

THE HELMHOLTZ-INSTITUTE FOR PHARMACEUTICAL RESEARCH SAARLAND (HIPS)

Helmholtz-Institute for Pharmaceutical Research Saarland







FOREWORD

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New findings of health research benefit people more directly than the results of almost any other field of research. The Federal Government therefore champions a vigorous health research community. We need effective methods for prevention, diagnosis and patient treatment.

Infection research in particular faces major new challenges. These include poverty-related and chronic infectious diseases as well as previously unknown pathogens which are spreading rapidly such as the Ebola virus. The best researchers need to cooperate in order to control infectious diseases at the national and global level and to develop effective methods for diagnosis and treatment.

It is gratifying to see the Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS) develop so successfully. The work done by the Helmholtz Centre for Infection Research (HZI) in Braunschweig and Saarland University to jointly establish the Institute clearly demonstrates that long-term cooperation on an equal basis between universities and non-university research institutions can create new opportunities and synergy.

The HIPS aims to identify new natural products and new treatments to combat infectious diseases. It can thus contribute substantially to closing a gap in the innovation chain of infection research.

As an institute of the Helmholtz Centre for Infection Research, the HIPS is also an important partner in the German Centre for Infection Research. It helps ensure the rapid transfer of research results into clinical practice.

I am convinced that the people working at the HIPS will continue to play a vital part in successfully addressing the national and international challenges of infection research.

Prof. Dr. Johanna Wanka

Federal Minister of Education and Research

FOREWORD



The Helmholtz Centre for Infection Research (HZI) in Braunschweig and its institutes at their various locations are some of the most outstanding research facilities in Germany. Their renowned scientists are engaged in health research and develop new pharmaceutical drugs and therapies against dangerous infectious diseases.

The antibiotic resistance of dangerous bacteria results in hospitals facing major challenges especially when performing vital surgery. The Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS) is taking up the challenge of discovering new active agents against resistant microbes. The Institute was founded in August 2009 by the Helmholtz Centre for Infection Research in Braunschweig and Saarland University with the goal of developing novel pharmaceuticals against dangerous and frequently life-threatening infectious diseases. The research pursued at the Helmholtz Centre is tremendously successful. Many people all over the world benefit from new, innovative methods of treatment for infectious diseases that are triggered by bacteria, viruses and other pathogens.

With the successes achieved to date, the Institute fits perfectly into the innovation strategy of the Saarland, which focuses on close-to-the-market research. Research, development and science are crucial vehicles for the further development of the Saarland as a business location.

I am delighted about the positive development of the HIPS, which has established itself as an internationally recognized, leading research facility within a very short time, and I hope that in the future the Institute and the renowned scientists working there will succeed in making even more groundbreaking discoveries within the field of health research.

Annegret Kramp-Karrenbauer State Prime Minister of Saarland



THE HELMHOLTZ-INSTITUTE FOR PHARMACEUTICAL RESEARCH SAARLAND (HIPS)

Increasing (multi)-resistance towards established antibiotics is a serious medical problem. Re-emerging and new infectious diseases are of equal concern. In addition, the development of new drugs against such illnesses is currently based mainly on known mechanisms of action and old molecule scaffolds, which allows bacteria to develop and spread resistance rapidly. There is thus an urgent need for new strategies aimed at the discovery and development of novel anti-infective pharmaceuticals: This is the research focus of the Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS).

Antibiotics have been used successfully for the last 70 years. Since their introduction the mortality rate from infectious diseases has fallen dramatically. However, these drugs have been applied so widely and for so long that the infectious organisms have adapted to them, making these drugs less effective. Once restricted almost exclusively to developing countries, resistant pathogens are now spreading in hospitals and in communities in developed countries as well. Research to develop novel antimicrobial drugs is required – and this is precisely the issue that is being tackled by the Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS).

