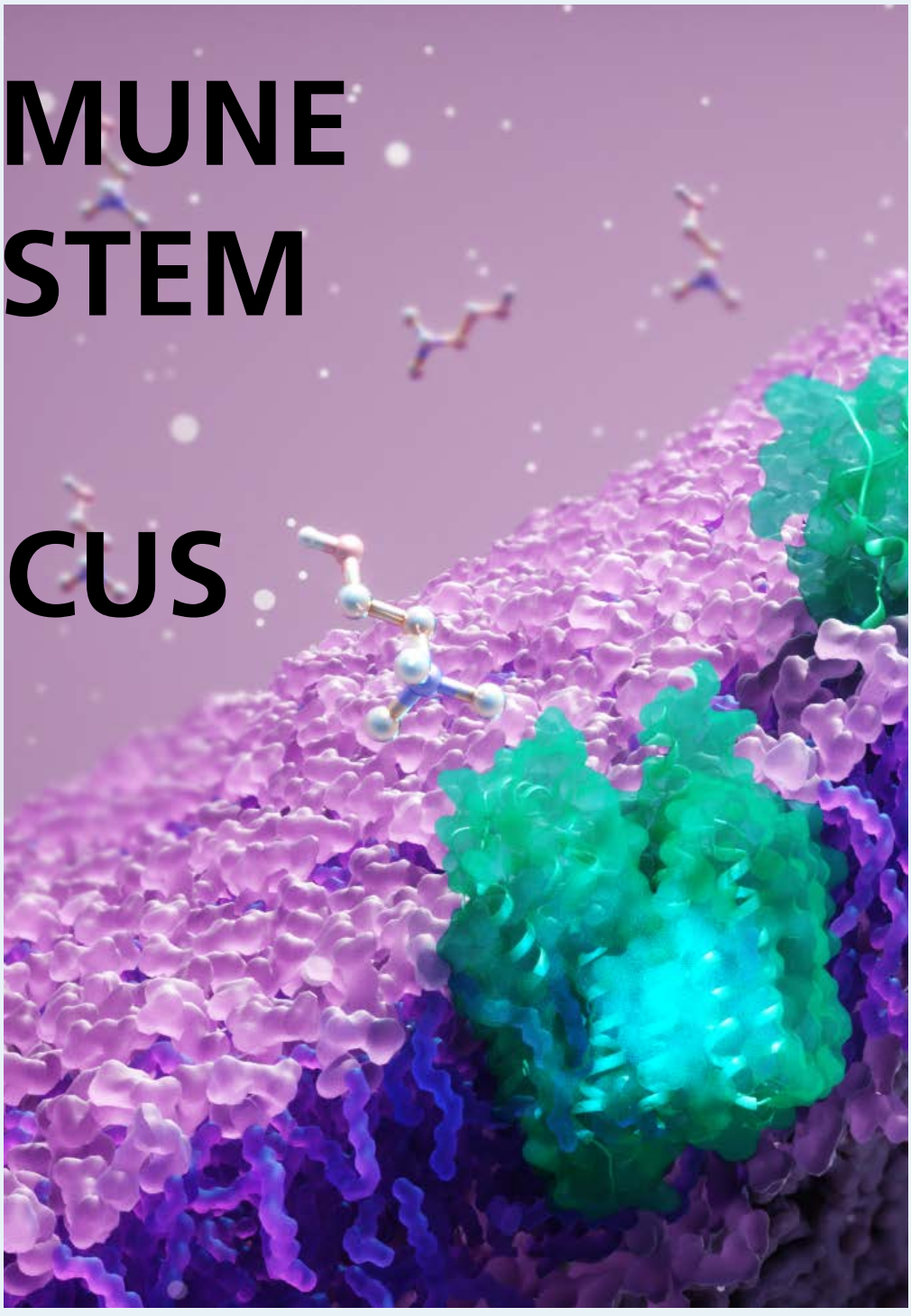
Fraunhofer
ITMP

IMMUNE SYSTEM IN FOCUS



Fraunhofer ITMP annual report **2024**

DEAR READERS,

» Last year in my foreword, I confidently mentioned the growth potential of the industrial healthcare sector, which has the potential to become a leading industry for Germany in the 21st century. «

In my view, one key to successfully exploiting this potential for value creation is even more intensive cooperation between all the players in our innovation system in order to transfer promising approaches from research into medical practice more quickly. This insight is also one of the key recommendations that the Fraunhofer Group for Health developed last fall together with the German Association of Research-Based Pharmaceutical Companies (vfa) in the strategy paper Pharma R&D 2035. I would be delighted if we could make a joint contribution to further strengthening the performance and attractiveness of Germany as a location for the industrial healthcare sector.

Despite some challenges, 2024 was a successful year for Fraunhofer ITMP, both from a scientific and a financial point of view. This is not least thanks to intensive cooperation with universities, our most important partners in the scientific system. Cooperation with the pharmaceutical industry was also stepped up and expanded in terms of the range of topics. I have great pleasure in presenting to you the 2024 Annual Report of the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP. Our transdisciplinary teams are working to build a solid bridge between basic research and clinical application. Through close cooperation with partners from industry, hospitals and other research institutions, we have succeeded in making significant progress in the translation of research results. This is reflected not only in the numerous publications and patents that we authored last year, but also in the promising projects that we have continued to develop both with the pharmaceutical industry and within our scientific ecosystem.

