DZIF
German Center
for Infection Research

DZG
DEUTSCHE ZENTREN DER
GESUNDHEITSFORSCHUNG

German Center for Infection Research

Annual Report 2023/24

The German Center for Infection Research (DZIF)

As one of eight German Centers for Health Research, the DZIF coordinates and oversees the strategic planning of translational infection research within Germany. Through its work, the DZIF ensures that patients can quickly benefit from findings in basic and clinical research on infectious diseases.

Cover image (electron micrographs by Manfred Rohde, HZI): The growing problem of antibiotic resistance calls for new approaches to treating bacterial infections—such as the use of bacteriophages. The front cover shows Pseudomonas phage JG005 (visible as small dots) attached to and penetrating rod-shaped Pseudomonas aeruginosa *bacteria. On the back cover, the destructive processes caused by the phages are visible, in which the bacterial cells are broken down (lysis).*

The DZIF in figures

35
Member institutions

9
Research areas

796
Employees

143
Patents

114
Preclinical efficacy studies

42
Clinical studies

43
Data and biobanks

87
Cohorts

8
Industry collaborations

1,782
Publications

133
Press releases

1,870,344
Website visitors

Data as of December 31, 2024 Total for 2023/24

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Editorial

The ongoing impact of the COVID-19 pandemic shaped public life in Germany well into the early months of 2023. Although the World Health Organization declared an end to the "public health emergency of international concern" in May of that year, the repeated emergence of new SARS-CoV-2 variants continued to cause significant health problems worldwide. These problems manifested, among other things, as late and long-term effects known as post-COVID, long COVID, or post-infectious syndrome.

In infection research, the years 2023 and 2024 saw intensified efforts to respond more effectively to future viral epidemics and to draw concrete lessons from the pandemic. For instance, a study presented on page 14 illustrates how a clinical trial on the efficacy of a prophylactic MERS vaccine, which had begun prior to the pandemic, gained valuable insights due to the pandemic. Another study on page 15 highlights the importance of sufficient testing capacity—particularly in the Global South—and strong international collaboration for effective pandemic management.

MILESTONES IN INFECTION RESEARCH

Significant progress was also made in 2023 and 2024 in characterizing multidrug-resistant mycobacterial strains, identifying blood-based biomarkers for extrapulmonary tuberculosis, developing antibiotic strategies against tropical helminth diseases, and working on a malaria vaccine (see pages 16–19).

On page 20, you will also find details on the cure of the "Düsseldorf patient" from HIV. Significant milestones were also reached in the fight against hepatitis B, C, and D, as well as in the development of the first Epstein-Barr virus vaccine (pages 22–23 and 26–27).

As the acute situation with the coronavirus subsided, the "silent pandemic" of antibiotic resistance once again became the focus of attention in 2023. DZIF researchers made significant contributions in this area—from discovering new antibacterial agents to characterizing innovative classes of drugs (pages 24–25, 28–29, and 30–31).

INFRASTRUCTURAL SUPPORT FOR RAPID TRANSLATION

Some of the DZIF's antiviral and antibacterial projects are accompanied by the product development team on their journey from basic research to clinical application. A selection of projects that receive particularly intensive support are highlighted on pages 10–13. Since late 2024, the new DZIF portal has further boosted collaboration among DZIF scientists. The portal combines the functions of a classic intranet with resource platforms, databases, and project management areas. Support for young scientists has also been further strengthened. Since 2023, this support has come in the form of a structured, cross-location mentoring program. Since late 2024, support has also come in the form of a short-term training program for young researchers at African partner institutions. Additionally, a film was produced in 2024 offering exciting insights into the research work and the DZIF network (pages 32, 36, and 50).

This DZIF annual report is the first to cover a two-year period. As always, the 2023/24 report provides a clear and concise overview of all the important facts and figures. We hope you find it inspiring and informative!

Yours sincerely,
The Executive Board of the German Center for Infection Research


Prof. Dr. D. Busch


Prof. Dr. H.-G. Kräusslich


Prof. Dr. M. Dandri


Prof. Dr. A. Peschel


Prof. Dr. T. Pietschmann

ABOUT THE DZIF

Successful translation at the DZIF: from knowledge to health

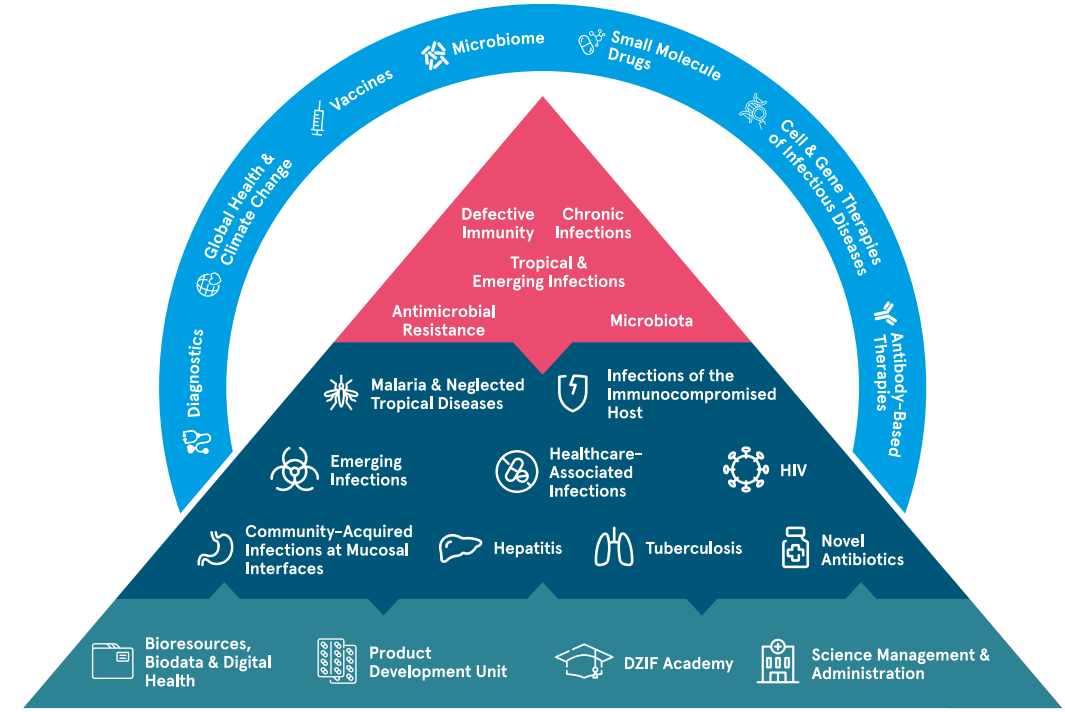
"Translation" refers to the process of bridging the gap between basic research and clinical application. Patients should benefit from new research findings as quickly as possible—for example, in the form of medicines, vaccines, or diagnostics. At the DZIF, the success of this approach is reflected in positive project progress, preclinical and clinical studies, spin-offs of start-up companies, and drug approvals.

Promising projects receive particular support within the framework of the DZIF's so-called flagship projects (see pages 10–13). Supporting the next generation of researchers is crucial for long-term translational success. The *DZIF Academy* paves the way for young talents to pursue scientific careers, securing the future of infectious disease research in Germany (see pages 36–37).

STRATEGIC FOCUS: KEY ISSUES IN INFECTION RESEARCH

At the DZIF, over 700 scientists and physicians conduct research to develop solutions to the global challenges in infection research. These grand challenges include antimicrobial resistance, chronic infections, defective immunity, and tropical and emerging infections (see image below).

In 2024, we added "microbiota" as another major research field. This term refers to the totality of microorganisms that colonize humans and the environment. The microbiota influence the immune system, protect against pathogens, and regulate inflammatory processes. Disruptions in the microbial balance (dysbiosis) have been associated with numerous diseases, including acute and chronic infectious diseases. The DZIF's activities are strategically focused on addressing these five grand challenges.



The focus and priorities of infection research at the DZIF include challenges, research areas, infrastructures, and overarching bridging topics. In 2023, two research areas were renamed: Gastrointestinal Infections *became* Community-Acquired Infections at Mucosal Interfaces*, and* Hospital-Acquired Infections and Antibiotic-Resistant Bacteria *became* Healthcare-Associated Infections.

RESEARCH STRUCTURES AT THE DZIF

DZIF researchers work at 35 member institutions across seven partner sites in Germany. Additionally, DZIF staff members come from associated partner institutions, as well as from transnational collaborations and alliances.

This synergistic DZIF network of universities, hospitals, and research institutions has created a globally unique infrastructure that brings together expertise from a wide range of fields—including medicine, biology, epidemiology, chemistry, and bioinformatics.

The DZIF organizes its projects into nine research areas. Each area is dedicated to a specific pathogen, disease, or common theme within infection research. Additionally, four "translational infrastructures" support all DZIF researchers with expertise and services.

BRIDGING TOPICS FOR INTERDISCIPLINARY APPROACHES

To address forward-looking questions, the DZIF has established several Bridging Topics. These interdisciplinary groups combine expertise from various DZIF research areas and infrastructures. This fosters innovative collaborations, including with external partners. Each group comprises four to ten DZIF experts.

To date, the DZIF has established the following Bridging Topics: *Diagnostics*, *Vaccines*, *Antibody-Based Therapies*, *Cell and Gene Therapies of Infectious Diseases*, and the *Microbiome*. *Global Health and Climate Change* and *Small Molecule Drugs* will be added as further Bridging Topics in 2025.

The figure on the left summarizes global challenges and the DZIF's research structures.

A STRONG VOICE FOR PATIENTS: THE NEW DZIF PATIENT ADVISORY BOARD

Established in 2024, the DZIF Patient Advisory Board currently consists of seven members. Each member represents a specific disease or research area and has been personally affected by a disease, either directly or through a family member. The Board's insights are now regularly incorporated into the planning, evaluation, and communication of research projects. The potential risks, obstacles, and consequences of DZIF's research strategies and projects are examined and discussed from the patients' perspective.

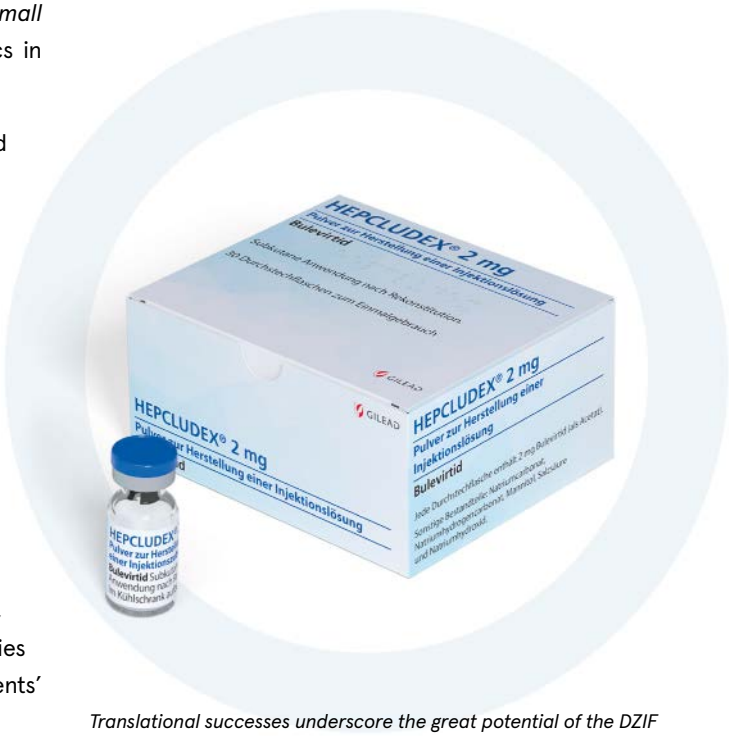
The board meets regularly, issues statements, and serves as a bridge between research and the public. Through its work, the board strengthens the societal relevance and acceptance of DZIF research, thereby making an important contribution to patient-centered science.

INTERNATIONALLY CONNECTED

Infectious diseases do not stop at national borders—nor should scientific research. Since its founding, the DZIF has fostered close collaborations with partner institutions in Eastern Europe and Africa, to conduct research on diseases such as tuberculosis and malaria directly in the regions most severely affected by them.

As a co-initiator of the UNITE4TB consortium, the DZIF is supporting the development of new therapeutic approaches against tuberculosis. In light of the growing threat posed by antibiotic-resistant pathogens, the DZIF participates in the European INCATE initiative, which promotes innovative research approaches from the initial development phases. Additionally, the DZIF is part of the international CARB-X network, dedicated to accelerating the development of drugs against resistant pathogens.

As part of the CEPI vaccine initiative, the DZIF collaborates on strategies to protect against emerging infectious diseases. The DZIF also participates in numerous other collaborations with industry and academia to find effective solutions to today's infectious disease challenges.



Translational successes underscore the great potential of the DZIF research network. For example, the DZIF successfully brought the world's first hepatitis D drug, Hepcludex®, from basic research to market approval.

FINANCES

DZIF financial data 2023 and 2024

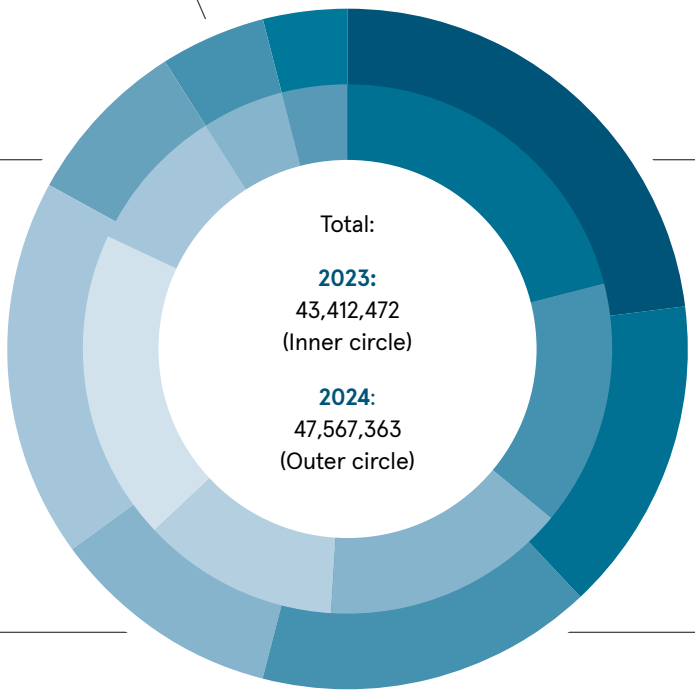
The DZIF's verified expenditures amounted to 43.4 million euros in 2023 and 47.6 million euros in 2024. A total of over 400 research projects and more than 250 *DZIF Academy* projects were carried out during the 2023–2024 period.

The majority of funding came from the federal government (90 percent) and from federal state funds (10 percent). Only the departmental research projects of the federal R&D institutions were fully funded by Germany's Federal Ministries. Associated partners contributed 10 percent of their own funds. The remaining 90 percent was also provided by federal funds.

The federal states transfer their share of the funding to the federal government, which then forwards the full amount to the Helmholtz Centre for Infection Research (HZI). The Funding Management at the HZI then distributes the funds to DZIF partner institutions for their projects.

Partner institutions report expenditures in their interim and final financial reports, which are reviewed by DZIF Funding Management. The contributions from the federal states and the associated partners were calculated based on these interim and final financial reports. The financial data presented here is preliminary and reflects the status of the review as of September 1, 2025.

EXPENDITURES BY PARTNER SITE IN EUROS



Gießen – Marburg – Langen
2023: 2,040,476
2024: 2,332,006

Associated Partners
2023: 1,738,383
2024: 1,914,922

Heidelberg
2023: 4,063,085
2024: 3,828,345

Hannover – Braunschweig
2023: 9,294,822
2024: 10,766,778

München
2023: 8,415,730
2024: 8,750,313

Hamburg – Lübeck – Borstel – Riems
2023: 6,322,547
2024: 7,264,265

Tübingen
2023: 5,131,492
2024: 5,082,105

Bonn – Köln
2023: 6,405,936
2024: 7,628,630

In **2023**, 66 percent of the budget was allocated to personnel costs, while 34 percent was spent on material expenses.

In **2024**, 67 percent was allocated to personnel costs and 32 percent to material expenses. One percent of the total budget was allocated to investments.

EXPENDITURES BY FIELD OF WORK IN EUROS

Field of work	2023	2024
Emerging Infections	2,694,872	2,969,783
Tuberculosis	2,094,824	2,076,937
Malaria and Neglected Tropical Diseases	3,483,747	3,559,338
HIV	2,270,738	2,400,024
Hepatitis	3,050,161	3,423,361
Community-Acquired Infections at Mucosal Interfaces	2,022,132	2,316,697
Infections of the Immunocompromised Host	6,204,616	6,910,652
Healthcare-Associated Infections	4,604,997	5,188,521
Novel Antibiotics	5,275,042	5,193,280
Product Development Unit	870,436	1,067,459
Clinical Trial Unit	300,978	418,752
DZIF Academy	2,910,229	2,684,873
Bioresources, Biodata and Digital Health	1,802,038	2,163,898
Special measures for the development of antiviral therapeutics	2,014,514	1,543,089
Bridging Topics	-	1,401,727
Administration	3,667,599	3,875,525
Cross-DZG projects	145,548	373,446
Total	**43,412,472**	**47,567,363**

EXPENDITURES BY FUNDERS IN EUROS

Funder	2023	2024
Baden-Württemberg	950,118	926,683
Bayern	860,584	897,221
Hamburg	423,972	500,156
Hesse	178,409	194,338
Lower Saxony	825,687	956,753
North Rhine-Westphalia	649,553	769,478
Schleswig-Holstein	211,369	231,619
Financial contributions from associated partners	173, 838	191,492
Federal Government	39,138,942	42,899,623
Total	**43,412,472**	**47,567,363**

FLEXFUNDS: A FLEXIBLE WAY TO SUPPORT EXCELLENT IDEAS

Approximately one-fifth of all DZIF funds are allocated through FlexFunds to provide flexible funding for particularly promising translational projects. FlexFunds are awarded competitively through a standardized, multi-stage review process depending on the amount of funding. The *Product Development Unit (PDU)* participates in the review process to provide input on patents, intellectual property, and regulatory aspects early on.

In **2023**, eleven FlexFunds applications with a total volume of €13,490,373 were approved.

In **2024**, 14 FlexFunds applications with a total volume of €12,138,877 were approved.

THIRD-PARTY FUNDED PROJECTS OF THE DZIF E. V.* IN EUROS

Project	Funding body	Funding		
		2023	2024	Total
UNITE4TB *A development partnership focused on accelerating the advancement of new tuberculosis (TB) therapies. The project unites academic institutions, public organizations, and pharmaceutical companies.*	Federal Ministry of Research, Technology and Space (BMFTR)	2,393,682	2,321,545	4,715,227
Global Antimicrobial Resistance Research & Development Hub *This international initiative coordinates and accelerates global research and development efforts to combat antimicrobial resistance. The hub's secretariat is operated by DZIF in Berlin.*	BMFTR	842,899	1,269,377	2,112,276
MVA-MERS: Development of a MERS vaccine *Development of a vaccine against the Middle East respiratory syndrome coronavirus (MERS-CoV).*	Coalition for Epidemic Preparedness Innovations (CEPI)	472,108	149,906	622,014
Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) *As a key player in the CARB-X and INCATE initiatives, the DZIF promotes the development of new antibiotics and therapies against drug-resistant pathogens through research, networking, and financial support.*	BMFTR	218,225	229,090	447,315
Total amount		**3,926,915**	**3,969,918**	**7,896,833**

Third-party funding refers to external financial resources provided by public or private entities for specific projects or purposes. Such funding supplements the regular core funding of DZIF e. V. It includes, for example, grants from ministries, the European Union, foundations, or industry partners.

These funds finance targeted projects that go beyond regular operations, such as research projects or infrastructure measures. The above table summarizes the third-party funded projects of DZIF e. V., the amount of funding received during the reporting period, and the respective funding bodies.

*e. V. = registered association under German law

PERSONNEL

DZIF staff

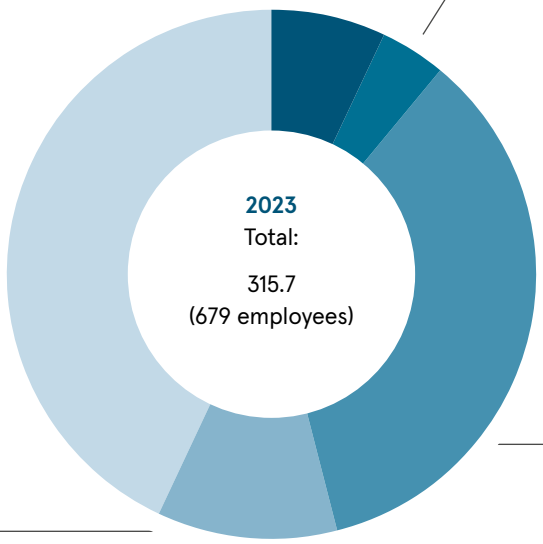
FULL-TIME EQUIVALENT BY PROFESSIONAL GROUP 2023

Professor and junior research group leader **23.3**

Employees: 30 (male (m): 19, female (f): 11)

Physician **13.7**

Employees: 32 (m: 12, f: 20)



Other **135.3**

Employees: 327 (m: 75, f: 252)

Senior scientist and postdoc **107.7**

Employees: 218 (m: 80, f: 138)

Doctoral student **35.7**

Employees: 72 (m: 29, f: 43)

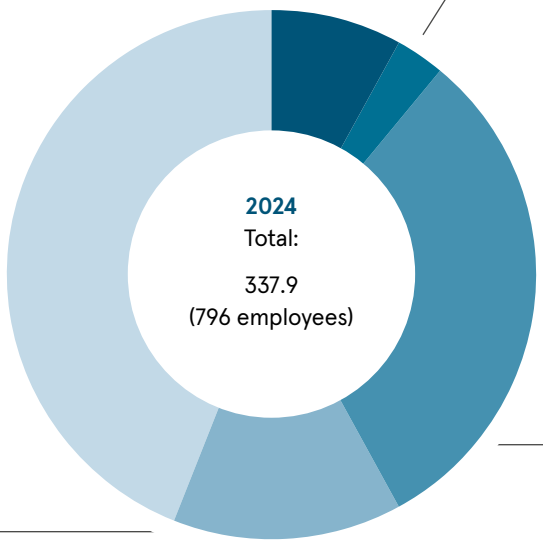
FULL-TIME EQUIVALENT BY PROFESSIONAL GROUP 2024

Professor and junior research group leader **26.1**

Employees: 34 (male (m): 19, female (f): 15)

Physician **10.2**

Employees: 33 (m: 13, f: 20)



Other **147.9**

Employees: 379
(m: 83, f: 295, divers (d): 1)

Senior scientist and postdoc **105.5**

Employees: 219 (m: 77, f: 141, d: 1)

Doctoral student **48.2**

Employees: 131 (m: 57, f: 74)

In 2023 and 2024, the DZIF recruited 16 employees from abroad and assisted 18 mothers and fathers on their return to work after taking parental leave. This is in addition to the 24 individuals who received support through the *DZIF Academy*'s Maternity Leave Program.

SUCCESSFUL TRANSLATION

Flagship projects funded by the DZIF

To accelerate the translation of research into clinical application, the DZIF provides long-term support for so-called flagship projects. These projects cover all phases from late preclinical development to clinical trials and are characterized by high innovation potential and clear product profiles with commercial orientation.