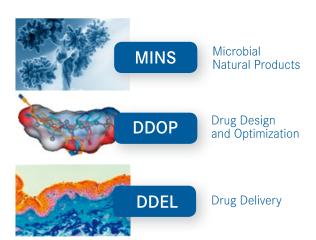
The Institute was founded in 2009 in Saarbrücken, Germany, following a positive international evaluation of a joint proposal from the Helmholtz Centre for Infection Research (HZI) and Saarland University (UdS). The HIPS is the first non-university based research facility in Germany that is explicitly devoted to pharmaceutical research, and it is closely integrated into UdS on the basis of a cooperation agreement between the HZI and UdS. As a branch of the HZI, the HIPS is involved in the activities of the "Health" research field of the Helmholtz Association and the "Infection and Immunity" research program.



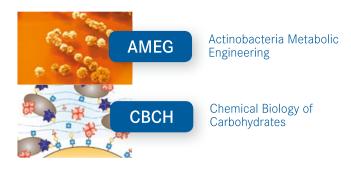
The range of scientific work at the HIPS comprises genetic and genome-based methods for optimizing natural product producers and lead compounds as well as methodologies to improve the transport of pharmaceutical agents to their target. The combination of the HZI's knowledge of infectious diseases and the HIPS' pharmaceutical research puts the HIPS in a unique position both in Germany and in Europe, especially regarding the development of anti-infectives.

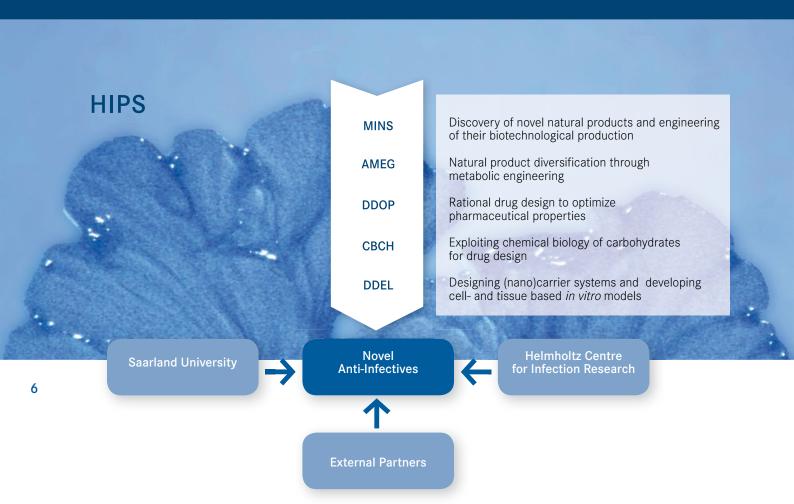
This complementary expertise allows concerted and synchronous approaches towards the discovery and mining of novel producers for potential drugs, their rational improvement and bioprofiling, as well as their optimal formulation. This combination of expertise greatly enhances the probability of identifying and utilizing novel natural products, and accelerates their advancement to (pre)clinical studies. The combined research activities and experience of scientists at the HIPS, the HZI and further regional and international cooperations in drug development make it possible to cover drug development in its entirety from early drug discovery to clinical phase studies. A successful implementation of translational research is thus achieved.

DEPARTMENTS AT THE HIPS



JUNIOR RESEARCH GROUPS





HIPS EVENTS TO EXCHANGE IDEAS

The HIPS regularly organizes events which bring together renowned scientists and young investigators from three pharmaceutical communities: Natural products, medicinal chemistry and drug delivery. The HIPS Symposium provides a forum for senior scientists to exchange ideas while crossing the boundaries of classical disciplines. At the same time it gives young investigators the opportunity to obtain valuable feedback on their projects from international experts in the respective fields. The plan is to establish the HIPS Symposium as a creative meeting with a regular place in the schedule of leading scientists from these research fields in Europe and beyond. The HIPS Talk invites scientists from different disciplines who are interested in pharmaceutical research from faculties and public research institutes to the Saarland University campus. Other events, like workshops, are an additional part of the creative development process.