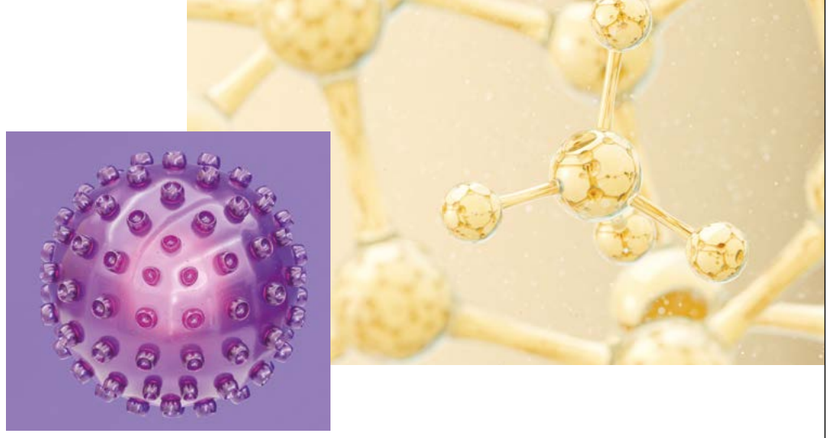
Prof. Dr. Dr. Gerd Geißlinger

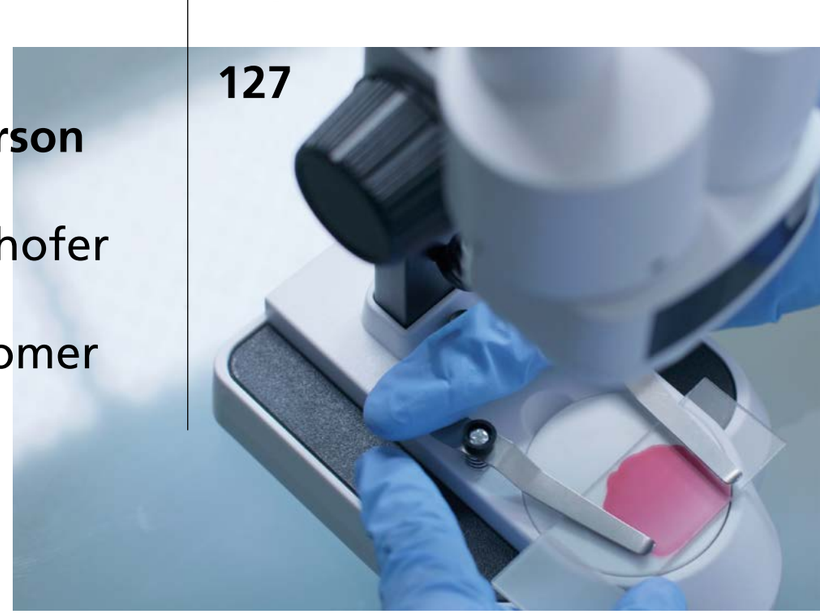
A particular focus this year was on the development of new therapeutic and diagnostic approaches and the improvement of existing treatment methods in the field of immune-mediated diseases.

I would like to thank our employees for their commitment and creativity. Their commitment is the key to our success and the positive developments. I would also like to thank our partners and sponsors who have supported us along the way.

We invite you to browse through the pages of this report and find out more about our projects, successes and future plans. Please get in touch with us.

Prof. Gerd Geißlinger
Executive Director of Fraunhofer ITMP





PROFILE OF FRAUNHOFER ITMP

Fraunhofer ITMP new building at its Frankfurt site, planned completion end of 2024;
© Wörner Traxler Richter Planungsgesellschaft mbH

Prof. Dr. Dr. Gerd Geißlinger
Executive Director
Fraunhofer ITMP

Prof. Dr. Frank Behrens
Deputy Institute Director
Fraunhofer ITMP

Dr. Lutz Zeitlmann
Deputy Institute Director
Fraunhofer ITMP

The Fraunhofer Institute for Translational Medicine and Pharmacology ITMP was founded from the Translational Medicine and Pharmacology institute branch of Fraunhofer IME on January 1, 2021. The institute's focus is on the research and development of innovative methods for the early detection, diagnosis and therapy of diseases resulting from disturbed functions of the immune system.

The guiding principle of Fraunhofer ITMP is the realization of superior, innovative solutions for cost-intelligent diagnostics and therapy for the benefit of patients. Research topics range along the value chain from drug discovery, through highly specialized methods in preclinical research, to selected indication areas in clinical research. The effective transfer of innovative ideas from biomedical research to medical application and industry is at the core of its scientific objectives. Based on the 4D concept (linking drugs, devices, diagnostics and data), this idea and technology transfer is intended to enable, for example, novel diagnostic and therapy options as well as early detection and prevention options for immune-mediated and neurodegenerative inflammatory diseases.

Fraunhofer ITMP currently employs around 425 people at its sites in Frankfurt am Main, Hamburg, Göttingen, Berlin and Penzberg/Munich. The institute is divided into two cross-site research divisions: Drug Discovery and Preclinical Research, and Clinical Research. Employees are organized in agile matrix teams across sites and divisions into what are known as innovation areas. This organizational structure allows rapid adaptation to current problems and issues.

The institute has close research links with many institutes and hospitals at the University Medical Center of Goethe University Frankfurt am Main, the University Medical Center Hamburg-Eppendorf, the University Medical Center Göttingen, the Charité Universitätsmedizin Berlin, the Ludwig-Maximilians-Universität (LMU) and the LMU Medical Center Munich. In addition, it enjoys lively scientific exchange with other national and international universities and research institutions. The aim of the collaboration is to identify trends and developments at an early stage and to develop and implement new research approaches and technologies. This being the case, Fraunhofer ITMP sees itself as a strong partner both for university medicine for the consistent translation of research findings into application and for the pharmaceutical and biotechnological industry.