Translational projects in late preclinical and early clinical phases can achieve flagship project status. These projects receive special support and advice from the DZIF *Product Development Unit* (see pages 38–39).

Achieving this status requires the establishment of clear goals and specific milestones on the path to translation, along with the subsequent transition to a start-up or collaboration with industry.

PREVENTION AND TREATMENT OF VIRAL INFECTIONS

Four flagship projects focus on preventing and treating acute and chronic viral infections using innovative approaches. These projects include developing prophylactic vaccines against the Epstein-Barr virus (EBV) and the Middle East respiratory syndrome (MERS) coronavirus, a therapeutic vaccine against hepatitis B virus (HBV), and broadly neutralizing antibodies against hepatitis E virus (HEV).

The DZIF is closely monitoring the development of prophylactic and therapeutic vaccines, as well as broadly neutralizing antibodies, as they transition from laboratory research to clinical application.

EBV-VLP: DEVELOPMENT OF A VACCINE AGAINST THE EPSTEIN-BARR VIRUS

The Epstein-Barr virus (EBV), which infects over 90 percent of people during their lifetime, causes diseases such as infectious mononucleosis (also known as Pfeiffer's glandular fever) and secondary diseases like multiple sclerosis, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), and certain tumors. A vaccine candidate based on non-infectious, EBV-derived virus-like particles, which has proven highly effective in animal studies, is being manufactured under Good Manufacturing Practice conditions for clinical trials in humans. This vaccine candidate is being developed as part of the start-up EBViously, a DZIF-supported spin-off from Helmholtz Munich (see also page 26).

Project lead:
Prof. Dr. Wolfgang Hammerschmidt
Helmholtz Munich/CSO EBViously

MVA-MERS: A VACCINE AGAINST THE MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS

The Middle East respiratory syndrome (MERS) coronavirus is transmitted to humans through droplet infection from dromedary camels. The virus causes respiratory infections, which are severe in about 35 percent of cases and can be fatal. Human-to-human transmission is also possible. The vector-based vaccine candidate MVA-MERS-S has been researched up to clinical phase Ib and will now be developed further in a phase II study funded by the Coalition for Epidemic Preparedness Innovations (CEPI), in collaboration with IDT Biologika. Alongside the clinical development of the MVA-MERS-S vaccine candidate, preclinical testing is underway for a new, stabilized MVA-MERS-ST vaccine.

Project lead:
Prof. Dr. Asisa Volz
University of Veterinary Medicine Hannover
Prof. Dr. Marylyn Addo
University Medical Center
Hamburg-Eppendorf

TherVacB: DEVELOPMENT OF A THERAPEUTIC VACCINE AGAINST HEPATITIS B

Around 254 million people worldwide are infected with the hepatitis B virus (HBV). As a result, over one million people die each year from liver failure or liver cancer. Current therapies suppress the virus, but they do not cure it. The DZIF TherVacB project is developing an immunotherapy that activates the immune system to control or eliminate the virus. The TherVacB vaccine is effective against over 95 percent of the HBV strains found worldwide. After a successful Phase Ia clinical trial, a European multicenter Phase Ib/IIa trial began in June 2025 to evaluate the vaccine's safety and efficacy in patients.

Project lead:
Prof. Dr. Ulrike Protzer
Technical University of Munich
Helmholtz Munich

HEVbnAb: DEVELOPMENT OF BROADLY NEUTRALIZING HEPATITIS E VIRUS (HEV) ANTIBODIES

Broadly neutralizing antibodies (bnAbs) against HEV were isolated from the serum of patients who had recovered from an acute HEV infection. Several of these antibodies recognized the capsid protein pORF2 of all human pathogenic HEV genotypes, as well as a recently emerging HEV transmitted by rats. Further development of the most promising bnAb candidate could provide a targeted treatment option for chronic and acute HEV infections, such as in pregnant women or patients with decompensated liver damage. It could also serve as a prophylactic option to protect immunocompromised patients from HEV infections and the diseases they cause.

Project lead:
Prof. Dr. Thomas Krey
Universität zu Lübeck

INNOVATIVE APPROACHES TO COMBAT BACTERIAL INFECTIONS

Conventional antibiotics are losing their effectiveness as pathogens become resistant to an increasing number of antibiotics. Therefore, new antibiotics and alternative treatment options are urgently needed.

At the DZIF, six projects focusing on infections caused by common bacterial pathogens are currently receiving special support as flagship projects. These projects take a wide variety of approaches to combating bacterial infections.

BTZ-043: DEVELOPMENT OF A NEW TUBERCULOSIS DRUG

With an estimated 10.8 million new cases in 2023, tuberculosis (TB) remains the most prevalent infectious disease worldwide. Approximately three to four percent of those affected have multidrug-resistant TB (MDR-TB). BTZ-043 is the first antibiotic developed in Germany in decades. Based on current findings, BTZ-043 is also effective against MDR-TB. Studies on its tolerability and efficacy have been conducted at the DZIF. Since 2021, the DZIF has participated in multinational consortia, such as UNITE4TB, to bring this drug candidate to market. Several phase II studies are currently underway.

Project lead:
Prof. Dr. Michael Hoelscher
LMU University Hospital Munich

CORALLOPYRONIN A: A NOVEL NATURAL PRODUCT ANTIBIOTIC

Corallopyronin A is a novel natural product antibiotic currently in preclinical development for the treatment of filarial infections caused by parasitic nematodes. At the DZIF, a robust production process has been established to supply sufficient quantities of the compound for preclinical studies. Phyton Biotech GmbH is responsible for transferring and adapting the process to GMP-compliant manufacturing. Corallopyronin A demonstrates promising efficacy, favorable tissue distribution, and activity against biofilms—key prerequisites for entry into first-in-human clinical trials, which are planned to begin in 2025.

Project lead:
Prof. Dr. Achim Hörauf
University Hospital Bonn

EVREA-PHAGE: ORAL PHAGE THERAPY AGAINST A RESISTANT INTESTINAL BACTERIUM

Vancomycin-resistant enterococci (VRE), particularly *Enterococcus faecium*, are major pathogens in healthcare-associated infections. In immunocompromised patients, VRE infections can be severe and are associated with high mortality. The EVREA-Phage project is developing a phage cocktail consisting of four well-characterized natural bacteriophages. The cocktail is designed to target and lyse a broad range of clinical *E. faecium* strains. Bacteriophages are viruses that selectively infect specific bacterial strains. First clinical trials are currently in preparation.

Project lead:
Dr. Johannes Wittmann
Leibniz Institute DSMZ–German Collection of Microorganisms and Cell Cultures

HY-133: A PHAGE-DERIVED LYSIN AGAINST *STAPHYLOCOCCUS AUREUS*

Staphylococcus aureus (*S. aureus*) is a common bacterium that naturally occurs in humans, but it can also act as an opportunistic pathogen, especially in hospitalized patients. It frequently colonizes the nasal mucosa. If it enters wounds or the bloodstream, it can cause severe and potentially life-threatening infections. HY-133 is a phage-derived lysin, a protein that specifically targets and breaks down bacteria, designed to act against *S. aureus*. In June 2024, HY-133 entered phase I clinical trials (see page 29 for further details).

Project lead:
Prof. Dr. Andreas Peschel
University of Tübingen

ALPHA-TOXIN INHIBITOR: SMALL-MOLECULE INHIBITORS AGAINST *STAPHYLOCOCCUS AUREUS*

Like the HY-133 project, this flagship project targets *Staphylococcus aureus*. The focus is on severe hospital-acquired pneumonia in mechanically ventilated intensive care patients. A key pathogenic factor is alpha-toxin, a bacterial protein that forms pores in cell membranes and thereby destroys immune and tissue cells. The small-molecule inhibitor H052 blocks the activity of this toxin and has been shown to protect against pneumonia in rodent models. Currently, preclinical studies, process development for producing clinical-grade material, and biomarker-based analyses of patient samples are underway. The goal is to initiate a phase I clinical trial in 2027.

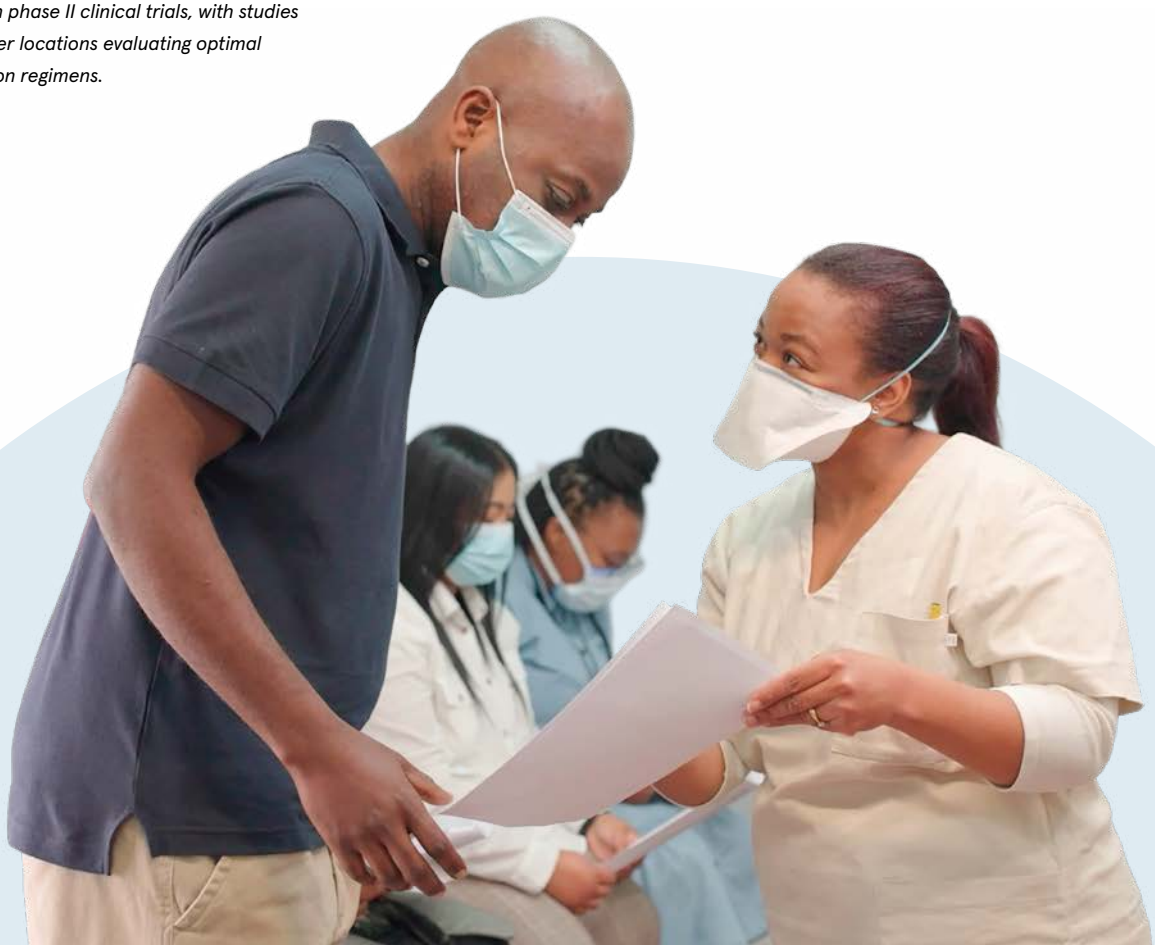
Project lead:
Prof. Dr. Mark Brönstrup
Helmholtz Centre for Infection Research

PANTIPA: PRECLINICAL DEVELOPMENT OF MONOCLONAL ANTIBODIES

Pseudomonas aeruginosa (*P. aeruginosa*) is a bacterium that is often multidrug-resistant and can cause life-threatening infections. DZIF researchers have found that patients with long-term *P. aeruginosa* infections develop antibodies against the PcrV protein, which plays a key role in bacterial virulence. Based on this finding, monoclonal antibodies (mAbs) targeting PcrV were generated in the laboratory. PANTIPA aims to identify the most suitable candidate from a panel of promising antibodies for further clinical development.

Project lead:
Prof. Dr. Jan Rybniker
Dr. Alexander Simonis
University Hospital Cologne

BTZ-043 is currently in phase II clinical trials, with studies in Cape Town and other locations evaluating optimal dosing and combination regimens.



EMERGING INFECTIONS

Prevention vs. restrictions: what works—and what doesn't

Coronaviruses include well-known, relatively harmless pathogens that only cause common colds. Severe respiratory diseases, on the other hand, can often occur from those that have only recently spilled over from animals to humans—such as MERS-CoV or SARS-CoV-2. Vaccinations and efficient laboratory diagnostics can slow their spread and reduce mortality rates.

DZIF researchers in Hamburg launched a randomized, double-blinded vaccine trial against the MERS coronavirus. Colleagues in Berlin tracked the spread of the SARS-CoV-2 Omicron variant in Africa.

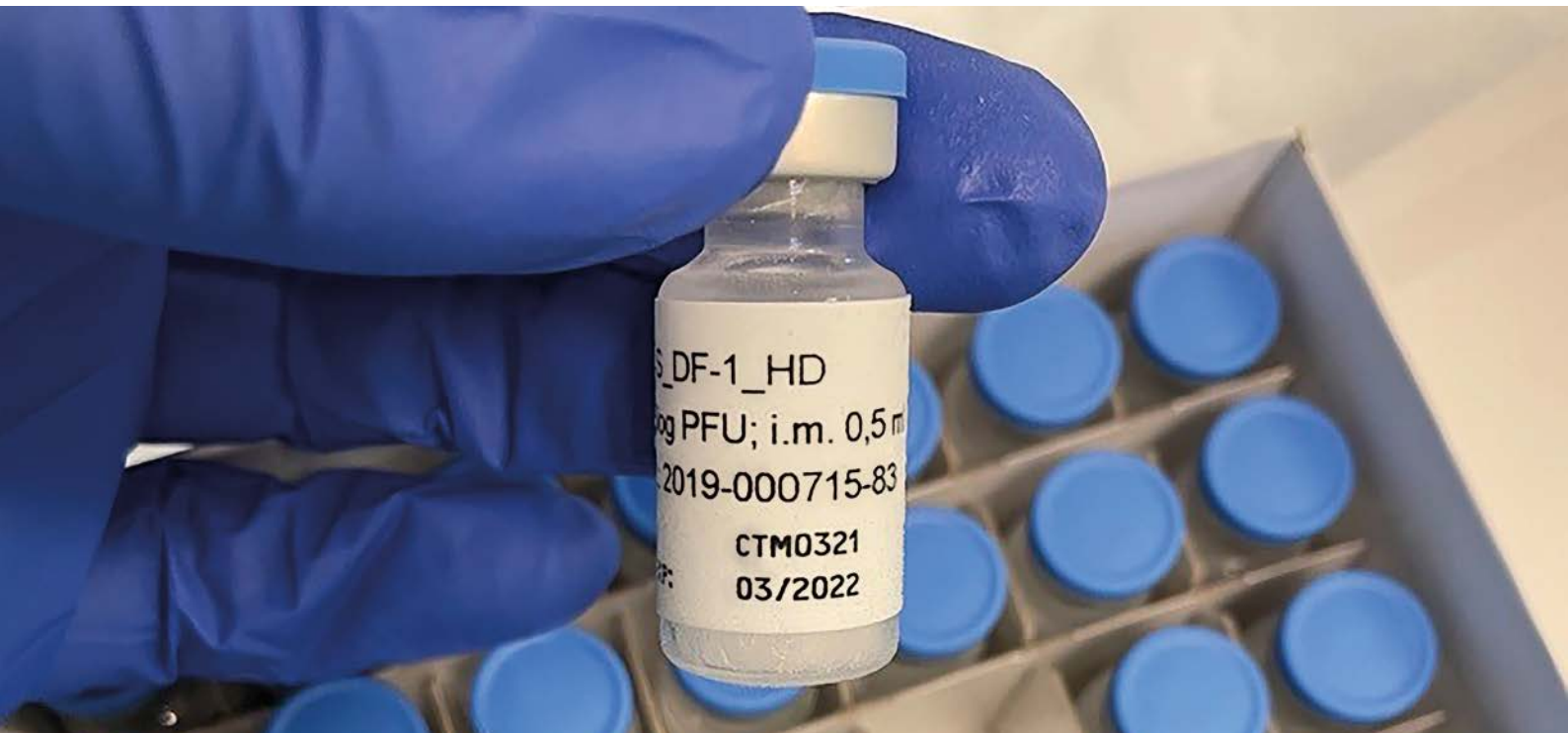
MERS VACCINE SUCCESSFULLY TESTED DESPITE COVID-19 PANDEMIC

Since its discovery in 2012, nearly 3,000 people have been infected with the MERS coronavirus (MERS-CoV), which causes the Middle East respiratory syndrome (MERS). One reason for the relatively low number of infections is probably that the MERS virus primarily affects the lower respiratory tract and is transmitted less efficiently from person to person than SARS-CoV-2. However, the case fatality rate of infection with MERS-CoV is as high as 36 percent, which is significantly higher than that of infection with either SARS-CoV-2 or SARS. MERS-CoV is transmitted to humans from dromedary camels and predominantly occurs on the Arabian Peninsula, but has been exported to 27 countries.

One of the reasons for developing a vaccine is to be prepared in case the MERS coronavirus mutates significantly or related viruses are discovered that are more efficient at spreading from person to person and could be as contagious as, for example, the Omicron variant of SARS-CoV-2, explains Prof. Marylyn Addo from the University Medical Center Hamburg-Eppendorf (UKE). It would be very concerning if people were to become infected with a highly contagious respiratory virus, for example during the pilgrimage to Mecca, and then carry the virus from there to the rest of the world.

When the researcher launched the first pilot study of the MERS vaccine candidate developed at the DZIF in 2018, she had no idea how significant the experiment would become beyond MERS itself. Suddenly, the SARS-CoV-2 pandemic hit. While many other studies were halted, the UKE was able to continue working with an adapted study protocol and test the MERS vaccine on 140 subjects. Some of the participants had already received a SARS-CoV-2 vaccine by the time they participated in the study. Others became infected with SARS-

The vaccine candidate MVA-MERS-S developed at the DZIF. It is based on an attenuated virus—the so-called "modified vaccinia Ankara virus" (MVA)—which has been supplemented with protein components of the MERS coronavirus.



At a hospital laboratory in Madagascar, a team of Madagascan and German scientists, including Prof. Jan Felix Drexler (second from left), are conducting PCR tests to determine the spread of the Omicron variant of SARS-CoV-2.

CoV-2 during the study, which unexpectedly provided valuable data on entirely new research questions. For example, researchers investigated how the MERS vaccination affects simultaneous or prior vaccination or infection with the related beta coronavirus, SARS-CoV-2. The vaccine proved to be equally safe and effective in all subjects in the long term, whether they had been infected with SARS-CoV-2 or vaccinated. Neutralizing antibodies were still detectable in their blood more than two years later.

TESTING CAPACITY AND INTERNATIONAL COOPERATION AS THE KEY TO EFFECTIVE PANDEMIC CONTROL

When the Omicron variant of SARS-CoV-2 was discovered in southern Africa in 2021, international travel restrictions were quickly implemented, causing significant harm to economy and affected people. But did these restrictions actually curb the spread of the new variant? To find out, an international research team led by Prof. Jan Felix Drexler from Charité – Universitätsmedizin Berlin analyzed respiratory samples from infected individuals both retrospectively and during the outbreak. With enormous logistical effort, specially developed PCR tests that can distinguish between the Delta and Omicron variants were developed with funding from the Bill & Melinda Gates Foundation and sent to 27 laboratories in 24 African countries. A total of 13,294 SARS-CoV-2-positive samples, collected between June 1, 2021, and April 14, 2022, were examined locally. Mobility-based mathematical modeling was then used to track the temporal and spatial spread of Omicron. The result: Omicron had already spread widely across nearly all of Africa before travel restrictions came into effect. The investigations also revealed that the actual infection rate in Africa had been underestimated by at least a factor of ten.

"With PCR tests developed and distributed at an early stage, databases on travel movements, and better international cooperation, measures to combat future pandemics, such as travel restrictions or physical distancing, could be implemented more effectively, and mistakes could be avoided," says Drexler. After all, genome sequencing capacities in Africa expanded significantly during the pandemic. However, there is a considerable need for investment in infrastructure and personnel in all regions of the Global South to ensure better preparedness for future outbreaks of highly transmissible viruses.

PUBLICATIONS ON THE STUDIES

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FOCUS OF THE RESEARCH AREA "EMERGING INFECTIONS"

Recent viral epidemics, including the SARS-CoV-2 pandemic, demonstrate the need for preparedness and the ability to swiftly develop countermeasures. This research area aims to deepen our understanding of respiratory viral pathogens and new, non-native viral infections. This includes the rapid development of novel diagnostic tools, antiviral strategies, and vaccines, as well as the rapid clinical testing of therapeutics and vaccines.

Coordination

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TUBERCULOSIS

Far more than just a lung problem

In 2023, 10.8 million people worldwide were newly diagnosed with tuberculosis—slightly more than in the previous year. Among other things, this is due to restrictions on diagnosis and treatment during the COVID-19 pandemic. Current research focuses on increasing multidrug resistance and extrapulmonary tuberculosis, which is often overlooked.

In Borstel, DZIF researchers are investigating the spread of multidrug-resistant tuberculosis (TB) in Mozambique. Colleagues in Cologne are searching for biomarkers that will enable the early detection of TB in organs other than the lungs.

RESISTANCE IS SPREADING UNDER THE RADAR

With 368 cases of TB per 100,000 inhabitants, Mozambique is one of the regions in Africa most severely affected by the disease. There, multidrug-resistant and rifampicin-resistant TB pathogens are on the rise. This is also confirmed by the results of a joint study conducted by the teams of Prof. Stefan Niemann from the Research Center Borstel, Leibniz Lung Center and the National Institute of Health of Mozambique. In this study, the genomes of rifampicin-resistant *Mycobacterium tuberculosis* strains were sequenced: 20 percent of all strains submitted to the national tuberculosis reference laboratory in Maputo between 2015 and 2021 included in the study were already resistant to fluoroquinolone. At the same time, resistance to bedaquiline increased in these strains—rising from three percent in 2016 to 14 percent in 2021. Both fluoroquinolones and bedaquiline are key drugs in new treatment regimens recommended by the World Health Organization (WHO) for patients with multidrug-resistant TB. In addition, the analysis data shows that these multidrug-resistant strains —especially those with fluoroquinolone and/or bedaquiline resistance—are transmitted extremely efficiently.

The researchers also found multidrug-resistant strains with a specific rifampicin resistance mutation—*rpoB* I491F. Strains with this genetic mutation are not detected by the WHO-recommended rapid molecular test, "Xpert MTB/RIF Ultra". As a result, these strains, known as "diagnostic escapes", some of which are resistant to bedaquiline or even have combined resistance to bedaquiline and fluoroquinolones, are spreading unnoticed and across borders in Eswatini, Mozambique, and South Africa, as comparative analyses have shown. This jeopardizes efforts to contain the drug-resistant TB epidemic in Mozambique and neighboring regions. Patients with highly resistant pathogens must be identified as early as possible to

Preparing samples for genome sequencing of resistant Mycobacterium tuberculosis *strains in Maputo, Mozambique. The nation is among the African countries with the highest incidence of tuberculosis.*

As part of the DZIF mEX-TB study, blood samples from patients with extrapulmonary tuberculosis are being analyzed to identify markers that enable early diagnosis of the disease and its severity.

avoid ineffective treatment and prevent the further spread of resistance. Otherwise, even newly developed drugs could become ineffective within a short period of time. Mozambique therefore plans to introduce genome-based diagnostics nationwide.