HIPS Symposium



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The HIPS originates from three pharmaceutical research departments of Saarland University headed by Professors Rolf Müller (Managing Director of the HIPS and former scientist at the HZI), Rolf W. Hartmann and Claus-Michael Lehr. Rolf Müller's research focuses on the exploitation of microbial agents, primarily from myxobacteria (MINS Department, Microbial Natural Products), Rolf Hartmann's Department specializes in pharmaceutical and medicinal chemistry (DDOP Department; Drug Design and Optimization) while Claus-Michael Lehr investigates the targeted transport of drugs to the source of disease (DDEL Department; Drug Delivery).

From 2009 to presumably 2014 (by when it is expected new appointments will have been made to the chairs of pharmacy at UdS), the three professors hold chairs of



pharmacy at UdS and are also department heads at the HIPS, so that their research groups originate from both UdS and the HIPS. Currently, two junior research groups are located at the HIPS: The AMEG group headed by Andriy Luzhetskyy specializes in the engineering of actinobacteria, while Alexander Titz's research focuses on the Chemical Biology of Carbohydrates (CBCH).

In 2015 the new HIPS building on the UdS campus will be completed, and all HIPS departments, junior research groups and infrastructures can then be accommodated under one roof.

he HIPS is funded by the German Federal Government and the Federal State of the Saarland and has an annual budget of 5.5 million euros. Since the foundation of the HIPS the Helmholtz Association has also been represented in the Saarland. As Germany`s largest scientific research organization the Helmholtz Association contributes to solving the grand challenges of society, science and industry by performing cutting edge research in the fields of Energy, Earth and Environment, Health, Key Technologies, Structure of Matter, Aeronautics, Space and Transport. The Association has an annual budget of 3.8 billion euros and almost 34 000 collaborators undertake research into systems of great complexity with large-scale facilities and scientific infrastructure, cooperating closely with national and international partners.

See also: www.helmholtz.de/en/partners.



THE DEPARTMENT "MICROBIAL NATURAL PRODUCTS"

Natural products of microbial origin continue to be very promising sources for the development of pharmaceuticals. Compared to synthetic compounds, natural products cover a unique chemical space and they are also thought to be evolutionarily optimized binders for various biological targets. They can exhibit diverse biological activities and modes-of-action, making them useful for numerous therapeutic applications like the treatment of infections or cancer. However, finding and developing new bioactive compounds, so-called secondary metabolites, from microorganisms is a challenging task. The overall success depends on good sources (proficient microbial producer strains) as well as the professional interplay of

The research in the "Microbial Natural Products" Department aims to exploit the rich biosynthetic potential of microorganisms, especially soil-dwelling myxobacteria, for the production of novel natural products.

various interdisciplinary approaches. 13.000 kb 0 kb Sorangium 3,000 kt 10,000 k cellulosum Genome 13.0 Mb

DISCOVERY OF NOVEL BIOACTIVE COMPOUNDS

An on-going, world-wide strain discovery program, in close collaboration with the "Microbial Drugs" Department at the HZI in Braunschweig, aims to identify new myxobacterial species, genera and families. Once new isolates have been successfully adapted to growth under laboratory conditions, cultivations are performed and culture extracts are then screened for promising bioactivities mainly against human pathogens. The discovery of novel natural products is underpinned by state-of-the art analytical

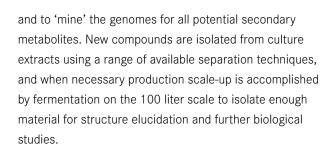
techniques, which allow an in-depth analysis of the strain`s secondary metabolite profiles.