RESEARCH DIVISIONS

Prof. Dr. Aimo Kannt
Drug Discovery, Preclinical Research
Fraunhofer ITMP Frankfurt am Main

Drug Discovery and Preclinical Research

Innovative therapeutics and biomarkers for precision medicine

This research area is concerned with elucidating disease mechanisms, validating drug targets and identifying and characterizing pharmacologically active molecules. The spectrum of therapeutic approaches ranges from small organic molecules to biopharmaceuticals, and research is also being done into novel drug entities such as proximity-inducing molecules. This work requires the development and use of innovative tools and technologies such as primary and stem cell models, high-resolution imaging, high-throughput screening, high-resolution mass spectrometry, targeted proteomics, methods for designing drugs and developing new substance libraries, innovative in vivo and ex vivo test systems and technologies for AI-assisted de novo protein design, protein engineering and structure elucidation. An additional focus is analyzing large data sets, developing knowledge graphs, merging data from different sources in federated database systems, processing it and storing it according to FAIR (findable, accessible, interoperable, reusable) principles. This also includes using real-world data to develop new active ingredients and for regulatory matters. In collaboration with the Clinical Research division at Fraunhofer ITMP, we use findings from clinical supply and molecular signatures obtained from patient samples to identify new target proteins, pharmacologically active substances and biomarkers for personalized medicine. The main indications are inflammatory diseases, neurodegenerative diseases, bacterial and viral infections and rare diseases.

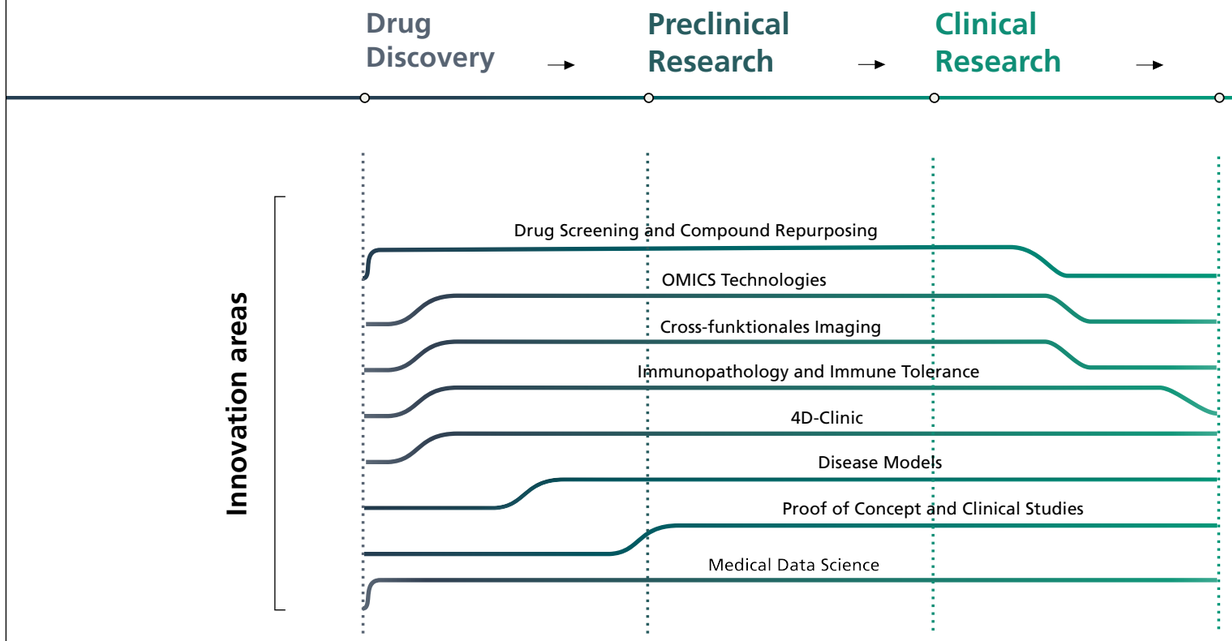


Fig.: Institute structure with cross-site and cross-divisional innovation areas.

Prof. Dr. Frank Behrens
Clinical Research
Fraunhofer ITMP Frankfurt am Main

Clinical Research

From idea to characterization of established products — successfully implementing innovative concepts through »Quality by Design«.

Our research focuses on designing, planning, implementing and evaluating clinical projects for patients with immune-mediated inflammatory diseases of various organ systems and for pain as an indication area (projects falling under the German Medicinal Products Act, or AMG, as well as non-AMG projects). In order to meet the medical challenges of immune diseases and related indications such as inflammation and pain in the field of translational research, we implement innovative clinical projects on the early detection, diagnosis, prevention and treatment of those diseases. As well as developing our own drug candidates, we also conduct proof-of-concept studies and investigator-initiated clinical trials. We use modern and clinically relevant study designs, which are developed in close cooperation with medical experts, to make sustainable improvements to patient care and address patients' specific needs. In our phase 1 research units at the sites in Frankfurt am Main and Göttingen, our direct connection to university hospitals means that drug candidates can be developed early, both for test subjects and for patients with the relevant indications.

