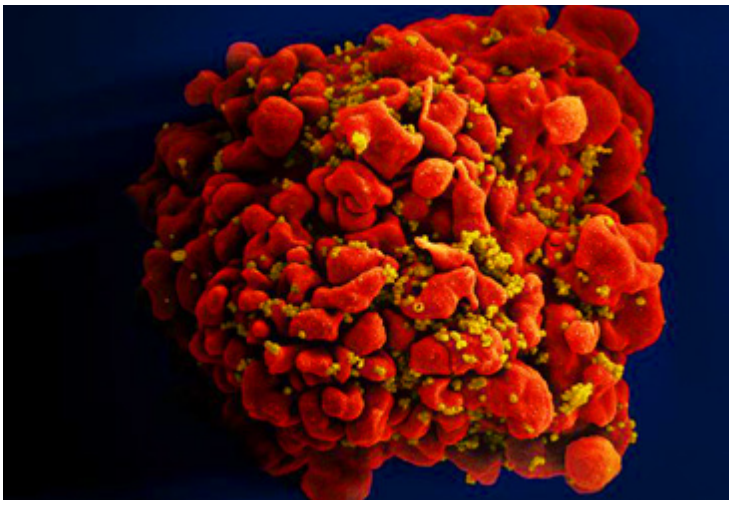
**NEW HIV ANTIBODY FOR TREATMENT AND VACCINATION**

HIV drugs are not able to cure the disease, instead merely suppressing the HIV virus. Therefore, HIV infection requires lifelong treatment. Because of the side effects of long-term treatment and growing drug resistance, researchers worldwide are exploring alternative treatments. One novel approach to the prevention and treatment of HIV entails broad-spectrum, neutralising antibodies. Only they are able to bind effectively to the viral envelope proteins and render the virus harmless.

*"Recent data on broad-spectrum neutralising antibodies foster hope: We have an increasing arsenal for researching a HIV cure."*

**Prof. Marcus Altfeld**, Hamburg
Coordinator

"Broad-spectrum" means that the antibodies are able to target as many different viral strains as possible. This is important because the HIV virus is constantly changing, giving rise to new viral variants. A group of German scientists led by Prof. Florian Klein, Dr Dr Philipp Schommers and Dr Henning Grüll from University of Cologne recently succeeded in isolating such a broad-spectrum antibody, which they simply called 1-18. To that effect, they screened more than 2,200 HIV patients. The 1-18 antibodies were very effective even at low concentrations and against 97 percent of the HIV variants tested. "1-18 binds to a structure on the surface of the virus which is of particular relevance in viral infection and replication," explained Schommers. "The blood viral load declined drastically and continually in mice we treated with these antibodies." The Cologne scientists consider 1-18 to be a very promising candidate that could soon be used against HIV. "The antibody's broad-spectrum activity makes it also a potential vaccine candidate for prevention of HIV infection," Schommers said.



*Scanning electron microscope of a T-cell (red) infected with HIV (yellow).*

**GOALS FOR 2020: OUTCOMES**

- ● *Investigation of the role of antioxidants as well as of iron metabolism in HIV-1 latency.*
- ● *Submission of a manuscript on highly effective genetic manipulation of quiescent CD4+ T-cells. This approach permits rapid functional analysis of dependency and restriction factors in HIV infection that regulate susceptibility and latency in these important HIV reservoir cells.*
- ● *Further characterization of the role of non-conventional T-cells in the viral HIV reservoir in a cohort of HIV-positive stem cell transplant recipients.*

◐ *Goal partially achieved/project is still ongoing*
● *Goal achieved*

**GOALS FOR 2021**

- ○ *Expansion of the cooperation with the French ANRS RHIVIERA consortium in the HIV-1 Cure field.*
- ○ *Development of synergies within the three main HIV research fields, focusing on immune control of HIV-1, the HIV reservoir and the clinical cohorts in HIV research.*
- ○ *Characterisation of the role of Fc gamma receptor-mediated trogocytosis – a mechanism that facilitates HIV-1 infection of quiescent CD4+ T-cells.*

*You can find more information at*

HEPATITIS

# Curing hepatitis D and B

The WHO wants to eliminate hepatitis worldwide by 2030. More than 365 million people are still carriers of hepatitis B and C viruses, of whom one million die as a result. Research on substances to combat the, in total, five different hepatitis viruses is progressing at full speed. Already now, treatment has improved.

With the development of new drugs, DZIF researchers are even hoping for a cure.

## Examples from research

**FIRST APPROVED DRUG**

It began 25 years ago with basic research on Peking ducks, culminating in 2020 in the approval of a drug for Europe. Hepcludex/Bulevirtide is the first drug against hepatitis D virus (HDV). The active substance was developed by a team led by Prof. Stephan Urban from Heidelberg University Hospital in collaboration with the DZIF and other partners. "With the approval, we are a big step closer to helping more than 12 million people infected worldwide with hepatitis D," said Urban, who since 2014 has held a DZIF professorship. HDV causes the most aggressive type of viral hepatitis, which can lead to liver cirrhosis and liver cancer. Infection always co-occurs with hepatitis B virus (HBV), which lends its envelope to HDV. Well-known HDV hotspots are Pakistan, Russia, the Balkans, Brazil, southern Italy, central Africa and the Middle East. "In Germany, too, the number of unreported cases is high," said Urban. Hepcludex is the first member of the "entry inhibitors", which prevent both HDV and HBV from penetrating a hepatocyte. It targets the bile salts transporter NTCP which is located only on hepatocytes and serves as a portal of entry for viruses. Hepcludex blocks the receptor lock like a broken key – HDV and HBV can no longer penetrate the hepatocyte. A multicentre phase III trial on the long-term efficacy, safety and tolerability is currently underway. In addition, research is ongoing to determine if Hepcludex is also effective against HBV. "We very much believe and hope that Hepcludex will also play an important role in future combination therapies for HBV," said Urban. With

*Prof. Stephan Urban from Heidelberg University Hospital is confident that Hepcludex can also be used to treat hepatitis B.*

his newly established foundation, and in addition to his scientific activities, Urban wants to further reinforce translational research – his team is currently developing a rapid test for HDV.

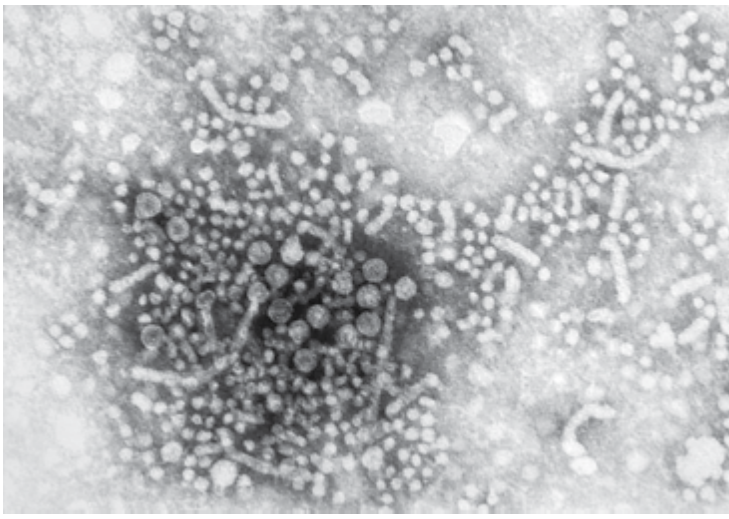
**HOPE FOR A CURE**

The team led by Prof. Ulrike Protzer from the Helmholtz Centre Munich, the Technical University of Munich and the DZIF has discovered how hepatitis B virus paralyses the body's defences – and how the immune system can be stimulated to control the virus. This makes the hope for a cure somewhat more realistic. An estimated 257 million people worldwide suffer from chronic HBV infection, of whom some 80,000 die every year from liver cirrhosis and liver cancer. The presently available treatments only prevent viral replication; a cure is not yet in sight. Protzer has now discovered how immune tolerance can be overcome in chronically infected persons.

*"We have used the know-how of our researchers and by means of impressive publications have helped to understand SARS-CoV-2 and COVID-19 disease. In doing so, we have contributed to the fight against the pandemic."*

**Prof. Ulrike Protzer**, München
Coordinator

"The hepatitis B virus produces a large quantity of viral proteins in the liver that inhibit induction of T-cell immunity," said the coordinator of the *Hepatitis* research field. "If one first suppresses the formation of proteins and then activates the immune system, this can eliminate the virus." In a murine model the infection was cured. Protzer's team inhibited protein formation by using small interfering RNAs (siRNAs). The small ribonucleic acid molecules bind to the messenger RNA (mRNA) of the viral proteins. The cell thus receives a signal to degrade the viral RNA, inhibiting protein production. "We combined the siRNA method with therapeutic vaccination," explained Protzer. "The TherVacB vaccine is designed to activate immune cells such as helper cells, antibodies and cytotoxic T-cells." It will be tested in a clinical trial starting 2022. Infected persons will receive three vaccinations four weeks apart. It will take seven to eight years until the therapeutic vaccine is ready for the market. "The aim is to further develop TherVacB as far as possible in the public sector," said Protzer. "Countries in which hepatitis B is prevalent need the vaccine at an affordable price."



*Hepatitis B viruses under the electron microscope.*

**GOALS FOR 2020: OUTCOMES**

- ● *Approval of Myrcludex B (trade name: Hepcludex) as the first antiviral drug developed in the DZIF Hepatitis research field.*
- ◐ *Definition of a combination therapy to enhance efficacy of a therapeutic hepatitis B vaccine.*
- ● *Preclinical investigation of the efficacy of an anti-HBV T-cell therapy for co-infection with hepatitis D virus.*

◐ *Goal partially achieved/project is still ongoing*
● *Goal achieved*

**GOALS FOR 2021**

- ○ *Development of bidirectional antibodies to direct T-cells to HBV-infected cells and eliminate them.*
- ○ *Development of a point-of-care test for detection of infection with HDV.*
- ○ *Identification and preclinical testing of therapeutic strategies affecting the in vivo activity of HBV-cccDNA.*

*You can find more information at*

GASTROINTESTINAL INFECTION

# Stopping the spread of gastrointestinal pathogens

In Western countries, diarrhoeal diseases are usually harmless. However, long-term shedders who spread the microbes to persons with a compromised immune system, for example in hospitals or nursing homes, are a problem.

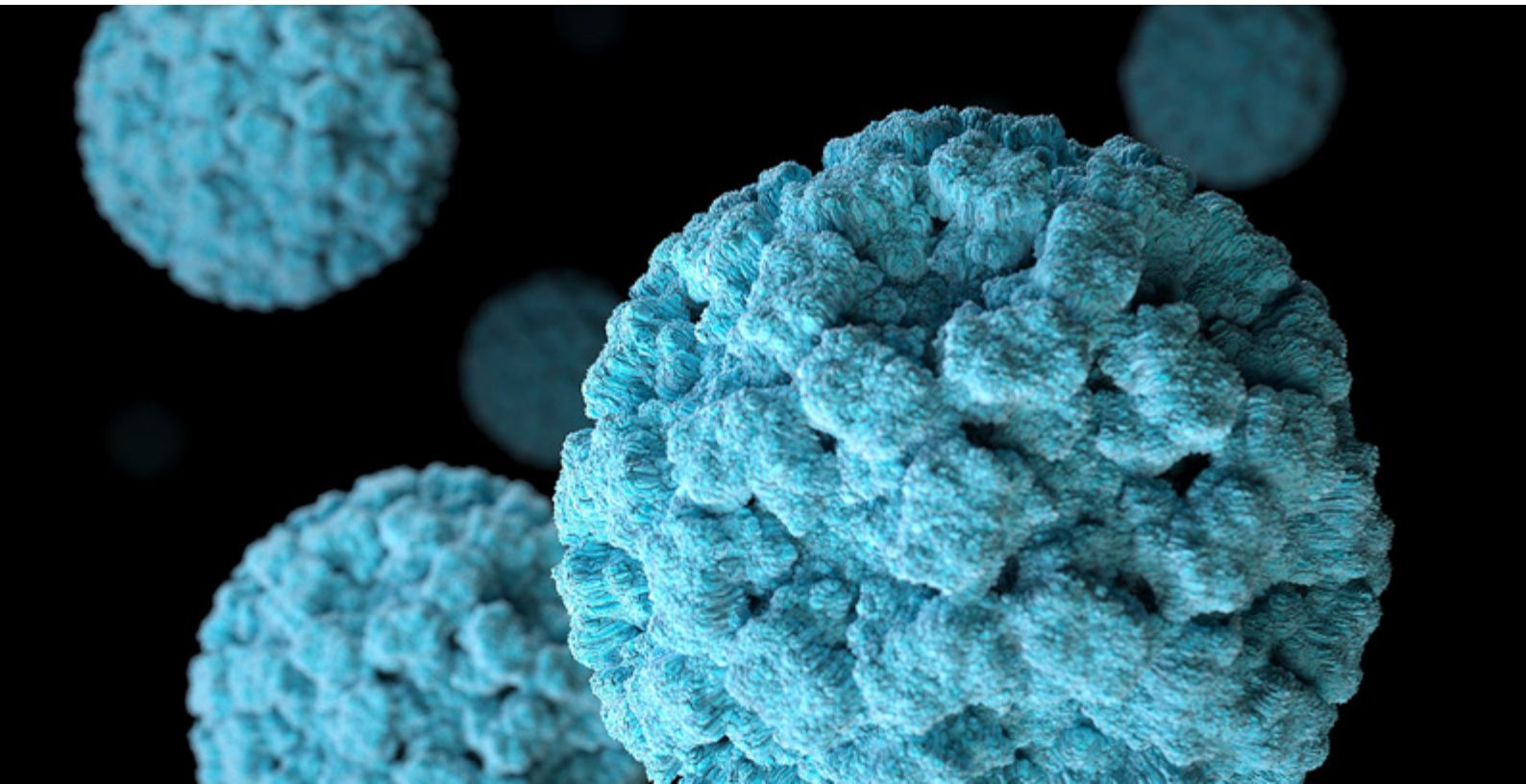
DZIF scientists from the *Gastrointestinal Infection* research field are exploring new ways to improve the treatment of gastrointestinal tract infections or completely prevent them through vaccination. They are also elucidating the composition of the natural gastrointestinal flora and the role of microorganisms in the development of disease.