> The scientists also decipher the genetic information of the bacteria

> > to obtain comprehensive

insights into their metabolic capabilities. As many natural product biosynthesis pathways are not active and considered to be 'silent' under standard cultivation conditions, several tricks are applied to activate these pathways

Map of the circular Sorangium cellulosum So ce56 genome



OPTIMIZATION OF BIOTECHNOLOGICAL PRODUCTION

Following the discovery of new natural products exhibiting promising activity, different strategies are applied to improve both their production yields and their structures, e.g. to optimize their pharmaceutical and pharmacological properties. To this end, an in-depth investigation of the underlying biosynthetic mechanisms and regulatory

networks controlling production is performed. Based on these results rational production engineering is carried out by genetic manipulation of the producer strains or by transferring complete natural product biosynthetic pathways into suitable host strains for heterologous production. Overall, these synthetic biotechnology endeavors aim at translating early natural product hits into clinical application.

Rolf Müller 's group provides a highly interdisciplinary research environment, where a broad spectrum of techniques, including microbiological, molecular-biological, genetic, biochemical, analytical and bioengineering methods, are combined to exploit microbial natural products for drug discovery and development approaches.





Molecular structure of Argyrin, a metabolite from myxobacteria showing antibacterial activity

Chondromyces crocatus fruiting body, containing large numbers of myxospores

High-resolution mass spectrometry platform for the in-depth analysis of secondary metabolomes

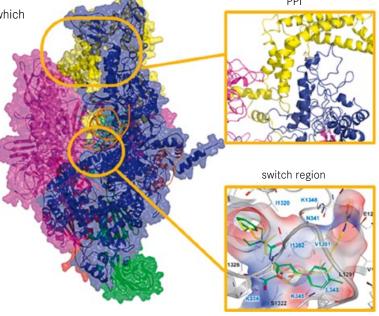


THE "DRUG DESIGN AND OPTIMIZATION" DEPARTMENT

Recent advances in microbiology have resulted in the identification of an increasing number of natural products which exhibit antibiotic activity. However, most of these structures are not suitable to be used as drugs due to their unfavorable pharmacokinetic properties, such as poor solubility or difficult large-scale synthesis. The Department of "Drug Design and Optimization" focuses on the development of novel synthetic antibiotics, which can either be derivatives of natural products with improved druglikeness or synthetic compounds based on a rational drug design. Diverse strategies of medicinal chemistry are applied. Currently, the Department is working on two projects: The synthesis of antibiotic compounds targeting either the bacterial growth or the cell-to-cell

communication.

Rational development of antivirulence compounds with improved physicochemical properties



Structure of *E. coli* RNA polymerase. Inhibitors can be designed to target e. g. protein-protein interactions (PPI); defined binding sites can be used to develop a pharmacophore (ph4) model.



NOVEL RNAP INHIBITORS STOP BACTERIAL GROWTH

The bacterial RNA polymerase (RNAP) is essential for bacterial growth and is well conserved between different bacteria.

However, marketed RNAP inhibitors have evoked resistant strains by point-mutations in their binding sites. Rolf Hartmann's group aims to develop bacterial RNAP inhibitors with novel modes of action. It applies different methods such as ELISA- and SPR-based experiments as well as classical enzyme inhibition assays. The group utilizes computer-aided drug design (CADD) strategies to understand RNAP inhibition and to spark new ideas for drug design. Besides improving the RNAP inhibitory and

Chemical synthesis of small molecule antibacterial agents

antibacterial activity, DDOP aims to elucidate the mode of action and to optimize the pharmacokinetic properties of novel compounds. These endeavors should lead to new and highly potent antibiotics to be used in therapeutic applications in humans.

INTERFERING WITH CELL-TO-CELL COMMUNICATION IN BACTERIA

In a second project, the scientists of the DDOP Department develop compounds that interfere with the cell-to-cell communication in the bacterium Pseudomonas aeruginosa. Lung infections caused by this pathogen are difficult to treat when bacteria arrange themselves into clusters, so called biofilms. These dense layers suppress the uptake of antibiotics. The formation of biofilms and also the production of virulence factors are controlled by cell-tocell communication systems (quorum sensing) in response to signal molecules. Pseudomonas aeruginosa has a third unique communication system which is regulated by PQS (Pseudomonas Quinoline Signal) as a signaling molecule. The DDOP Department aims to develop compounds that interfere with the PQS-dependent signaling in order to prevent the formation of biofilms and the production of virulence factors, without affecting the microbial viability.