MARKER FOR EXTRAPULMONARY TUBERCULOSIS SOUGHT

Many patients undergo a years-long odyssey from specialist to specialist before it is recognized that they are suffering from TB. This is because in almost 30 percent of patients in Germany it is not the lungs which are affected but other organs such as lymph nodes, bones, or brain. This so-called extrapulmonary TB can affect any organ in principle—and the symptoms are correspondingly diffuse and diverse. In 2022, PD Dr. Isabelle Suárez and Prof. Jan Rybniker from the University Hospital Cologne launched a multicenter DZIF study (mEX-TB) to identify those affected at an early stage and treat them in a more targeted manner. To this end, clinical data and samples from patients with extrapulmonary TB in Bonn, Borstel, Frankfurt, Hamburg, Heidelberg, and Cologne are collected, analyzed, and evaluated in a central biobank. Over 130 patients have already been enrolled in the study, and more than 500 blood samples have been collected.

The search is on for markers in the blood that are specific to extrapulmonary TB and its severity. This would also make it possible to determine when the usually lengthy antibiotic therapy can be discontinued. The study's findings are expected to improve care for patients with extrapulmonary TB not only in Germany, but especially in regions with high TB incidence in Africa, Asia, and Eastern Europe. The team hopes these findings will contribute to the WHO's goal of eliminating TB worldwide.

PUBLICATIONS ON THE STUDIES

Barilar I et al. Emergence of bedaquiline-resistant tuberculosis and of multidrug-resistant and extensively drug-resistant Mycobacterium tuberculosis strains with rpoB Ile491Phe mutation not detected by Xpert MTB/RIF in Mozambique: a retrospective observational study. *Lancet Infect Dis*. 2024 Mar;24(3):297-307. doi: 10.1016/S1473-3099(23)00498-X. Epub 2023 Nov 10.

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FOCUS OF THE RESEARCH AREA "TUBERCULOSIS"

Scientists in the *Tuberculosis* research area are working to improve TB management, monitor the emergence of drug resistance, develop new diagnostics, and identify novel anti-TB agents. In personalized medicine, they develop and evaluate pathogen- and host-specific biomarkers to tailor treatments for optimal effectiveness and duration. They also focus on predictive biomarkers for post-TB disease and its management and treatment.

Coordination

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MALARIA AND NEGLECTED TROPICAL DISEASES

Wandering worms and the search for the slowest parasites

Although malaria is easily treatable, only a vaccine can prevent infection. Therefore, researchers are working diligently to develop efficient vaccines. Meanwhile, there is hope for an effective drug against the various pathogens that cause tropical worm diseases.

At the University of Bonn, Prof. Marc Hübner is coordinating a therapy study against several tropical worm diseases. Colleagues in Heidelberg are pursuing a new vaccination concept against malaria.

WHAT HELPS DOGS AND CATS...

Behind the flowery name *Loa Loa* lie nasty nematodes, also known as African eye worms. Transmitted by flies, these threadworms migrate through the subcutaneous fatty tissue, causing itchy swelling. Sometimes, they even crawl across the conjunctiva of the eyes. Loiasis and other worm infections, such as onchocerciasis (river blindness), mansonelosis, and trichuriasis (whipworm infection), can cause serious, chronic health problems and affect hundreds of millions of people in tropical regions. In the joint project "eWHORM", which is funded with €11.5 million by the European Union and the Swiss government, DZIF researchers led by Prof. Marc Hübner at the University of Bonn aim to eliminate the roundworms that are widespread in sub-Saharan Africa. The main goal is to test the broad-spectrum drug oxfendazole, which is successfully used in veterinary medicine against intestinal worms, on humans to treat nematodes. "We expect it to have a pan-nematicidal effect, so we are testing the tablets against all four worm species in Gabon, Cameroon, Tanzania, and the Democratic Republic of Congo," says Hübner. The "basket approach" allows for the inclusion of patients colonized by more than one parasite.

Oxfendazole kills adult worms, but it does not directly affect the first larval stage: the microfilariae. However, it results in a gradual decrease in microfilariae, and good tolerability is expected. As long as there is no new infection with the third larval stage, no more adult worms can develop. Nematode infections are not only extremely unpleasant and lead to prolonged illnesses but they also modulate the immune system. This increases the risk of viral infections, such as HIV.

A microfilaria of the "African eye worm" (Loa loa) *is visible under a microscope in a blood smear. The European joint project eWHORM is making important contributions to the elimination of worm infections such as loiasis. Further information on eWHORM: https://www.ewhorm.org.*

Malaria pathogens enter the host when an Anopheles *mosquito feeds on blood. Sexual recombination of the genes of the malaria parasite* Plasmodium *during its development in the mosquito results in high genetic variability, which complicates vaccine development.*

WHERE THE SLOWEST CROSSES THE FINISH LINE FIRST

Every year, 250 million people contract malaria and 600,000 die from it. The fact that the world is still waiting for an effective vaccine is due, on the one hand, to the complicated life cycle of the *Plasmodium falciparum* parasite. On the other hand, it is also because many of the parasite's approximately 5,000 genes can recombine sexually each time it passes through the *Anopheles* mosquito. A tiny virus would also be much easier to neutralize than the 100 times larger single-celled organism, which can move by itself and replicate in different cells. Researchers led by Prof. Friedrich Frischknecht and Dr. Julia Sattler at Heidelberg University are therefore pursuing a new vaccination approach that they have successfully tested in a mouse model. The trick: they "vaccinate" the rodents with genetically modified pathogens that develop normally in mosquitoes but much more slowly than usual in rodents. This gives the immune system more time to fight the parasites itself. When the mice were infected with normal *Plasmodium* parasites three, six, or twelve months later, they were either completely protected or only developed mild infections without symptoms.

The mouse parasite reproduces every 24 hours and causes severe malaria symptoms in rodents. By selectively switching off specific genes, the research team succeeded in slowing down the parasite to a quarter of its normal reproduction rate. "Unfortunately, this is more difficult with the human parasite: it takes 48 hours to reproduce, and so far, we have only managed to reduce its reproduction rate by about 30 percent," says Frischknecht. The search for slower parasites is therefore still ongoing. Current efforts are focused on doubling the reduction in growth by switching off two genes that are important for growth in parallel.

The particular appeal of this concept lies in the fact that not all residents in malaria-endemic areas would need to be vaccinated. This is because the mosquitoes would ingest the slowed-down parasites with their next blood meal and thus spread the vaccine so to speak by themselves.

PUBLICATIONS ON THE STUDIES

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FOCUS OF THE RESEARCH AREA "MALARIA AND NEGLECTED TROPICAL DISEASES"

This research area is dedicated to the clinical development of new diagnostic tools, vaccination strategies, and drugs for the control and elimination of the most widespread poverty-related infectious diseases in the Global South. In collaboration with African partner institutions of the DZIF, the therapeutic and preventive potential of novel malaria drugs and combination therapies as well as the effects of insecticide resistance in malaria pathogens are being investigated. In addition, researchers are focusing on the clinical testing of novel diagnostics and therapeutics for worm diseases such as filariasis and schistosomiasis.

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HIV

How a cure could be achieved

In rare cases, stem cell transplants also eliminate HIV in blood cancer patients who are HIV-positive. Some infected individuals produce highly potent, long-lasting HIV-neutralizing antibodies. Researchers hope that both groups will provide clues for new therapies and a vaccine.

DZIF researchers in Hamburg have been closely monitoring the healing process of the "Düsseldorf patient" over a period of ten years. Their colleagues in Cologne are investigating the dynamics of long-lasting neutralizing antibodies in people infected with human immunodeficiency virus type 1 (HIV-1).

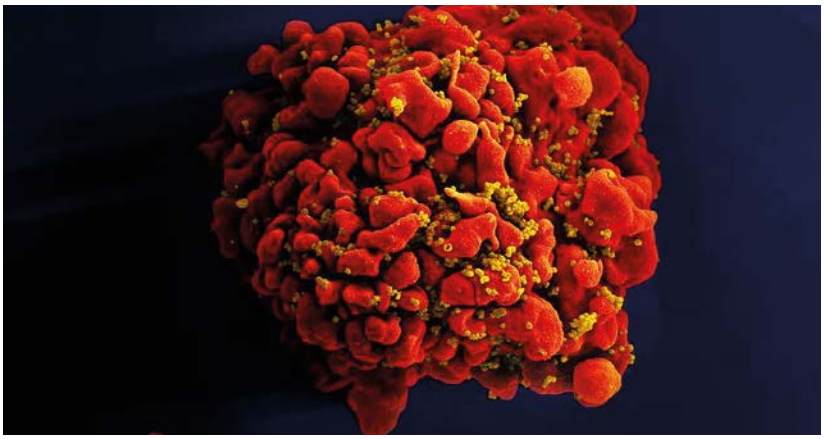
IS HIV CURABLE? NEW PERSPECTIVES THANKS TO STEM CELL TRANSPLANTATION

What could be worse for people living with HIV than also developing blood cancer? Paradoxically, for a few, this could open the way to a cure for HIV. Namely, when they receive a so-called allogeneic hematopoietic stem cell transplant from a donor who carries the rare CCR5 gene mutation. This mutation provides genetic protection against HIV for about one percent of Europeans. The protection is transferred to patients through the stem cells and can cure them of AIDS.

As part of the European cooperation project "IciStem", physicians such as Prof. Julian Schulze zur Wiesch from the University Medical Center Hamburg-Eppendorf (UKE) as well as stem cell researchers, virologists, and immunologists are following people such as the "Düsseldorf patient" for years after their transplants. They want to understand what happens in detail in the tissue and when HIV therapy can be safely discontinued. Ten years after the transplant (and four years after the end of therapy), traces of viral RNA were still found in the tissue, but no replication-competent HIV. The "Düsseldorf patient" is therefore considered cured.

Researchers now suspect that the CCR5 mutation may not be necessary at all. Rather, the transplant itself may be sufficient to essentially restart the patient's immune system so that it can eliminate the virus on its own. The search is now on for even more sensitive methods that can detect even the smallest virus reservoirs throughout the body, as well as immunological markers that reliably indicate replication-competent

Marc Franke (right), the "Düsseldorf patient" cured of AIDS through a stem cell transplant, together with DZIF scientist Prof. Julian Schulze zur Wiesch from the UKE during their visit to the "AIDS 2024" conference in Munich.



A digitally colored scanning electron microscope image shows numerous spherical, mustard-colored HIV particles adhering to the surface of a red-colored T cell. Broadly neutralizing antibodies against HIV are now being further developed for therapeutic purposes.

virus. This would benefit not only the few patients who can actually be cured by transplantation, but also all others affected by HIV.

WHAT MAKES AN "ELITE NEUTRALIZER"?

There are now effective antiretroviral drugs that mean HIV infection is no longer fatal, but has become a chronic disease. However, around 1.2 million people are still newly infected with the virus every year, and a vaccine is still not in sight. Broadly neutralizing antibodies, administered as an infusion every three to six months, could be an intermediate step in protecting people at high risk of infection or controlling the virus in infected individuals. They could even help to induce lasting immune control and thus achieve a "functional cure."

To better understand the dynamics of these antibodies, an international team led by DZIF scientists Prof. Florian Klein and Prof. Philipp Schommers from the University Hospital Cologne investigated the formation and longevity of HIV antibodies in over 2,300 people living with HIV from Germany, Tanzania, Cameroon, and Nepal. This apparently depends on various factors: What type of virus is present? How long has someone been infected? Was the viral load high or low? Was the person treated very early on or only later?

"We found good antibodies in many people. But only about one percent are what we call elite neutralizers, which produce really potent, broadly neutralizing antibodies," says Florian Klein. However, it will not be easy to induce these antibodies through vaccination. This is because these special antibodies are highly mutated and have repeatedly adapted to changes in the virus over many years. The researchers have isolated various antibodies from elite neutralizers and further developed them for therapeutic purposes. One of these is already scheduled to enter clinical trials in the coming months.

PUBLICATIONS ON THE STUDIES

Jensen BO et al. In-depth virological and immunological characterization of HIV-1 cure after CCR5Δ32/Δ32 allogeneic hematopoietic stem cell transplantation. *Nat Med*. 2023 Mar;29(3):583-587. doi: 10.1038/s41591-023-02213-x. Epub 2023 Feb 20.

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FOCUS OF THE RESEARCH AREA "HIV"

Despite continuous antiretroviral therapy, HIV—integrated into the human genome—can persist in the body for life. This complicates the healing process, requires long-term treatment, and carries the risk of developing resistance. At five DZIF partner sites in Germany and at African Partner Institutions, scientists are working together to characterize reservoirs and develop new therapeutic approaches for the long-term control and cure of HIV-1 infections.

Coordination

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HEPATITIS

Hepatitis B and D: what works, how, and why?

Approximately 250 million people worldwide have chronic hepatitis B. Of those, 20 million are also infected with the hepatitis D virus (HDV). Fortunately, a new drug offers an effective treatment option. A therapeutic vaccine that strengthens the immune system's ability to fight hepatitis B is also undergoing clinical trials.

DZIF researchers in München and Hamburg are testing a therapeutic vaccine against hepatitis B virus (HBV). Meanwhile, colleagues in Heidelberg, Gießen and Hannover are investigating the mode of action of bulevirtide.

A THERAPEUTIC VACCINE AGAINST CHRONIC HEPATITIS B

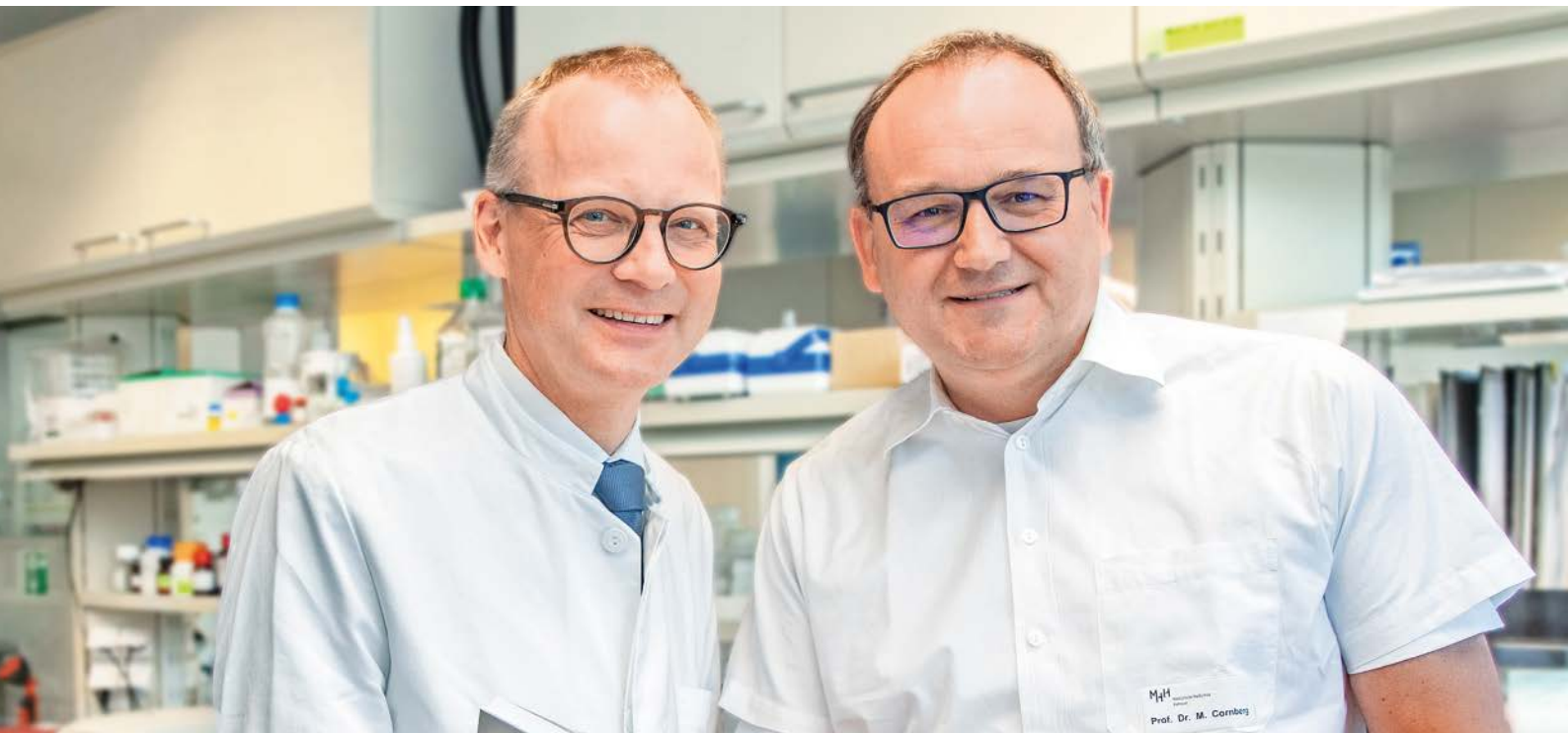
Although antiviral drugs used to treat hepatitis B virus infections prevent the virus from multiplying, they do not eliminate it from infected liver cells. Consequently, the infection can persist. Therefore, a complete cure is currently not possible and therapy must be continued lifelong. The risk of developing liver cancer remains despite antiviral therapy. Given that HBV infection remains associated with high mortality worldwide, scientists are keen to change this. Currently, 1.1 million people worldwide die each year as a result of HBV infection, most of them from liver cancer.

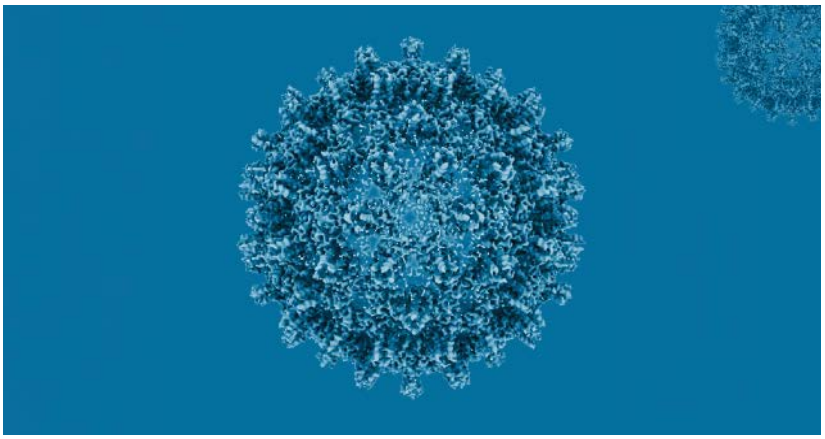
A vaccine for the prevention of hepatitis B has been available for a long time. However, it only works preventatively and is ineffective for those who are already infected. For this reason, Prof. Marylyn Addo of the University Medical Center Hamburg-Eppendorf, Prof. Ulrike Protzer of Helmholtz Munich and the Technical University of Munich (TUM), and scientists from Ludwig-Maximilians-Universität München are conducting a phase Ia clinical trial to test the safety and immunogenicity of a novel therapeutic vaccine candidate in healthy volunteers.

The candidate vaccine was able to clear HBV infection in preclinical mouse models. Not only did the rodents produce antibodies, but CD4 and CD8 T immune cells, which play an important role in defending against HBV, were also activated.

In another study, Prof. Protzer and her colleagues at TUM discovered that the success of therapeutic vaccination actually depends on the efficient activation of HBV-specific CD4 T cells. These cells coordinate the immune response against foreign pathogens and are therefore crucial for eliminating viruses from liver cells. An optimal protein vaccine formulation during the initial vaccination enabled the desired activation

They have demonstrated the efficacy and safety of the new drug Hepcludex® against hepatitis D: Prof. Heiner Wedemeyer (left) and Prof. Markus Cornberg from Hannover Medical School.





Reconstruction of the structure of an HBV core capsid using cryo-electron microscopy. The capsids of the hepatitis B virus (HBV) are protein shells that enclose the viral DNA genome and are formed from several copies of the HBV core protein.

of CD4 T cells and laid the foundation for a booster vaccination to control HBV infection. A therapeutic vaccine would be a game changer, as the global need is enormous—especially in Asia and Africa, where many people die from the consequences of HBV infection. Even the uninfected participants benefit from the DZIF study, as they are now protected against hepatitis B.

HEPCLUDEX®: THE FIRST DRUG AGAINST HEPATITIS D

After Prof. Stephan Urban in Heidelberg discovered how hepatitis B viruses invade liver cells—and thus also hepatitis D viruses, which use HBV as a vehicle for cell invasion—the way was clear for developing a virus blocker. Bulevirtide, a peptide drug whose clinical development was also accomplished with the help of the DZIF, was provisionally approved in the EU in 2020 and definitively approved in 2023 under the name Hepcludex®. Hepcludex® treats hepatitis D and reduces the viral load by a factor of one million within 48 weeks. In one out of three infected individuals, the HDV pathogens are completely eliminated. Hepcludex® is the first drug ever to be developed against hepatitis D, and researchers hope it will soon be approved to treat hepatitis B as well.

At Hannover Medical School, Prof. Heiner Wedemeyer led an international, multicenter phase III study with Hepcludex®. Approximately half of the 150 patients in the study had early cirrhosis. Even in these patients, liver inflammation improved significantly. The 144-week treatment was highly effective and safe with no side effects.

Professors Dieter Glebe from Justus Liebig University Giessen and Stephan Urban from Heidelberg University Hospital, along with Swiss and US colleagues, have elucidated the mechanism of action of bulevirtide. According to their findings, the active ingredient blocks the cellular bile salt transporter protein NTCP at the precise points where the virus attaches in order to penetrate the liver. Now that this mechanism is understood, more simplified active ingredients can be developed.

PUBLICATIONS ON THE STUDIES

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Su J et al. Activation of CD4 T cells during prime immunization determines the success of a therapeutic hepatitis B vaccine in HBV-carrier mouse models. *J Hepatol*. 2023 Apr;78(4):717-730. doi: 10.1016/j.jhep.2022.12.013. Epub 2023 Jan 9.

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Wedemeyer H et al. A Phase 3, Randomized Trial of Bulevirtide in Chronic Hepatitis D. *N Engl J Med*. 2023 Jul 6;389(1):22-32. doi: 10.1056/NEJMoa2213429. Epub 2023 Jun 22.

FOCUS OF THE RESEARCH AREA "HEPATITIS"

Scientists at the DZIF collaborate closely to combat viral hepatitis, a disease that claims well over a million lives each year. To this end, they are developing novel diagnostic tools and testing therapeutic approaches in various preclinical models and clinical trials. They aim to cure chronic hepatitis B and D, develop a hepatitis C vaccine, and prevent and treat hepatitis E.

Coordination

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Helmholtz Munich

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COMMUNITY-ACQUIRED INFECTIONS AT MUCOSAL INTERFACES

Mechanisms of bacterial stress and control

Once *Helicobacter pylori* has established itself in the stomach, it can contribute to the development of gastric cancer. Can vaccination prevent colonization of the gastric mucosa? Meanwhile, antibiotics disrupt the entire microbial ecosystem of the intestine. But how exactly does the microbiome respond?

In Munich, DZIF researchers are developing a vaccine against the bacterium *Helicobacter pylori*. At the same time, teams in Munich and Braunschweig are investigating how the microbiome responds to antibiotic exposure and how commensal bacteria can counteract pathogens such as *Salmonella*.