THE FRAUNHOFER ITMP NETWORK

Headquarters
Institute site
Fraunhofer-project group

Frankfurt am Main

Translational Medicine and Pharmacology

Prof. Gerd Geisslinger | Prof Frank Behrens

Our expertise lies in researching therapeutic and diagnostic innovations for immune-mediated diseases. We use state-of-the-art technologies and multi-omics approaches for biomarker discovery, develop predictive disease models to characterize drugs, use our pharmaceutical expertise to identify and optimize chemical and biological active ingredients, and translate findings into applications through clinical research projects. In clinical research, our core expertise lies in the design and quality-assured execution of clinical trials, as well as the early clinical development of drug candidates in our phase I unit. Our own biomaterial bank supports basic research into our key indications.

Hamburg

Discovery Research ScreeningPort

Dr. Philip Gribbon | Prof. Carsten Claussen

Our expertise lies in high-throughput drug discovery using high-quality compound and re purposing libraries (in silico and in vitro screening), which enables us to identify pharmacologically active compounds. A comprehensive portfolio of phenotypic and biochemical assays, as well as in vitro models based on induced pluripotent stem cells are used to investigate the mechanisms of action. We are also developing workflows to ensure the analysis of drug discovery data and the highest standards of FAIR data management, as well as algorithms and AI tools for the statistical analysis of patient cohorts in different medical indications, thus covering the broad field of medical data science with our range of services.

Göttingen

Translational Neuroinflammation and Automated Microscopy TNM

Prof. Stefan Jakobs | Prof. Martin Weber

We use innovative high- and super-resolution microscopy techniques to visualize sub-cellular structures at the nano scale. The automation of these techniques and innovative image analysis algorithms allows us to investigate the influence of pharmacologically active compounds on the nanostructure of (living) cells with high throughput. In various preclinical models, these compounds are examined for their in vivo efficacy within the central nervous system. A modern phase I unit as well as an excellent interdisciplinary team guarantees the translation into the hospital and completes our portfolio in the research into new drug candidates for neuroinflammation.

Berlin

Immunology and Allergology IA

Prof. Torsten Zuberbier | Prof. Marcus Maurer

We research disease mechanisms in inflammatory, immune-mediated, neuroinflammatory and neurodegenerative diseases. We use bioanalytical high-throughput technologies such as omics methods to analyze biomolecules and pathomechanisms in patient samples that are involved in complex physiological and pathophysiological processes. We investigate identified target molecules (targets) and their modulators (drugs) in suitable in vitro, ex vivo and in vivo disease models of varying complexity, through to highly predictive models for the human and patient situation. The adverse outcome pathways, or undesirable influences on certain (patho-)mechanisms, can also be explored.

Penzberg/Munichen

Immunology, Infection and Pandemic Research IIP

Prof. Michael Hoelscher | Dr. Andreas Wieser

We research the interactions between infectious agents and the immune system with the aim of improving the prevention, screening and early detection of future pandemics and optimizing the treatment of infectious diseases.
As part of epidemiological surveillance, we identify potential pathogens that could cause a pandemic. A modular system can be used to create sequencing data, antigens and antibodies for prototype strains, and develop suitable rapid test systems.
The establishment of multi-parameter diagnostic platforms is intended to improve the diagnosis of infectious diseases: Viral and bacterial pathogens can be detected at the same time and the status of the immune system or organ functions can be determined.

FRAUNHOFER ITMP
WITHIN THE FRAUNHOFER-GESELLSCHAFT

Fraunhofer headquater in Munich; © Markus Jürgens

www.fraunhofer.de/en

The Fraunhofer-Gesellschaft is at the global forefront of applied research. Founded in 1949, it now operates 76 institutes and research units in Germany. It has just under 32,000 employees, most with a background in natural sciences or engineering, who generate a total annual research volume of 3.4 billion euros. Contract research accounts for 3.0 billion euros of this total.

The Fraunhofer-Gesellschaft plays an important role in the innovation process through its focus on innovative key technologies and its implementation of research results in business and industry. As a trailblazer and driving force when it comes to forward-looking developments and scientific excellence, it also contributes significantly to the shaping of our society and our future.

The various Fraunhofer institutes operate autonomously, and so certain structures, programs and processes have been established within the Fraunhofer-Gesellschaft to pool their expertise together. The aim is to strengthen both field-specific and interdisciplinary networking between the individual Fraunhofer institutes and to expand their competitiveness by opening up new, joint business units. Within the Fraunhofer-Gesellschaft, Fraunhofer ITMP is involved in various structures and initiatives in the field of health research.

Fraunhofer Strategic Research Fields (FSFs)

The seven Fraunhofer Strategic Research Fields (FSFs) of the Fraunhofer-Gesellschaft form the focus of the research portfolio — especially with a view to the markets and needs of tomorrow.

https://www.fraunhofer.de/en/research.html

Fraunhofer lead markets

Fraunhofer defines strategic customer segments (lead markets), which offer customers industry-oriented access to the range of services offered by Fraunhofer. Through innovations, the lead markets create global competitive advantages for Germany, secure Germany's and Europe's technological sovereignty and generate sustainable value creation for society.

https://www.fraunhofer.de/en/for-customers-and-partners.html

Fraunhofer Groups

Related Fraunhofer institutes join together in Fraunhofer groups in order to pool their expertise, present themselves jointly on the research and development market and play an active role in shaping corporate policy.

https://www.fraunhofer.de/en/institutes/institutes-and-research-establishments-in-germany/fraunhofer-groups.html

Fraunhofer Health

Health Research at the Fraunhofer-Gesellschaft or Fraunhofer Health for short, is made up of the **Fraunhofer Group for Health**, the **Fraunhofer Strategic Research Field Digital Healthcare** and the **Lead Market Healthcare Sector.** The overarching goal is to transform innovation from biomedical research into medical application for the benefit of patients. The healthcare sector is a key industry with considerable economic importance for Germany as a business location and is characterized by the development of innovative high-tech products in medical engineering and pharmaceuticals as well as new treatment and examination methods.