## Examples from research

**INDIRECT INHIBITION**

Pathoblockers are an effective means of fighting gastrointestinal infections. They block pathogenic mechanisms of bacteria, for example by preventing the pathogens from penetrating the intestinal wall or by neutralising their toxins. This has the major advantage of preserving the endogenous microbiome. In addition, the pathogens do not become resistant or resistance development is much slower than when using antibiotic treatment. Currently, DZIF researchers led by Dr Monika Schütz from the Institute of Medical Microbiology and Hygiene at the University of Tübingen are developing a pathoblocker against *Escherichia coli*. This bacterium causes, inter alia, travel diarrhoea or severe diarrhoea in young children. The pathoblocker targets a periplasmic chaperone of the pathogen, which is an important stabilizer of the cell wall. "If this chaperone is blocked, the bacterial envelope becomes more permeable," Schütz explained. Antibiotics that would otherwise have difficulty penetrating the cell wall are more effective. The immune system is also better able to fight the weakened bacteria. Besides, the bacterium is overall less infectious because chaperone blockade also blocks pathogenic virulence factors on the outer membrane of *E. coli*. The partnership with the European Lead Factory – a consortium

*Aesthetic in the illustration, dangerous in reality: noroviruses are highly infectious.*



aimed at expediting the drug development process in Europe – has enabled the research group to test 300,000 substances that potentially block the target protein. Several active substances have been identified and are being investigated in greater detail by the team using modelling and simulation techniques. "Based on these data we will modify the molecules to work even better," Schütz said. Since the target protein of *E. coli* is similar to that of other bacteria such as *Klebsiella, Shigella* or *Salmonella*, the inhibitor could also be effective against them.

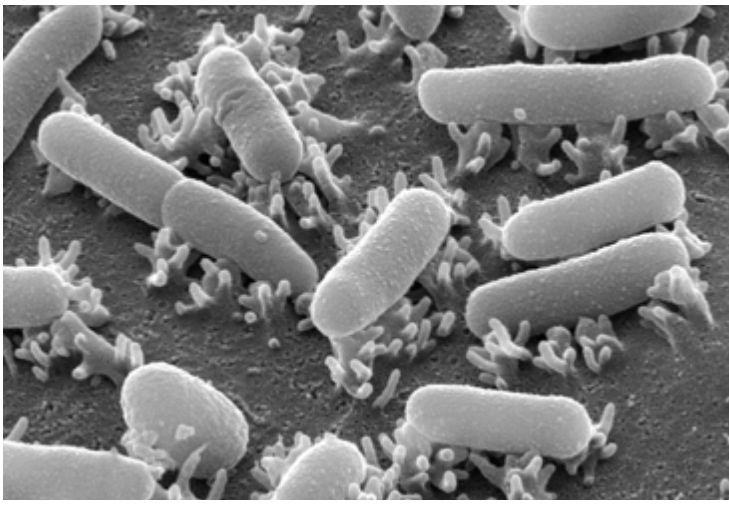
**A VACCINE AGAINST NOROVIRUSES**

Noroviruses (NoV) are a very common cause of viral gastrointestinal infections. "Infants and young children as well as elderly and immunocompromised persons would particularly benefit from a vaccine against this highly contagious diarrhoeal pathogen," said Dr Dieter Hoffmann, deputy director of the Institute of Virology at the Technical University of Munich (TUM). But there are several obstacles to be overcome for its development: For example, noroviruses cannot be grown in cell cultures and hence large amounts of antigen cannot be produced. Therefore, a vaccine composed of viral fragments, as used for example for influenza, would make little sense, as it would be very expensive.

*"Filing the first patent and the first FlexFunds application from the Pathoblocker research field marked especially important milestones for me in 2020."*

**Prof. Sebastian Suerbaum**, München
Coordinator

Hence, DZIF researchers at TUM are applying a different concept: "We stimulate the host organism with DNA and RNA constructs to produce the noroviral antigens itself, similar to the mRNA vaccines used against the coronavirus," the virologist said. The blueprint for the viral components is delivered to the body. The benefit: only minimal amounts of vaccine are needed to elicit an effective immune response. "This saves costs and makes it possible to rapidly adapt the vaccine if the norovirus undergoes genetic change," Hoffmann said. But scientists must still overcome another hurdle: Noroviruses that are infectious to humans are harmless to animals. As such, it is not possible to conduct trials to investigate whether vaccination prevents infection in animals. "However, we are able to measure in mice how their immune system responds to vaccination," Hoffmann pointed out. Researchers are currently exploring which of the vaccine construct candidates induce a particularly good immune response.



*Scanning electron micrograph of E. coli attached to human cells. Small protrusions, the microvilli, are visible on the cell surface.*

**TARGETS FOR 2020: OUTCOMES**

- *Signing of the cooperation agreement for the HelicoPTER trial by all project partners and approval by all the ethics committees; launch of the HelicoPTER pilot study at the München site.*
- *Filing of a patent application in at least one of the pathoblocker projects.*
- *Completion of patient recruitment for the CROSSDIFF trial and publication of the findings of the SPECTRUM trial.*

◐ *Goal partially achieved/project is still ongoing*
● *Goal achieved*

**TARGETS FOR 2021**

○ *Expansion of the HelicoPTER trial to at least two additional trial centres outside München.*

○ *Filing of another patent from the Pathoblocker Development project area.*

○ *Completion of the trial protocol for characterisation of human tissue samples for the potentially protective commensal bacterium Mucispirillum spp. and granting of the ethics vote.*

*You can find more information at*

HEALTHCARE-ASSOCIATED AND ANTIBIOTIC-RESISTANT BACTERIAL INFECTIONS

# Fighting antimicrobial resistance

The excessive use of antibiotics is among the leading causes of antimicrobial resistance as it promotes bacterial resilience through point mutations or gene exchange and a subsequent selection process. Consequently, many antimicrobials are no longer effective. WHO has declared antibiotic resistance one of the ten greatest global health threats.

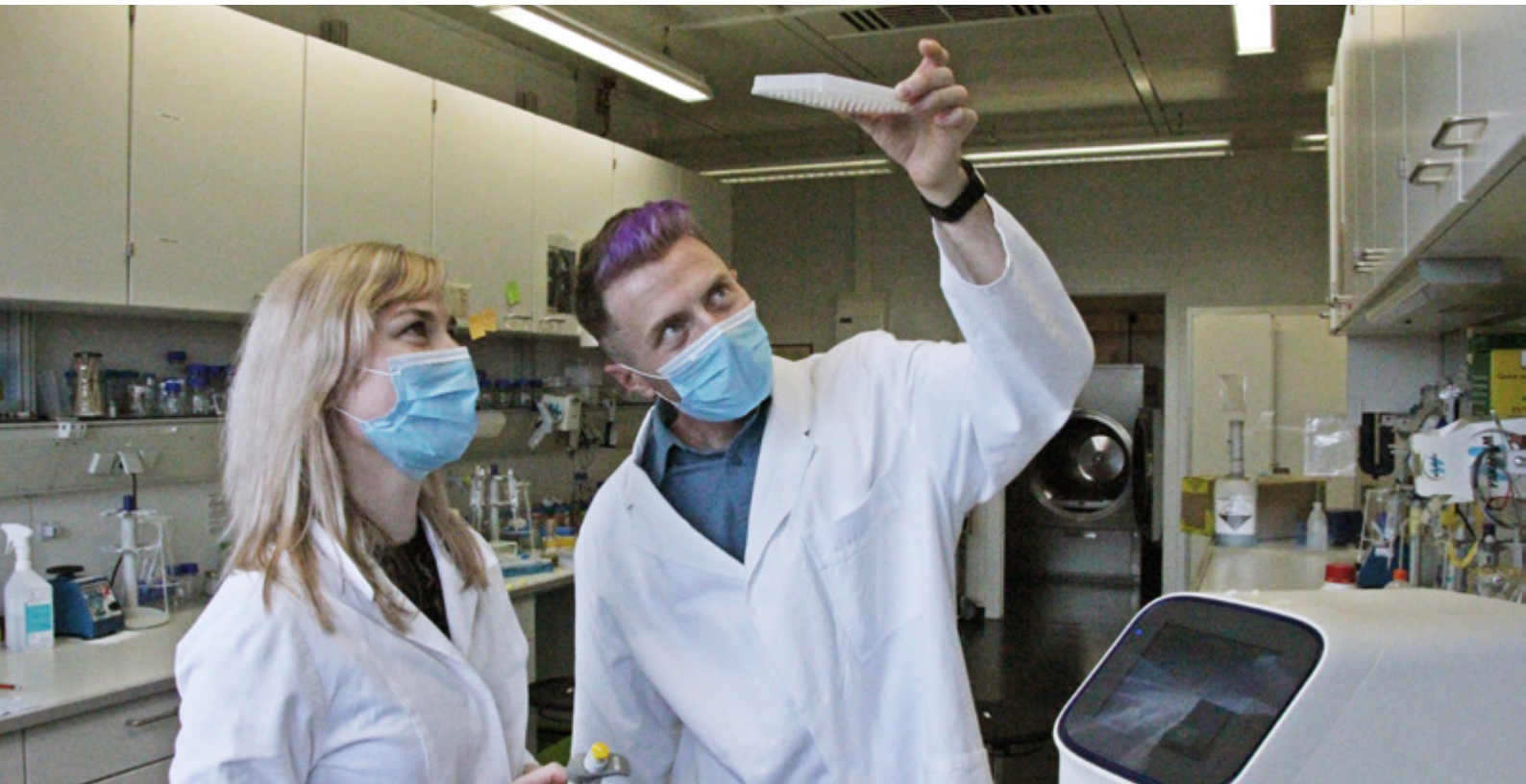
Scientists of the German Center for Infection Research (DZIF) are therefore adopting new research strategies to prevent the further spread of resistant bacteria.

## Examples from research

**HOW BACTERIA PREVAIL**

Bacteria gain a survival advantage or prevail over competitors by developing a resistance against antibiotics. The precise occurrences in the genome of the single-celled organisms in this situation have been uncovered by the team led by Dr Simon Heilbronner at the University of Tübingen using the bacterium *Staphylococcus aureus* as a model. Like all bacteria, this pathogen reproduces through simple cell division; the daughter cells are a clone of the parent cell. Hence, the cells have the same genetic makeup and the same properties. Adding to this knowledge, Heilbronner and his team have now discovered how pathogenic bacteria can nevertheless generate genetic variants among sibling cells. "If new properties are needed in the fight against the human immune system, the bacteria randomly amplify certain sections of their genetic material," stated the microbiologist. In addition to gene exchange, these amplifications are an effective means by which bacteria increase their chances of survival in hostile environments: "These duplicated gene sequences give rise to umpteen genetically new cells within a few generations." Amplifications always occur randomly and lead to the formation of higher amounts of certain proteins due to the expanded genome of the bacterial cell. If the affected proteins transport antibiotics out of the cell or fight the immune system, amplification confers a survival advantage to the bacteria. Therefore, instead of looking exclusively for antibiotic resistance

*Darya Belikova (left) and Jeffrey Power (right) in Simon Heilbronner's lab at University of Tübingen.*



genes as in the past researchers are now searching for highly amplified gene segments in supposedly resistant or particularly virulent bacterial strains. Proteins formed as a result of the amplifications could then be prospectively used as biomarkers to more easily identify these dangerous strains.

**DZIF STOOL BANK ESTABLISHED**

*Clostridioides difficile* infection (CDI) is a severe and often recurrent, diarrheal disease. In case of multiple recurrences of CDI despite adequate antibiotic treatment, affected patients may be potential candidates for what is known as a faecal microbiota transfer (FMT). Through a FMT, which can be administered via enema, colonoscopy or oral capsules, patients receive gut bacteria from a healthy fecal donor. For this purpose, the University of Cologne has established a so called Good Manufacturing Practice (GMP) Laboratory to safely process and manufacture bacteria-based FMT products. This project has already been initiated in 2014 by the infectious disease specialist Prof. Maria Vehreschild. The first-time inspection of the laboratory then occurred in 2020 by the responsible government authorities of Cologne and the German Federal Institute for Drugs and Medical Devices (BfArM).

*"Although 2020 was challenging because of the pandemic, we were able to promote young researchers focussing on healthcare-associated and multidrug-resistant bacterial infections."*

**Prof. Maria Vehreschild, Köln**
Coordinator

"The laboratory requires certification before we can conduct a registration trial for our FMT products in CDI patients," said Vehreschild. In perspective, the stool bank is to be established as a broadly accessible translational infrastructure within the DZIF as well as for external institutes and hospitals. "The objective is to manufacture various GMP-accredited products to facilitate randomised controlled trials and quality-assured products even for indications such as recurrent urinary tract infections or multidrug-resistant bacteria," outlined the scientist, who has been researching CDI and treating affected patients for many years. Her team was the first to introduce encapsulated FMT products in Europe and to treat over 300 patients with compassionate use FMT products. In the future, Vehreschild's FMT laboratory in Köln intends packaging microbiota into capsules after freeze-drying, in order to facilitate storage until they are used for treatment.

*Illustration of Clostridioides difficile bacteria, formerly known as Clostridium difficile.*

**GOALS FOR 2020: OUTCOMES**

- ● *Development and validation of prognostic models for short- and long-term mortality in patients with bloodstream infection.*
- ● *Establishment of an in vitro gut model under anaerobic conditions to optimise decolonisation strategies.*
- ● *Commissioning of a Faecal Microbiota Transfer (FMT) Facility (stool bank) in Köln to produce FMT products under GMP conditions for future use in clinical trials.*

◐ *Goal partially achieved/project still ongoing*
● *Goal achieved*

**GOALS FOR 2021**

- ○ *Development of a new project in collaboration with the Bioresources, Biodata and Digital Health infrastructure to identify lytic phages for treatment of vancomycin-resistant enterobacterial infections.*
- ○ *Enrolment of the first patients in the recently launched TIARA cohort (The Impact of Colonization and Infection with MDRO in a Cohort of Complex Surgical Patients).*
- ○ *Establishment of a DZIF-wide culturomics platform with which the dynamics of microbial communities can be analysed after co-cultivation.*
- ○ *Establishment of an overarching "DZIF Bacteriophage Task Force".*

*You can find more information at*

INFECTIONS OF THE IMMUNOCOMPROMISED HOST

# New therapeutic approaches for immunocompromised persons

People who have received an organ or bone marrow transplant, for example, or suffer from AIDS have a weakened immune system and often become very ill because of harmless viruses. Some pathogens hide inside the body for life. The search for new drug targets and a better understanding of the immune response are contributing to the development of innovative therapies.