THE STOMACH LINING—A CHALLENGE FOR THE IMMUNE SYSTEM

Almost half of the world's population is infected with *Helicobacter pylori*. This is of major clinical relevance, as the bacterium can cause chronic gastritis and peptic ulcer disease and is associated with approximately 750,000 new cases of gastric cancer worldwide each year. Meanwhile, antimicrobial resistance is steadily increasing. An effective vaccine would therefore be a highly desirable preventive strategy. However, inducing protective immunity in the gastric mucosa poses a particular challenge: how can immune responses be directed against *H. pylori* without disrupting the beneficial local microbiome? This question has been a central focus of Prof. Markus Gerhard's group at the Technical University of Munich (TUM) for over 15 years. Using murine models, the team demonstrated that protection against particularly virulent *H. pylori* strains is mediated primarily by specific T-cell populations rather than humoral responses. To effectively exert their function, these cells must be guided to the appropriate mucosal sites. This requires a tailored vaccination strategy involving repeated administration—typically two intramuscular doses followed by a mucosal booster, either sublingual or oral. Currently, different vaccine platforms, including protein-, vector-, and mRNA-based approaches, are being evaluated in Munich.

H. pylori is transmitted via the oral route. While colonization rarely occurs in adults, children are susceptible, often through close contact such as maternal saliva. In early childhood, the gastric environment is less acidic and the immune system is still developing, creating a window of susceptibility that typically closes around age ten. Accordingly, a vaccine would likely need to be administered in early childhood, in line with established pediatric immunization schedules. The

Scanning electron microscope image of the stomach pathogen Helicobacter pylori *(green) on epithelial cells (red). The bacterium is responsible for around 750,000 new cases of stomach cancer worldwide every year.*

Electron microscope image of bacteria of the species Klebsiella oxytoca. *Through competition for food and other mechanisms, this type of bacterium can help kill* Salmonella *bacteria in the human intestine.*

DZIF-funded project has now entered the EU Horizon program. Given limited commercial incentives for vaccine development, early-stage academic research remains essential. "We use *H. pylori* as a model to understand mucosal immunity in gastrointestinal infections more broadly. There is an urgent need for vaccines against pathogens such as noroviruses, *Salmonella*, *Escherichia coli*, and *Shigella*," Gerhard emphasizes. The first mucosally active adjuvant developed within DZIF is expected to support such approaches across multiple indications.

HOW DOES THE GUT MICROBIOME RESPOND TO ANTIBIOTICS—AND CAN IT DEFEND ITSELF?

Antibiotic treatment disrupts the gut's complex microbial ecosystem and promotes the emergence and spread of resistant strains. Prof. Bärbel Stecher (TUM) and Prof. Alice McHardy (Helmholtz Centre for Infection Research, HZI) studied how repeated antibiotic exposure affects microbiome composition and dynamics. They colonized mice with a defined microbial community and monitored species-specific responses for 80 days using metagenomic and culture-based analyses of stool samples. The results were highly heterogeneous: some bacterial species entered a dormant, low-metabolic state; some showed reduced growth rates; and some rapidly acquired resistance. In addition, certain antibiotics triggered the activation of bacteriophages—viruses that infect bacteria and whose genetic material can integrate into bacterial genomes. Upon activation, these phages replicate and lyse their host cells, releasing new viral particles. This illustrates that antibiotics can also exert indirect effects on microbial communities. "These mechanisms are highly complex, making it difficult to predict precisely how individual species will respond to specific treatments," McHardy concludes.

Some members of the microbiome can directly suppress pathogenic bacteria. For example, the intestinal bacterium *Klebsiella oxytoca* can inhibit *Salmonella*, as shown by Prof. Till Strowig and Dr. Lisa Osbelt of HZI and their collaborators. *K. oxytoca* produces a toxin that can damage intestinal tissue but also reduces *Salmonella* viability. While this may benefit the host, it is not suitable as a therapeutic strategy. However, other mechanisms may have potential: *K. oxytoca* and *Salmonella* compete for similar nutrient resources. When these resources become limited, *Salmonella* growth is suppressed. Such ecological interactions within the microbiome could offer promising therapeutic approaches and are currently being explored in further studies.

PUBLICATIONS ON THE STUDIES

Gong R et al. CagA-dependent Hobit+ gastric tissue-resident memory T cells confer full protection from Helicobacter pylori reinfection. *Gut*. 2025 Jun 5:gutjnl-2025-334781. doi: 10.1136/gutjnl-2025-334781. Epub ahead of print.

Münch PC et al. Pulsed antibiotic treatments of gnotobiotic mice manifest in complex bacterial community dynamics and resistance effects. *Cell Host Microbe*. 2023 Jun 14;31(6):1007-1020.e4. doi: 10.1016/j.chom.2023.05.013. Epub 2023 Jun 5.

Osbelt L et al. Klebsiella oxytoca inhibits *Salmonella* infection through multiple microbiota-context-dependent mechanisms. *Nat Microbiol*. 2024 Jul;9(7):1792-1811. doi: 10.1038/s41564-024-01710-0. Epub 2024 Jun 11.

FOCUS OF THE RESEARCH AREA "COMMUNITY-ACQUIRED INFECTIONS AT MUCOSAL INTERFACES"

Gastrointestinal diseases caused by pathogenic bacteria—especially multi-drug-resistant strains—viruses, and parasites constitute a major global health burden. Examples include peptic ulcer disease, gastric cancer and antibiotic-associated diarrhea. Scientists in this research area are developing innovative, pathogen-specific approaches to prevent and treat gastrointestinal and other community-acquired infections of mucous membranes while preserving the microbiome.

Coordination

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INFECTIONS OF THE IMMUNOCOMPROMISED HOST

New vaccination strategies against well-known viruses

Some pathogens can be handled by a strong immune system, but not by a weak one. Certain viruses, such as Epstein-Barr and hepatitis C, can remain undetected in the body for long periods of time and cause severe organ damage, immune disorders, or even cancer decades later. Early vaccination could prevent this—if only there were a vaccine...

In Munich, DZIF researchers are founding the start-up "EBViously" to develop the first EBV vaccine. In Lübeck, researchers are working on a vaccine against hepatitis C.

JUST ONE PRICK TO PREVENT MANY DISEASES

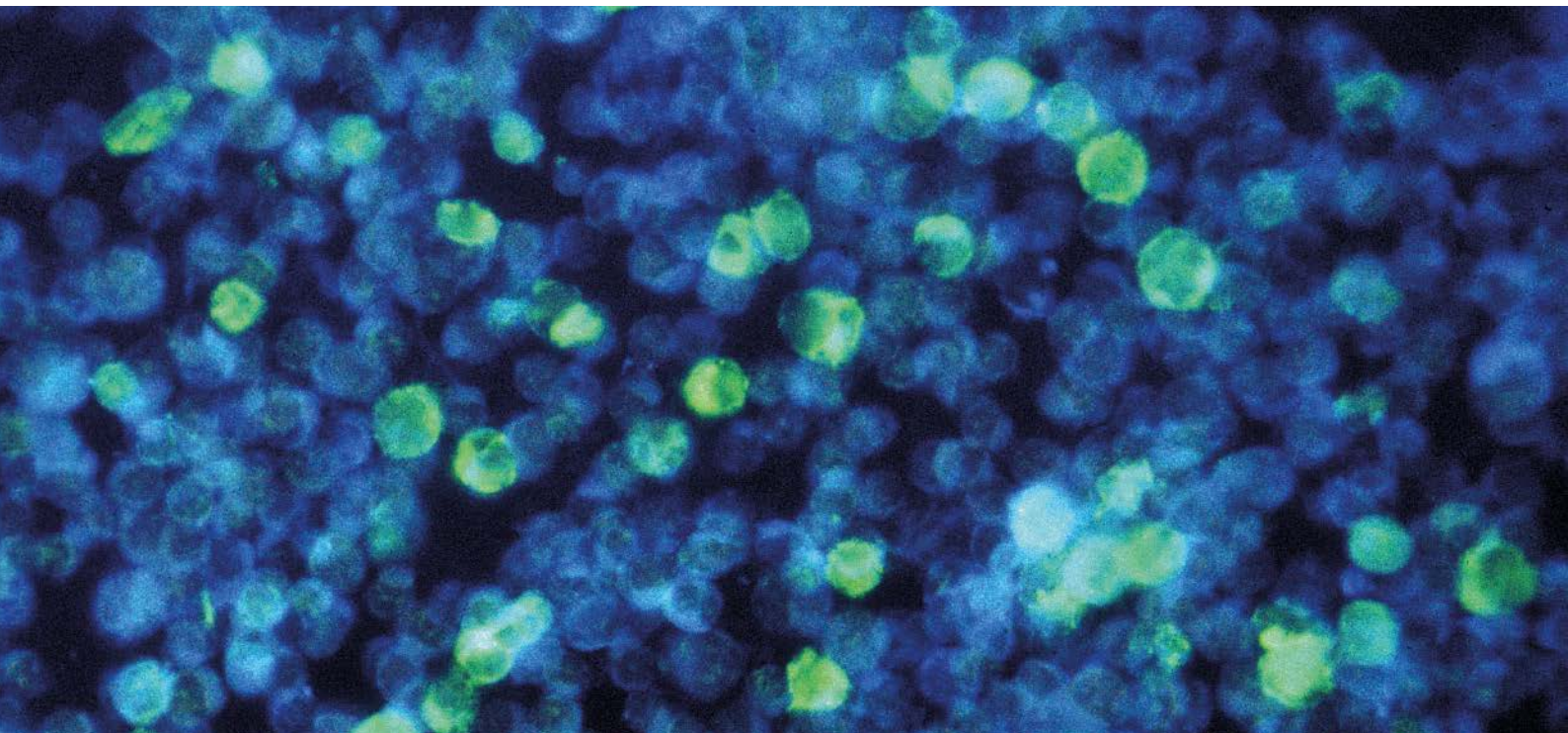
Almost every adult is infected with the Epstein-Barr virus (EBV), even if they have never had Pfeiffer's glandular fever. This herpes virus is transmitted through bodily fluids and usually infects people during childhood or adolescence. Although it is often asymptomatic, the virus remains in the body for life. This is treacherous because EBV is suspected of triggering immune diseases such as lupus erythematosus and rheumatoid arthritis, but it is also linked to Hodgkin's disease and other forms of lymphoma, i. e., lymph node cancers. In addition, EBV has been proven to be a prerequisite and thus a main risk factor for multiple sclerosis. The search for a vaccine has been unsuccessful for a long time. However, Prof. Wolfgang Hammerschmidt from Helmholtz Munich now appears to be close to achieving this goal.

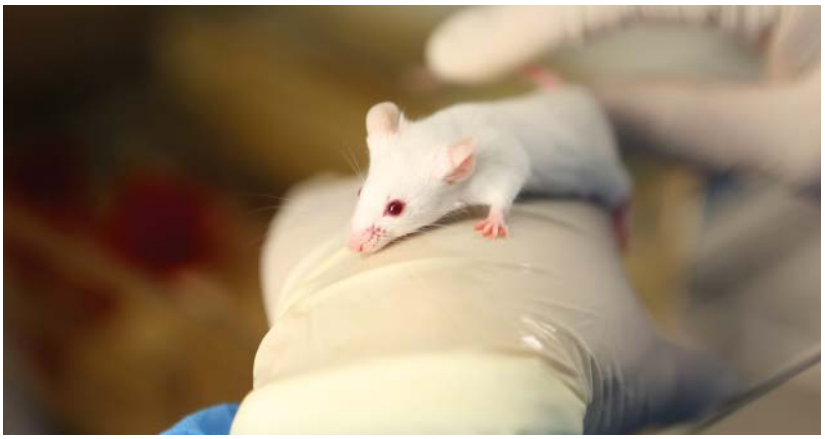
The vaccine candidate EBV-001 uses virus-like particles (VLPs) that are structurally derived from EBV. However, since these particles lack viral genetic material, they are not infectious. The start-up company EBViously was founded in Munich in 2024. In collaboration with the LMU University Hospital Munich, EBV specialists are developing the vaccine further. To date, the project has received around twelve million euros in funding from the Helmholtz Validation Fund and the DZIF. The first production of VLPs under Good Manufacturing Practice conditions in cell cultures is scheduled to begin in the first quarter of 2026. Assuming subsequent clinical trials are as successful as preclinical laboratory testing, the EBV vaccine will be available to EBV-seronegative young adults, and eventually to children before puberty, similar to the vaccination against papillomaviruses.

HOPE FOR A HEPATITIS C VACCINE!

There are vaccines available that protect against infection with either the hepatitis A virus (HAV) or the hepatitis B virus (HBV).

Fluorescence microscope image of leukemia cells infected with the Epstein-Barr virus (EBV). EBV particles labeled with fluorescent antibodies cause the cells to glow (green) under UV light. EBV is a herpesvirus and one of the most common viruses in humans.





The vaccine developed by Prof. Thomas Krey and his team at the Universität zu Lübeck has already successfully triggered the formation of the desired antibodies against the hepatitis C virus in mice. The vaccine is now being further developed to strengthen the immune response.

"Unfortunately, there is still no vaccine against the hepatitis C virus (HCV)," says Prof. Thomas Krey from the Universität zu Lübeck. This is dramatic because, unlike HAV, HCV can lead to chronic liver inflammation and liver cancer if left untreated. The infection is like a sleeping dragon: Although it can be effectively treated, since it often has no symptoms it is often only discovered 20 to 30 years later. By then, it's often too late! Approximately 50 million people worldwide are chronically infected with HCV, and every year, 240,000 people die from the consequences of infection, such as cirrhosis or liver cancer.

Prof. Krey has been working on an HCV vaccine for 15 years. He considers the question of why it is taking so long to be easy to answer. On the one hand, HCV is far more variable than most other viral pathogens. On the other hand, there has been no suitable animal model in recent years because studies on chimpanzees—the only animals that can be infected with HCV—have long been banned. In the near future, a "Controlled Human Infection Model" (CHIM) will be used instead. In this model, volunteers are vaccinated and then intentionally infected with the virus. These studies are ethically acceptable because effective antiviral drugs are now available.

Krey's team developed a vaccine based on only two short sections of the virus's envelope proteins. These sections, called neutralization epitopes, alone trigger a powerful immune response. They were grafted onto carrier proteins and displayed on a virus-sized nanoparticle. In mice, these nanoparticles have already triggered the formation of the desired, potently neutralizing antibodies. To further enhance the immune response, the team plans to equip the particles with additional HCV-neutralization epitopes.

PUBLICATIONS ON THE STUDIES

Roessler J et al. SARS-CoV-2 and Epstein-Barr Virus-like Particles Associate and Fuse with Extracellular Vesicles in Virus Neutralization Tests. *Biomedicines*. 2023 Oct 25;11(11):2892. doi: 10.3390/biomedicines11112892.

Nagarathinam K et al. Epitope-focused immunogens targeting the hepatitis C virus glycoproteins induce broadly neutralizing antibodies. *Sci Adv*. 2024 Dec 6;10(49):eado2600. doi: 10.1126/sciadv.ado2600. Epub 2024 Dec 6.

FOCUS OF THE RESEARCH AREA "INFECTIONS OF THE IMMUNO-COMPROMISED HOST"

A weakened immune system can have various causes, including chemotherapy, biologics, transplants, or congenital immune defects. This makes those affected more susceptible to infections. The research area aims to improve diagnostic and therapeutic options, for example through tailored antiviral therapies, vaccines, and new concepts for combating infection.

Coordination

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HEALTHCARE-ASSOCIATED INFECTIONS

Using sophistication to combat resistant hospital germs

Around 500,000 people contract a bacterial infection in German hospitals every year, often from multidrug-resistant bacteria. The search for ways to prevent the infections or quickly neutralize the pathogens is in full swing.

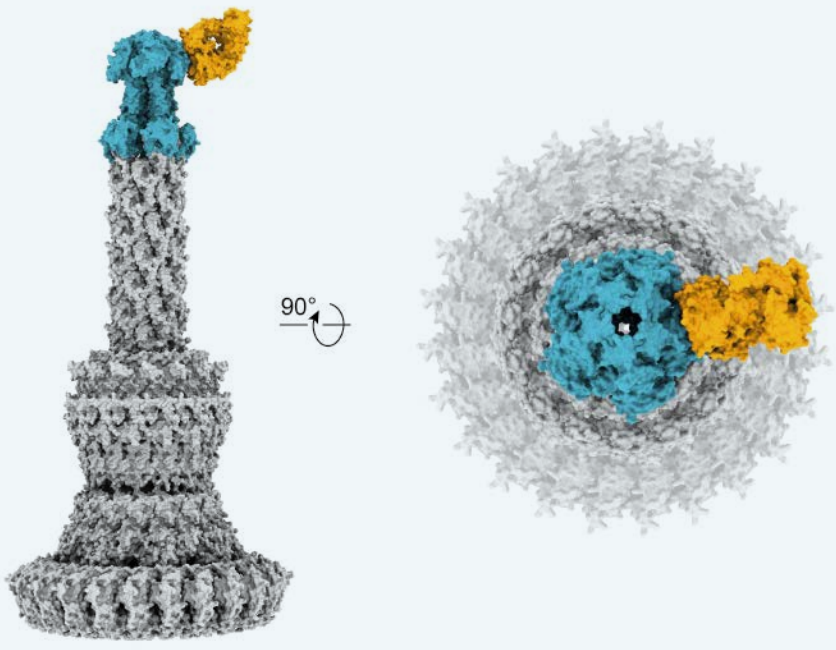
DZIF researchers in Cologne and Braunschweig are targeting *Pseudomonas aeruginosa*. They are using antibodies to combat the bacterium. In Tübingen and Greifswald, researchers are testing a phage lysin against *Staphylococcus aureus* infections.

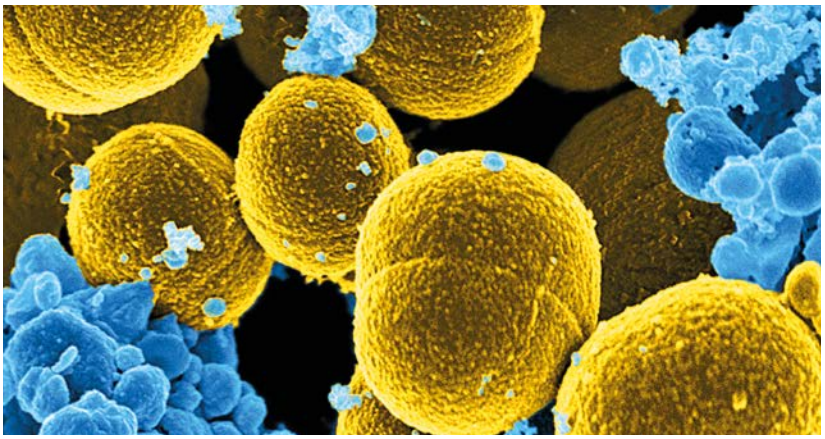
SUCCESSFULLY BLOCKING BACTERIAL VIRULENCE

Patients hospitalized with severe burns, on ventilators, or undergoing cancer treatment are at high risk of becoming infected with multidrug-resistant bacteria such as *Pseudomonas aeruginosa*. In addition to causing acute infections, *P. aeruginosa* can colonize people with chronic lung diseases, such as cystic fibrosis, for years. Could prolonged exposure to *P. aeruginosa* have led these patients to develop antibodies that could be used therapeutically to neutralize the bacterium? A team led by Prof. Jan Rybniker and Dr. Alexander Simonis from the University Hospital Cologne sought to answer this question. They found what they were looking for in the blood of people with cystic fibrosis and isolated multiple highly effective antibodies. DZIF colleagues in Braunschweig demonstrated in an animal model that these antibodies are as effective as classic antibiotics against *P. aeruginosa*. Unlike antibiotics, however, these antibodies are effective for weeks without causing the typical side effects of antibiotics.

The mechanism is now also clear. Using cryo-electron microscopy, research partners at the University Medical Center Hamburg-Eppendorf showed that some of the antibodies bind to the tip of the type III secretion system of *P. aeruginosa*, thereby disarming the bacterium. With €1.7 million in funding from the DZIF and an additional €1.5 million from the ForTra gGmbH for Research Transfer of the Else Kröner-Fresenius Foundation, the most effective of these antibodies will be developed into a drug and tested in clinical trials. This antibody could protect patients in oncology or intensive care units from infection through passive immunization. It could also be used therapeutically in infections caused by *P. aeruginosa*, especially multidrug-resistant strains.

Cryo-electron microscopic reconstruction of the antigen-binding region of a human antibody (yellow) on the needle-tip protein (blue) of the type III secretion system of Pseudomonas aeruginosa. *Binding of the antibody inhibits the secretion system, thereby weakening an important virulence factor.*





Digitally colored scanning electron microscope image of spherical, mustard-colored Staphylococcus aureus *bacteria surrounded by attacking white blood cells (here: colored blue).*

THE PROBLEM LITERALLY SOLVED AT THE DOORSTEP

The natural habitat of *Staphylococcus aureus* is the human nasal cavity. Through nose-hand contact, the bacteria can spread to the rest of the body. "Eighty percent of wound infections in surgical patients can be traced back to the strain found in the patient's nose," says Prof. Karsten Becker, a microbiologist at Greifswald University Hospital. To prevent the introduction and transmission—in particular of methicillin-resistant *S. aureus* (MRSA)—in hospitals, an antibiotic nasal ointment has been used to date. It must be applied for a week and usually destroys the entire microbiome in the nose. "Wouldn't it be possible to do this in a gentler, more sophisticated, and more targeted way?" asked Becker and his colleague, Prof. Andreas Peschel of the University of Tübingen.

In an initial study conducted in cooperation with HYpharm, a nasal spray containing the company's patented phage agent, HY-133, is being tested on healthy volunteers who are tested positive for *S. aureus* colonization in the nose but do not exhibit any symptoms of disease. HY-133 is a lysin, a protein derived from a bacteriophage that specifically attacks and dissolves the cell wall of *S. aureus* bacterial strains, including MRSA. The normal microbiome in the nose shall remain unaffected.

Unlike phage therapies, which remain controversial in Western Europe, this treatment relies solely on a specific phage-derived enzyme rather than on a "cocktail" of whole phages. The enzyme was optimized in the laboratory and subsequently produced synthetically. In nature, phages use this enzyme to release themselves from the host cell after replication. In the case of HY-133, the phage enzyme should rapidly and reliably destroy its bacterial host in the human nasal cavity within just 20 to 30 minutes.

PUBLICATIONS ON THE STUDIES

Simonis A et al. Discovery of highly neutralizing human antibodies targeting Pseudomonas aeruginosa. *Cell*. 2023 Nov 9;186(23):5098-5113. e19. doi: 10.1016/j.cell.2023.10.002. Epub 2023 Nov 1.

Kaspar U et al. Exploration of Bacterial Re-Growth as In Vitro Phenomenon Affecting Methods for Analysis of the Antimicrobial Activity of Chimeric Bacteriophage Endolysins. *Microorganisms*. 2022 Feb 15;10(2):445. doi: 10.3390/microorganisms10020445.

Idelevich EA, Becker K. Phagenendolysine – eine neue Wirkstoffklasse mit vielfältigen Einsatzmöglichkeiten. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2025 Jun;68(6):660-669. doi: 10.1007/s00103-025-04059-9. Epub 2025 May 6.