The nucleus of Fraunhofer Health Research is formed by the Fraunhofer Group for Health, a medical, scientific and technological community of highly qualified experts from six Fraunhofer institutes and one Fraunhofer research unit, who bring together their expertise from the fields of medicine, pharmacology, medical engineering, digital health applications and biotechnology on an interdisciplinary level in the four key areas of drugs, diagnostics, devices and data (Fraunhofer 4D concept). The goals of this specialized research group are to coordinate this research within the Fraunhofer-Gesellschaft, pool core areas of expertise and harmonize the market presence of the respective group members.

The network-driven research activities are supplemented by market-specific working groups which, based on a bottom-up approach, promote cross-institute cooperation on handling complex research questions and drive the development of medical innovations, which often arise at the interfaces between the various specialist fields. This technology-driven approach can produce innovations to give Germany a global competitive edge, secure Germany's and Europe's technological sovereignty and generate sustainable value creation for society. The political agenda is set jointly with a view to the markets and needs of tomorrow. The focus here is on building up the sovereignty of medicine and medical device supply, improving the usability of medical data, decoding the immune system and defining transdisciplinary translation cycles to accelerate the usability of innovative drugs and medical devices.

https://www.gesundheit.fraunhofer.de/en.html

Further links:

Fraunhofer Strategic Research Field
https://www.fraunhofer.de/en/research/fraunhofer-strategic-research-fields/digital-healthcare.html

Healthcare sector
https://www.fraunhofer.de/en/for-customers-and-partners/healthcare-sector.html

Fraunhofer Group for Health
https://www.fraunhofer.de/en/institutes/institutes-and-research-establishments-in-germany/fraunhofer-groups/health-research.html

Fraunhofer Clusters of Excellence

The Fraunhofer Clusters of Excellence bundle inter-institute research activities on system-relevant topics and act as "virtual institutes." They not only pursue individual projects, but also follow a concrete roadmap for the long-term development of a complex technological trend.

https://www.fraunhofer.de/en/institutes/institutes-and-research-establishments-in-germany/cluster-of-excellence.html

Fraunhofer High-Performance Centers

Fraunhofer High-Performance Centers are regional cooperation projects between Fraunhofer institutes, university and non-university research institutions, companies and stakeholders from civil society. The aim is to work together to further develop regionally specific research priorities and to improve the economic impact and societal benefits of R&D projects by successfully transferring this research into practical application.

https://www.fraunhofer.de/en/institutes/cooperation/high-performance-centers.html

Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

The Fraunhofer Cluster of Excellence Immune-Mediated Diseases (Fraunhofer CIMD) pools Fraunhofer's specific strengths in the field of translational medicine, interdisciplinarity and transdisciplinarity. Its purpose is the use of scientific findings on the complex function, dysregulation and modulation of the immune system. This work makes research findings on early detection and diagnosis and new treatment options for immune-mediated diseases (IMDs) available for the benefit of patients. Fraunhofer CIMD conducts modern, forward-looking health research that is tailored to the indication area and has an interdisciplinary structure and organization. In Fraunhofer CIMD, established and new technologies are integrated in ways that are tailored to IMD applications. Data science and artificial intelligence, as well as medical technologies, are adopted into health research on IMDs in a targeted and medically moderated manner. Fraunhofer CIMD is developing into a central core for a national German network in the field of immune diseases, in cooperation with partners from universities, medical schools, non-university research institutions and industry.

https://www.cimd.fraunhofer.de/en.html

High-Performance Center Innovative Therapeutics TheraNova

Fraunhofer high-performance centers work together with university and non-university research partners to serve the needs of industry. Universities, higher education institutes, Fraunhofer institutes and other stakeholders work together at a single location on specific topics in order to rapidly implement the latest innovations. Together with the Goethe University Frankfurt am Main, the Max Planck Institute for Heart and Lung Research in Bad Nauheim and the Fraunhofer Institute for Computer Graphics Research IGD, as well as pharmaceutical and biotechnological companies in the Rhine-Main region, Fraunhofer ITMP has founded the High-Performance Center Innovative Therapeutics TheraNova. The focus of TheraNova is on the development of novel therapeutic approaches and drug classes for the treatment of diseases with a high unmet medical need. A key focus is the development and use of AI methods and quantum technologies for the design of complex biological agents and the analysis of multidimensional data sets (clinical data and findings, molecular and genetic profiles) for personalized therapy.

https://www.theranova.eu/

TOTAL BUDGET 2024

Budget

The **operating budget** in **2024** of Fraunhofer ITMP amounted to

€ 33.4 Mio.

(incl. start-up financing).

In addition, around

€ 4.8 Mio.

were invested in **equipment**.

Expenditure relating to **construction activities** for the new institute building in Frankfurt amounted to

€12.5 Mio.

Income

62.1 %

of the operating budget for the **contract research area** of the parent institute was financed by **external income.**

The **economic income** of

€ 4.49 Mio.

is at a good level.

Employees

At the **end of 2024,** a total of

387

people were employed at the Fraunhofer ITMP sites in Frankfurt am Main, Hamburg, Göttingen, Berlin and Penzberg/Munich.