THE DEPARTMENT "DRUG DELIVERY"

Advances in molecular biotechnology and medicinal chemistry have led to the discovery of new drug candidates. However, developing these molecules into actual pharmaceuticals first requires the screening of their biochemical properties and their ability to cross biological barriers.

Scientists must establish new technologies to ensure the safe and effective delivery of the drug candidate to the site of action, for example the site of infection or components of the immune system. Therefore, the main focus of the "Drug Delivery" Department is on the exploration of the biological barriers themselves, which are present between the sites of drug administration and drug action.

DISEASE-RELEVANT MODELS WITHOUT ANIMAL EXPERIMENTS

An important line of the research focuses on laboratory cell culture models to study the epithelial barriers of the lungs, the gastro-intestinal tract, and the skin under controlled conditions *in vitro*. The establishment of disease-relevant *in vitro* models for infections and/or inflammation of the respective barriers allows the therapeutic efficacy of novel drug candidates to be demonstrated via adequate

biomarkers without using animal experiments. Such models make it possible to perform pre-screening or high throughput screenings of drug candidates as well as a detailed investigation of transport mechanisms in an environment which is less complex than the *in vivo* situation – the situation in living organisms. Similarly, such models also have considerable potential as alternatives to animal testing in the drug development process.

The Department headed by Claus-Michael Lehr has developed an in vitro co-culture model for inflamed intestinal mucosa. The model, honored by two animal welfare awards from the German Federal Ministry of Food, Agriculture and Consumer Protection (BMELV) and the State of Rhineland-Palatinate, has been successfully applied to the testing of first anti-inflammatory formulations. In collaboration with other groups at the HZI, this in vitro model will be applied to identify epithelial inflammation markers and to study mechanisms of bacterial adhesion and invasion of enteropathogens. Understanding and mimicking the bacterial invasion pathway will allow even more effective targeting of diseased areas and increased cellular internalization of drug carriers, by using invasion decorated particles, for example. Furthermore, other complex, disease-relevant in vitro models are being studied by developing both a co-culture model of the blood-airbarrier and a pulmonary biofilm model.

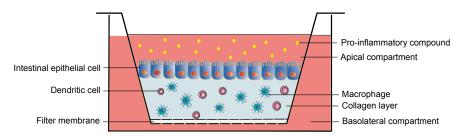


A second major research line of the "Drug Delivery" Department consists of developing appropriate carrier systems that are capable of crossing biological barriers and thereby improving the delivery of the active molecule to the target. This is particularly relevant in the context of macromolecular biopharmaceuticals such as peptides, proteins, and RNA or DNA based drugs. In parallel, the nanotechnology platform, part of the Department, is



Developing carrier systems that are capable of crossing biological barriers

to be advanced and broadened in terms of formulating multifunctional nanocarriers that allow tracking of the carriers, targeting to the site of action and release of the payload in a controllable manner both *in vitro* and *in vivo*. Last but not least, the carrier systems must be safely eliminated from the body, preferably by biological degradation of their constituents. Taken together, DDEL researchers are interested in a deeper understanding of the function of biological barriers in the healthy and the diseased state as well as in their interaction with (nano) particulate drug carriers.



Experimental set-up of the co-culture consisting of an intestinal epithelial cell line, macrophages and dendritic cells



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JUNIOR RESEARCH GROUP:

"NATURAL PRODUCT DISCOVERY BY ACTINOBACTERIA METABOLIC ENGINEERING"

Actinomycetes are a well-known and very intensively investigated group of bacteria. They have produced various antitumor drugs and are used industrially to produce antibiotics. Despite their track record in antibiotic production, a huge potential still remains to be revealed: Actinomycetes have about 30 biosynthetic gene clusters which are responsible for natural product biosynthesis - the function of most of them is still unknown. Whole complexes of genes are not active under normal laboratory conditions. In most cases it is not yet known how these "silent genes" are switched on and which substances they produce in an active state.