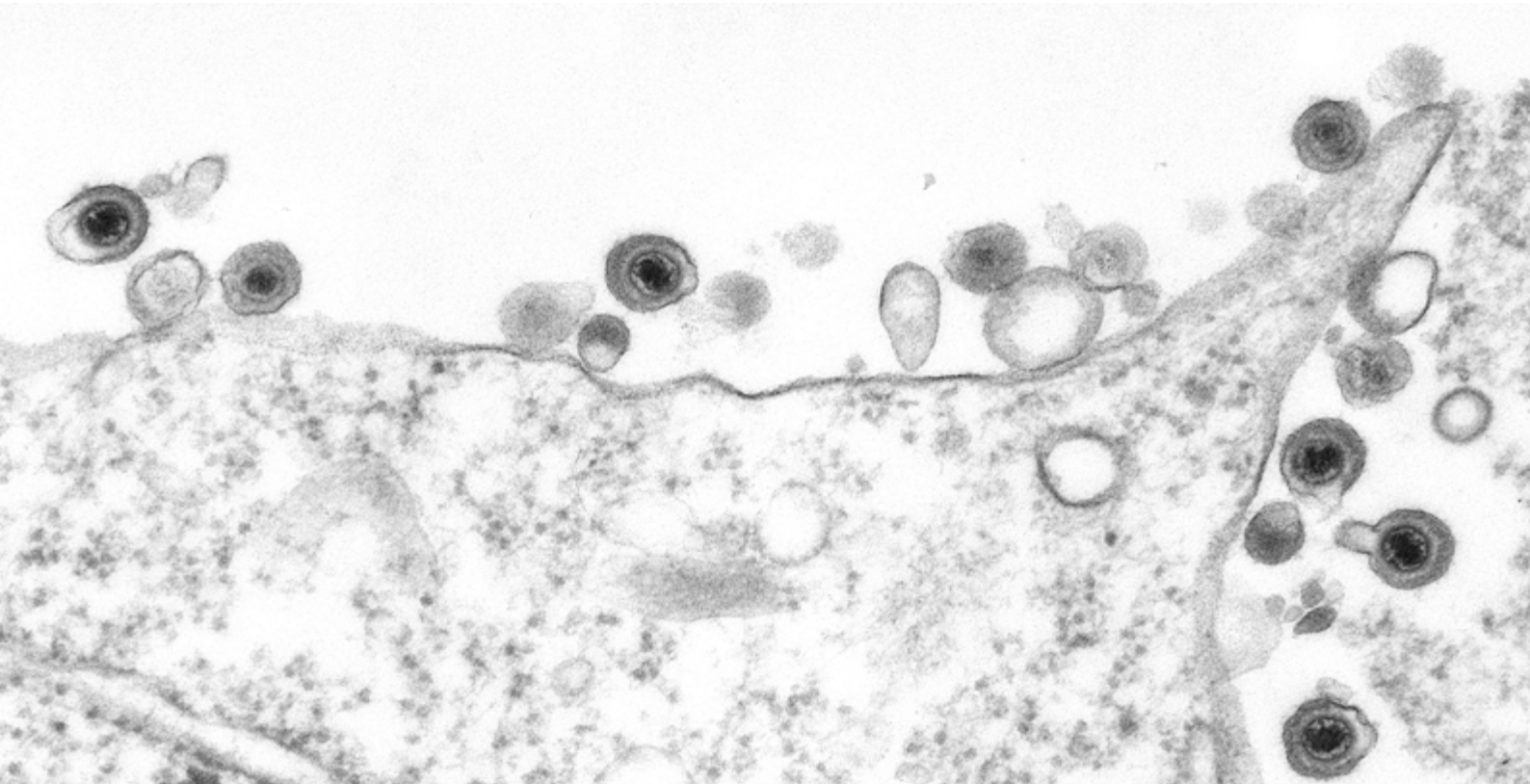
DZIF scientists are investigating the cellular mechanisms of the immune system and are searching for vaccines and new antiviral drugs.

## Examples from research

**T-CELL EQUILIBRIUM KEEPS VIRUS IN CHECK**

One in every two persons worldwide is a carrier of cytomegalovirus (CMV). In immunocompromised persons, CMV infection causes neurological damage or inflammation of the lungs and liver. Healthy people do not notice the latent, i.e. chronic quiescent, infection. Their immune system and, in particular, their T-cells keep the virus in check. An interdisciplinary team led by Prof. Dirk Busch from the Technical University of Munich has now for the first time analysed in detail the quality and composition of the T-cell response throughout CMV infection. Using a specially developed method, T-cells were isolated and characterised from the blood of infected persons as well as from samples of chronically infected mice. The study data published in the journal Nature Immunology demonstrate: Different T-cells with different receptors are active in the various stages of infection. Depending on the receptor, they exhibit variable binding avidity to infected body cells. “In the early stage a variety of T-cells, some of which bind strongly, fight the virus,” Busch said. In the late stage this diversity is no longer manifested. Instead, equilibrium is established between T-cells with lower binding avidity and the virus. While the findings are surprising, this dynamic could have advantages for the body. “Even though T-cells with high binding avidity are initially more effective at fighting the pathogen, they also elicit a more potent, harmful inflammatory reaction,” said Busch.

*Kaposi’s sarcoma, a malignant tumour, can develop in people infected with human herpesvirus 8 (shown as particles in the image).*



"In the late stage the body continues to be largely unharmed despite viral infection when the virus is kept in check only by T-cells with lower binding avidity." For future T-cell therapies these findings could mean that a "mixture" of different T-cells is particularly effective – and tolerable.

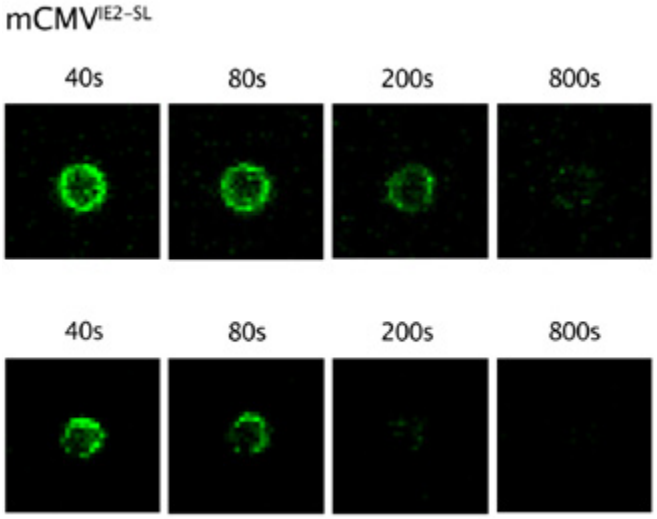
**LEARNING FROM ONCOLOGY**

Kaposi's sarcoma-associated herpesvirus (KSHV) is life-threatening for immunocompromised patients. For example, it can cause skin cancer in people with AIDS. A study conducted in 2020 by a research group led by virologist Prof. Thomas Schulz at the Hannover Medical School demonstrated that certain tyrosine kinase inhibitors are able to block the activity of various KSHV enzymes. Tyrosine kinases are enzymes that activate certain metabolic pathways in the cell – and for example promote the proliferation and motility of cells. If they are blocked, the virus cannot replicate and multiply. The new drugs also prevent the virus from being suddenly reactivated after lying dormant for years in the body. Tyrosine kinase enzymes are often overactive in malignant tumours. But good results have been achieved with tyrosine kinase inhibitors to treat certain cancers: In oncology they are already used to effectively block the increased enzyme activity of various cancers such as chronic myeloid leukaemia. "We have now been able to demonstrate that the viral tyrosine kinase of KSHV can also be inhibited by such tyrosine kinase inhibitors (TKIs)," reported Schulz.

*"In 2020, the development of new CRISPR-Cas9-based methods for editing T-cell receptors for adoptive T-cell therapy was the greatest success achieved in our research field."*

**Prof. Thomas Schulz**, Hannover
Coordinator

"From the approximately 20 active substances commonly used in oncology, we have identified three potentially effective antiviral candidates." At least one of these TKIs was able to inhibit KSHV-induced vascular tumours in an *in vivo* murine model. The selected, already clinically approved, TKIs may prove suitable in future for use as an established drug for a new indication. "For this, the next step is to now test the active substances in AIDS patients or transplant recipients for treatment of KSHV-associated tumours," Schulz said.




*The Koff rate assay developed by the research group led by Prof. Dirk Busch can be used to measure T-cell receptor binding avidity to viral antigens. The illustrated microscopy images each show a T-cell with high (top row) and low (bottom row) binding avidity.*

**GOALS FOR 2020: OUTCOMES**

◐ *With the "DZIF ETB Database", the aim is to establish an expert-edited database of clinically relevant, pathogen-specific T-cell epitopes as well as T- and B-cell receptors, thus driving forward the development of novel treatment strategies for infections of the immunocompromised host.*

◐ *Identification of biomarkers for CMV de novo infection in transplant patients based on spontaneous interferon-stimulated gene-expression.*

◐ *Identification of at least three genetic defects in patients with primary immunodeficiencies.*

◐ *Goal partially achieved/project is still ongoing*
● *Goal achieved*

**GOALS FOR 2021**

○ *Start with in vivo trials of new antiviral inhibitors in an animal model.*

○ *Continue patient recruitment in the DZIF transplant cohorts.*

○ *Publications from the Biomarker and New antiviral therapies research themes.*

*You can find more information at*

NOVEL ANTIBIOTICS

# New strategies in the fight against bacteria

According to the World Health Organisation, infectious diseases will be the most common cause of death in 2050. With ten million deaths worldwide, they would then rank before cancer. One reason for this is antibiotics that are no longer sufficiently effective because many bacteria have become resistant to them. Novel antibiotics are hardly in sight.

Antibiotics are increasingly becoming less effective. DZIF scientists are therefore specifically screening, identifying and optimising substances to weaken and kill bacterial pathogens.

## Examples from research

**KNOWING THE BACKGROUND, UNDERSTANDING MECHANISMS OF ACTION**

Daptomycin is a reserve antibiotic that is effective against methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant enterococci. Until recently, the precise target of this drug was unknown. "Daptomycin has different effects that for a long time we were unable to join together," said Prof. Tanja Schneider, deputy coordinator of the DZIF's *Novel Antibiotics* research field. The head of Pharmaceutical Microbiology at University Hospital Bonn and her team together with Dr Fabian Grein from the DZIF's *Healthcare-Associated and Antibiotic-Resistant Bacterial Infections* research field have solved the puzzle: Daptomycin blocks the incorporation of key building blocks into the bacterial cell wall. Two molecules are especially important, said Schneider: Lipid II and the membrane lipid phosphatidylglycerol. "Daptomycin binds to these specific areas of the cell membrane." Phosphatidylglycerol creates a kind of landing platform for daptomycin, so that it can target lipid II. If lipid II is then blocked by the antibiotic, the bacterium can no longer incorporate it into its cell envelope. The cell wall becomes unstable and the bacteria die. "Knowledge of the target structures and function of antibiotics lays the groundwork for targeted modification and further development," according to the microbiologist.

*Lab discussion at HIPS: Anna Hirsch (left) and colleague Jörg Haupenthal.*

Knowledge of the targets of antibiotics in the bacterium is also necessary for a second strategy in the fight against resistance: getting a better grip on complex bacteria with antibiotic combinations. “We need to know exactly which target structure each individual drug attacks in the bacterial cell in order to combine antibiotics more effectively,” Schneider said.

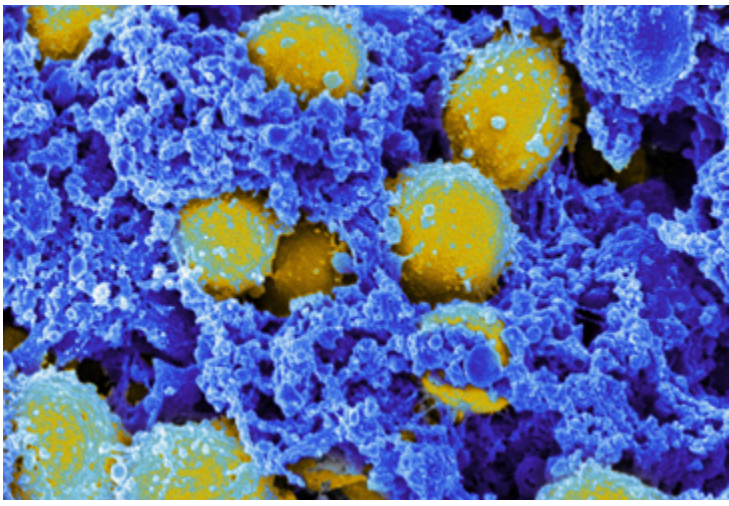
**NOVEL PATHOBLOCKERS AGAINST PSEUDOMONAS**

In addition to MRSA and enterococci, *Pseudomonas aeruginosa* is a bacterium that gives rise to major multidrug-resistance problems. The enzyme elastase is responsible for many of the bacterium’s pathogenic properties: elastase is able to cleave components of human tissue and thus enables pseudomonads to penetrate deeper into the body. It is also able to inactivate various components of the human immune system, making it easier for the pathogen to evade it. Elastase is also thought to play a role in the formation of the bacterium’s own biofilm – a layer of mucus that helps *Pseudomonas* to seal itself off from its environment. “We are developing and optimising molecules that specifically inhibit elastase,” said Prof. Anna Hirsch, DZIF researcher at the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS). Such “pathoblockers” or antivirulence agents mitigate the pathogenic effects of bacteria, without killing them.

*“Transferring and upscaling Corallopyronin production from the academic-translational to the industrial sector was the most important milestone in 2020.”*

**Prof. Rolf Müller**, Braunschweig/Saarbrücken
Coordinator

One important advantage is that resistance development is much slower in bacteria treated in this way than when treated with antibiotics. In the search for suitable molecules, the scientist and her team first screened several substances for effectiveness. And they found what they were looking for. In the next step, the team investigated how these molecules that were effective in the test bind to elastase. “With this knowledge, the substances can be further optimised,” said the chemist. Thanks to funding from the international public-private partnership CARB-X, this process is running at full speed for the time being until March 2022. “By then we should have selected one or two classes of compounds, which we will then further improve,” Hirsch said. By 2027, the preclinical research could be complete. “We are pleasantly surprised at how well our compounds are doing,” Hirsch pointed out. “Things are progressing in a way that a scientist could otherwise only dream of.”



*The image shows a scanning electron micrograph of Staphylococcus aureus bacteria (stained yellow).*

**GOALS FOR 2020: OUTCOMES**

- ● *Expansion of the DZIF natural compound library to > 1,000 pure substances.*
- ● *Completion and publication of the ARTS 2.0 online platform for ”genome mining“ that extends across strains and is target-related for new antibiotics.*
- ◐ *Transfer of the established production of high-grade, pure Corallopyronin A to an industrial producer.*

◐ *Goal partially achieved/project is still ongoing*
● *Goal achieved*

**GOALS FOR 2021**

- ○ *In the Corallopyronin A development, completion of transfer to the industrial Clinical Research Organisations and upscaling of the production to large scale (15,000 litres), as well as key toxicology studies in dogs.*
- ○ *Elaboration and publication of a roadmap for antibiotic development from translational academic research within the framework of the DZIF participation in JPI-AMR.*
- ○ *Demonstration/confirmation of in vivo proof-of-concept for adjuvant treatment of Pseudomonas aeruginosa infections using PqsR inverse agonists in combination with an aminoglycoside antibiotic.*

*You can find more information at*

PRODUCT DEVELOPMENT UNIT

# Accelerator for drug development

*During the development of vaccines and therapeutics, the product developers ensure the necessary contacts with industry.*

The *Product Development Unit* (PDU) supports DZIF scientists from the initial project idea through to the first clinical trials of potential drugs. Without this professional support, new drug candidates would often fail to reach the first clinical trial stage. In order to identify appropriate measures in the development of new vaccines, therapeutic agents and diagnostics, the PDU works closely together with various DZIF research fields. The aim is to develop innovative agents up to the point from where the pharmaceutical industry – or other suitable third parties – can assume the following stages of drug development through to the final approval or marketing stages.