The proportion of **women** (permanent staff incl. doctoral students) at Fraunhofer ITMP was

61 %

Summary

Fraunhofer ITMP with its sites in Frankfurt am Main, Hamburg, Göttingen, Berlin and Penzberg/Munich recorded considerable growth in 2024 and was thus able to strengthen and expand health research at Fraunhofer in cooperation with excellent university locations.

ADVISORY BOARD 2024

The members of the advisory board advise the various bodies of the Fraunhofer-Gesellschaft as well as the institute management and promote the connection of Fraunhofer ITMP to partners from industry, science and the public sector.

Fig.: The members of the Fraunhofer ITMP Board of Trustees at the annual meeting at the Westend Campus of Goethe University Frankfurt. © Fraunhofer

The fourth annual meeting of the members of the Fraunhofer ITMP advisory board took place on June 6, 2024 at the Westend Campus of the Goethe University Frankfurt. The Chair of the Advisory Board Prof. Löw-Friedrich, the President of Goethe University Prof. Enrico Schleiff and the former Minister-president of the German state of Hesse Dr. Volker Bouffier addressed the members of the advisory board and representatives of the five Fraunhofer ITMP sites. During the meeting, current developments at the Fraunhofer-Gesellschaft and Fraunhofer ITMP were discussed, and innovative technologies and methods from the individual Fraunhofer ITMP sites were presented.

In his report on the current situation for the Fraunhofer-Gesellschaft, Dr. Peter Neu, representing the Executive Board, focused in particular on the development of new efficiency programs designed to simplify a more stringent organization of processes.

Prof. Gerd Geisslinger, Executive Director of Fraunhofer ITMP and Medical Research Officer of the Fraunhofer-Gesellschaft, addressed the importance of the healthcare sector and discussed the development of the institute's sites. He emphasized the role of Fraunhofer in the translation of research results into clinical application.

The focus at next year's meeting will be on cooperation between Fraunhofer ITMP and industry, especially with regard to optimizing clinical trials.

Members of the advisory board in the 2024 reporting year

Prof. Iris Löw-Friedrich (chair)
UCB Pharma GmbH, Monheim

Prof. Heyo Kroemer (deputy chair)
Chief executive officer Charité — Universitätsmedizin Berlin, Berlin

Volker Bouffier
Minister-president of Hesse (ret.)

Prof. Klaus Cichutek
President of the Paul-Ehrlich-Institut (ret.), Langen

Dr. Carolin Daamen
Bristol Myers Squibb GmbH & Co. KGaA, Munich

Dr. Claudia Fleischer
Roche Diagnostics GmbH, Mannheim/Penzberg

Dr. Rolf Greve
Science, Research, Equality and Districts Authority (BWFGB), Hamburg

Prof. Stefan Hell
Max Planck Institute for Multidisciplinary Sciences, Göttingen

Dr. Claudia Jentzsch
Berlin-Chemie Menarini, Berlin

Dr. Joachim Kreuzburg
Chief executive officer Sartorius AG, Göttingen

Dr. Volker Lodwig
Roche Diagnostics GmbH (ret.), Mannheim

Dr. Ulrike Mattig
Hessian Ministry of Science and the Arts (HMWK), Wiesbaden

Prof. Michael Popp
Bionorica SE, Neumarkt in der Oberpfalz

Prof. Enrico Schleiff
President of Goethe University, Frankfurt am Main

Prof. Blanche Schwappach-Pignataro
Dean of the University Medical Center Hamburg-Eppendorf (UKE), Hamburg

Prof. Angelika Vollmar
Ludwig-Maximilians-Universität München, Munich

Dr. Marion Zerlin
Sanofi-Aventis Deutschland GmbH, Frankfurt am Main

FRAUNHOFER ITMP FRANKFURT

Prof. Dr. Dr. Gerd Geißlinger
Executive Director Fraunhofer ITMP
Frankfurt am Main

Prof. Dr. Frank Behrens
Deputy Institute Director
Fraunhofer ITMP, Frankfurt am Main

»We research and develop innovative approaches for the early detection, diagnosis and treatment of immune diseases.«

January 2021 / at Fraunhofer **since 2012**, then as the Translational Medicine and Pharmacology project group of Fraunhofer IME. **179** permanent staff (**197** in total).

Close collaboration/cooperation with (local university/university hospital)
- Goethe University Frankfurt am Main
- Frankfurt University Medical Center of Goethe University
- Frankfurt Alliance
- Helmholtz Health Centers

Indication area(s)
- Immune-mediated inflammatory diseases (IMIDs), especially in the fields of rheumatology, dermatology and gastroenterology
- IMID-associated diseases in other indication areas (e.g., psychiatry, neurology)
- Pain

Research focus(es)
- Development of therapeutic and diagnostic innovations
- Design and optimization of chemical and biological active ingredients
- Biomarker identification for diagnosis and personalized therapy
- Functional characterization of drugs (efficacy, safety) in human model systems
- Proof of concept (PoC) studies and clinical trials in all phases with innovative study design

Particular expertise
- Pharmaceutical chemistry and biological test systems for optimizing active ingredients
- Mass spectrometric analyses and targeted proteomics
- De novo protein design, biological degraders
- Design and quality-assured implementation of clinical trials
- Implementation of trial ideas as IITs and providing sponsorship in clinical trials
- Early clinical development of drug candidates in own phase I unit

Special technologies
- Multi-omics method for biomarker development
- Predictive disease models (in vitro, ex vivo, in vivo)
- Own biomaterial bank for the basic scientific characterization of IMIDs
- Interdisciplinary outpatient study clinic

Highlight
The time has finally come in 2025: The new building is on schedule and anticipation is mounting! We will soon be pooling our strengths at a central location in Frankfurt.