The HIPS "Actinobacteria Metabolic Engineering" Junior Research Group activates such genes in the microbial genome: Powerful and efficient instruments for highthroughput genetic analysis of actinobacteria are provided by special enzymes like site-specific recombinases, transposases, I-Scel meganuclease and beta-glucuronidase based systems. Those recently developed genetic tools are being used for the construction of synthetic biobricks, the identification of regulatory networks, which are responsible for "silencing" natural products biosynthesis, and the generation of suitable hosts for the antibiotic production and activation of "cryptic" biosynthetic gene clusters. Andriy Luzhetskyy's group anticipates that the methods will provide new possibilities for the study of functional gene expression in actinomycetes and eventually lead to natural product discovery.





Different transposon mutants of Streptomyces coelicolor M145



CBCH

"CHEMICAL BIOLOGY OF CARBOHYDRATES"

Carbohydrates and glycoconjugates belong to the three major classes of biopolymers. Complex carbohydrates play important roles in biological recognition processes, which are represented by the presence of dense glycoconjugate layers on cells, known as the glycocalyx. Despite their importance, the study of carbohydrates suffers because of the limited methods available for their synthesis and analysis, a problem not experienced with the study of nucleic acids or proteins.

TREATMENT OF CHRONIC INFECTIONS: DISRUPTING LECTIN-MEDIATED BIOFILMS

Many human pathogens can establish chronic infections with the help of a biofilm mode of life. As a protective shield, the matrix of the biofilm renders antibiotics ineffective and ensures the survival of the embedded pathogen. Novel ways for treatment address the disintegration of such biofilms, and thus restore the activity of antibiotics. The architecture of biofilms is frequently maintained by carbohydrates and so-called

lectins, which recognize and crosslink carbohydrate motifs of the glycocalyx, both on human cells and pathogens. The inhibition of such structural components leads to the disruption of a biofilm and thereby allows treatment of the infection. *Pseudomonas aeruginosa* is an important pathogen in hospital-acquired infections and for cystic fibrosis patients. This Gram-negative bacterium can establish chronic infections in various tissues by accumulating into protective biofilms. One focus of the research here is on two *P. aeruginosa* lectins, which are crucial elements of the biofilm architecture.

The group headed by Alexander Titz aims to develop antibacterial drugs using a combination of medicinal chemistry, biochemistry and microbiological methods. Recently, a competitive binding assay was developed for the *in vitro* evaluation of inhibitors of the *Pseudomonas* lectins. In collaboration with other groups at the HIPS and the HZI, potent molecules obtained by the group are then evaluated further in biofilm and infection models. Such compounds may ultimately lead to the successful treatment of chronic infections without evoking resistance among the pathogens.

INTERVIEW



Prof. Dr. Rolf Müller, Managing Director of the Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS) and Head of the "Microbial Natural Products" Department

Rolf Müller studied pharmacy at Bonn University and obtained his PhD at the Department of Pharmaceutical Biology. In 1996, he went to the Department of Chemistry at the University of Washington in Seattle, USA. This was when he began to investigate the production of antibiotics in bacteria. Two years later he returned to Germany as a junior group leader at the German Research Centre for Biotechnology (GBF, now the HZI) in Braunschweig. In 2000, he completed his habilitation thesis at the Technische Universität Braunschweig on the biosynthesis of antibiotics in actinomycetes and myxobacteria. Since October 2003, Rolf Müller has held a chair as professor of Pharmaceutical Biotechnology at Saarland University. His research has already earned the Phoenix-Pharmacy Research Award twice, the DECHEMA Award for Natural Products Research, the BioFuture Award of the German Federal Ministry for Education and Research, and the DECHEMA Award of the Max-Buchner Research Foundation. Since 2012 he has been a member of the German National Academy of Science and Engineering.