The Office for Scientific and Regulatory Advice (OSRA) is part of the PDU. It is located at the Paul-Ehrlich-Institut (PEI) and at the Federal Institute for Drugs and Medical Devices (BfArM). The OSRA supports in clarifying regulatory matters and technical issues within scientific concerns and consulting procedures. The Translational Project Management Office (TPMO) at the Helmholtz Centre for Infection Research (HZI) in Braunschweig, also forms part of the PDU and provides its support in the operational and commercial aspects of drug development.

In 2020, the PDU structures could be used to accelerate the development of vaccines and therapeutics against the SARS-CoV-2 pandemic from within the DZIF and to cooperate with industrial partners for this purpose. In addition, the first two workshops of a series on product development were held.

**Prof. Klaus Cichutek** *Langen*
Coordinator

CLINICAL TRIAL UNIT

# Clinical trials in pandemic times


*Everything at a glance: The DZIF study register for all COVID-19 studies.*

New drugs and vaccines must also be tested on humans before they are launched on the market. The DZIF has twelve clinical trial centres specialised in infectious diseases, organised in the *Clinical Trial Unit* (CTU) infrastructure. The central Coordinating Office is based in Köln, also supporting DZIF scientists in the planning and implementation of clinical trials.

In 2020, the work of the CTU was dominated by the corona pandemic. The DZIF study register for COVID-19 studies was introduced in April. It is the first to provide an overview of such studies that are planned or have already been conducted in Germany. "In addition to voluntary study participants, the approval of COVID-19 vaccines also requires study centres that are able to reliably test safety and efficacy," said Prof. Oliver Cornely. The Coordinating Office developed the EUVAP platform to identify and characterise suitable vaccination study centres throughout Europe. This is complemented by the first Germany-wide register for vaccination study participants, which places volunteers at nearby study centres.

Together with the Advisory Board for Dialysis and Kidney Transplantation, the CTU is conducting the DOPPIO observational study. DOPPIO investigates the protective effect of pneumococcal vaccinations in dialysis patients. Results are expected to be available by the end of 2021.

**Prof. Oliver Cornely** *Köln*
Coordinator

AFRICAN PARTNER INSTITUTIONS

# Growing together and growing closer

*In Kumasi (Ghana), the DZIF is working on joint projects with local researchers.*

The DZIF infrastructure *African Partner Institutions* strengthens the long-standing partnerships between German DZIF institutions and African research institutes in Kumasi (Ghana), Lambaréné (Gabon), Nouna (Burkina Faso) and Mbeya (Tanzania). Joint research projects on poverty-related diseases such as malaria as well as on neglected tropical diseases and bacterial infections strengthen the links between the institutes. Furthermore, a new generation of well-connected scientists is being trained through laboratory rotations and workshops.

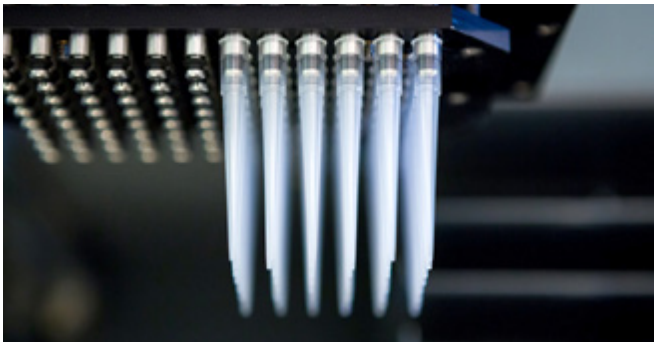
The diagnostics for bacterial pathogen determination set up in the rural partner hospitals, as well as the testing of antibiotic resistances, contribute significantly to a more targeted treatment and improve the sparse data on the effectiveness of antibiotics in these countries. In the future, a combination of epidemiological, clinical and microbiological data will make it possible to identify resistance patterns and transmission pathways and to investigate the effectiveness of interventions. The African institutions make an important contribution to the research infrastructure, but also to disease control on the ground.

In recent years, there has already been a growing interest in connecting the laboratories to the National Reference Centres in Africa. Meanwhile, some of the African partner institutes are directly involved in national COVID-19 diagnostics, but also in large clinical drug trials on COVID-19.

**Prof. Jürgen May** *Hamburg*
Coordinator

NOVEL ANTIVIRALS

# New “hits” are being added



*High-throughput screening robots enable the search for active substances in biobanks.*

There is a lack of effective drugs not only for emerging viruses such as SARS-CoV-2, Ebola or Zika. Even for many well-known viral diseases such as flu or hepatitis, the search for successful formulas remains in vain. At the end of 2017, the DZIF set up an overarching infrastructure especially for the research of new substances with antiviral activity. In the search for active substances, biobanks with small molecule substances are increasingly being screened for possible drug candidates. All DZIF partner sites have access to appropriate screening platforms as well as substance banks; on request, the scientists can be supported in carrying out screening experiments. Screening platforms are found in München, Heidelberg, Hannover and Braunschweig.

In 2020, 30,000 substances acquired in the previous year were tested for their effectiveness against various viruses, and cooperation with medicinal chemists was further intensified. They are on hand to advise the DZIF scientists in the *Novel Antivirals* infrastructure. Even during the early stages, they will provide their assessment as to whether active substances identified in screenings, known as “hits”, would be promising drug candidates from a chemical perspective. In 2020, medicinal chemists synthesised further hit derivatives and then successfully tested them for their antiviral effect. Some potential target molecules of the antiviral substances have also been identified.

**Prof. Thomas Schulz** *Hannover*
Coordinator

BIOBANKING

# COVID-19 biosamples as a new challenge

*Biosamples can be safely stored in nitrogen tanks for long periods of time.*

Human biosamples such as tissues or body fluids are indispensable for infection research. Within the DZIF, the *Biobanking* infrastructure is available specifically for this purpose: It offers scientists high-quality, accurately characterised and systematically recorded biosamples as well as the associated clinical information. A central biosample registry (ZBR) at the Helmholtz Centre Munich has simplified the search for infectious disease biosamples.

This infrastructure made it possible in 2020 to respond quickly and purposefully to the challenges of the COVID-19 pandemic and to provide all scientists with access to fluid and tissue samples from COVID-19 patients. To this end, a comprehensive COVID-19 collective was established within the DZIF tissue bank and expanded in the course of the pandemic through continuous autopsies of deceased COVID-19 patients. Studying the tissue included the analysis of the pathophysiological mechanisms of this infectious disease and made it possible to adapt the treatment of severe disease progressions.

In this context, the *Biobanking* infrastructure has also been involved in the national Network of University Medicine (NUM) from its inception; it also plays a leading role in both the tissue sample-based „DEFEAT PANDEMIcs“ project and the fluid sample-based „Biosample Core“ project within the NAPKON cohort network.

**Prof. Peter Schirmacher** *Heidelberg*
Coordinator

PATHOGEN REPOSITORY

# Pathogen collections for research purposes

*More than 2,600 strains of pathogens are stored in the pathogen bank of the Leibniz Institute DSMZ.*

Are newly occurring bacteria related to known common ones? How do antibiotics affect different bacterial strains? What role do microorganisms play in humans? To answer these and other questions, infection researchers need access to isolates of pathogens. A wide range of pathogens is stored in the DZIF *Pathogen Repository* at the Leibniz Institute DSMZ–German Collection of Microorganisms and Cell Cultures in Braunschweig. Bacteria, fungi or bacteriophages – viruses that specialise in infecting bacteria – are provided in a quality-controlled and well-documented manner for use in research. Training courses are held for the professional handling of pathogens. In recent years, the DZIF pathogen collections have grown to include over 2,600 microbial pathogen strains and active substance producers. An important role is played by multidrug-resistant bacteria and antibiotic-sensitive “negative control strains”. More than 500 genome sequencings have already been performed in cooperation with the following research areas: *Healthcare-Associated and Antibiotic-Resistant Bacterial Infections, Gastrointestinal Infections (GI)* and *Novel Antibiotics*. Thanks to the cooperation with the research area GI and other partners, there is a collection of bacteria from the intestinal tract of the mouse. Scientists can also draw upon a collection of strains from the intestinal tract of pigs, chickens and humans.

**Prof. Jörg Overmann** *Braunschweig*
Coordinator

BIOINFORMATICS

# Complex analyses at the push of a button

*The alphabet of life contains only a few letters - but their infinite combinations challenge bioinformaticians.*

The approaches of bioinformatics are indispensable in today's medical research. Genomes and patient samples are being sequenced in ever shorter time spans, and functional analyses (genomics, metagenomics, proteomics) generate huge amounts of data. Collecting and evaluating this data correctly requires the expertise of bioinformaticians as well as specialised soft- and hardware.

The *Bioinformatics* infrastructure supports DZIF scientists by evaluating and interpreting their infection research data. This includes developing and evaluating analysis pipelines for DZIF researchers to use independently as required. Automated and reproducible complex analyses, such as the genome-based prediction of bacterial phenotypes and antibiotic resistance, can be performed simultaneously for thousands of isolates "at the push of a button". The automated structural and functional analyses of microbial communities are also possible.

The bioinformaticians pass on their knowledge through workshops and through project consulting. The need for these training sessions is rising. Particularly in demand were workshops on microbiome data analysis and viral sequencing analysis, but also on the basics of Linux pipelines and statistical data analysis as well as data visualisation in free software such as "R".

**Prof. Alice McHardy** *Braunschweig*
Coordinator

EPIDEMIOLOGY

# Controlling pathogen outbreaks

*Prof. Gérard Krause and colleagues use their specially developed software as an aid in combatting the pandemic.*

Epidemiology deals with the occurrence, spread and distribution of diseases within a given population. Infectious diseases have different prevalences in different regions. The DZIF *Epidemiology* infrastructure supports the DZIF research areas in epidemiological questions. It offers methodological workshops, prepares reviews and develops new tools for studies in clinical and epidemiological research. This includes, for example, the development of mobile health apps with which pathogen outbreaks can be recorded and controlled in real time (the "SORMAS" project) as well as e-health research platforms ("PIA") for conducting epidemiological studies.

During the COVID-19 pandemic, experts from *Epidemiology* have methodologically supported the conduct of one of the largest seroprevalence studies in Germany together with the establishment of a SARS-CoV-2 multiplex serology and a platform for integrating data from different seroprevalence studies. The SORMAS software played a key role in the fight against the pandemic to increase the efficiency of contact tracing in Germany, Europe and internationally. Through fast and targeted evidence synthesis as well as infection-dynamic modelling, epidemiologists from this infrastructure supported the guidance of federal and state ministries, parliaments and committees as well as public communication.

**Prof. Gérard Krause** *Braunschweig*
Coordinator

DZIF ACADEMY

# Career opportunities in translational research

The DZIF attaches great importance to the promotion of young researchers in translational research, a fact that has been taken into account from the outset with the establishment of an Academy. From the Universität zu Lübeck, Professor Jan Rupp and Dr Nadja Käding coordinate and manage the Academy's various funding programmes to train physicians and scientists for infection research. The programmes offer special career opportunities in the fields of clinical infectious diseases, microbiology, virology, immunology, and molecular medicine.

*The infection researchers of the future are trained in the DZIF Academy funding programmes.*

**SUCCESSFUL: SCHOLARSHIP HOLDERS AT THE DZIF**

The Academy's most popular programme is the Clinical Leave Programme. It enables doctors to get away from the daily routine of the clinic for a year or two and devote themselves to infection research. In this way, translational research can come to life, because clinicians make their knowledge of bedside problems the basis of their research and vice versa. As it happened, the Clinical Leave Stipend has been the beginning of a career in infection research for some. In 2020, 18 doctors were able to conduct research in medicine with such a scholarship. Another extraordinary support at the DZIF is the Maternity Leave Stipend. It makes it easier for mothers – including fathers if necessary – to re-enter research after parental leave by temporarily financing half of their salary. Twelve women benefited from this offer in 2020. In addition to maternity scholarships, the Academy awards doctoral scholarships to medical students and doctors who wish to obtain the medical doctorate or the internationally recognised PhD degree. In 2020, 70 MD and six MD/PhD scholarship holders were funded.

**DIFFICULT: NETWORKING IN CORONA TIMES**

Promoting the next generation always means getting the young scientists to talk to each other, paving their way to other laboratories and conveying the advice of the "old hands". But none of this – in the DZIF Academy provided through workshops, laboratory rotations and travel grants – could take place in the corona year 2020. In that year, even the prizes for translational infection research, offered annually by the DZIF Academy, had to be awarded digitally to the award winners Prof. Stephan Becker and Prof. Gerd Sutter. "In terms of networking, this has been a sad year for the Academy and for its scholarship holders," explained Prof. Jan Rupp, the Academy's coordinator. The coveted autumn and summer schools had to be cancelled due to corona. For 2021, however, at least the autumn school, traditionally taking place in Lübeck, is firmly scheduled.

**Prof. Jan Rupp** *Lübeck*
Coordinator

SUCCESSFUL TRANSLATION

# Flagship projects in the DZIF on the road to success

Translation is the goal of the DZIF: The effective implementation of research results into practice is the focus of all German Centers for Health Research. The fact that there will be a number of projects in 2020 that are well on the way to application is also due to the fact that an infrastructure has been created specifically for this purpose at the DZIF. Product Development staff keep a close eye on the translational projects and support the researchers on their path towards development.

*At DZIF, translational projects are specifically supported by the Product Development infrastructure.*

"Our flagship projects currently include ten projects – which aim at the development of new therapeutics as well as new vaccines," explained Dr Thomas Hesterkamp, in charge of the project management of the translational projects. In the corona year 2020, most of the projects could be continued; the first hepatitis D drug has been approved in Europe. In some other projects, too, important steps towards application have been taken.

**VACCINES FOR THE FUTURE**

Ulrike Protzer's research group at the Institute of Virology of the Helmholtz Zentrum München is developing a therapeutic vaccine for the immunotherapy of chronic hepatitis B. The year has been dominated by the preparation and quality-assured manufacturing of the vaccine components. After the preclinical toxicological trials, the first clinical trials are scheduled to begin in 2021. The development of a vaccine against the MERS coronavirus that the team of Gerd Sutter, Stephan Becker and Marylyn Addo is driving forward is already one step further. The MVA-MERS-S vaccine had already proven to be well tolerated in a first clinical pilot study on 23 subjects back in 2018/19, triggering a persistent antibody formation. The randomised, placebo-controlled phase Ib trial now starts, aiming to test the vaccine on a total of 145 people. For SARS-CoV-2, the development of a vaccine based on the MVA vector platform technology began in 2020.