FOCUS OF THE RESEARCH AREA "HEALTHCARE-ASSOCIATED INFECTIONS"

Infections with multidrug-resistant bacteria, particularly those acquired in hospitals, are among the leading causes of illness and death worldwide. To reduce the incidence of such infections, researchers are developing novel diagnostic procedures and personalized prognosis methods, as well as innovative preventive and therapeutic interventions, particularly against nosocomial multidrug-resistant pathogens of the ESKAPE group such as *S. aureus* and *P. aeruginosa*.

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NOVEL ANTIBIOTICS

Take that, microbe!

Bacteria live in the most bizarre places. The competition they encounter there is correspondingly challenging—and they keep it at bay with complex defense molecules. Some of their chemical weapons work via previously unknown mechanisms, qualifying them as novel antibiotics.

In Bonn, DZIF researchers elucidated the mode of action of clovibactin. Meanwhile, their colleagues in Saarbrücken successfully modified and tested darobactin in animal models.

TARGET STRUCTURE CAPTURED IN MOLECULAR CAGE

Many soil bacteria grow slowly or not at all under standard laboratory conditions, so they are often overlooked when culturing samples. However, with the iChip technology developed in Boston, researchers are far less likely to overlook these microorganisms. In this approach, a plastic chip is immersed in diluted soil samples, trapping the contained microbes in 380 tiny cavities. After twelve long weeks of cultivation, colonies of *Eleftheria terrae* were discovered and isolated from soil samples in the U.S. The wait proved worthwhile, as the microbe produced two extraordinary defense molecules: teixobactin and clovibactin. In 2015, an international team led by Prof. Tanja Schneider from the University of Bonn elucidated the mode of action of teixobactin. They have now succeeded in doing the same for clovibactin.

The molecule is aptly named after the Greek word "klouvi" (meaning "cage"), as it specifically encloses the pyrophosphate moieties of several bacterial cell wall precursors. Prof. Markus Weingarth, Schneider's cooperation partner in the Netherlands, discovered this using solid-state NMR spectroscopy. Furthermore, once docked, clovibactin forms fiber-like supramolecular structures that tightly enclose the target and cause additional damage. It also triggers the unregulated release of autolysins—enzymes that break down their own cell wall, leading to lysis. According to Schneider, this complex antibiotic strategy will make it difficult for bacteria to develop resistance.

Clovibactin is particularly effective against Gram-positive bacteria, including major clinical pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Mycobacterium tuberculosis*, the causative agent of tuberculosis. For further analysis, the researchers first want to have the substance produced by its natural producers. In addition, an eleven-step total synthesis already exists, which will also enable the development and production of even more effective derivatives.

The team, led by Prof. Tanja Schneider from the Institute of Pharmaceutical Microbiology at the University of Bonn, is working to elucidate the mode of action of the antibiotic "cage molecule" clovibactin. From left to right: Annika Krüger, Prof. Tanja Schneider, Dr. Stefania De Benedetti, and Dr. Fabian Grein.

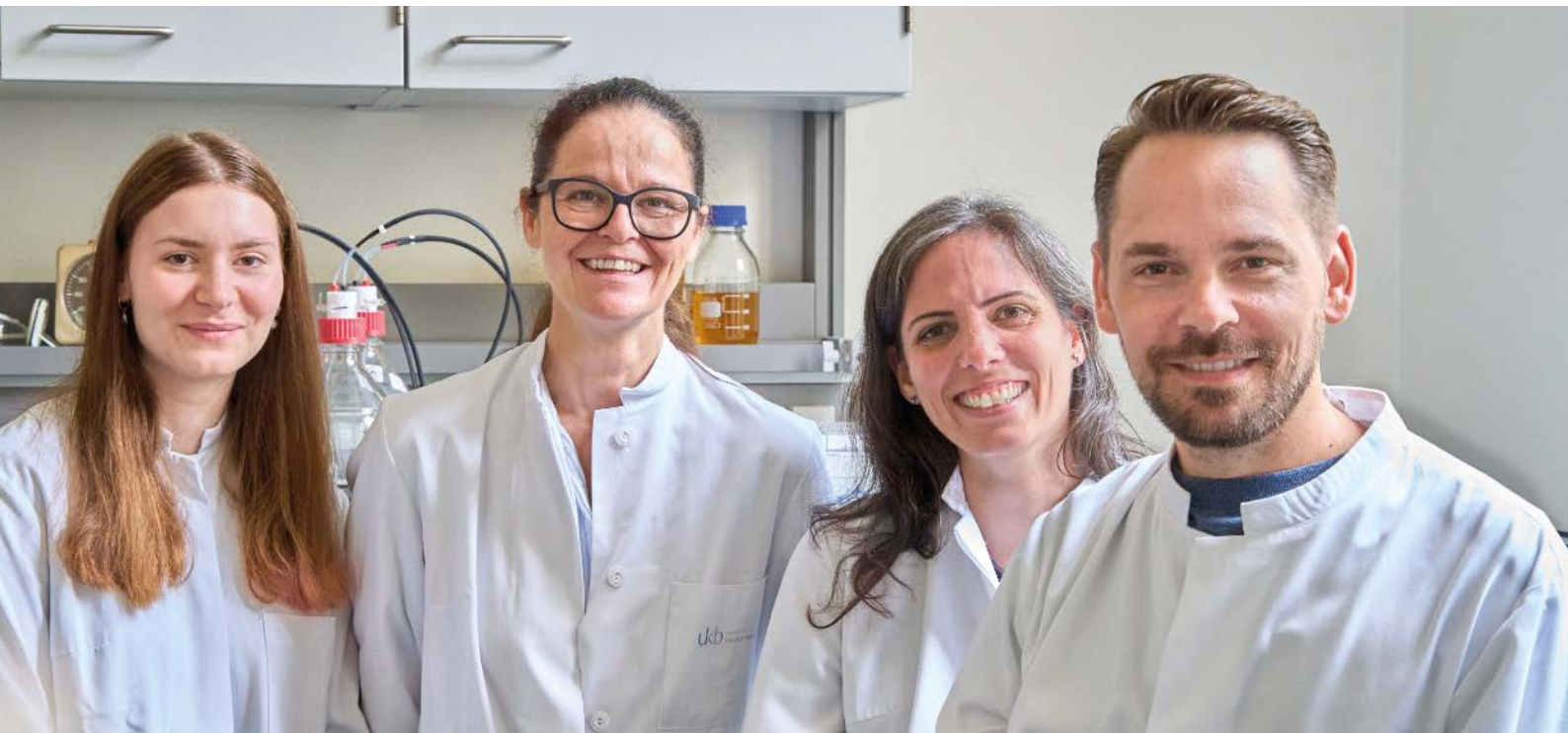

Illustration of the multi-resistant pathogen Pseudomonas aeruginosa*, classified as critical by the World Health Organization. The darobactin derivative D22 has been shown to be highly effective against it.*

HEPTAPEPTIDE TARGETS EASILY ACCESSIBLE CELL WALL PROTEIN

Darobactin was discovered in 2019 in bioluminescent *Photorhabdus* bacteria. These bacteria inhabit the digestive tracts of parasitic nematodes that infect insect larvae. Darobactin, the active agent, is considered a promising candidate for a new, resistance-breaking antibiotic against Gram-negative bacteria. In the laboratory, darobactin has been shown to be effective against pathogens classified as critical by the World Health Organization, such as *Escherichia coli*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, which are often multi-drug-resistant.

Darobactin acts by blocking the BamA protein. Located in the cell wall of Gram-negative bacteria, BamA is essential for the renewal of membrane proteins. The particular advantage of BamA as a target structure is that the protein is located in the outer shell of the bacteria, meaning that a BamA-targeting antibiotic does not first have to penetrate the double membrane of the bacterial cell in order to be effective.

Researchers from DZIF, led by Prof. Rolf Müller and Drs. Andreas Kany, Carsten Seyfert and Jennifer Herrmann of the Helmholtz Institute for Pharmaceutical Research Saarland, optimized the seven-amino-acid peptide darobactin. They expressed the darobactin-encoding gene from *Photorhabdus* in the foreign host *E. coli* and mutated it specifically. The work was supported by *in silico* modeling, in which individual amino acids of the peptide chain were exchanged in a computer model to create additional interaction surfaces with the target structure, BamA. This process generated numerous darobactin derivatives, some of which showed improved activity *in vitro*. The particularly promising derivative D22 was shown to be active in zebrafish and murine models, including urinary tract infections and peritonitis/sepsis. It could also be shown that D22 exhibits significantly improved *in vivo* efficacy compared to natural darobactin A.

PUBLICATIONS ON THE STUDIES

Shukla R et al. An antibiotic from an uncultured bacterium binds to an immutable target. *Cell*. 2023 Sep 14;186(19):4059-4073.e27. doi: 10.1016/j.cell.2023.07.038. Epub 2023 Aug 22.

Seyfert CE et al. New Genetically Engineered Derivatives of Antibacterial Darobactins Underpin Their Potential for Antibiotic Development. *J Med Chem*. 2023 Dec 14;66(23):16330-16341. doi: 10.1021/acs.jmedchem.3c01660. Epub 2023 Nov 21.

Kany AM et al. In Vivo Activity Profiling of Biosynthetic Darobactin D22 against Critical Gram-Negative Pathogens. *ACS Infect Dis*. 2024 Dec 13;10(12):4337-4346. doi: 10.1021/acsinfecdis.4c00687. Epub 2024 Nov 20.

FOCUS OF THE RESEARCH AREA "NOVEL ANTIBIOTICS"

Antibiotic resistance is increasingly becoming a major global challenge. This makes it all the more urgent to close the gap between the discovery of new active substances and their actual therapeutic application. Progress in chemical processes, identification of innovative target molecules, and *in vivo* proof-of-concept studies are crucial in this regard. These approaches are central to the search for new antibiotic producers, such as in microbiomes, and to the optimization of active substance structures.

Coordination

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Helmholtz Centre for Infection Research

Deputy Coordination

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University of Bonn

Prof. Dr. Wolfgang Wohlleben
University of Tübingen

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BIORESOURCES, BIODATA AND DIGITAL HEALTH

Connecting researchers and data across DZIF

Across five DZIF partner sites, experts from the *Bioresources, Biodata and Digital Health (BBD)* infrastructure are working to standardize biomedical and clinical data across institutions. They are interconnecting database systems to improve access to biosamples, biodata, (digital) tools, and methods, and to facilitate the reuse of data.

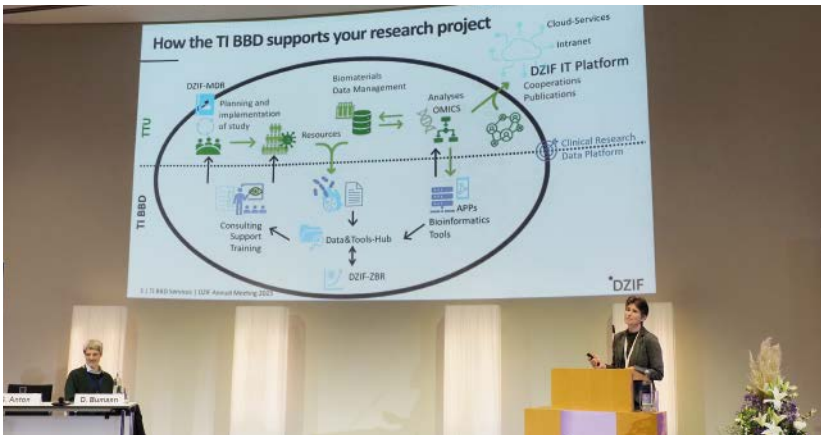
The *BBD* infrastructure, established in 2021, focuses on developing a comprehensive IT and data platform for the DZIF-wide exchange of resources, tools, and information. To this end, BBD experts have worked closely with the DZIF community and engaged intensively with other German Centers for Health Research (DZG) as well as publicly funded consortia in related fields.

DZIF PORTAL FOR COLLABORATION

After several years of intensive development work, the *BBD* successfully launched the DZIF portal in the second half of 2024 and began its promotion within DZIF in 2025. Among other features, the DZIF portal offers functionalities of a classic intranet to facilitate communication and collaboration across DZIF. For example, the portal includes an internal DZIF cloud that enables users to collaborate on documents. It is integrated with the user management system, allowing automatic control of accessibility within user groups, such as research areas and infrastructures. In addition, the *BBD* has developed the Data & Tools Hub (DT-Hub), a searchable resource platform that is also integrated into the DZIF portal. The DZIF DT-Hub includes documents, digital health tools, workflows, and information on registries, studies and databases. The currently integrated resources are already widely used by the DZIF community, with access numbers continuing to increase.

In collaboration with the German Human Genome-Phenome Archive (GHGA), diverse types of molecular data from research projects—including genetic and other omics data—are being consolidated. At the same time, data protection procedures for the associated metadata are being developed. In addition, population-based health and serology data from the Serohub, which contains more than 40,000 participant records, are being integrated. The newly established ability to combine all these sources highlights a core service of the *BBD*: the harmonization and integration of large, heterogeneous datasets from both new and ongoing studies.

The long-term storage of biological samples ensures that research material remains available for future studies. As part of the DZIF biobanking initiative for liquid biological samples, material can be stored centrally and securely—as shown here, for example, in a semi-automatic nitrogen tank.



Dr. Gabriele Anton, then BBD *coordinator, presented the wide range of services offered by the infrastructure's experts at the DZIF Annual Meeting in Hannover in September 2023. Her presentation highlighted how the* BBD *supports researchers across all stages of their projects.*

FAIR RESEARCH DATA THROUGH THE DZIF CORE DATASET

The *BBD* worked extensively on defining DZIF-specific clinical and epidemiological datasets and finalized the DZIF core dataset by the end of 2024. The DZIF core dataset incorporates, among other data items, items from the DZG data set. Once implemented, it will enable the reuse of data collected in DZIF studies both within and beyond DZIF.

In addition, information from DZIF cohorts, long-term and population-based studies, and the already established DZIF Central Biosample Register (DZIF-ZBR) was integrated. By the end of 2024, three tissue collections had been transferred from the DZIF Tissue Bank to the DZIF-ZBR. The DZIF Tissue Bank is one of the first biobanks in Germany to be accredited according to the new biobanking standard DIN EN ISO 20387 and is the only tissue bank for infectious diseases in Germany.

SHARING THE EXPERTISE OF *BBD* EXPERTS

One of the *BBD's* major strengths is its ability to translate methodological work directly into decision-making at both the national and European levels. Its activities have contributed to the development of public health guidelines. With the *BBD's* support, digital health tools and databases have been developed and implemented both nationally and internationally. All DZIF researchers can benefit from this expertise. *BBD* experts support the entire process of conducting epidemiological studies, from study design and the collection and storage of biosamples to data analysis and interpretation. Support starts early, with a structured, questionnaire-based review of FlexFunds applications (see page 8), ensuring targeted support from the outset.

FOCUS ON THE RESEARCH INFRASTRUCTURE "BIORESOURCES, BIODATA AND DIGITAL HEALTH"

The goal of the infrastructure is to standardize biomedical data and make it available in an interoperable format.

THE INFRASTRUCTURE'S SERVICES

3,000 strains in the DZIF Pathogen Bank

In addition to the DZIF Pathogen Bank based at the DSMZ, "EnteroBase" enables web-based genome analyses, and "BacDive" is the world's largest database for standardized information on bacterial strains.

472,450 samples in the Central Biosample Register (DZIF-ZBR)

The *BBD's* metadata repositories provide a comprehensive overview and context for biomedical data. In addition to the DZIF-ZBR, there is also the DZIF Metadata Repository (DZIF-MDR) with structured information following FAIR principles and the clinical core dataset, which supports DZIF researchers in study design and standardizes datasets.

> 2,000,000 tissue samples in the DZIF Tissue Bank

The Heidelberg partner site makes collections of relevant tissue samples available for DZIF research projects. The DZIF biobank for liquid biological samples is located at Helmholtz Munich.

1 portal for over 700 employees

The DZIF portal serves as a central platform connecting researchers from all DZIF partner sites and other centers within the Network of German Centers for Health Research (DZG).

Coordination

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Prof. Dr. Berit Lange
(2024)
Helmholtz Centre for Infection Research

Dr. Gabriele Anton
(2023)
Helmholtz Munich

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CLINICAL TRIAL UNIT

From the laboratory to clinical application

Before new drugs or vaccines are approved, their safety and efficacy are evaluated. To this end, the DZIF operates twelve clinical trial centers specializing in infectious diseases, collectively forming the Clinical Trial Unit infrastructure. The central unit is the Coordinating Office in Cologne, which supports researchers in planning and conducting clinical trials.

The DZIF's *Clinical Trial Unit* provides an infrastructure that enables infectious disease studies to be conducted at a high standard of quality. Clinical trials can be coordinated across sites and implemented across multiple institutions. The infrastructure comprises twelve trial centers at all seven DZIF partner sites. "Our centers across Germany are ready to conduct clinical trials—with a high level of expertise and established structures for a wide variety of infectious diseases. Our expertise ranges from selecting an appropriate study design and calculating costs to the practical implementation of clinical trials," explains Prof. Oliver Cornely as head of the Coordination Office (since 2024: Clinical Trial Office – CTO).

In 2023 and 2024, the CTO supported DZIF researchers with more than 60 individual consultations on over two dozen clinical trial projects, including the translationally relevant "StaphAcute" phase I/IIa trial for the treatment of *Staphylococcus aureus* infections.

Among other things, the CTO supported "StaphAcute" with grant applications and protocol development. As part of the review of FlexFunds applications (see page 8), the CTO also provided 19 individual expert assessments and six summary reports to support the work of the DZIF's Internal Advisory Board.

CLINICAL RESEARCH SETTING STANDARDS

When the COVID-19 pandemic began, the CTO faced a massive challenge—and turned it into an opportunity. To better coordinate clinical trials, the team developed the "European Vaccine Trial Accelerator" (EUVAP), funded by the Federal Ministry of Research, Technology and Space. This initiative gave rise in 2021 to the EU-wide network VACCELERATE, which officially concluded in January 2025 after a four-year run. "With VACCELERATE, the DZIF has created a sustainable foundation for European vaccine research—fast, coordinated, and scientifically robust," says Prof. Cornely.

Prof. Marylyn Addo speaking with a patient at the University Medical Center Hamburg-Eppendorf (UKE). Among other things, a phase Ib clinical trial with the vaccine candidate MVA-MERS-S against Middle East respiratory syndrome (MERS) was conducted at the UKE.

Before the start of a clinical trial, the Clinical Trial Unit *prepares all the necessary steps and actively supports DZIF researchers, for example in selecting suitable study designs and analysis methods.*

By the end of 2024, the VACCELERATE network comprised 525 study sites in 57 countries worldwide and has become an important component of European pandemic preparedness. It connects research groups with study opportunities and builds capacity for large-scale vaccine trials. A particularly successful element is the volunteer registry for vaccine trials, in which over 100,000 people in 24 European countries have now registered. The network and volunteer registry will continue to be operated by the CTO even after the VACCELERATE funding ends.

The *Clinical Trial Unit* was involved in several clinical trials within the VACCELERATE framework alone, including the "AGED study," which was a unique randomized controlled trial of SARS-CoV-2 vaccines in participants over 75 years of age. In addition, the "Auto-COVID-VACC study" was launched, which investigates the immune response following autologous stem cell transplantation and CAR-T cell therapies—another important contribution to the protection of particularly vulnerable patient groups.

ADVANCING CLINICAL TRIAL METHODOLOGY

In early 2024, the CTO organized an expert workshop on adaptive platform trials (APTs) for vaccines. These trial designs had previously been used only in therapeutic settings, but not for disease prevention. Through discussions among approximately 60 European experts from various disciplines, regulatory authorities, ethics committees, the European Commission, and patient advocacy groups, it was concluded that the APT approach is also highly suitable for clinical vaccine research. The results can be found in a white paper (doi: 10.1007/s15010-024-02347-1).

EXPERTISE IN ACTION—COMBINING STRENGTHS WITHIN A SHARED INFRASTRUCTURE

The *Product Development Unit (PDU)* (see pages 38–39) and the CTO support DZIF scientists in bridging the gap between basic research and clinical application. In early 2024, the CTO merged with the *PDU*. This is expected to enable improved support for clinical, regulatory, and product-related aspects from a single source in the future.

FOCUS ON THE RESEARCH INFRASTRUCTURE "CLINICAL TRIAL UNIT"

The local clinical trial centers support DZIF researchers in planning, conducting, and ensuring the quality of clinical trials—from early feasibility studies to multicenter, international trials. The Clinical Trial Office (CTO), as a central unit, provides researchers with specific guidance on, among other things, the preparation of FlexFunds grant applications.

THE "CLINICAL TRIAL UNIT" IN NUMBERS

12 trial centers

The Clinical Trial Office (CTO) at the University Hospital Cologne forwards study inquiries to the affiliated clinical trial centers at seven partner sites. The goal is to conduct clinical trials according to uniformly high-quality standards.

> 100,000 volunteers in the VACCELERATE registry

Coordinated by the CTO, VACCELERATE has become an important component of the EU's pandemic preparedness efforts. In addition, VACCELERATE now offers substantial support to DZIF researchers: In 2023 and 2024, more than 30,000 outreach contacts were made to inform potential participants about studies conducted at DZIF sites, including the clinical trials BOOSTAVAC, TherVacB and PANHPVAX. The Phase Ib trial of the vaccine candidate MVA-MERS-S also benefited significantly from collaboration with the volunteer registry (see pages 14-15).

Coordination

Prof. Dr. Oliver Cornely
University Hospital Cologne

You can find more information at

DZIF ACADEMY

Support builds the future

Since it was founded, the DZIF Academy has supported more than 650 young researchers in their career development—with lasting impact: About 90 percent of them have remained in the field of infectious disease research, and roughly 40 percent now lead their own research groups. Nearly a quarter have completed their habilitation, and six percent have since taken on a professorship.

In 2023 and 2024, the *DZIF Academy's* activities were further expanded: A cross-partner site mentoring program was launched, and by the end of 2024, a tailored short-term training program for early-career scientists of African Partner Institutions was introduced. The established programs continued to see strong demand—a sign of their appeal and effectiveness.

Today, the *DZIF Academy* is a vibrant network for young researchers at the DZIF. It combines individual support with structured talent development—both nationally and internationally, in clinical and basic research. This helps ensure that translational research is not only excellent but also remains sustainable for the future.