In 2009 Rolf Müller became the Director of the Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS) and heads the Department of "Microbial Natural Products" (MINS).

Professor Müller, the HIPS has set itself the goal of combining pharmaceutical research and research into infectious diseases, why is that important?

The number of dangerous pathogens is increasing globally. But the problem is certainly not just limited to developing countries, as the increasing incidence of multidrugresistant tuberculosis clearly shows. Neither must the significance of infectious diseases here in Germany be underestimated. With more and more organisms developing resistances to available antibiotics, there are simply not enough new active agents currently under development. Our parent organization, the Helmholtz Centre for Infection Research (HZI) in Braunschweig, has extensive expertise in the field of infection research. However, until recently there

was a lack of pharmaceutical know-how to drive forward the development of new drugs. The key motivation behind the creation of the HIPS was therefore to combine the skills and knowledge at the HZI and Saarland University so that both institutions could work together to develop new anti-infective strategies and agents.

Why was the Saarland chosen as the location for the new Institute?

Saarland University has an excellent reputation for pharmaceutical research, covering areas such as medicinal chemistry, pharmaceutical technology, pharmaceutical biology as well as pharmacology and toxicology. Much of the work involves natural products – and about 80 percent

of anti-infectives currently in clinical use are based on natural products. Personal ties to the HZI certainly also played a role. I myself spent almost eight years at the HZI in Braunschweig before I took up an endowed professorship at Saarland University in the area of pharmaceutical biotechnology in 2003.

The HIPS was established jointly by Saarland University and the Helmholtz Centre for Infection Research. Founding the new Institute must have required close collaboration between Braunschweig and Saarbrücken.

Yes, that's right, but despite their relatively large geographical separation, collaboration was excellent right from the start. And I'd like to take this opportunity to thank all those involved at the HZI, particularly the late Jürgen Wehland, and at Saarland University. The state government here in the Saarland has also given us outstanding support, for example by providing the funding for the new HIPS building. We are very pleased to see that establishing Saarbrücken as a major centre of pharmaceutical research has received such strong political backing. It is also nice to see that the work we do is now getting positive feedback from a very broad political base at both the regional and national levels.

Regular events such as the HIPS Symposium and the HIPS Talks are also helping to raise public awareness of the HIPS and what it does.

The HIPS Talks are well attended and we've been able to invite some very distinguished speakers. The HIPS Symposium is generally held at the same time as the meeting of our Scientific Advisory Board (SAB). The SAB is made up of world renowned scientists, who also make excellent speakers at the symposium. The SAB has been established to support, advise and supervise the scientific and organizational development of the Institute and regularly meets in Saarbrücken to discuss current progress.

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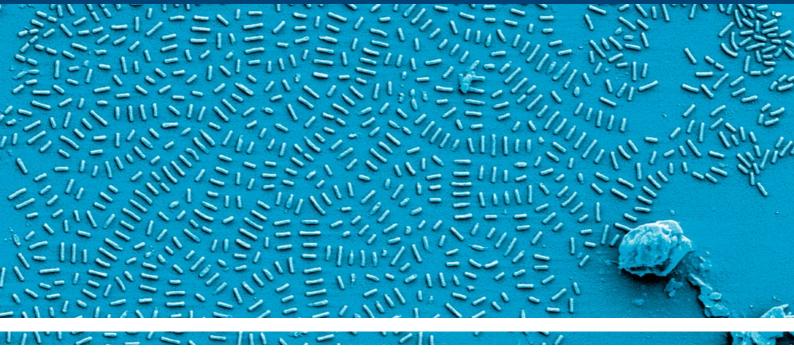
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HIPS was established in 2009. What are some of your successes to date?