**FROM CANDIDATE DRUGS TO MEDICINE**

New candidate therapeutics are being developed in various areas. The lighthouse projects include a recombinant phage lysine against hospital pathogens, an antibiotic against filarial worms, a SARS-CoV-2 neutralising antibody and a drug against tuberculosis. This new anti-tuberculosis agent, BTZ-043, has been in clinical development in Africa since last year. Drug development, costing several million euros, is only possible through joint financing from the public and private sectors and is a good example of the fact that translation needs many partners. "Our main task as DZIF is to produce candidate drugs and vaccines from discovery to early clinical trials," Hesterkamp emphasised. "In this way, we are laying the foundation for an efficient drug development in a partnership model with third parties." The increasing cooperation with companies in the pharmaceutical industry shows that this concept is working.

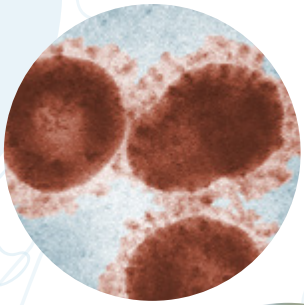
DZIF HIGHLIGHTS 2020

# News Ticker

## JANUARY

DZIF scientists at the Charité – Universitätsmedizin Berlin developed the first test for the detection of the SARS-CoV-2 virus, at that time as yet only raging in China.

A research group at the University Hospital Cologne discovered a new, highly effective antibody against HIV, known as 1-18 and able to suppress virus replication continuously.



## JUNE

More than half of the world's population carries the cytomegalovirus. Many feel none of this – their immune system keeps the viruses at bay. Groups of T cells with virus-specific receptors play a key role in this. A research team at the Technical University of Munich were the first to analyse their interaction in detail.

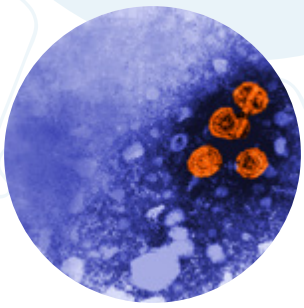
## APRIL

Prof. Christian Drosten, Director of Charité's Institute of Virology, has received the "Special Award for Outstanding Achievements in Scientific Communication during the COVID-19 Pandemic". The prize of the German Research Foundation and the Donors' Association is endowed with 50,000 euros.

## FEBRUARY

A München research team discovered a new approach to curing chronic hepatitis B. The hepatitis B virus produces large amounts of proteins in the liver, which inhibit the immune defence, thus preventing an effective therapy. Suppression of these viral proteins makes therapeutic vaccination possible. Clinical trials will start in 2022.

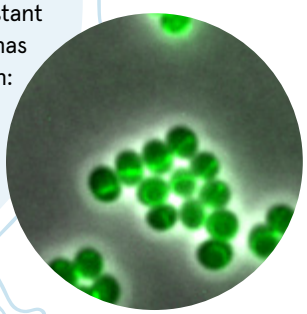
At University Hospital Frankfurt, SARS-CoV-2 was detected for the first time in symptom-free returnees from China. The virus can thus potentially be transmitted by people who are not yet aware of their disease.



## MARCH

Since SARS-CoV-2 first appeared in China, the scientists and doctors at the DZIF have been working on rapid vaccine development against the new coronavirus.

Daptomycin is used as a reserve antibiotic when conventional active substances fail against resistant germs. A DZIF team at the University of Bonn has now uncovered daptomycin's mode of action: It blocks the incorporation of important building blocks into the bacterial cell wall, thus causing the bacteria to die.



## AUGUST

The virus blocker bulevirtide (brand name Hepcludex) was the first drug against hepatitis D to be approved by the European Commission. It was developed by researchers from the Heidelberg University Hospital and Medical Faculty in collaboration with the DZIF and is the first representative of so-called "entry inhibitors".

## OCTOBER

On October 9, the first subject of the DZIF vaccine study MVA-SARS-2-S against COVID-19 received her injection at the University Medical Center Hamburg-Eppendorf.

Based on data involving more than 80,000 patients, an international research group, including DZIF scientists at Research Center Borstel-Leibniz Lung Center, developed a programme able to predict the individual risk of tuberculosis.

## NOVEMBER

The DZIF was reviewed by the Scientific Advisory Board and external reviewers. Some of their questions were: Does the DZIF meet the requirements for translation? Are scientists able to get new drugs, vaccines and diagnostics off the ground faster than before? The result: The successes to date were rated as "impressive", the plans for 2021 to 2024 as "outstanding".

What COVID-19 vaccine trials are underway and where can volunteers get in touch if they want to participate? In order to be able to place interested parties in specific studies, a central volunteer database for Germany has been created at the DZIF and a Europe-wide platform set up, recording all of the centres where SARS-CoV-2 vaccines can be tested.

## DECEMBER

In 2020, the DZIF honoured two scientists who have long been involved in virus research and who are currently working on a vaccine against COVID-19: Prof. Stephan Becker and Prof. Gerd Sutter both receive an award for translational infection research, each endowed with 5,000 euros.

Scientists from the University Hospital Cologne, the Philipps-Universität Marburg and the DZIF, together with Boehringer Ingelheim, have succeeded in developing a new antibody that renders SARS-CoV-2 harmless in preclinical tests.

SCIENCE AND PUBLIC

# Focus on media response

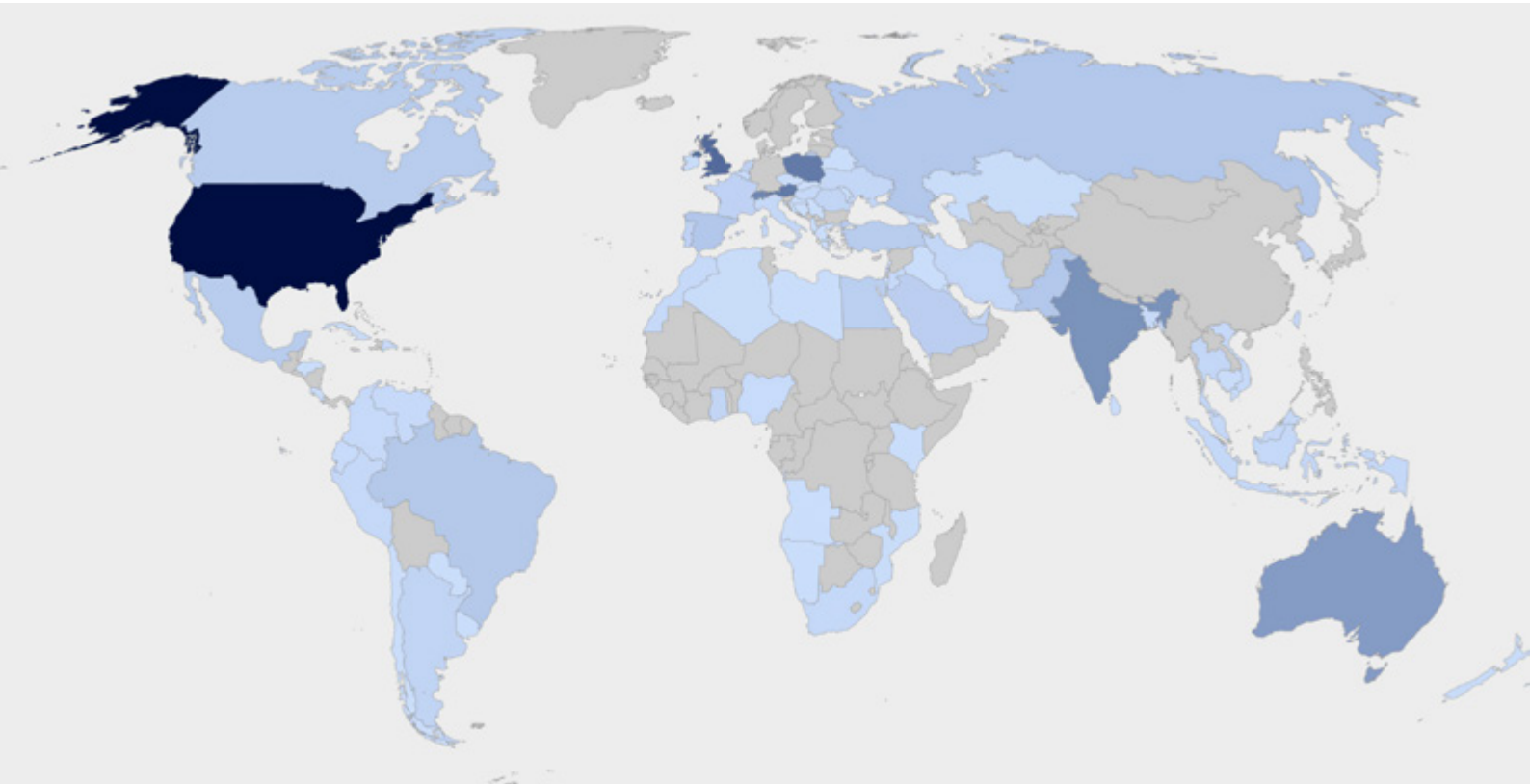
Looking back at the media and public relations activities of 2020, there has been no way around the corona pandemic. Nothing has required more work with the media than the novel virus. With the support of the scientists at the DZIF, it has been possible time and again to inform the interested public in a factual manner and to support the media in their reporting. However, the newly emerging infections were only one focus at the DZIF, because the coronavirus raised the general interest in infection research.

We have taken this extraordinary year as an opportunity for having the responses to our media work measured and analysed. As expected, the results show 2020 to have been a "successful" year in terms of our public image. The importance of infection research has become visible and has also brought other challenges into the public interest, such as antibiotic resistance or hepatitis diseases. For us as communicators, content remains important, which must be prepared with competence and objectivity. The media response analysis of 2020 shows that in public relations, old and new media formats complement each other sensibly.

**WEBSITE TRAFFIC, MEDIA RESPONSE & REACH**

The website is still at the centre of press and public relations. Keeping it as up-to-date as possible, quickly mapping new research results and addressing current issues are crucial for a successful communication. The DZIF welcomed 1.17 million visitors to its website in 2020. The increased interest is also reflected in the media response: Almost 9,000 online articles reported on our research projects. This had the potential of reaching 6.8 billion people. An online medium that has reported particularly frequently and that is probably one of the most clicked is t-online. But also traditional daily

*The work of the DZIF is reported across the globe: Around a fifth of all online articles appeared in non-German-speaking countries - most of them in the USA and the UK. In addition to SARS-CoV-2, results of hepatitis research were the ones to be picked up the most outside of Germany.*



newspapers such as Frankfurter Rundschau, DIE WELT or Hamburger Abendblatt have reported on the DZIF on their websites.

**CORONA, VACCINE & EVEN MORE CORONA**

It is hardly surprising that in 2020 no infectious disease has been able to compete in popularity with COVID-19. The top ten topics from the analysis of German-language media revolved around corona, with vaccine development in first place with 44 percent, and corona tests as well as COVID-19 treatments as further frequent topics. The top article by reach could be found at merkur.de: 17.9 million people had access to the article on May 14: "Will I be able to go swimming in the summer?" A question understandably particularly close to the hearts of many people. Fortunately, a DZIF expert was able to provide an answer to this question, too. The analysis by research area revealed: *Emerging Infections* with about 5,000 online articles were followed by the subject areas of *Novel Antibiotics* with 55 and *Hepatitis* with 15 online articles.

**DROSTEN, BECKER & CO.**

The DZIF scientists have played a major role in the now frequent mentioning of the German Center for Infection Research in connection with infections. The inquiries from journalists show that some individuals are already being connected to the DZIF. The top three ranks were occupied by Stephan Becker, Klaus Cichutek and Christian Drosten: Stephan Becker, who coordinates the research area *Emerging Infections* at the DZIF and is jointly responsible for vaccine development, was named in almost 3,000 online articles in connection with the DZIF.

**PRESS RELEASES, TWITTER & LINKEDIN**

In 42 press releases, research results from the DZIF were publicised in a timely manner last year. In parallel, they were also communicated via social media and thus made more quickly accessible to other target groups in addition to media representatives. The analysis showed that almost all press releases were picked up by the press, 561 articles were based on them. Their content has been shared 43,000 times on social media. First and foremost has been a press release about the start of the first clinical trial of the DZIF vaccine, accessible to 7.3 million readers via an article in DIE WELT alone and picked up in a total of 89 articles.

In addition to the website, social media offer the opportunity of placing short messages quickly and target-group appropriately and of entering into a dialogue. Within the press and public relations work of the DZIF, the social media sector saw a further expansion. The numbers speak for themselves: The DZIF published 186 tweets on Twitter in 2020 and 65 posts on LinkedIn, gaining around 2,000 followers.


*The increased awareness of the DZIF in 2020 was also reflected in numerous donations: In May, Verena Streich and Ina Schulenburg from the Hanseatische Personalkontor GmbH personally handed over the proceeds of a charity run to Timo Jäger. A big thank-you also goes to all other supporters of DZIF research!*

**NETWORKING, COOPERATING & COMMUNICATING**

Communication with the media is a major task of press and public relations. But it is only one segment. Equally important is the communication with other target groups, also supported by our team. A centre such as the DZIF thrives on networking. The internal cooperation of basic researchers and clinicians is essential, as is the cooperation with external research institutions and with industry, indispensable for translational development. In the corona year 2020, the cooperation with the other German Centers (DZG) has been further strengthened, with many projects being launched jointly. This has also been reflected in the research magazine SYNERGIE, jointly published by the DZGs' press offices since 2019. In 2020, the third and fourth editions were published on the topics of "Diagnosis" and "Therapy".

**Tatiana Hilger, Janna Schmidt, Karola Neubert und Martina Lienhop**

*Braunschweig,* Press Office

COLLABORATIONS

# External Partnerships

Numerous associated partnerships and other external collaborations reinforce the DZIF's position as a top-class institution in the field of infection research.

**THE DZIF'S ASSOCIATED PARTNERS**

**Charité – Universitätsmedizin Berlin**

The Charité Institute of Hygiene and Environmental Medicine is one of six partners in the DZIF network „Multidrug-resistant Bacteria" (MDRO Network: R-Net). This network is focusing on investigating the epidemiology of multidrug-resistant bacteria, bloodstream infections and *Clostridioides difficile* infections.

The research group „Virus Detection and Preparedness" forms a major part of the DZIF *Emerging Infections* research field. It is led by Professor Christian Drosten at the Charité's Institute of Virology (Campus Charité Mitte) and is responsible for identifying emerging pathogens and for developing diagnotic tests for both novel and epidemic pathogens. The „Innate Immunity and Viral Evasion" research group is also located at the Institute of Virology and is part of the DZIF *HIV* research field. It is led by Professor Christine Goffinet and characterises the mechanisms of intrisic cellular immune responses and HIV-1 induced antagonising strategies. The research group „Virus Epidemiology", led by Prof. Jan Felix Drexler, coordinates Zika outbreaks in Latin America projects across several DZIF partner sites and collaborates closely with the *Hepatitis* research field, conducting research on novel hepatitis viruses from animal reservoirs.