TAILORED SUPPORT FOR DIVERSE NEEDS

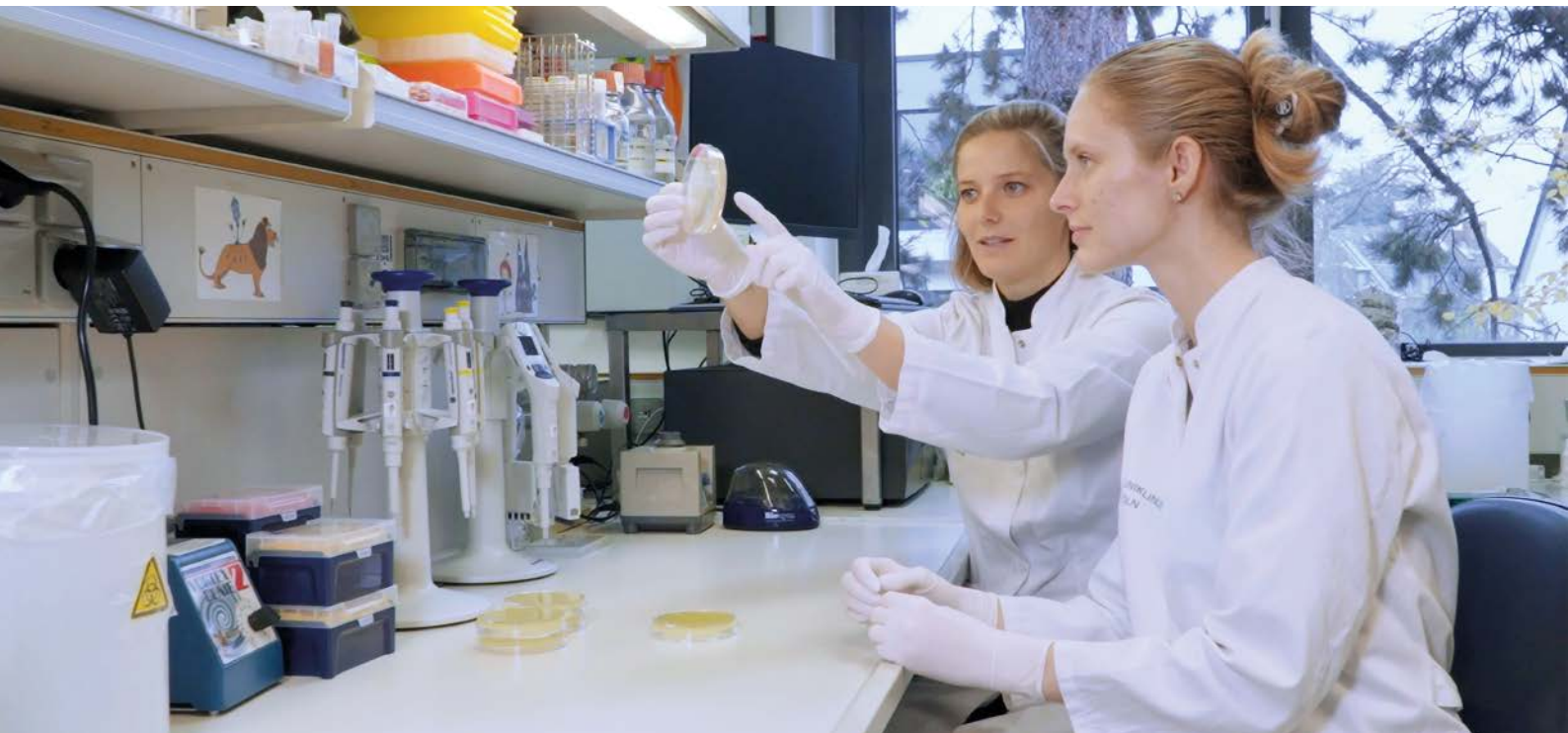
Regular Autumn and Summer Schools, workshops, and laboratory rotation grants foster exchange, generate new ideas, and promote methodological diversity. Travel grants support early-career researchers in presenting their research findings at national and international workshops and conferences.

Since 2023, the *DZIF Academy* has offered a structured mentoring program that supports young researchers across partner sites and disciplines. The program is complemented by coaching and training sessions designed to strengthen both professional and personal skills.

FOCUS ON TRANSLATION

With the Advanced Clinician Scientist Program launched in 2021, the *DZIF Academy* aims to pave the way for outstanding, research-oriented physicians to take on future leadership roles or professorships. A 50 percent reduction in clinical duties enables fellows to advance their research projects and effectively balance responsibilities in research, teaching, and patient care within academic medicine. In this way, innovative ideas and methods are incorporated into translational infection research, and new findings reach clinical practice more

Working in phage research as a physician: DZIF Academy *fellow Dr. Annika Claßen (in the background) with colleague Vivien Persy in a laboratory at the University Hospital Cologne. A full-time fellowship for physicians through the* DZIF Academy *allows her to focus entirely on her research.*



During the 2024 Autumn School in Lübeck, DZIF Academy *Coordinator Prof. Jan Rupp emphasized how important the* DZIF Academy's *regular training sessions and workshops are for fostering exchange and collaboration among early-career researchers.*

quickly. At the same time, the grant recipients ensure continuity by training the next generation of clinical scientists. By the end of 2024, six Advanced Clinician Scientists had been funded at four DZIF partner sites and in three research areas—an important contribution to building bridges between the laboratory, the clinic, and patients.

INTERNATIONAL EXPANSION—SHORT-TERM TRAINING PROGRAM FOR EARLY CAREER SCIENTISTS OF DZIF AFRICAN PARTNER INSTITUTIONS

In collaboration with the *Malaria and Neglected Tropical Diseases* research area, the *DZIF Academy* launched a short-term training program in late 2024 that creates new opportunities for young African researchers. It enhances their visibility in the international research community, provides targeted additional skills, and facilitates access to collaborations within the DZIF. The flexible design of the modules allows individual interests and needs to be addressed. This is a key component in supporting the development of independent research profiles and building successful long-term career paths.

DRIVING COLLABORATION WITHIN THE GERMAN CENTERS FOR HEALTH RESEARCH (DZG)

The *DZIF Academy* serves as a driving force far beyond the DZIF's boundaries. Dr. Nadja Käding, project manager of the *DZIF Academy*, took over as spokesperson for the DZG working group Promotion of Young Scientists in 2023: "Our goal is to strengthen networking among young researchers across the individual centers. This is essential to creating a vibrant, interdisciplinary environment that strengthens health research in Germany in a sustainable way," says Käding. Newly developed formats such as the DZG Science & Career Days, which took place for the second time at the end of 2024 and bring together young researchers from all eight DZG centers for two days each year, help achieve this.

FOCUS OF THE RESEARCH INFRASTRUCTURE "DZIF ACADEMY"

Supporting early-career researchers is a cornerstone of the German Center for Infection Research. Through the *DZIF Academy*, young scientists and clinicians are supported at various stages of their careers.

OVERVIEW OF CAREER DEVELOPMENT PROGRAMS

172 Programs for Medical Students

Support for up to six medical students per DZIF partner site per year.

33 Clinical Leave Programs

Leave of absence of up to 18 months for physicians in training to work at a DZIF partner site e. g., to carry out a research project.

7 MD/PhD Programs

Three-year full-time grants enabling trained physicians to earn an additional doctoral degree (Dr. rer. nat., PhD, or equivalent).

11 Advanced Clinician Scientist Programs

Funding for scientifically qualified medical specialists through partial release from clinical duties to pave the way for leadership roles and professorships.

24 Maternity Leave Programs

Support for female scientists returning to infectious disease research after maternity leave or parental leave.

The figures indicate the total number of individuals who received funding in the respective programs during the 2023/24 reporting period. During the same period, eleven Lab Rotations and 16 Travel Grants were awarded.

Coordination

Prof. Dr. Jan Rupp
Universität zu Lübeck

You can find more information at

PRODUCT DEVELOPMENT UNIT

Accelerating translation—from concept to product

The DZIF *Product Development Unit (PDU)* supports researchers from preclinical stages through early clinical trials and provides the specific expertise required for the successful development of vaccines, therapeutics, and diagnostics—expertise that is not always readily available in academic settings.

There remain significant unmet medical needs in the treatment of viral, bacterial, and parasitic infectious diseases. Infectious diseases continue to pose a major global health challenge. Through the *PDU*, the DZIF offers a structured framework that helps translate research findings into product candidates for patients by creating interfaces between academia, industry, and regulatory authorities, thereby enabling early and targeted support for innovative approaches. The *PDU* not only provides advisory services but also takes on active project management, supports grant applications, and facilitates access to regulatory expertise.

"The demand for support from the *PDU* has increased significantly in recent years—not least during the COVID-19 pandemic, when several vaccine and antibody projects were supported through to clinical development," says Dr. Klaus Schwamborn, current coordinator of the *PDU* and head of vaccine development in the DZIF's Translational Project Management Office.

OSRA AND TPMO AS KEY FACTORS FOR SUCCESSFUL TRANSLATION

The *PDU* consists of closely collaborating teams: the Office for Scientific and Regulatory Advice (OSRA) and the Translational Project Management Office (TPMO).

The OSRA, based at the Paul-Ehrlich-Institut (PEI)—the Federal Institute for Vaccines and Biomedicines—and at the Federal Institute for Drugs and Medical Devices (BfArM), provides researchers with priority access to scientific and regulatory advice. "This enables DZIF projects to benefit from up-to-date regulatory expertise, the flexible application of frameworks for drugs and medical devices, and the international networks of Germany's federal regulatory institutes responsible for medicinal products," summarizes Prof. Klaus Cichutek, former President of the PEI.

The TPMO contributes its industry experience to the DZIF. In drug and vaccine development, it develops tailored

Participants of a workshop on the Bridging Topics Antibody-Based Therapies *and* Vaccines*, including members of the* PDU *team. The* PDU *team is also organizing workshops to share knowledge on regulatory issues and product development strategies.*

Precision from the outset: Regulatory requirements are considered early in the analysis of manufacturing samples and the selection of analytical methods to ensure quality, traceability, and safety in drug development.

development plans for research projects, oversees their implementation step by step, and ensures that external experts are involved when needed—for example, specialized research organizations or expert groups that provide guidance and support.

THE CLINICAL TRIAL OFFICE—ADDED VALUE FOR TRANSLATION AND CLINICAL TRIALS

To leverage synergies even more effectively, the Clinical Trial Office (CTO) team was integrated into the *PDU* in 2024. Based at the University Hospital Cologne, the CTO contributes methodological expertise in the design and conduct of clinical trials. This allows aspects such as patient recruitment and the appropriate selection of endpoints in clinical trials to be incorporated into development planning at an even earlier stage (see pages 34–35).

Through workshops, consultations, and training sessions on regulatory issues and product development strategies, the *PDU* also helps strengthen expertise and awareness throughout the DZIF network and in other German Centers for Health Research.

FOCUS ON FLAGSHIP PROJECTS

The *PDU* has been and continues to be involved in many major DZIF flagship projects—from preclinical development to clinical trials of vaccine and therapeutic candidates. These include the vaccine candidates TherVacB and EBV-VLP, the antibiotic BTZ-043, and the therapeutic candidates HY-133, CorA, and StaphAcute (see pages 10–13). Annual meetings involving external industry and regulatory experts ensure continuous evaluation of development progress.

In addition, the *PDU* supports international partnerships: It acts as an accelerator within the global CARB-X network to support the development of novel antibiotics and, together with partners, co-founded the European incubator INCATE for antimicrobial technologies.

FOCUS OF THE RESEARCH INFRASTRUCTURE "PRODUCT DEVELOPMENT UNIT"

With its integrated structure and regulatory expertise, coupled with industrial experience in pharmaceutical and biological product development, the *PDU* is today a key driver of translational infection research at the DZIF.

THE "PDU" DRIVES INNOVATION AND TRANSLATION

49 Regulatory consultations

The OSRA plays an important role in facilitating coordination between researchers and drug regulatory authorities and agencies. Regulatory consultations are a key step on the path from research to application. The *PDU* experts from the federal institutes serve on committees and working groups, including at the European Medicines Agency (EMA) and in global regulatory networks such as the WHO.

2 Spin-offs

In 2023/24, the TPMO was involved in two company spin-offs: the spin-off EBViously from Helmholtz Munich and the spin-off MyxoTech from the Helmholtz Centre for Infection Research.

Coordination

Dr. Klaus Schwamborn
(since April 2025)
DZIF e. V.

Prof. Dr. Oliver Cornely
(2024 to April 2025)
University Hospital Cologne

Prof. Dr. Klaus Cichutek
(2023)
Former President of the Paul-Ehrlich-Institut

You can find more information at

DZIF partner sites

Hamburg - Lübeck - Borstel - Riems

- Bernhard Nocht Institute for Tropical Medicine (BNITM)
- Friedrich-Loeffler-Institut (FLI)
- Leibniz Institute of Virology (LIV)
- Research Center Borstel, Leibniz Lung Center (FZB)
- Universität zu Lübeck (UzL)
- University of Hamburg (UHH)
- University Medical Center Hamburg-Eppendorf (UKE)

Hannover - Braunschweig

- Hannover Medical School (MHH)
- Helmholtz Centre for Infection Research (HZI)
- Leibniz Institute DSMZ–German Collection of Microorganisms and Cell Cultures (DSMZ)
- Robert Koch Institute (RKI)
- Technische Universität Braunschweig (TU BS)
- TWINCORE - Centre for Experimental and Clinical Infection Research (TC)
- University of Veterinary Medicine Hannover (TiHo)

Bonn - Köln

- Federal Institute for Drugs and Medical Devices (BfArM)
- University of Bonn (Uni BN)
- University of Cologne (Uni K)
- University Hospital Bonn (UK BN)
- University Hospital Cologne (UK K)

Gießen - Marburg - Langen

- Justus Liebig University Giessen (JLU)
- Marburg University (Uni MR)
- Technische Hochschule Mittelhessen (THM)
- Paul-Ehrlich-Institut (PEI)

Heidelberg

- German Cancer Research Center (DKFZ)
- Heidelberg University (Uni HD)
- Heidelberg University Hospital (UK HD)

Tübingen

- Max Planck Institute for Biology Tübingen (MPI B)
- University of Tübingen (Uni TÜ)
- University Hospital Tübingen (UK TÜ)

München

- Bundeswehr Institute of Microbiology (IMB)
- Helmholtz Munich (HMGU)
- LMU University Hospital Munich (KUM)
- Ludwig-Maximilians-Universität München (LMU)
- Technical University of Munich (TUM)
- TUM University Hospital (TUM MRI)

Research Areas

- Emerging Infections
- Tuberculosis
- Malaria and Neglected Tropical Diseases
- HIV
- Hepatitis
- Community-Acquired Infections at Mucosal Interfaces
- Infections of the Immunocompromised Host
- Healthcare-Associated Infections
- Novel Antibiotics

Infrastructures

- Bioresources, Biodata and Digital Health
- Clinical Trial Unit
- Product Development Unit
- DZIF Academy

DZIF partner sites and member institutions

DZIF partner sites and member institutions

The DZIF unites 35 member institutions across seven partner sites in Germany, including universities, university hospitals, and non-university research institutions, thereby furnishing researchers with access to the entirety of available infrastructure. Each partner site contributes significantly to the success of the translational research program by providing expertise, resources, and equipment. In addition, the DZIF enters into associated partnerships with other institutions to respond flexibly to current issues and integrate specific expertise. The DZIF also maintains international collaborations, is an established partner in national, European, and global networks on infectious diseases and conducts translational research and clinical trials with African partners (see also pages 48–51).

PARTNER SITES

Hamburg – Lübeck – Borstel – Riems (HH – HL – BO – RI)

RESEARCH FOCUS

- Novel antiviral therapies
- Novel antibacterial & antiparasitic therapies
- Vaccine studies
- Surveillance of antibiotic resistance
- Epidemic and pandemic preparedness

FLAGSHIP PROJECTS

- Anti-tuberculosis drug – BTZ-043
- Broadly neutralizing hepatitis E virus antibodies – HEVbnAb
- MERS coronavirus vaccine development – MVA-MERS-S
- Therapeutic hepatitis B vaccine – TherVacB

DZIF PROFESSORSHIPS AND JUNIOR RESEARCH/WORKING GROUPS (JRG/WG)

- **Prof. Dr. Ralph Holl** "Medicinal Chemistry of Novel Anti-Infective Agents," UHH
- **Prof. Dr. Christoph Lange** "Eastern European Partner Institution," UzL/FZB
- **Prof. Dr. Stefan Niemann** "Molecular and Experimental Mycobacteriology," UzL/FZB
- **Prof. Dr. Esther Schnettler** "Surveillance of Arthropods and Arthropod-Borne Pathogens," BNITM
- **Dr. Beatriz Escudero Pérez** (BNITM)/ **Dr. Toni Luise Meister** (UKE) JRG "Clinical Management and Epidemiology of Emerging Infections," BNITM/UKE

Partner Site Speaker
Prof. Dr. Julian Schulze zur Wiesch
University Medical Center Hamburg-Eppendorf

Deputy Partner Site Speaker
Prof. Dr. Esther Schnettler
Bernhard Nocht Institute for Tropical Medicine

The HH – HL – BO – RI site brings together seven university and non-university institutions with complementary expertise and infrastructure. The scientists at the site are active in eight of the nine DZIF research areas and coordinate or co-coordinate five of them: *Healthcare-Associated Infections*, *HIV*, *Malaria and Neglected Tropical Diseases*, *Emerging Infections*, and *Tuberculosis*. The site also heads the DZIF Academy, which promotes young scientists. Strong international collaborations—especially with the DZIF's African partner institutions—as well as the five DZIF professorships and junior research groups ensure close national and international networking.

HH – HL – BO – RI is involved in five DZIF bridging topics and coordinates three of them: *Diagnostics*, *Vaccines*, and *Cell and Gene Therapies of Infectious Diseases*. The site has excellent infrastructure for the development and evaluation of new vaccines and preventive and therapeutic anti-infectives. Unique *in vivo* and *in vitro* models for bacterial and viral pathogens, some of which are located in high-security laboratories with BSL-3 and BSL-4 safety levels, make it a central hub for European infection research.

Humanized mouse models at the UKE and BNITM are being used to investigate new active agents against hepatitis viruses and the efficacy of vaccines against hemorrhagic fever viruses. The DZIF working group "Humanized Mouse Platform" at the site made an important contribution to the evaluation of the hepatitis B/hepatitis D virus inhibitor bulevirtide (trade name Hepcludex®), a flagship project of the DZIF (see page 23). In addition, the researchers are involved in surveillance of pathogens, developing diagnostic procedures, and implementing new measures in regions with a high disease burden.

PARTNER SITES

Hannover – Braunschweig (H – BS)

RESEARCH FOCUS

- Antibacterial and antiviral therapies
- Vaccine development
- Transplant Cohort

FLAGSHIP PROJECTS

- Antibiotic corallopyronin A
- Broadly neutralizing hepatitis E virus antibodies – HEVbnAb
- Small-molecule inhibitors against *Staphylococcus aureus* – alpha-toxin inhibitor
- Phage therapy against *Enterococcus faecium* – EVREA-Phage
- Therapeutic hepatitis B vaccine – TherVacB

DZIF PROFESSORSHIPS AND JUNIOR RESEARCH/WORKING GROUPS (JRG/WG)

- **Prof. Dr. Mark Brönstrup** "Chemical Biology", HZI
- **Prof. Dr. Markus Cornberg** "Infectious Diseases in Hepatology", MHH
- **Prof. Dr. Daniel Depledge** "Systems Virology", MHH
- **Prof. Dr. Guntram Graßl** "Medical Microbiomics", MHH
- **Prof. Dr. Ulrich Nübel** "Functional Genomics of Novel Microbial Producers", DSMZ
- **Prof. Dr. Alexander Titz** "Medicinal Chemistry with Focus on Natural Products", HZI/HIPS

Partner Site Speaker
Prof. Dr. Mark Brönstrup
Helmholtz Centre for Infection Research

Deputy Partner Site Speaker
Prof. Dr. Asisa Volz
University of Veterinary Medicine Hannover

At the H – BS partner site, scientists and clinicians from seven member institutions—including six DZIF professorships—coordinate several DZIF research areas and infrastructures, such as bioinformatics, epidemiology, and pathogen repositories. They also contribute to all Bridging Topics of the DZIF.

The site combines natural product research and medicinal chemistry with expertise in the biology of pathogens to develop novel antibiotics and antiviral agents. Bioinformatics, genetic, and chemical methods are used to identify and optimize anti-infective compounds. The Pharmacokinetics and Pharmacodynamics Department at the HZI evaluates the pharmacological properties of drug candidates *in vivo* and supports target identification and compound optimization in DZIF projects.

The H – BS partner site is closely involved in the DZIF flagship project on corallopyronin A (see page 12) and in five of seven DZIF projects on small molecules. These include cystobactamides, a promising class of natural compounds with broad-spectrum activity.

The site also has strong expertise in epidemiology and in the development of therapies and vaccines against various hepatitis viruses. It played a central role in the evaluation of the antiviral drug bulevirtide (see page 23), which has been approved in the EU since 2023 as Hepcludex® for the treatment of hepatitis D.

Researchers at the HZI are also involved in studies on the decolonization of multidrug-resistant Gram-negative bacteria in the gut using fecal microbiota transfer. At the MHH, clinicians treat immunosuppressed patients with infectious complications. These patients play an important role in the DZIF Transplant Cohort and support translational research into the mechanisms underlying increased susceptibility to infection.

PARTNER SITES

Bonn – Köln (BN – K)

RESEARCH FOCUS

- Cohorts and registries
- Cologne Microbiota Bank
- Novel antibiotics
- Antibody-based therapy and diagnosis
- Neglected tropical diseases

FLAGSHIP PROJECTS

- Antibiotic corallopyronin A
- Monoclonal antibodies targeting *Pseudomonas aeruginosa* – PANTIPA
- Phage therapy against *Enterococcus faecium* – EVREA-Phage

DZIF PROFESSORSHIPS AND JUNIOR RESEARCH/WORKING GROUPS (JRG/WG)

- **Prof. Dr. Aleksandra Pandyra**
  "Translational Immunology," Uni BN
- **Prof. Dr. Jörg Janne Vehreschild**
  "Translational Cohorts in HIV Research," UK K
- **Prof. Dr. Christoph Ernst**
  "Antimicrobial Resistance," UK K
- **Prof. Dr. Marc Hübner**
  "Translational Microbiology," Uni BN
- **Dr. Fabian Grein**
  JRG "Bacterial Interference," Uni BN
- **Dr. Ute Klarmann-Schulz**
  JRG "Preclinical and Clinical Development of Anti-Infectives," Uni BN
- **Dr. Alexander Klimka**
  WG "Antibacterial Vaccine Development," Uni K

Partner Site Speaker
Prof. Dr. Oliver Cornely
University Hospital Cologne

Deputy Partner Site Speaker
Prof. Dr. Achim Hörauf
University Hospital Bonn

The BN – K partner site brings together the University of Bonn, the University Hospital Bonn, the University of Cologne, the University Hospital Cologne, and the Federal Institute for Drugs and Medical Devices (BfArM). The BfArM is Germany's federal regulatory authority for medicinal products and also conducts research as part of the federal government.

Infection research at the BN – K site is integral to several DZIF research areas, in particular *Healthcare-Associated Infections*, *HIV*, *Infections of the Immunocompromised Host*, *Malaria and Neglected Tropical Diseases*, and *Novel Antibiotics*. The latter also includes the development of novel antifungal drugs. In addition, BN – K acts as a central resource provider for all DZIF partner sites, offering digital infrastructure, cohorts, and surveillance platforms.

The Office for Scientific and Regulatory Advice (OSRA), based at the BfArM, offers scientific and regulatory support. The Clinical Trial Office (CTO) at the University Hospital Cologne contributes methodological expertise in the design and conduct of clinical trials. Both OSRA and CTO form part of the DZIF *Product Development Unit*.

The importance of the site within the DZIF network is highlighted by four DZIF professorships and additional researchers who lead or co-lead research areas. They are also involved in the Bridging Topics *Antibody-Based Therapies* and *Microbiome*, as well as in the flagship project corallopyronin A (see page 12).

Key projects include "Antibody-based therapeutics and diagnostics," "PAACT—Precision access to antibiotic compounds and targets," the "BSL-3 platform for drug research against *Mycobacterium tuberculosis*," the "Cologne Microbiota Bank (CMB)," "Molecular diagnostics and drug development for neglected tropical diseases," and the "Clinical microbiology platform for surveillance of multidrug-resistant organisms (MDRO)."