We have already made a substantial contribution to drug discovery and drug development. Researchers from around the globe have been attracted to the Saarland and part of this work has involved establishing some new and innovative technologies. We have also been very successful in mentoring young research scientists to become future leaders in industry and academia. Our research is published in a range of highly respected academic journals, including Angewandte Chemie, Journal of the American Chemical Society, Proceedings of the National Academy of Sciences USA, Chemistry & Biology and also in various Nature Journals. We have additionally acquired substantial amounts of external research funding from funding providers such as the German Federal Ministry of Education and Research (BMBF), the German Research Foundation (DFG), the European Union (EU) as well as through collaborative projects with a variety of industrial partners.

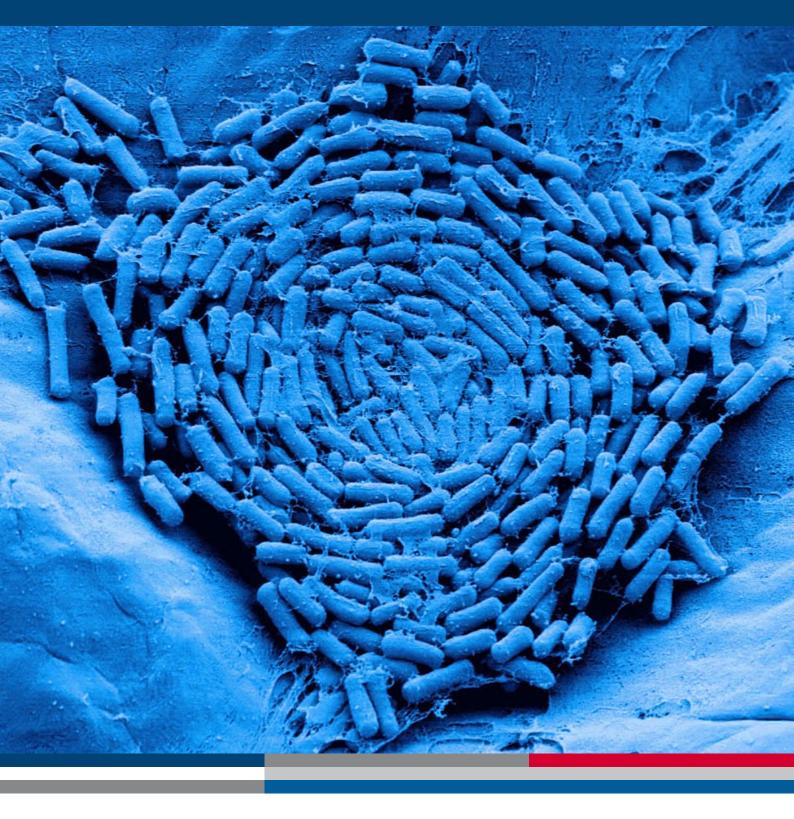
The plan is for the HIPS to relocate to its new building on the Saarland University campus in 2015. By then the number of employees working at the HIPS will have grown to 150. What's going to be happening over the next few years?

We plan to set up a third and possibly a fourth independent junior research group. One of them will be funded by the German Centre for Infection Research (DZIF). In addition, my colleagues Professor Lehr and Professor Hartmann and I will soon be working predominantly for the Helmholtz-Institute once our three professorial positions in pharmaceutical science at Saarland University have been filled. Taken together, the HIPS and Saarland University will then be one of the largest centres of pharmaceutical research in Germany – a very pleasing result for all of us who have been involved in this exciting project.



he DZIF is a close collaboration of experts from translational research, epidemiology and clinical practice to combat pathogens that are increasingly becoming resistant to the anti-infectives on the market. The HIPS works on the DZIF Natural Compound Library and within the Thematic Translational Unit "Anti-Infectives", making new natural products accessible and optimizing lead substances with the help of methods from medicinal chemistry, molecular biology and biotechnology.





Helmholtz-Institute for Pharmaceutical Research Saarland