**Essen University Hospital**

A hepatitis C project involving scientists from the Essen University Hospital and others (see also Goethe University Frankfurt) aims to point out individually tailored patient treatment options to the treating physician. Therapy recommendations include both hepatitis C virus genome sequences and the patient data. Scientists at the Essen University Hospital also research hepatitis delta virus

*In collaboration with BioNTech, the DZIF is researching RNA-based vaccines for selected virus families. The image shows an mRNA production facility of BioNTech in Marburg.*

(HDV) infections, the most severe form of viral hepatitis. In addition, the Essen University Hospital is involved in a project in the research field of *HIV*. Among other things, new treatment strategies for viral emission or destruction will be tested there in a cohort of patients with early HIV infection.

**Friedrich Schiller University Jena**
The Institute of Organic Chemistry and Macromolecular Chemistry at the University of Jena has been participating in a study in the research field of *Tuberculosis* since 2019. Thiopeptide derivatives and their effectiveness as antibiotics against multi-resistant tuberculosis bacteria are being investigated. Various semi-synthetically produced thiopeptides showed promising activities and are now being further developed up to preclinical studies.

**German Liver Foundation/HepNet Study-House, Hannover**
The HepNet Study-House has been networking study centres and is expanding nationwide networking across Germany with medical practices and physicians who are interested in taking part in hepatitis research. As a central point of contact for scientists and cooperation partners, it creates a platform for carrying out clinical trials. The DZIF can use the infrastructures and cohorts for its projects.

**Goethe University Frankfurt, Frankfurt am Main**
A project of the DZIF *Hepatitis* research field is currently underway at the Goethe University Frankfurt. It aims to improve the treatment of hepatitis C patients with novel drugs (directly acting antivirals, DAA). It defines treatment algorithms that maximise clinical success whilst minimising healthcare costs.

**Greifswald University Medical Center**
Greifswald University Medical Center is a partner in a project of the *Healthcare-Associated and Antibiotic-Resistant Bacterial Infections* research unit in which the lytic phage protein HY-133 is being investigated. The protein has been shown to be highly effective against methicillin-resistant *Staphylococcus aureus* bacteria in the nasal cavity. Currently, the promising compound is being investigated in preclinical studies to ensure safety in subsequent human clinical trials.

**Hans Knöll Institute, Jena**
The Hans Knöll Institute (HKI) provides the DZIF with different natural compounds. Scientists from the HKI and the Ludwig-Maximilians-Universität München (LMU) lead a project involving a clinical trial on a newly developed antibiotic against tuberculosis. The newly developed investigational agent, termed BTZ-043, is also effective against multidrug-resistant pathogens.

**Julius-Maximilians-Universität Würzburg**
In a clinical trial at the DZIF research area *Infections of the Immunocompromised Host*, leukaemia patients are administered specially purified immune cells, so-called memory T-cells, after a bone marrow transplant for the first time. These special immune cells are to protect patients from infection until their own immune systems function. Some of the trial patients are being treated in Würzburg, and also at the DZIF sites in München (coordination), Tübingen and Hannover.

**Medical Center – University of Freiburg**
The Medical Center of the University of Freiburg is a partner of several DZIF projects which are located in the research areas *Hepatitis*, *Infections of the Immunocompromised Host* and *Healthcare-Associated and Antibiotic-Resistant Bacterial Infections*. Reducing healthcare-associated infections is an important goal of these projects. To this end, for example, antibiotics are being used more selectively and hygiene measures improved. Freiburg is one of six partner sites at which the epidemiology of multidrug-resistant bacteria and the epidemiology of bloodstream infections and *Clostridioides difficile* infections are being studied longitudinally over a several-year period. In addition, a system is being developed that is designed to indicate outbreaks of multi-resistant bacteria in the clinic in good time.

Human cytomegalovirus (HCMV) infections pose a risk for immunocompromised individuals (such as AIDS or transplant patients). The researchers are looking for new drugs against HCMV.

**University of Bayreuth**
The *Mycobacterium tuberculosis* (MTB) pathogen is in the focus of a major tuberculosis screening project in which the University of Bayreuth is involved. The goal is to create a preclinical model, based on which new drugs against tuberculosis can be identified, and both known and newly discovered drugs can undergo efficacy testing.

**University of Münster**
The University of Münster is partner in a project of the research area *Gastrointestinal Infections* and is working on new pathogen-specific inhibitors, for example against salmonella.

Scientists at the University of Münster are also involved in the development of new antibiotics against multi-resistant tuberculosis bacteria. The aim of this project is to develop a drug candidate that proves its efficacy against tuberculosis in preclinical studies.

## INDUSTRY COLLABORATIONS

**BioNTech AG, Mainz**
The DZIF is researching RNA-based vaccines for selected virus families with potential human pathogens in collaboration with the BioNTech Institute and the TRON Research Institute, subsequently bringing the vaccines into preclinical and early clinical development.

**Coris BioConcept, Gembloux (Belgium)**
DZIF scientists from the Institute of Medical Microbiology at the University of Cologne have generated antibodies against the carbapenemases OXA-23, -40 and -58, which are being used in collaboration with the Belgian company Coris BioConcept in a now commercially available rapid test for the detection of carbapenem-resistant *Acinetobacter baumannii*. Dr Alexander Klimka's research group „Antibacterial Vaccine Development" is being funded by the DZIF.

**HYpharm GmbH, Bernried**
HYpharm GmbH and a consortium funded by the DZIF are collaborating to manufacture and preclinically develop phage lytic protein HY-133 (also see Greifswald University Medical Center). They are specifically planning joint early-stage clinical development for nasal decolonisation of *Staphylococcus aureus*.

**IDT Biologika GmbH, Dessau-Rosslau**
Together with the company IDT Biologika, the DZIF is developing a vaccine against the MERS coronavirus in a consortium of scientists and clinicians. The company IDT Biologika developed its own cell line for the production of the vaccine on a larger scale. The company is also a partner and the consortium leader in the currently ongoing clinical trial of the vaccine candidate MVA-SARS-2-ST.

**Juno Therapeutics GmbH, a Bristol Myers Squibb Company, Göttingen**
Juno Therapeutics, formerly Stage Cell Therapeutics, is collaborating and exploitation partner of a research group led by Prof. Dirk Busch, Technical University of Munich, working in the field of GMP quality-assured manufacture of central memory T-cells for the treatment of infections and cancer. The DZIF is funding Prof. Busch's group.

**Gilead Sciences, Inc.**
Together with the University of Heidelberg, an active agent which inhibits hepatitis B viruses from penetrating cells was being developed and could potentially be used to prevent hepatitis B and D infections. MYR GmbH was coordinating the entire project. At the end of July 2020, the European Commission approved the active ingredient under the name Hepcludex – initially for hepatitis D. In March of this year, the full acquisition of MYR GmbH by Gilead Sciences, Inc. became public.

ABOUT THE DZG

# German Centers for Health Research

The main objective of the Federal Government's health research programme is to develop more effective ways to combat common diseases. With the establishment of the German Centers for Health Research (DZG), the federal and state governments have put into place the prerequisites.


*Eye-catcher: The joint research magazine "SYNERGIE" by the German Centers for Health Research.*

The German Centers for Health Research are long-term, equal partnerships of non-university research institutions, such as the Max Planck, Helmholtz and Leibniz Institutes as well as universities with university hospitals. The German Center for Infection Research (DZIF) is one of the six DZGs, established between 2009 and 2012 on the initiative of the Federal Ministry of Education and Research. They bundle existing competencies, thus contributing significantly to closing knowledge gaps and improving the prevention, diagnosis and therapy of common diseases. The centres are dedicated to the following diseases: cancer (DKTK), diabetes (DZD), cardiovascular diseases (DZHK), infectious diseases (DZIF), lung diseases (DZL) and neurodegenerative diseases (DZNE). Two other centres for child and adolescent health and for mental health are in the process of being established. The strategic cooperation of the leading researchers in the DZGs strengthens Germany as a science location in international competition and significantly increases its attractiveness for young scientists at home and abroad. The bundling of different disciplines and competencies has already led to a significantly increased international visibility of translational, clinical-application-oriented research in Germany.

The six DZGs have been working closely together from the outset to exchange experiences and exploit synergies. In recent years, cross-DZG cooperation has been further expanded, with the establishment of working groups for biobanking, artificial intelligence, data management, promotion of young researchers, public relations, prevention, global health and regulatory aspects of clinical trials and others. At the end of 2020, a strategy paper for the future cooperation of the DZG and the use of subsidies was adopted.

In 2020, the DZGs have jointly conducted various corona projects – such as the establishment of a Europe-wide database for the collection of clinical data and biomaterials of patients with COVID-19. As part of the promotion of young talent, last year they were offered a course on science communication in the DZG in collaboration with the National Institute for Science Communication. In order to inform the members of the Bundestag about the work of the DZGs and to exchange ideas with the parliamentarians, a parliamentary evening had been planned for 2020, which sadly had to be cancelled at short notice due to the pandemic. At the beginning of 2019, the first issue of jointly conceived health research magazine "SYNERGIE" was published – both as a high-quality print product and as an online edition. Two more issues followed in 2020.

ORGANISATION AND BODIES

# The DZIF's structure

## GENERAL ASSEMBLY

The General Assembly is the central decision-making organ of the DZIF and comprises representatives of the DZIF member establishments. The General Assembly elects the Executive Board members and the Executive Director, and decides on the allocation of funds to the research fields and infrastructures (TTUs and TIs).

## COMMISSION OF FUNDING AUTHORITIES

The Commission of Funding Authorities is made up of the Federal Government and respective states (Länder) and decides on important matters of finance, organisation and personnel. The Executive Board and the Managing Director report to the Commission on all funding measures.

## EXECUTIVE BOARD

The Executive Board represents the DZIF externally. It implements the resolutions and tasks assigned by the General Assembly and is responsible for routine administrative affairs.

## SCIENTIFIC ADVISORY BOARD

The association is supported by the Scientific Advisory Board, consisting of internationally renowned experts from the field of infection research. The Scientific Advisory Board advises the Executive Board and General Assembly on all scientific and programme-related matters.

## MAIN OFFICE

The Main Office is located in Braunschweig and supports the Executive Board in its work. Its duties include organising research initiatives and coordinating the DZIF's press and public relations activities.

## INTERNAL ADVISORY BOARD

The members of the Internal Advisory Board are DZIF scientists representing all research fields and locations of the centre. The council advises the Executive Board on all scientific, programme-related and technical matters and performs representative duties.

## THEMATIC TRANSLATIONAL UNITS (TTUS)

The Thematic Translational Units (Research Areas) pool the DZIF's research activities. Each unit is dedicated to one pathogen or to one specific problem in infection research.

- Emerging Infections
- Tuberculosis
- Malaria
- HIV
- Hepatitis
- Gastrointestinal Infections
- Infections of the Immunocompromised Host
- Healthcare-Associated and Antibiotic-Resistant Bacterial Infections
- Novel Antibiotics

## TRANSLATIONAL INFRASTRUCTURES (TIS)

Strategically aligned translational infection research requires modern infrastructures. These are provided in the form of the Translational Infrastructures, and can be used by all DZIF members.

- Product Development Unit
- African Partner Institutions
- Biobanking
- Pathogen Repository
- Bioinformatics
- Novel Antivirals
- Epidemiology
- Clinical Trial Unit
- DZIF Academy

## PARTNER SITES

The DZIF conducts its research in 35 research establishments at seven locations across Germany. At each site, two scientists are appointed to coordinate the collaboration and to advise the Main Office. Various external research partners are also involved in DZIF projects.

| | | | |
|---|---|---|---|
| Bonn-Köln | Gießen-Marburg-Langen | Hamburg-Lübeck-Borstel-Riems | Hannover-Braunschweig |
| Heidelberg | München | Tübingen | Associated Partners |

# Central bodies

**EXECUTIVE BOARD**

- Prof. H.-G. Kräusslich,
  (Chair)
  *Heidelberg University and University Hospital*
- Prof. D. Busch,
  (Vice Chair)
  *Technical University of Munich*
- Prof. M. Dandri,
  *University Medical Center Hamburg-Eppendorf*
- Prof. D. Heinz,
  *Helmholtz Centre for Infection Research, Braunschweig*
- Prof. A. Peschel,
  *University and University Hospital Tübingen*

**MANAGING DIRECTOR**

- Dr T. Jäger, DZIF e.V.

**SCIENTIFIC ADVISORY BOARD**

- Prof. R. Burger,
  (Chair)
  *former President of the Robert Koch Institute, Germany*
- Dr A. Ammon,
  *European Centre for Disease Prevention and Control, Sweden*
- Dr H. Feldmann,
  *National Institute of Allergy and Infectious Diseases, USA*
- Dr K. Klumpp,
  *Riboscience LLC, USA*
- Prof. R. Laxminarayan,
  *Center for Disease Dynamics, Economics & Policy, USA*
- Prof. C. Mgone,
  *former Executive Director of the European &*
  *Developing Countries Clinical Trials Partnership, Tanzania*
- Prof. D. Moradpour,
  *Lausanne University Hospital, Schweiz*
- Prof. C. Rooney,
  *Baylor College of Medicine, USA*
- Prof. R. Wallis,
  *The Aurum Institute, South Africa*
- Prof. S. Ward,
  *Liverpool School of Tropical Medicine, Great Britain*

**INTERNAL ADVISORY BOARD**

- Prof. G. Sutter,
  (Chair)
  *Ludwig-Maximilians-Universität München*
- Prof. H. Brötz-Oesterhelt,
  (Vice Chair)
  *University of Tübingen*
- Dr S. Castell,
  *Helmholtz Centre for Infection Research, Braunschweig*
- Prof. K. Cichutek,
  *Paul-Ehrlich-Institut, Langen*
- Prof. O. Cornely,
  *University Hospital Cologne*
- Prof. K. Heeg,
  *Heidelberg University Hospital*
- Prof. C. Meier,
  *Universität Hamburg*
- Prof. T. Pietschmann,
  *TWINCORE, Centre for Experimental and*
  *Clinical Infection Research, Hannover*

as at August 2021

PARTNER SITES AND MEMBER ESTABLISHMENTS

# Partner sites and member establishments

# Germany-wide infection research

## BADEN-WÜRTTEMBERG

The DZIF partner site in Heidelberg co-coordinates the *Hepatitis* and *Infections of the Immunocompromised Host* research fields. Alongside this, scientists in Heidelberg also coordinate the DZIF translational *Biobanking* infrastructure with a focus on establishing tissue banks. One focus of the research activities is on imaging methods in order to render infections visible in various complex systems ranging from clonal cells to mixed cell populations through to organs and animal models. Research on HIV is also conducted here.