IN
FOCUS

PD Dr. Lena M. Biehl
Attract Group Manager
Fraunhofer ITMP Frankfurt am Main
lena.biehl@itmp.fraunhofer.de

Development of New Microbiota-Based Drugs From Idea to Application

In recent years, understanding of the role that human microbiota play in the development or progression of certain diseases has increased. Although research in this area is growing, there are still only a few microbiota-based therapies that have achieved clinical approval. Many therapeutic approaches are based on donor samples, while the development of live biotherapeutic products (LBPs) is more promising. LBPs are tailored bacterial consortia that are more efficient and economical. The proposed Attract group aims to research the clinical development of LBPs from idea to application.

The starting position

The microbiota — the multitude of microorganisms that colonize the human body — and their effects on human health and the development of diseases are currently being intensively studied. This means that we now know many of the important functions of the intestinal microbiota in particular for the physiological regulation of target organs. Damage to the microbiota leads to a reduction in diversity, causes a less favorable microbiota signature and can promote certain diseases. The correlations identified in previous research include numerous clinical pictures such as metabolic, rheumatic, cardiological, gastrointestinal, hepatic, renal, neurological, psychiatric and oncological diseases.

This results in enormous potential for the therapeutic use of the microbiota. Fecal microbiota transplantation (FMT) has established itself as the best microbiota-based therapy. It is used worldwide in the clinical treatment of Clostridioides difficile infections. Other diseases with promising research results in the use of FMT are chronic inflammatory bowel diseases, the decolonization of multi-resistant bacteria and the optimization of the response to immunotherapies in oncology. An FMT always requires the processing of individual donor samples, which means that its composition cannot be reproduced. Bacterial consortia selected for a specific indication, the live biotherapeutic products (LBPs), offer the advantage of reproducibility and promise greater safety and scalability. So far, there are still too few research groups that are translating these preclinical ideas into applications.

The aim of the new MicroThera research group

The newly established MicroThera Attract group at Fraunhofer ITMP aims to decisively address the lack of translation in microbiome research. The research group is working on a platform for innovative microbiome-based therapeutic approaches such as LBPs or other forms of therapeutic microbiome modulation — particularly in immunological and infectiological areas of application — and on bringing these into clinical development. In addition to its own research projects, the company also offers scientific services for academic or industrial partners, including the design and planning of potential studies, the production of initial prototypes and investigational medicinal products and the final implementation of clinical trials..

Application example: Vancomycin-resistant enterococci

Besonders vielversprechend ist die gezielte Entwicklung eines LBP zur Dekolonisierung
The targeted development of an LBP for the decolonization of vancomycin-resistant enterococci is particularly promising. Colonization with this pathogen is caused in particular by a disturbed microbiota and is dependent on reduced diversity due to antibiotic pre-treatment. This in turn leads to subsequent bloodstream infections, particularly in immunocompromised patients. The spread of VRE has increased worldwide and in Germany too in recent years. However, there has been no successful eradication of VRE colonization to date. The MicroThera Group is currently involved in preparing a clinical trial on the use of FMT for the decolonization of VRE, which is scheduled to start next year. The bioinformatic analysis of potentially protective microbiota signatures will be of great importance for the future work of the MicroThera group. By analyzing the data and incorporating nutrient competition models, promising LBP candidates for the effective decolonization of VRE will be identified. The resulting findings will serve as the basis for future research projects with the long-term goal of advancing an innovative treatment approach from indication to application in clinical trials.

In the coming years, the Attract Group plans to lay the foundations for firmly establishing applied research into microbiota-based therapies as a new research area at Fraunhofer ITMP.

RESEARCH

Green Light for the PREPARE Project LinCA

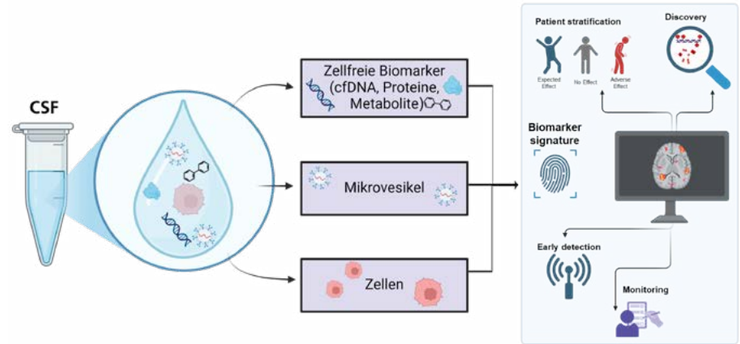
Low-input CSF Analysis (LinCA) is a new PREPARE project that received funding this year. Researchers from Fraunhofer ITMP (Frankfurt and Göttingen), Fraunhofer ITEM (Regensburg) and Fraunhofer IZI-BB (Potsdam) are focusing on the molecular diagnostic possibilities for diseases of the central nervous system, which are often still inadequate. The basic idea of LinCA is to gain maximum information with minimum use of samples. Its aim is to establish a cross-institutional platform for multi-omics analyses to identify biomarkers in cerebrospinal fluid (CSF).

Caption: The LinCA project focuses on the development of a platform for multi-omics analyses to identify biomarkers in cerebrospinal fluid (CSF). The limited volume of a CSF biopsy can thus be optimally utilized to obtain the most complex information possible through the use of different technologies. The collected data is combined in a multimodal analysis, helping to provide information on disease-associated and patient-specific changes that can be used for diagnostics and therapy monitoring in CNS diseases.