PARTNER SITES

Gießen – Marburg – Langen (GI – MR – LA)

RESEARCH FOCUS

- Development of emergency vaccines
- Cohort studies on infections caused by multidrug-resistant pathogens
- Surveillance of multidrug-resistant organisms
- Animal models for the study of highly pathogenic viruses (BSL-3/4)

FLAGSHIP PROJECTS

- MERS coronavirus vaccine development – MVA-MERS-S

DZIF PROFESSORSHIPS AND JUNIOR RESEARCH/WORKING GROUPS (JRG/WG)

- **Prof. Dr. Volker Winstel**
  "Translational Microbiology and Immunopathology of Infections," JLU

Partner Site Speaker
Prof. Dr. Stephan Becker
Marburg University

Deputy Partner Site Speaker
Prof. Dr. Susanne Herold
Justus Liebig University Gießen

The DZIF partner site GI – MR – LA comprises the Justus Liebig University Giessen (JLU), Marburg University (Uni MR), the Technische Hochschule Mittelhessen – University of Applied Sciences (THM) as well as the Paul-Ehrlich-Institut (PEI), the German Federal Institute for Vaccines and Biomedicines, in Langen.

Researchers at the site coordinate the DZIF research areas *Emerging Infections* and *Healthcare-Associated Infections*, addressing both emerging viral diseases and infections caused by multidrug-resistant bacteria. They also contribute to the research areas *Hepatitis* and *Novel Antibiotics*. The site is equipped to study a wide range of highly pathogenic viruses at biosafety levels up to BSL-4 for advanced translational research and to respond rapidly to viral outbreaks when needed. The JLU Faculty of Veterinary Medicine supports research on zoonotic pathogens in the One Health context.

The site hosts the National Reference Center for Hepatitis B and D Viruses, which contributes to the *Hepatitis* research area. Through the Office for Scientific and Regulatory Advice (OSRA), which is part of the DZIF *Product Development Unit*, GI – MR – LA provides regulatory guidance and expertise for DZIF-developed products such as vaccines, monoclonal antibodies, and therapeutic biopharmaceuticals, as well as *in vitro* diagnostics.

Close collaboration with other DZIF sites is reflected in the site's leading role in cross-site projects and its key contributions to the Bridging Topics *Antibody-Based Therapies*, *Diagnostics*, *Microbiome*, and *Vaccines*.

PARTNER SITES

Heidelberg (HD)

RESEARCH FOCUS

- Antiviral therapies
- Vaccine development
- Diagnostics and operational research
- Transplant Cohort

FLAGSHIP PROJECTS

- Anti-hepatitis D drug bulevirtide / Hepcludex®

DZIF PROFESSORSHIPS AND JUNIOR RESEARCH/WORKING GROUPS (JRG/WG)

- **Prof. Dr. Dr. h.c. Stephan Urban**
  "Translational Virology," UK HD
- **Prof. Dr. Victoria Ingham**
  JRG "From Bench to Bedside: The Impact of Insecticide Resistance on Vector Competence in the Major Malaria Vector *Anopheles coluzzii*," UK HD
- **Dr. Marina Lusic**
  "Preclinical HIV-1 Research," UK HD
- **PD Dr. Dr. Angelika Riemer**
  WG "Molecular Vaccine Design," DKFZ

Partner Site Speaker
Prof. Dr. Dr. h.c. Stephan Urban
Heidelberg University Hospital

Deputy Partner Site Speaker
Prof. Dr. Claudia Denkinger
Heidelberg University Hospital

The DZIF's Heidelberg partner site brings together the closely collaborating institutions associated with Heidelberg University (Uni HD), including its two medical faculties in Heidelberg and Mannheim, Heidelberg University Hospital (UK HD), and the German Cancer Research Center (DKFZ). Both Uni HD and the DKFZ have long been engaged in research on infectious diseases and have made significant contributions to the DZIF's preclinical and clinical research. These include the development of novel drugs and the study of their mechanisms of action, new vaccine approaches, innovative diagnostics, and advances in implementation science.

The site contributes to seven of the nine DZIF research areas and co-coordinates two of them: *Hepatitis* and *Infections of the Immunocompromised Host*. Heidelberg also provides key infrastructure for the DZIF. This includes the DZIF Tissue Bank, which offers unique samples and expertise as part of one of the first accredited biobanks in Germany; the Heidelberg First-In-Human (FIH) unit for early clinical trials; and advanced imaging techniques, including animal imaging under BSL-2 and BSL-3 conditions. Experts at the site are involved in five Bridging Topics—including the site-initiated topic *Global Health and Climate Change*—and play a key role in the DZIF Transplant Cohort.

Notable developments at the site include bulevirtide (Hepcludex®), the first approved drug for hepatitis D; a therapeutic vaccine against human papillomaviruses (HPV); a potential malaria vaccine using attenuated parasites; new genetic approaches to HIV therapy; and innovative tuberculosis diagnostics.

PARTNER SITES

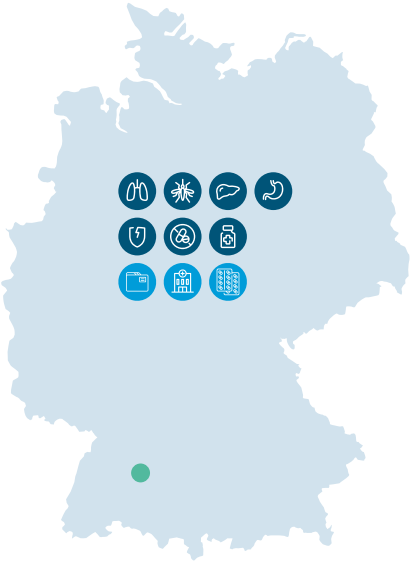
Tübingen (TÜ)

RESEARCH FOCUS

- Malaria vaccine development
- *Salmonella* pathoblockers
- Novel anti-infective agents
- ESKAPE cohort studies

FLAGSHIP PROJECTS

- Phage lysin HY-133 against *Staphylococcus aureus*



DZIF PROFESSORSHIPS AND JUNIOR RESEARCH/WORKING GROUPS (JRG/WG)

- **Prof. Dr. Ayola Akim Adegnika**
  "Clinical Research Group," Uni TÜ and Centre de Recherches Médicales de Lambaréné (CERMEL), Gabon
- **Prof. Dr. Sabine Bélard**
  "Clinical Trial Platform," Uni TÜ
- **Prof. Dr. Nadine Ziemert**
  "Applied Natural Products Genome Mining," Uni TÜ
- **Prof. Dr. Andreas Dräger**
  JRG "Computational Systems Biology of Infections and Antimicrobial Resistant Pathogens," Uni TÜ
- **Dr. Thales Kronenberger**
  JRG "Computational Drug Development," UK TÜ
- **Prof. Dr. Simon Heilbronner**
  JRG "Healthcare-Associated Bacterial Pathogens," LMU

Partner Site Speaker
Prof. Dr. Peter Kremsner
University Hospital Tübingen

Deputy Partner Site Speaker
Prof. Dr. Heike Brötz-Oesterhelt
University of Tübingen

The Interfaculty Institute of Microbiology and Infectious Diseases in Tübingen is at the core of the Cluster of Excellence "Controlling Microbes to Fight Infections", which focuses on antibacterial agents. DZIF-funded clinical trials are conducted both at the Institute of Tropical Medicine and at international research centers coordinated from Tübingen. These include the Centre de Recherches Médicales de Lambaréné (CERMEL) in Gabon, one of the DZIF's African Partner Institutions, as well as centers in the Republic of Congo (Fondation Congolaise pour la Recherche Médicale, FCRM) and in Vietnam (Vietnamese-German Center for Medical Research, VGCARE). Their directors are affiliated with the University of Tübingen.

Pioneering studies on the use of bacteria to protect against pathogens on mucosal surfaces inspired the Bridging Topic *Microbiome*. Natural product research in Tübingen is a key interdisciplinary focus with a long-standing tradition and strong international visibility. The DZIF flagship project "Phage lysin HY-133 against *Staphylococcus aureus*" (see also pages 12 and 29), led by researchers in Tübingen, is based on a public-private partnership with the company HyPharm and the University of Greifswald. The controlled malaria infection model established at the site has become an international standard for malaria infection studies. It is used to test new drugs and promising vaccine candidates, employing radioactively, chemically, and genetically attenuated sporozoites.

Another project supported by the *DZIF Product Development Unit* focuses on pathogenicity blockers against microbiome-associated bacterial infections. All four sites of the *Novel Antibiotics* research area, as well as scientists from the *Healthcare-Associated Infections* and *Community-Acquired Infections at Mucosal Interfaces* research areas, are involved in a project to identify and characterize antibacterial compounds. The goal is to ensure a continuous stream of new lead compound candidates for the DZIF's early-stage antibiotic pipeline.

PARTNER SITES

München (M)

RESEARCH FOCUS

- Vaccine development
- Immunotherapies
- Antiviral therapies
- Transplant Cohort
- National and international clinical trials

FLAGSHIP PROJECTS

- Anti-tuberculosis drug – BTZ-043
- EBV vaccine development
- MERS coronavirus vaccine development – MVA-MERS-S
- Therapeutic hepatitis B vaccine – TherVacB

DZIF PROFESSORSHIPS AND JUNIOR RESEARCH/WORKING GROUPS (JRG/WG)

- **Prof. Dr. Michael Hoelscher** "International Clinical Trials Unit (iCTU)," KUM
- **Prof. Dr. Andreas Pichlmair** "Immune Pathology of Viral Infection," TUM
- **Dr. Elvira D'Ippolito** JRG "Non-viral Editing for the Manufacturing of TCR-T Cells to Prevent Virus-Related Diseases in Immunocompromised Patients," TUM
- **Dr. Andreas Moosmann** WG "Host Control of Viral Latency and Reactivation," KUM
- **Dr. Riccardo Vasapolli** JRG "Gastrointestinal Infections," KUM

Partner Site Speaker
Prof. Dr. Michael Hoelscher
LMU University Hospital Munich

Deputy Partner Site Speaker
Prof. Dr. Ulrike Protzer
Technical University of Munich, Helmholtz Munich

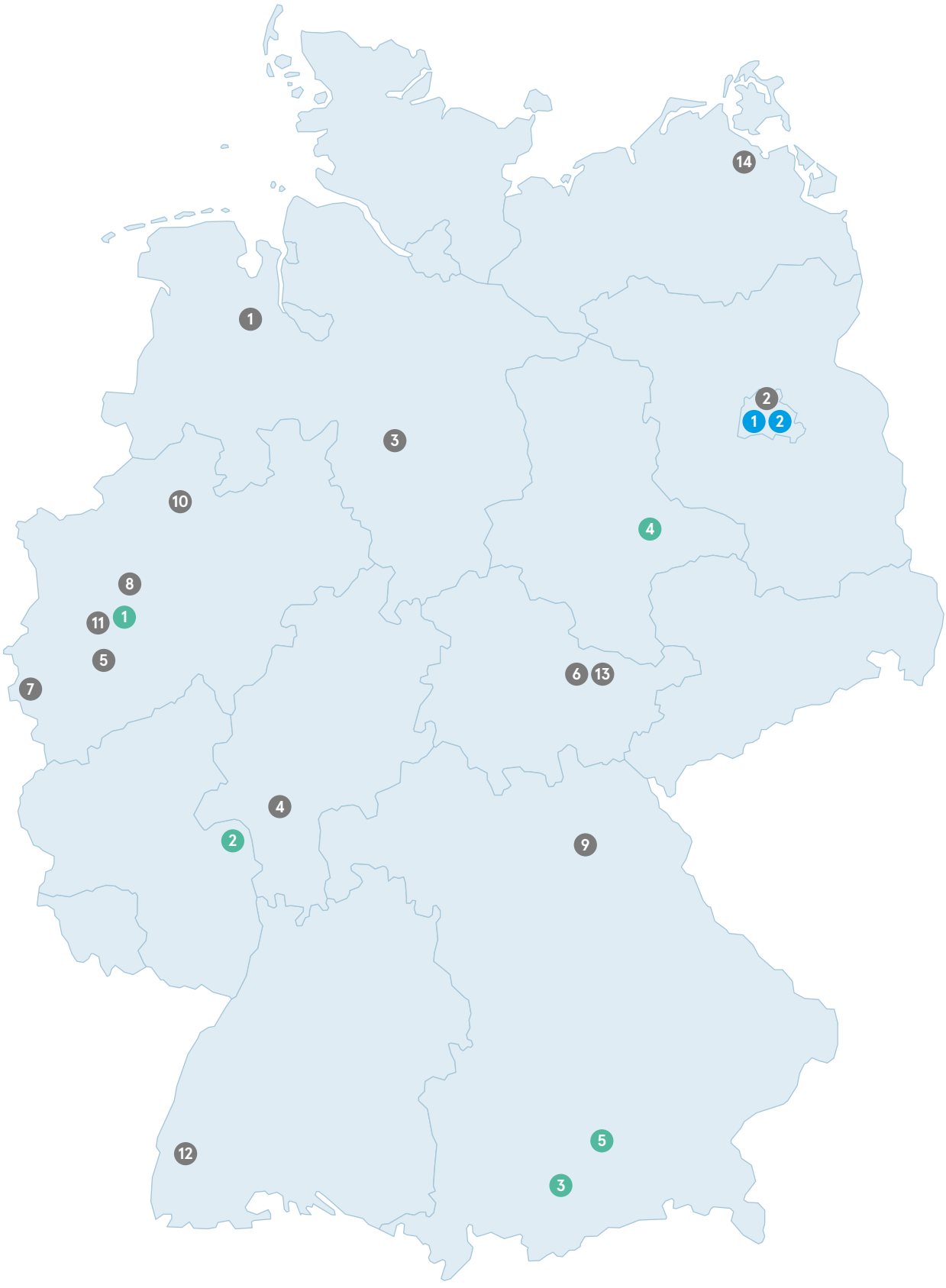
At the partner site München, six institutions pool their expertise in infectious disease and immunology research. The goal is to understand immune mechanisms and host-pathogen interactions in order to develop new approaches for the diagnosis, prevention, and treatment of infectious diseases. The site operates platforms for the development and production of vector-, nucleic acid-, and protein-based vaccines to address emerging infections and antibiotic resistance. State-of-the-art BSL-3 facilities enable proof-of-concept studies in animal models. A pipeline of preclinical developments targets infections caused by the Epstein-Barr virus (EBV), mycobacteria, hepatitis B and E viruses, coronaviruses and noroviruses, *Helicobacter pylori*, as well as antibiotic resistance. A special focus is on emerging infections.

Vaccines against hepatitis B and the Middle East respiratory syndrome (MERS) coronavirus, developed at the München site as part of DZIF flagship projects, were clinically tested at specialized clinical trial centers in München (iCTU) and at the HH - HL - BO - RI site in collaboration with African Partner Institutions. The Mbeya Medical Research Center (NIMR-MMRC) is an African Partner Institution of the DZIF in Tanzania that works closely with the site. It has expertise in the areas of tuberculosis, HIV, hepatitis, parasitic diseases, malaria, neglected tropical diseases, and emerging infections—covering both epidemiological and clinical studies. Several DZIF clinical research projects are currently being conducted in Mbeya, including the flagship projects BTZ-043 and TherVacB, as well as the HEVbnAb project (see also pages 11–12).

The München site supports all phases of immunotherapy and drug development. Using screening platforms, targeted biologics design, structural biology analyses, and AI-supported methods, researchers identify and evaluate new drug candidates. Close collaboration with other DZIF partner sites as well as with the biotech and pharmaceutical industry within the Munich Biotech Cluster facilitates the rapid translation of promising approaches into the clinics.

COOPERATION

Partnerships in Germany



ASSOCIATED PARTNERS

Associated partners of the DZIF are researchers based at the following German universities and research institutions that are not among the DZIF's 35 member institutions. DZIF funding is provided for specific projects.

1 Carl von Ossietzky University Oldenburg
The University of Oldenburg provides isolates and data for research on antibiotic resistance.

2 Charité – Universitätsmedizin Berlin
Charité is involved in projects in the research areas of *Emerging Infections* and *HIV*.

3 German Liver Foundation/HepNet Study-House, Hannover
The German Liver Foundation provides a Germany-wide study platform for hepatitis research as well as infrastructure and cohorts for clinical trials.

4 Goethe University Frankfurt, Frankfurt am Main
Goethe University is active in the research areas *Hepatitis* and *Healthcare-Associated Infections*.

5 Kliniken der Stadt Köln
The Kliniken der Stadt Köln (Clinics of the City of Cologne) are investigating the spread of carbapenem-resistant enterobacteria as part of a Germany-wide pilot study.

6 Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute (Leibniz-HKI), Jena
The Leibniz-HKI is active in the DZIF research area *Novel Antibiotics*.

7 RWTH Aachen University
RWTH Aachen University is researching how stool transplants can displace multidrug-resistant intestinal bacteria and reduce the risk of infection.

8 Ruhr University Bochum
Ruhr University Bochum is participating in a project on hepatitis E and respiratory syncytial virus (RSV).

9 University of Bayreuth
The University of Bayreuth is participating in a large-scale screening project to identify new tuberculosis drug candidates.

10 University of Münster
The University of Münster is a partner in a project within the research area *Community-Acquired Infections at Mucosal Interfaces*.

11 University Hospital of Düsseldorf
The University Hospital of Düsseldorf is participating in a study on the management of hepatitis C.

12 Medical Center – University of Freiburg
The Medical Center of the University of Freiburg is a partner in the research areas *Hepatitis*, *Infections of the Immunocompromised Host*, and *Healthcare-Associated Infections*.

13 Jena University Hospital
Jena University Hospital is involved in DZIF research on a new antibiotic to combat Gram-positive bacterial infections.

14 Greifswald University Medicine
Greifswald University Medicine is a partner in a project within the *Healthcare-Associated Infections* research area that is investigating the phage protein HY-133.

INDUSTRIAL PARTNERS HEADQUARTERED IN GERMANY

To advance the development of drugs and diagnostics, the DZIF collaborates with industrial partners in Germany and internationally.

1 AiCuris Anti-infective Cures AG, Wuppertal
AiCuris and DZIF are collaborating on the identification of new antiviral drug candidates for the treatment of infections in immunocompromised patients.

2 BioNTech SE, Mainz
In collaboration with BioNTech, the DZIF is researching RNA-based vaccines for selected virus families.

3 Hypharm GmbH, Bernried
Hypharm and DZIF are collaborating on the development and production of the phage-derived lysin HY-133.

4 IDT Biologika GmbH, Dessau-Roßlau
Together with IDT Biologika, the DZIF is developing a vaccine against the MERS coronavirus.

5 Merck Sharp & Dohme GmbH, Munich
As part of the INCATE consortium, MSD Germany is collaborating with the DZIF on the development of new antibiotics and strategies to combat severe infectious diseases.

ALLIANCES WITH A NATIONAL FOCUS

To promote translational research, the DZIF is involved in a range of strategic alliances in Germany and beyond.

1 German Network against Antimicrobial Resistance (DNAMR), Berlin
The DNAMR advocates the development of new antibiotics and works to raise awareness among German policymakers of the urgency of antimicrobial resistance.

2 German Association of Research-Based Pharmaceutical Companies (vfa), Berlin
The vfa is working with the DZIF on strategies to combat antimicrobial resistance.

COOPERATION

International partnerships

INDUSTRIAL PARTNERS HEADQUARTERED ABROAD
To advance the development of drugs and diagnostics, the DZIF collaborates with industrial partners in Germany and internationally.

6 Coris BioConcept, Gembloux, Belgium
In collaboration with Coris BioConcept, the DZIF has developed a rapid test to detect carbapenem-resistant *Acinetobacter baumannii*.

7 Sanaria Inc., Rockville, MD, USA
In cooperation with the DZIF, Sanaria is working on the continued development and evaluation of malaria vaccine candidates.

8 CR2O, Maarssen, Netherlands
CR2O is involved in the development of a vaccine against the MERS coronavirus.

ALLIANCES WITH AN INTERNATIONAL FOCUS
To promote translational research, the DZIF is involved in a range of strategic alliances in Germany and beyond.

3 French National Agency for Research on HIV, Viral Hepatitis, and Emerging Infectious Diseases (ANRS MIE), Paris, France
DZIF and ANRS MIE are collaborating in the research areas of *HIV*, *Hepatitis*, *Tuberculosis*, and *Emerging Infections*.

4 BEAM (Biotech companies in Europe combating antimicrobial resistance), Lyon, France
This alliance of approximately 70 SMEs and associated organizations such as the DZIF develops innovative products with the goal of combating antibiotic resistance.

5 CARB-X Global Accelerator Network, Boston, MA, USA
The Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) supports projects worldwide that aim to develop new drugs against antibiotic-resistant bacteria.

6 7 8 Coalition for Epidemic Preparedness Innovations (CEPI), Oslo, Norway; London, UK; Washington, D.C., USA
The DZIF is involved in the CEPI vaccine initiative with the aim of helping stop epidemics at an early stage and developing preventive vaccines.

9 Drugs for Neglected Diseases initiative (DNDi), Geneva, Switzerland
In collaboration with DNDi, the DZIF is working on a nucleoside booster project to identify compounds with broad antiviral activity.

10 Global AMR R&D Hub, Berlin, Germany
The Global Antimicrobial Resistance Research and Development Hub promotes international, cross-sector collaboration in research on antimicrobial resistance.

11 H3D Research Centre, Rondebosch, South Africa
H3D and the DZIF are collaborating to establish a pipeline for joint projects aimed at the discovery and development of new drug candidates.

12 ICE-HBV, Doylestown, PA, USA
The International Coalition to Eliminate HBV aims to eliminate chronic hepatitis B as a global public health threat.

13 INCATE – Incubator for Antimicrobial Therapies in Europe, Basel, Switzerland
INCATE drives the development of new drugs by bringing together partners from the academic, industrial, and public sectors.

14 McMaster University, Hamilton, ON, Canada
McMaster University and the DZIF aim to improve preparedness for future pandemics through scientific collaboration.

15 Marius Nasta Institute, Bucharest, Romania
The Eastern European Study Site, which includes an affiliated hospital, collaborates with the Research Center Borstel on clinical tuberculosis studies.

16 UNITE4TB, Munich, Germany
The consortium of 30 partners in 13 countries is working on new treatment options for patients with tuberculosis. The DZIF plays a central role in this effort.