### HEIDELBERG

**Spokesperson:** Prof. Klaus Heeg (Heidelberg University Hospital) till 09/2020,
Prof. Stephan Urban (Heidelberg University Hospital) since 10/2020
**Establishments:** German Cancer Research Center in the Helmholtz Association, Heidelberg University, Heidelberg University Hospital
**TTU Coordination:**

- Hepatitis (co-coordination)
- Infections of the Immunocompromised Host (co-coordination)

**TI Coordination:**

- Biobanking (coordination)

The DZIF partner site in Tübingen coordinated the *Malaria* research field till 10/2020. It also co-coordinates *Gastrointestinal Infections, Healthcare-Associated* and *Antibiotic-Resistant Bacterial Infections, Novel Antibiotics* and now also *Malaria*. Scientists in Tübingen focus on translating research results into drug and vaccine development as well as on infection models and epidemiology. For infections caused by bacterial pathogens that are resistant to antibiotics, scientists in Tübingen focus on multidrug-resistant pathogens such as methicillin-resistant staphylococci (MRSA) and gram-negative pathogens (e.g. so-called ESBLs).

### TÜBINGEN

**Spokesperson:** Prof. Peter Kremsner (University of Tübingen)
**Establishments:** University of Tübingen, Max Planck Institute for Developmental Biology, University Hospital Tübingen
**TTU Coordination:**

- Malaria (coordination till 10/2020, co-coordination since 11/2020)
- Gastrointestinal Infections (co-coordination)
- Healthcare-Associated and Antibiotic-Resistant Bacterial Infections (co-coordination)
- Novel Antibiotics (co-coordination)

## BAVARIA

The DZIF partner site in **München** coordinates the *Gastrointestinal Infections, Hepatitis* and *Tuberculosis* research fields. Scientists at the DZIF site in München are also involved in researching the immune control of infections, the defence against emerging infections and the development of new treatment methods. Pathogen-specific immunotherapies (e.g. vaccinations or (adoptive) T-cell transfer) aim to strengthen the body's immune system in order to better control or completely cure specific infectious diseases. The München partner site further focuses on HIV and Biobanking.

**MÜNCHEN**

**Spokesperson:** Prof. Michael Hoelscher (LMU University Hospital Munich)

**Establishments:** Helmholtz Zentrum München – German Research Center for Environmental Health, Bundeswehr Institute of Microbiology, LMU University Hospital Munich, Klinikum rechts der Isar of the Technical University of Munich, Ludwig-Maximilians-Universität München, Technical University of Munich

**TTU Coordination:**

- Gastrointestinal Infections (coordination and co-coordination)
- Hepatitis (coordination)
- Infections of the Immunocompromised Host (co-coordination)
- Tuberculosis (coordination)

**TI Coordination:**

- DZIF Academy (coordination till May 2020)
- Biobanking (co-coordination)

## HAMBURG/SCHLESWIG-HOLSTEIN

The **Hamburg - Lübeck - Borstel - Riems** site has a unique concentration of expertise and infrastructure for research on national and globally relevant emerging pathogens and for the development of strategies to combat them. Scientists at the site are involved in clinical, entomological and virological studies. It is also the DZIF base for medical chemistry, active ingredient discovery, the epidemiology of malaria and translational research studies on tuberculosis, viral haemorrhagic fever and hepatitis. The site coordinates the *HIV* research field and the TI *African Partner Institutions*.

**HAMBURG - LÜBECK - BORSTEL - RIEMS**

**Spokesperson:** Prof. Marylyn Addo (University Medical Center Hamburg-Eppendorf)

**Establishments:** Bernhard Nocht Institute for Tropical Medicine, Research Center Borstel - Leibniz Lung Center, Friedrich-Loeffler-Institute, Leibniz Institute for Experimental Virology (HPI), University of Hamburg, University Medical Center Hamburg-Eppendorf, University of Lübeck

**TTU Coordination:**

- HIV (coordination)
- Tuberculosis (co-coordination)
- Emerging Infections (co-coordination)
- Healthcare-Associated and Antibiotic-Resistant Bacterial Infections (co-coordination)
- Malaria (co-coordination; coordination since 1/2021)

**TI Coordination:**

- African Partner Institutions (coordination)
- DZIF Academy (coordination since May 2020)

## HESSE

In **Gießen - Marburg - Langen**, DZIF researchers identify emerging pathogens, develop new agents and vaccines and use quality-assured production processes to produce them for scientific industrial partners. Research activities focus on developing strategies which enable quick, effective action to combat outbreaks of new or re-emerging infectious diseases, for example, through vaccine development. Scientists in Marburg concentrate on viral pathogens while the main focus in Giessen is on bacteria and antibiotic resistance. The institutions involved provide infrastructures such as the BSL-4 laboratory in Marburg and the BSL-3 laboratory at the Paul-Ehrlich-Institut (PEI) in Langen. The PEI contributes towards the rapid translation of research results into clinical practice by providing expertise with regard to drug approval and development.

**GIESSEN - MARBURG - LANGEN**

**Spokesperson:** Prof. Trinad Chakraborty (Giessen University) till 12/2020,
Prof. Stephan Becker (Philipps-Universität Marburg) since 1/2021

**Establishments:** Giessen University, Paul-Ehrlich-Institut Langen, Philipps-Universität Marburg, Mittelhessen University of Applied Sciences

**TTU Coordination:**

- Emerging Infections (coordination)
- Healthcare-Associated and Antibiotic-Resistant Bacterial Infections (co-coordination)

**TI Coordination:**

- Product Development Unit (coordination)

## LOWER SAXONY

Seven partner institutes work together within the DZIF **Hannover – Braunschweig** site. The *Infections of the Immunocompromised Host* and *Novel Antibiotics* research fields are coordinated from here. Scientists are involved in the establishment of a national transplant cohort and their research projects make considerable contributions towards developing new methods for the treatment and diagnosis of herpesvirus and hepatitis virus infections as well as for the vaccine development for hepatitis C virus. They also focus on developing new approaches for the effective treatment and control of multidrug-resistant bacteria and examine different molecular target sites for active agents. Another key aspect of this site is the identification and development of agent candidates as potential antibiotics.

**HANNOVER - BRAUNSCHWEIG**

**Spokesperson:** Prof. Thomas Pietschmann (TWINCORE)

**Establishments:** Helmholtz Centre for Infection Research, Braunschweig, Leibniz Institute DSMZ–German Collection of Microorganisms and Cell Cultures, Hannover Medical School, Robert Koch Institute, University of Veterinary Medicine Hannover, Technische Universität Braunschweig, TWINCORE – Centre for Experimental and Clinical Infection Research.

**TTU Coordination:**

- Infections of the Immunocompromised Host (coordination)
- Novel Antibiotics (coordination)
- Gastrointestinal Infections (co-coordination)
- Hepatitis (co-coordination)
- HIV (co-coordination)

**TI Coordination:**

- Bioinformatics (coordination)
- Epidemiology (coordination)
- Novel Antivirals (coordination)
- Pathogen Repository (coordination)

## NORTH RHINE-WESTPHALIA

DZIF activities at the **Bonn - Köln** site concentrate on the research and development of new antibiotics. In cooperation with the TPMO and BfArM, the preclinical development of Corallopyronin A, a new antibiotic, continues to be a top priority for the Bonn-Köln site. In vaccine research, vaccines against bacterial pathogens such as *S. aureus* and *A. baumannii* are developed up to the clinical application stage. Scientists at the TTU *Healthcare-Associated and Antibiotic-Resistant Bacterial Infections* research bacterial colonisation and infections with multidrug-resistant pathogens with regard to both their type and prevalence. They also examine treatment options and the effectiveness of infection control measures. With regard to HIV research, scientists bring new antibody mediated treatment approaches into translational research. In addition, SARS-CoV-2 research at the Bonn-Cologne site is also a top priority. This site also coordinates the DZIF *Clinical Trial Unit*.

**BONN - KÖLN**

**Spokesperson:** Prof. Achim Hörauf (University of Bonn) till 7/2020, Prof. Oliver Cornely (University Hospital Cologne) since 8/2020

**Establishments:** Federal Institute for Drugs and Medical Devices, University of Bonn, University Hospital Bonn, University of Cologne, University Hospital Cologne

**TTU Coordination:**

- Healthcare-Associated and Antibiotic-Resistant Bacterial Infections (coordination)
- HIV (co-coordination)
- Novel Antibiotics (co-coordination)

**TI Coordination:**

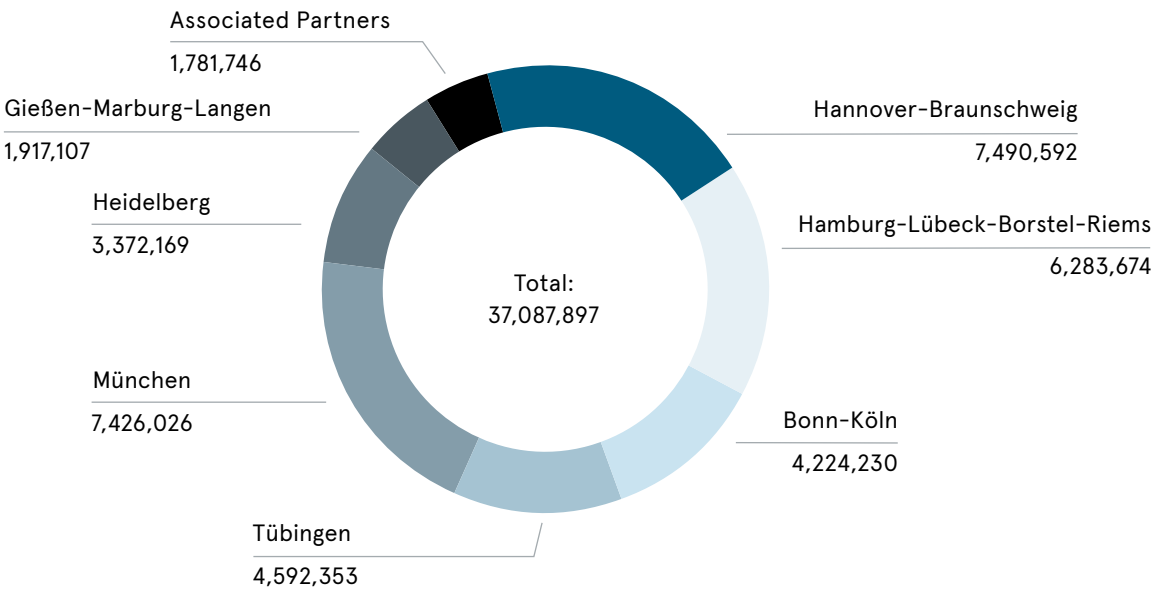
- Clinical Trial Unit (coordination)

FINANCES

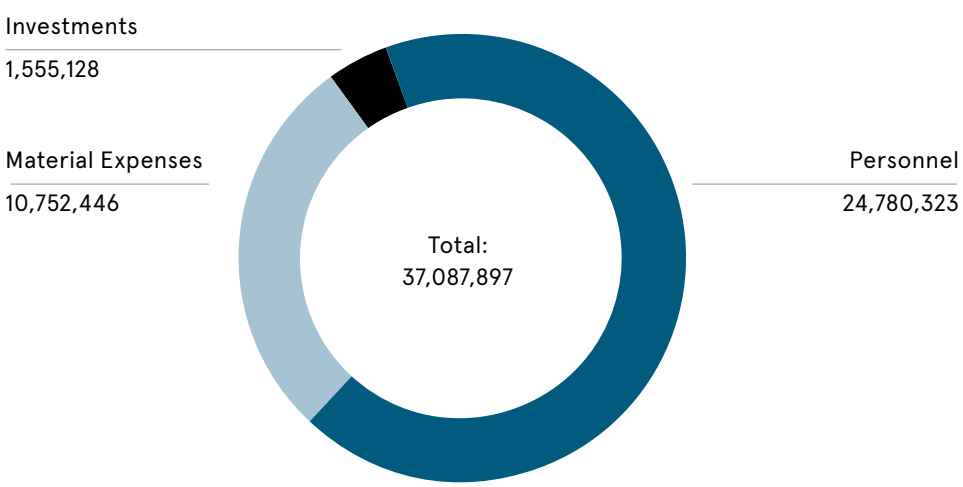
# DZIF financial data 2020

## REPORTED EXPENDITURE IN EUROS

### BY PARTNER SITE




### BY TYPE OF EXPENDITURE



### BY FIELD OF WORK

| FIELD OF WORK | Euro |
|---|---|
| Emerging Infections | 3,894,465 |
| Tuberculosis | 1,912,511 |
| Malaria | 1,742,563 |
| HIV | 2,078,481 |
| Hepatitis | 3,936,257 |
| Gastrointestinal Infections | 1,800,479 |
| Infections of the Immunocompromised Host | 5,719,857 |
| Healthcare-Associated and Antibiotic-Resistant Bacterial Infections | 2,584,998 |
| Novel Antibiotics | 3,144,117 |
| Product Development Unit | 702,096 |
| Clinical Trial Unit | 622,177 |
| African Partner Institutions | 790,571 |
| Biobanking | 454,321 |
| Bioinformatics | 271,063 |
| DZIF Academy | 2,516,572 |
| Pathogen Repository | 177,953 |
| Epidemiology | 242,829 |
| Novel Antivirals | 223,439 |
| Administration | 4,273,149 |
| **Total** | **37,087,897** |

### BY FUNDERS

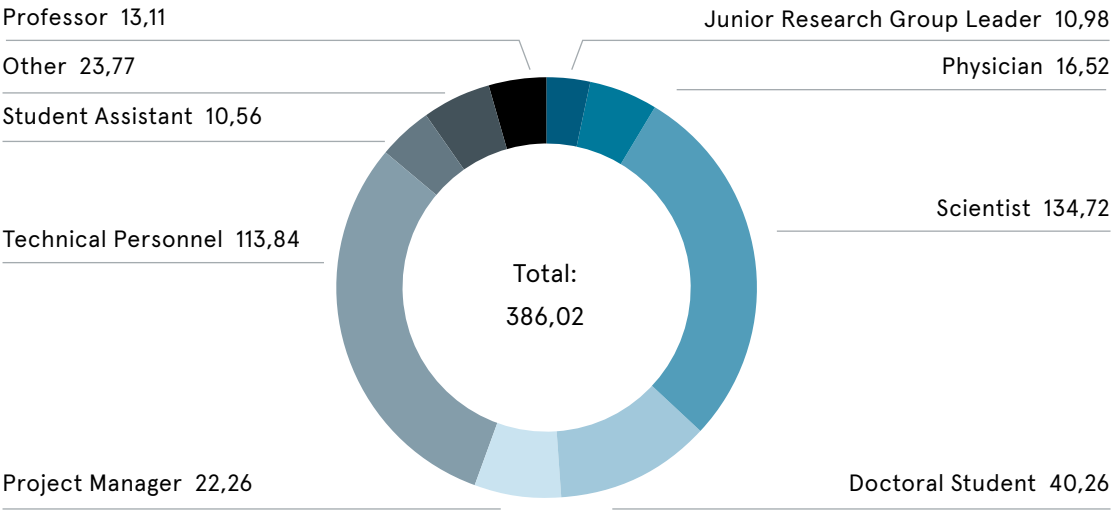
| FUNDER | Euro |
|---|---|
| Baden-Württemberg | 846,267 |
| Bavaria | 772,717 |
| Hamburg | 453,488 |
| Hesse | 157,782 |
| Lower Saxony | 708,581 |
| North Rhine-Westphalia | 439,453 |
| Schleswig-Holstein | 192,596 |
| Financial contributions from associated partners | 178,175 |
| Federal Government | 33,338,839 |
| **Total** | **37,087,897** |

In 2020, the German Center for Infection Research's reported expenditure amounted to approximately 37,09 million Euros. 208 projects and 107 stipends were funded within DZIF in 2020. The majority of funding came from the Federal Government (90 %) and from Länder funds (10 %). Only departmental research projects of the federal R&D institutions were fully funded by Germany's Federal Ministries. Funding management at the Helmholtz Centre for Infection Research in Braunschweig transfers the funds to the DZIF partner institutes for their projects. The expenditures amounting to the BMBF funding were reported by the DZIF partners in the interim and final financial report 2020 and will be investigated by the DZIF Funding Management. The amounts of state and associated partner funding were calculated on the basis of these interim and final financial reports. The calculated expenses for 2020 are preliminary and refer to the audit status as of 23.06.2021.

PERSONNEL AND AWARDS

# DZIF staff

## FULL-TIME EQUIVALENT BY PROFESSIONAL GROUP




## NUMBER OF EMPLOYEES BY PROFESSIONAL GROUP AND GENDER

| PROFESSIONAL GROUPS | MEN | WOMEN | TOTAL |
|---|---|---|---|
| Professor | 14 | 5 | 19 |
| Junior Research Group Leader | 6 | 8 | 14 |
| Physician | 16 | 26 | 42 |
| Scientist | 113 | 136 | 249 |
| Doctoral Student | 37 | 48 | 85 |
| Project Manager | 7 | 38 | 45 |
| Technical Personnel | 57 | 194 | 251 |
| Student Assistant | 7 | 16 | 23 |
| Other | 11 | 35 | 46 |
| **Total** | **268** | **506** | **774** |

In 2020, the DZIF recruited five employees from abroad and assisted 15 mothers and fathers respectively on their return from maternity leave.

## AWARDS AND COMMENDATIONS

**Prof. Marylyn M. Addo**
*University Medical Center Hamburg-Eppendorf*
Medical Scientist of the Year (German Medical Club)

•

**Prof. Stephan Becker**
*Philipps-Universität Marburg*
DZIF Prize for Translational Infection Research

•

**Prof. Christian Drosten**
*Charité - Universitätsmedizin Berlin*
DFG Special Award for Outstanding Science Communication in the COVID-19 Pandemic
Grimme Online Award
KlarText Special Award for Science Communication (Klaus Tschira Stiftung)
Order of Merit of the Federal Republic of Germany

•

**PD Oliver Koch**
*University of Münster*
Innovation Award for Medicinal and Pharmaceutical Chemistry (DPhG und GDCh)

•

**Julia Matthias**
*Technical University of Munich*
Young Investigator Award for Multiple Sclerosis of the Eva and Helmer Christoph Lehmann Foundation

•

**Prof. Ulrike Protzer**
*TU Munich, Helmholtz Zentrum München, German Research Center for Environmental Health*
Heinz Maier Leibnitz Medal

•

**Prof. Gerd Sutter**
*LMU München*
DZIF Prize for Translational Infection Research

•

**Dr Karin Wisskirchen**
*Helmholtz-Zentrum München - German Research Center for Environmental Health*
**& Dr Janine Kah**
*University Medical Center Hamburg-Eppendorf*
YAEL-Preis for the best publication 2019 (GASL)

INDICATORS 2020

# The DZIF in figures

## FLEXFUNDS*

29 Number of FlexFunds projects approved in 2020; thereof 5 Fast-Track projects for SARS-CoV-2

10,778,080 total budget in euros. Corresponding to

29.06 % of the annual DZIF budget

* funds available at short notice for translational projects

## DZIF ACADEMY PROGRAMMES*

18 Clinical Leave Stipends

06 MD/PhD Stipends

12 Maternity Leave Stipends

70 MD Stipends

01 Lab Rotation

* Travel Grants could not be used due to the pandemic.

## WORKSHOPS AND SYMPOSIA

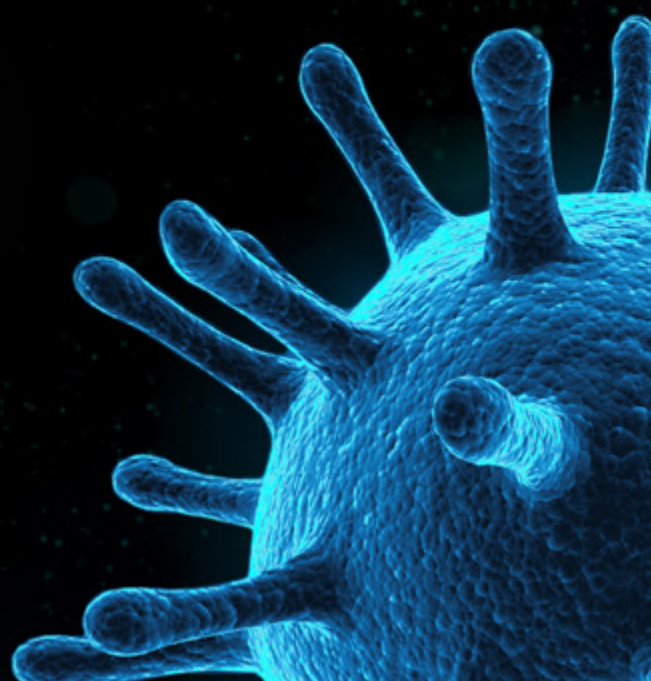
13 mostly online events

## PUBLICATIONS WITH DZIF AFFILIATIONS

758

## PUBLICATIONS WITH IMPACT FACTOR >10

93



**CONFERENCE CONTRIBUTIONS**
141 mostly online events

**INDUSTRY COLLABORATIONS**
6

**PATENTS AND PROPERTY RIGHTS**
56

**DATA- AND BIOBANKS**
39

**PRESS RELEASES/ NEWS**
55

**COHORTS**
54

**CLINICAL STUDIES**
40

**CONFIRMATORY PRECLINICAL STUDIES**
25

**WEBSITE VISITORS**
1,170,000

**SOCIAL MEDIA***
1,954 New Followers
602,825 Impressions
251 Social Media Posts

* Cumulative figures from the presences on Twitter and LinkedIn

PUBLICATIONS

# Scientific achievements 2020

The following shows a list of selected 2020 publications
(impact factor greater than 10*).
Please see our website for a complete list of DZIF publications.

## BASIC RESEARCH


1. Augestad EH, Castelli M, Clementi N, Ströh LJ, Krey T, Burioni R, Mancini N, Bukh J, Prentoe J (2020) *Global and local envelope protein dynamics of hepatitis C virus determine broad antibody sensitivity.* **Sci Adv**, 6(35): eabb5938

2. Ballhausen A, Przybilla MJ, Jendrusch M, Haupt S, Pfaffendorf E, Seidler F, Witt J, Hernandez Sanchez A, Urban K, Draxlbauer M, Krausert S, Ahadova A, Kalteis MS, Pfuderer PL, Heid D, Stichel D, Gebert J, Bonsack M, Schott S, Bläker H, Seppälä T, Mecklin JP, Ten Broeke S, Nielsen M, Heuveline V, Krzykalla J, Benner A, Riemer AB, von Knebel Doeberitz M, Kloor M (2020) *The shared frameshift mutation landscape of microsatellite-unstable cancers suggests immunoediting during tumor evolution.* **Nat Commun**, 11(1): 4740

3. Bankwitz D, Bahai A, Labuhn M, Doepke M, Ginkel C, Khera T, Todt D, Ströh LJ, Dold L, Klein F, Klawonn F, Krey T, Behrendt P, Cornberg M, McHardy AC, Pietschmann T (2020) *Hepatitis C reference viruses highlight potent antibody responses and diverse viral functional interactions with neutralising antibodies.* **Gut,** 70(9): 1734-1745

4. Bauernfried S, Scherr MJ, Pichlmair A, Duderstadt KE, Hornung V (2021) *Human NLRP1 is a sensor for double-stranded RNA*. **Science**, 371(6528): eabd0811

5. Bennett AJ, Paskey AC, Ebinger A, Pfaff F, Priemer G, Höper D, Breithaupt A, Heuser E, Ulrich RG, Kuhn JH, Bishop-Lilly KA, Beer M, Goldberg TL (2020) *Relatives of rubella virus in diverse mammals*. **Nature,** 586(7829): 424-428

6. Bojkova D, Klann K, Koch B, Widera M, Krause D, Ciesek S, Cinatl J, Münch C (2020) *Proteomics of SARS-CoV-2-infected host cells reveals therapy targets*. **Nature**, 583(7816): 469-472

7. Brown RJP, Tegtmeyer B, Sheldon J, Khera T, Anggakusuma, Todt D, Vieyres G, Weller R, Joecks S, Zhang Y, Sake S, Bankwitz D, Welsch K, Ginkel C, Engelmann M, Gerold G, Steinmann E, Yuan Q, Ott M, Vondran FWR, Krey T, Ströh LJ, Miskey C, Ivics Z, Herder V, Baumgärtner W, Lauber C, Seifert M, Tarr AW, McClure CP, Randall G, Baktash Y, Ploss A, Thi VLD, Michailidis E, Saeed M, Verhoye L, Meuleman P, Goedecke N, Wirth D, Rice CM, Pietschmann T (2020) *Liver-expressed Cd302 and Cr1l limit hepatitis C virus cross-species transmission to mice.* **Sci Adv**, 6(45): eabd3233

8. Carpentier A, Sheldon J, Vondran FWR, Brown RJ, Pietschmann T (2020) *Efficient acute and chronic infection of stem cell-derived hepatocytes by hepatitis C virus*. **Gut**, 69(9): 1659-1666

9. Cohen-Dvashi H, Zehner M, Ehrhardt S, Katz M, Elad N, Klein F, Diskin R (2020) *Structural Basis for a Convergent Immune Response against Ebola Virus*. **Cell Host Microbe**, 27(3): 418-427.e4

10. Cortese M, Lee JY, Cerikan B, Neufeldt CJ, Oorschot VMJ, Köhrer S, Hennies J, Schieber NL, Ronchi P, Mizzon G, Romero-Brey I, Santarella-Mellwig R, Schorb M, Boermel M, Mocaer K, Beckwith MS, Templin RM, Gross V, Pape C, Tischer C, Frankish J, Horvat NK, Laketa V, Stanifer M, Boulant S, Ruggieri A, Chatel-Chaix L, Schwab Y, Bartenschlager R (2020) *Integrative Imaging Reveals SARS-CoV-2-Induced Reshaping of Subcellular Morphologies*. **Cell Host Microbe**, 28(6): 853-866.e5

11. Dao Thi VL, Wu X, Belote RL, Andreo U, Takacs CN, Fernandez JP, Vale-Silva LA, Prallet S, Decker CC, Fu RM, Qu B, Uryu K, Molina H, Saeed M, Steinmann E, Urban S, Singaraja RR, Schneider WM, Simon SM, Rice CM (2020) *Stem cell-derived polarized hepatocytes*. **Nat Commun**, 11(1): 1677

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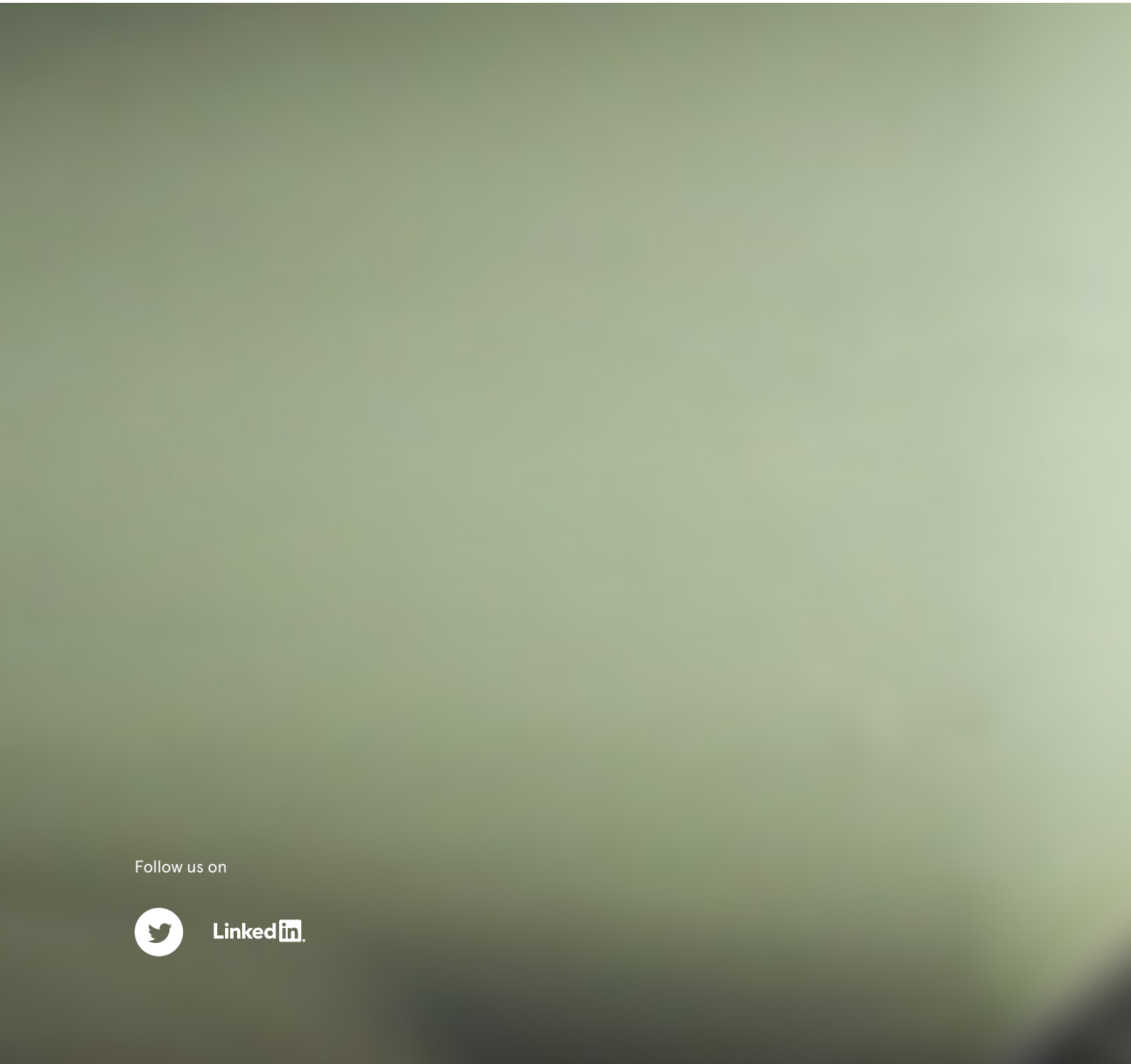

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