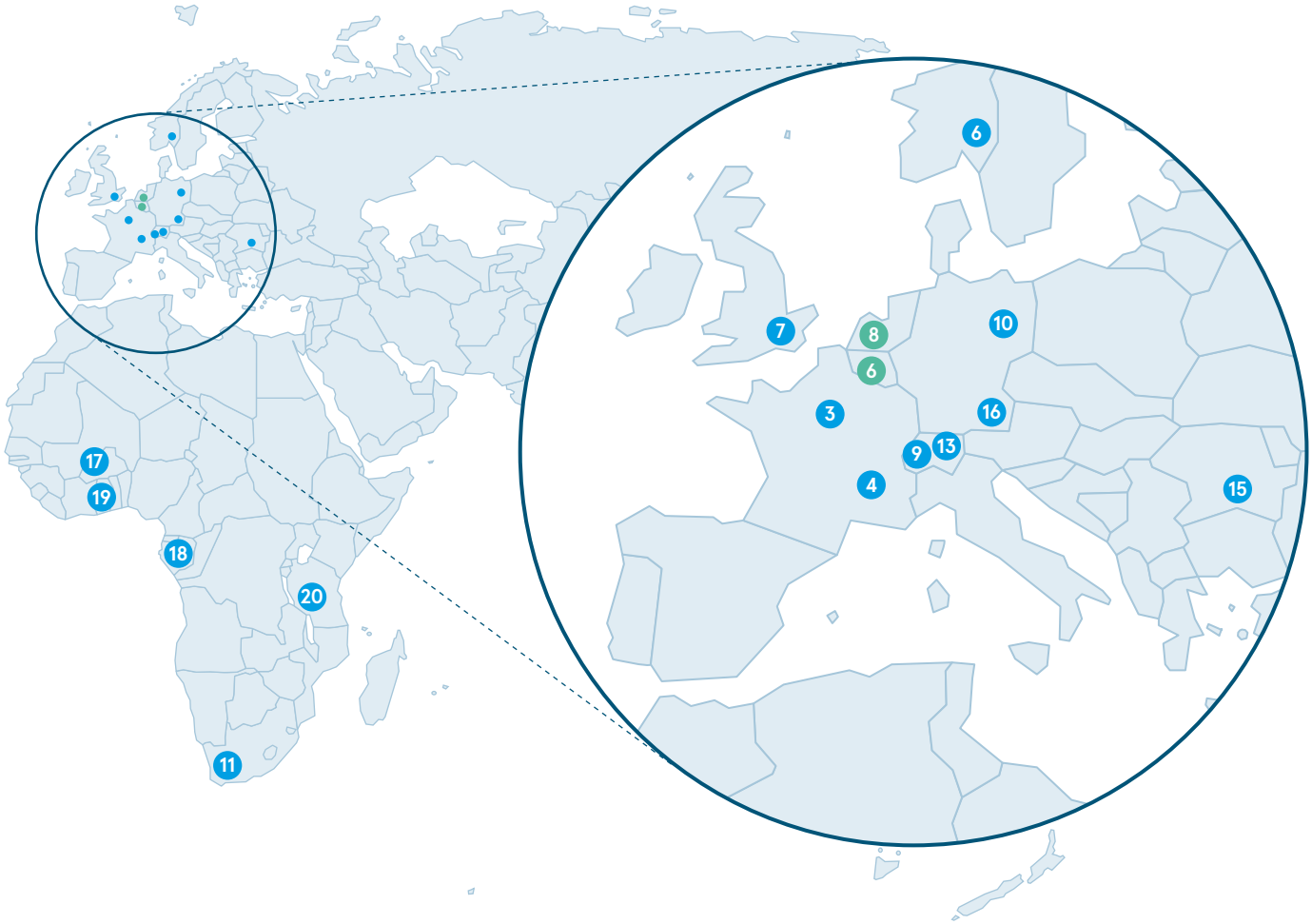
AFRICAN PARTNER INSTITUTIONS
The DZIF has maintained long-standing collaborations with the following four African Partner Institutions.

17 Centre de Recherche en Santé de Nouna (CRSN), Nouna, Burkina Faso
Research into and treatment of malaria, HIV/AIDS, and bacterial meningitis form the focus of joint projects with the CRSN.

18 Centre de Recherches Médicales de Lambaréné (CERMEL), Lambaréné, Gabon
Joint projects with CERMEL advance research in areas such as the prevention, diagnosis, and treatment of malaria.

19 Kumasi Centre for Collaborative Research (KCCR), Kumasi, Ghana
KCCR's research priorities include malaria, tuberculosis, salmonellosis, and Buruli ulcer.

20 NIMR-MMRC Mbeya Medical Research Center, Mbeya, Tanzania
In collaboration with LMU University Hospital Munich, MMRC conducts DZIF clinical trials on tuberculosis vaccines and therapeutics.



GERMAN CENTERS FOR HEALTH RESEARCH

Creating synergies through networking

The German Centers for Health Research (DZG) are long-term, equal partnerships between non-university research institutions—such as Helmholtz Centers, Leibniz Institutes, and Max Planck Institutes—and universities, as well as university and specialty hospitals. The DZIF is one of the DZG established between 2009 and 2012 at the initiative of the Federal Ministry of Education and Research (BMBF).

The German Centers for Health Research are part of the German government's health research program. They are funded by the Federal Ministry of Research, Technology and Space (BMFTR; formerly the BMBF) and the federal states. Their goal is to combat common and widespread diseases, including infectious diseases, more effectively. The centers combine existing knowledge and ensure that new scientific findings on prevention, diagnosis, and therapies benefit patients more quickly. Several thousand basic scientists, clinical researchers, and physicians collaborate on medical progress within one of Germany's largest health research networks, spanning research disciplines and organizational boundaries.

WORKING TOGETHER AGAINST COMMON DISEASES

Strategic collaboration between leading researchers strengthens Germany's position as a center of scientific excellence in international competition and increases its attractiveness for young scientists, both domestically and internationally. This has already led to a significant increase in the international visibility of translational, clinically oriented research in Germany.

The DZG conduct research in the following areas: cancer (DKTK), diabetes (DZD), cardiovascular diseases (DZHK), infectious diseases (DZIF), diseases affecting children and adolescents (DZKJ), lung diseases (DZL), neurodegenerative diseases (DZNE), and mental illnesses (DZPG).

At the annual German Academic International Network (GAIN) conferences in Boston in 2023 and San Francisco in 2024, the DZG presented themselves with a joint appearance. GAIN is the largest networking event for academic careers in Germany outside of Europe.

Four more issues of SYNERGIE, a high-quality German-language research magazine jointly conceived by all DZG, were published in 2023 and 2024. These issues focused on the topics of "Organ Crosstalk," "Blood," "Exposome," and "Intelligent Medicine."

STRUCTURES FOR EFFECTIVE COOPERATION

The DZG Head Office serves as an important link between the individual centers and coordinates working groups on topics such as biobanks, research IT, global health, promoting young talent, public relations, patient participation, and the regulatory aspects of clinical trials.

Monthly management team meetings, quarterly executive board meetings, and biannual consultations with federal and state governments promote cooperation and ensure the conceptual development of the DZG.

INNOVATION FUND: SETTING NEW IMPULSES

The joint research funding program, the "DZG Innovation Fund," was continued in 2023/24 with the theme "Microbiome." In 2024, the third call for proposals in the field of "Inter-Organ Metabolomics" was issued for the years 2025/26. Symposia were held in Dresden, Heidelberg, and Munich by the respective local DZG to promote cross-disciplinary collaboration.

YOUNG TALENT DEVELOPMENT AND NETWORKING

The training and networking of highly qualified young scientists is an important foundation for continuing successful research in the future. For this reason, the DZG are particularly active in this area. The Young Talent Promotion Working Group organizes an annual "DZG Science & Career Day," which promotes the interdisciplinary network of clinicians and medical scientists from all DZG institutions. Additionally, the quarterly online "DZG Lunchtime Career Talks" highlight the diversity of career paths.

For the first time, the DZG are offering the "DZG Training Program Translational Research". Combining workshops on translational health research (i.e., from the lab to the clinic) with a mentoring program, this program has been running since last year. Notable events included the joint presence of all DZG centers at the GAIN annual conferences in Boston in 2023 and San Francisco in 2024. Outside of Europe, GAIN is the largest networking event for scientific careers in Germany.

STRENGTHENING VISIBILITY

The DZG have an online presence at www.deutschezentren.de and on the social media platforms Facebook, Instagram, LinkedIn, and X (until 2024). Four additional issues of the high-quality, jointly conceived research magazine SYNERGIE were published in 2023 and 2024 on the topics of "Organ Crosstalk," "Blood," "Exposome," and "Intelligent Medicine." The German-language magazine is available online at https://dzg-magazin.de, and a print subscription is available.

SCIENCE AND THE PUBLIC

Diverse audiences– one mission

Science communication faces unique challenges: It must reach researchers, journalists, policymakers, patients, and the wider public—target audiences that often have very different information needs and media consumption habits.

What scientists consider precise wording may be incomprehensible to the general public. A press release about research findings requires a distinct approach from information intended for health policymakers. Tailoring communication for specific audiences was therefore a central focus of the DZIF Press Office's work in 2023 and 2024.

One of the greatest challenges when addressing these very different stakeholders is bridging the gap between the various communication contexts and channels.

In recent years, the Press Office has developed various formats to facilitate this communication across audiences, such as press conferences for science journalists, press releases written in plain language, and events with members of parliament.

WEBSITE TRAFFIC, MEDIA COVERAGE & REACH

The sustained interest in the DZIF's work is reflected in the traffic figures for the DZIF's digital channels. In 2023 and 2024, at least 1.5 million visitors from around the world used the DZIF website as their primary source of information. The glossary pages, which explain technical terms in accessible language, were among the most frequently accessed pages.

Overall, media coverage remained at a high level: Over the past two years, approximately 4,000 online sources reported on DZIF's research findings. Notably, a large portion of this coverage came from international sources. In 2023, more than half of the media reports were published outside German-speaking countries. In 2024, the figure was just under 30 percent. This demonstrates the international recognition of DZIF research and underscores the need to reach audiences worldwide.

A major milestone in 2024 was the production of a film that presents the work of the DZIF in an accessible way to a broad audience. Through authentic insights and explanations, it reaches a wide range of viewers—from members of the public and early-career researchers to potential collaboration partners.

On June 13, 2024, the cross-party "Parliamentary Group Against Antimicrobial Resistance" was founded. As spokesperson for the "German Network Against Antimicrobial Resistance" (DNAMR), DZIF Managing Director Dr. Timo Jäger (second from the right) attended the founding meeting together with Prof. Achim Hörauf (far right in the picture) and other representatives of the DNAMR

PRESS RELEASES AND SOCIAL MEDIA

With 133 press releases and shorter news items over the past two years, the Press Office has consistently provided updates on progress across all nine research areas. In doing so, it has struck a balance between scientific precision and accessibility—a key challenge in reaching diverse audiences. Numerous DZIF press releases were picked up by both international media and leading German media outlets.

One example is the appeal by Prof. Mark Brönstrup and other experts to create lasting economic incentives for the development and marketing of new antibiotics. This press release was covered by the German media outlets "Focus," "Welt," and "Stern." The highest potential reach was achieved by articles featured on "MSN.com," including coverage based on the press release "Learning from the COVID Pandemic: On the effectiveness of non-pharmaceutical interventions against pathogens," with a potential reach of over 150 million people. The DZIF was featured in media outlets worldwide, including the "Hindustan Times" (India), "Sohu" (China), "New York Post" (USA), and "News Medical" (UK).

Social media channels remain important tools for targeted communication: The 322 tweets and 426 LinkedIn posts from the Press Office generated approximately 490,000 impressions and 5,190 new followers. By the end of 2024, however, the Press Office had made an important strategic decision: The Twitter/X channel was discontinued because DZIF's values were no longer compatible with the platform's policies. Instead, DZIF has been active on Bluesky since early 2025. On this social media platform, communication continues in an environment that better aligns with the principles of responsible science communication. LinkedIn remains the DZIF's primary channel for reaching stakeholders in industry, politics, and the scientific community.

NETWORKING AS A COMMUNICATION STRATEGY

The DZIF's strength lies in its network—and this also applies to its communication efforts. Through close cooperation with the other German Centers for Health Research (DZG), resources can be pooled and various stakeholders reached more efficiently. The joint magazine SYNERGIE, with a total of four issues in 2023 and 2024, is an example of this successful collaboration.

Collaboration with professional societies, patient organizations, and industry partners also enables the DZIF to specifically target its audiences. Exchange and networking are fostered through the organization of and participation in scientific conferences, collaborations with professional associations, and a presence at national and international congresses.

In a decentralized network like the DZIF, internal communication is also of central importance. DZIF employees receive information tailored specifically to them in the form of internal emails and newsletters, as well as via the new DZIF portal.

The DZIF will continue to work toward building bridges between different worlds: between basic research and clinical application, between science and society, and between national and international partners. Research findings can only achieve their full impact—for the benefit of patients and society as a whole—when they reach all relevant audiences.

From left : **Stephanie Aue** (starting in 2025), **Tatiana Hilger** (until the end of 2024), **Martina Lienhop**, **Janna Schmidt**, **Sandra Winter** (Trainee since October 2024), **Dr. Nicola Wittekindt**
The DZIF Press Office team

DZIF-HIGHLIGHTS 2023/24

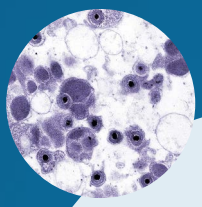
News in focus*

MARCH 2023

The human immunodeficiency virus (HIV-1) can infect various tissues. After entering cells, HIV-1 integrates its genome into the cellular genome, leading to persistent infection. However, the role of the structure and organization of the host genome in this process is not yet well understood. An international research team led by Dr. Marina Lusic has analyzed the integration patterns of HIV-1 into the genome of microglia immune cells of the brain using a cell culture model.

APRIL 2023

Mosquito nets treated with insecticides are the most important tool in the fight against malaria. However, mosquitoes are becoming increasingly resistant. Prof. Victoria Ingham and her team are researching the mechanism of action of the new insecticide chlorfenapyr for a dual attack on both the vector mosquitoes and the malaria parasite itself. The project is funded by the Bill & Melinda Gates Foundation.



MAY 2023

Researchers at the HZI have discovered that certain connective tissue cells not only serve as sites for cytomegalovirus (CMV) replication, but also as a reservoir for CMV in a latent state. This challenges the previous dogma that herpesviruses use different cells in the body for replication and latency. Another research finding was that CMV controls the use of fibroblasts not only via cell factors, but also through interaction with the immune system.

JULY 2023

The Else Kröner-Fresenius Foundation is funding two DZIF projects with a substantial sum of money: the antibiotic corallopyronin A for the treatment of tropical worm diseases and multi-resistant bacteria, and the probiotic bacterium *Staphylococcus lugdunensis* for the elimination of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria from the noses of high-risk patients. The funding will support the legally compliant production of new drug candidates for direct use in first-in-human clinical trials.

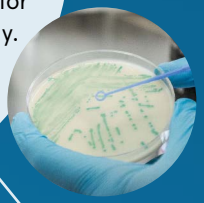
OCTOBER 2023

Around 240,000 children worldwide die of tuberculosis every year. This makes the disease one of the top ten causes of death in children under five. One reason for this high mortality rate is that the disease is often misdiagnosed or not diagnosed in time. A new diagnostic tool could bring about progress. It was tested by an international research consortium as part of a study in five countries.

*Selection

JANUARY 2024

Mobile genetic elements, known as plasmids, enable bacteria to exchange resistance genes. This horizontal gene transfer makes the recipients resistant to broad-spectrum antibiotics. Researchers at Justus Liebig University Giessen have identified a stable plasmid responsible for most bacterial resistance in Germany. This high-risk plasmid can be transferred to different types of bacteria and remains active for years.



JULY 2024

In chronic hepatitis B, immune cells accumulate in the liver. However, since these cells are inactive, they cannot fight the virus-infected liver cells. An international team led by Prof. Percy Knolle and Prof. Ulrike Protzer discovered a "sleep timer" mechanism in the blood vessel cells of the liver that switches off the immune cells after a certain period of time, rendering them inactive. This finding could lead to new approaches for immunotherapies.

AUGUST 2024

Established vaccines against the SARS-CoV-2 virus are quickly losing their protective effect, necessitating repeated booster vaccinations. In contrast, a novel vector vaccine developed at the HZI elicits a sustained immune response in animal models. In this vaccine, the genetic information for the spike protein of the coronavirus is incorporated into the mouse cytomegalovirus (MCMV), which is harmless to humans.

OCTOBER 2024

Bacteria in the gut microbiome are important for defending against pathogens. Sometimes, they occur in increased numbers in diseases. One example is the bacterium *Segatella copri*. Prof. Till Strowig at the HZI has investigated the conditions under which colonization with this widespread bacterium occurs and the processes involved. During their research, the team discovered a small RNA molecule that plays a crucial role in the bacterium's reproduction and spread.

NOVEMBER 2024

As bacteria are increasingly developing resistance to current drugs, there is an urgent need for new active substances. Researchers led by Prof. Rolf Müller and Dr. Jennifer Herrmann confirmed the effectiveness of genetically optimized derivatives of the bacterial natural product darobactin against the bacteria *Escherichia coli* and *Acinetobacter baumannii* in various *in vivo* models. These bacteria are known for frequently developing resistance.

DECEMBER 2024

On World AIDS Day 2024, the International Antiviral Society–USA (IAS-USA) published new guidelines for the treatment and prevention of HIV. The recommendations of the expert committee, which includes Prof. Clara Lehmann from Cologne University Hospital, are based on significant advances in antiretroviral therapies and new prevention strategies. The 2024 guidelines acknowledge the progress made in the fight against HIV but also highlight the challenges of accessing life-saving measures.

DZIF-HIGHLIGHTS 2023/24

Awards and honors*

2023/2024
CROSS OF THE ORDER OF MERIT OF THE FEDERAL REPUBLIC OF GERMANY

2023: Prof. Dr. Marylyn Addo, University Medical Center Hamburg-Eppendorf

2023: Prof. Dr. Sandra Ciesek, Goethe University Frankfurt Frankfurt a. Main

2024: Prof. Dr. Klaus Cichutek, Paul-Ehrlich-Institut, Langen

2023
GERMAN UNIVERSITY MEDICINE AWARD

Prof. Dr. Julian Schulze zur Wiesch, University Medical Center Hamburg-Eppendorf

2023
BIOMÉRIEUX DIAGNOSTICS AWARD

Dr. Janko Sattler, University Hospital Cologne

2023
META ALEXANDER PRIZE

Dr. Anahita Fathi, University Medical Center Hamburg-Eppendorf

2023
CHARLES THOM AWARD

Prof. Dr. Rolf Müller, Helmholtz Institute for Pharmaceutical Research Saarland

2023
ESPID FELLOWSHIP AWARD

Dr. Laura Olbrich, LMU University Hospital Munich

2024
MEMENTO RESEARCH AWARD

Prof. Dr. Michael Ramharter, University Medical Center Hamburg-Eppendorf

2023/2024
DZIF PRIZE FOR TRANSLATIONAL INFECTION RESEARCH

2023: Prof. Dr. Ralf Bartenschlager, Heidelberg University Hospital

2024: Prof. Dr. Peter Kremsner, University Hospital Tübingen

*Selection

2024
WALTER SIEGENTHALER MEDALS

Prof. Dr. Dr. Philipp Schommers, University Hospital Cologne

Dr. Alexander Simonis, University Hospital Cologne

2024
IAS/ANRS LANGE/ VAN TONGEREN PRIZE FOR YOUNG INVESTIGATORS

Dr. Kira Elsbernd, LMU University Hospital Munich

2024
PHOENIX PHARMACY SCIENCE AWARD

Prof. Dr. Tanja Schneider, University of Bonn

2023/2024
EUROPEAN RESEARCH COUNCIL (ERC) GRANTS

ERC Proof of Concept Grant 2023:
Prof. Dr. Anna Hirsch, Helmholtz Institute for Pharmaceutical Research Saarland

ERC Synergy Grant 2024:
Prof. Dr. Mark Brönstrup, Helmholtz Centre for Infection Research, Braunschweig

ERC Starting Grant 2024:
Dr. Florian Wimmers, University of Tübingen

2024
JÜRGEN MANCHOT RESEARCH PROFESSORSHIP FOR EXPERIMENTAL INFECTION MEDICINE

Prof. Dr. Jürgen Ruland, Technical University of Munich

2024
FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS

Prof. Dr. Dr. h.c. Christoph Lange, Research Center Borstel, Leibniz Lung Center

2023/2024
APPOINTMENT TO THE GERMAN SCIENCE AND HUMANITIES COUNCIL

2023: Prof. Dr. Christine Falk, Hannover Medical School

2024: Prof. Dr. Petra Dersch, University of Münster

PUBLICATIONS

Publication statistics and highlights

Publications are at the heart of scientific communication. They allow researchers around the world to build on, critically evaluate, and incorporate the findings of others into their own research. At the same time, publications serve as an important measure of scientific visibility and reputation. Those with a high impact factor demonstrate that research findings are recognized within the scientific discourse. These publications are considered particularly influential and are frequently used to evaluate scientific success.

463 ≥ 10

The Magic Ten: The Impact Factor (IF) is a key metric that indicates, on average, how often a journal's articles have been cited over the past two years based on citations in the current year. An IF of ten or higher is generally considered "excellent." A total of 463 publications involving DZIF (including reviews) had an IF of at least 10 during the 2023/24 period.

11 x Top 1 %

In both 2023 and 2024, eleven DZIF researchers were among the world's most frequently cited scientists in their respective fields. Ten of them maintained their place on the prestigious "Highly Cited Researchers" list for two consecutive years. The company "Clarivate Analytics" publishes an annual list of the world's most influential researchers whose publications ranked in the top 1% most cited in their field over the past ten years. This is a remarkable achievement, as only about 7,000 people worldwide make it onto this list each year.

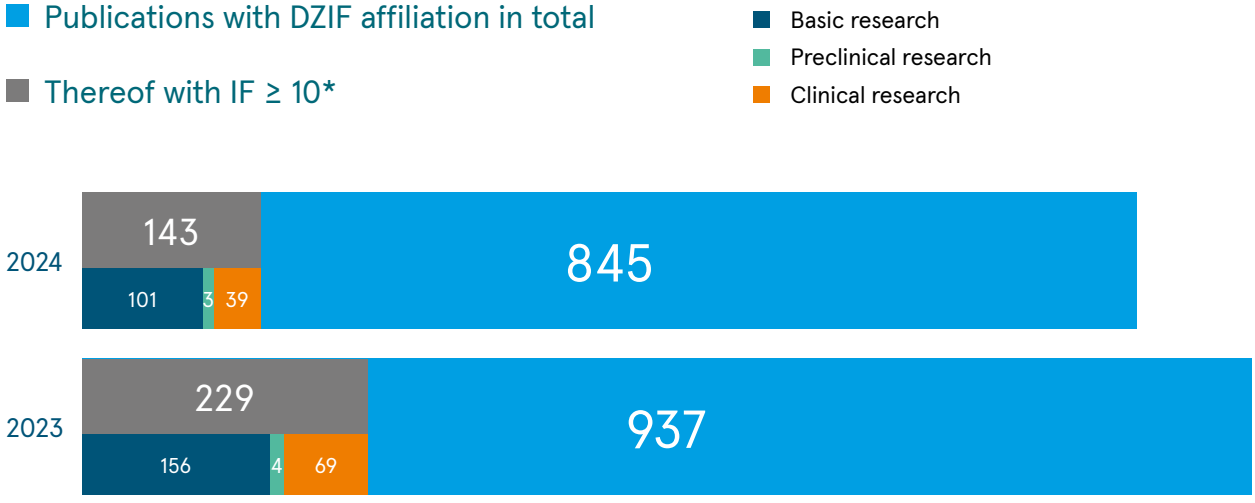
161 ≥ 2

The DZIF aims to bring together cutting-edge research. At least two different DZIF sites collaborated on 70 publications in 2023 and 91 publications in 2024. Most of the publications involving at least one other site were published by the Bonn – Köln and Hamburg – Lübeck – Borstel – Riems partner sites.

1,782

This is the number of publications involving DZIF that were published during the reporting period. After a significant increase during the pandemic years, the number declined slightly in 2024—but remained above pre-pandemic levels.

The following figure summarizes the trends in publication numbers for 2023 and 2024, as well as the proportions of publications in basic, preclinical, and clinical research.



The graph shows the number of scientific publications with DZIF affiliation during the 2023/24 reporting period (sources: PubMed and Scopus). The publication numbers for basic, preclinical, and clinical research refer to publications with an impact factor (IF) of 10 or higher.
**Review articles are not included in this overview of publications with an IF of 10 or higher.*

The complete DZIF publication lists are available at:

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