Dr. Nicole Ziegler
LinCA sub-project management
Fraunhofer ITMP Frankfurt am Main
nicole.ziegler@itmp.fraunhofer.de

The analysis of biomarkers from liquid biopsies is an essential component of the concept of personalized medicine and therefore indispensable for differential diagnostics, individual therapy decisions and predicting the success of treatment. The ability to take regular samples means that therapy can be monitored in real time and treatment can be tailored to the patient. Optimizing treatment using biomarker analysis therefore not only holds great potential for patients, most of whom are seriously ill, but is also fast and cost-effective.

In diseases of the central nervous system (CNS), access to disease-associated biomarkers poses a particular challenge, as they are retained from the bloodstream by the blood-brain barrier. Instead, they are increasingly found in the cerebrospinal fluid (CSF). Although CSF is taken as part of routine diagnostics for many CNS diseases, the minimal sample volume and the very low analyte concentrations limit the diagnostic possibilities enormously. This is where the LinCA projects wants to start by focusing its attention.

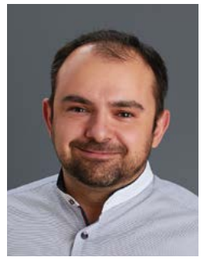


Multi-omics analyses of very small quantities

During the course of the project, the team will work on two clinical application examples. The first will involve working with biomarker analysis in multiple sclerosis, which can contribute to the selection of an optimal therapy by precisely predicting the course of the disease. A second application is leptomeningeal metastases in cancer, where precise diagnostics are essential for treatment but are currently still inadequate. In both cases, there is therefore a great need for highly sensitive and complex analysis methods to make patient treatment faster and more efficient.

At the end of the project, LinCA aims to provide solutions for the development and validation of biomarkers, as well as methods for predictive and therapy-accompanying diagnostics. In addition to the two clinical examples, these solutions can be applied to other CNS diseases and to the analysis of minimal sample quantities of other origins.

PUBLICATION HIGHLIGHTS



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Integrative Interface Research to Decode Rare Diseases

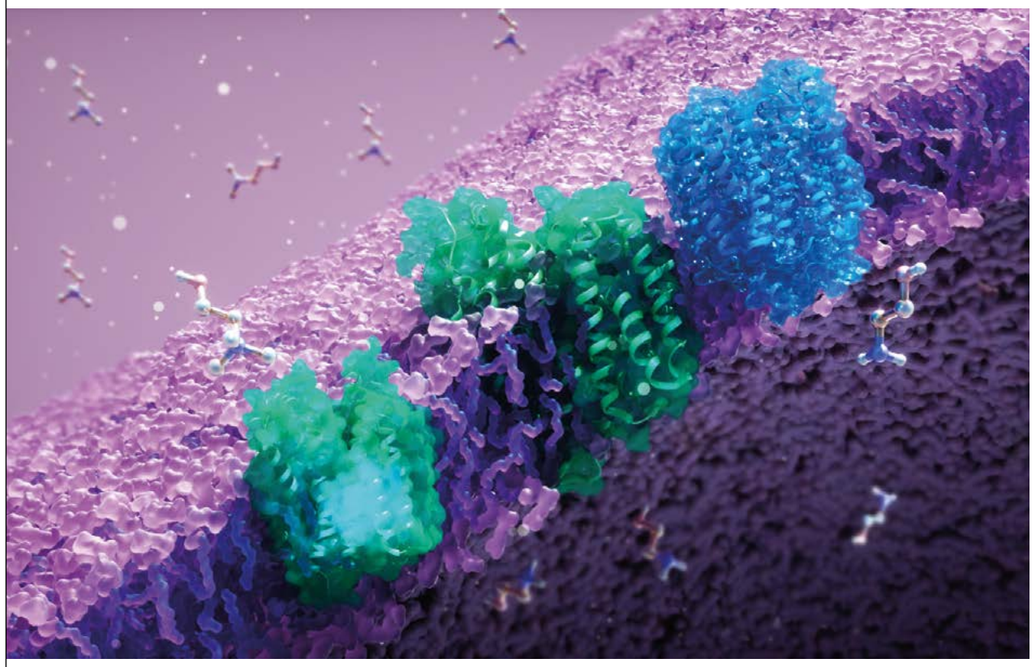
Membrane transport proteins of the solute carrier superfamily (SLCs) play a central role in the uptake of important nutrients and cellular building blocks. They influence metabolic processes and are essential for metabolic homeostasis in the human body. Genetic mutations in SLCs can cause rare diseases such as Fowler's syndrome. Our study reveals the molecular function of the SLC transporters FLVCR1 and FLVCR2, their substrate specificity and the mechanistic basis on which genetic mutations in these transporters cause rare diseases.

Membrane transport proteins of the solute carrier superfamily (SLCs) play a central role in metabolic processes and are essential for metabolic homeostasis in the human body. In numerous tissues and cell types, they regulate the uptake of important nutrients and cellular building blocks such as sugars, amino acids, lipids and ions. They therefore play a key role in metabolic adaptations and pharmacokinetic mechanisms.

The clinical relevance of SLCs was particularly recognized in the context of Fowler's syndrome and proliferative vasculopathy with hydranencephaly-hydrocephaly (PVHH), an autosomal recessive disorder first documented in an autopsy study by Malcolm Fowler et al. in 1972. It was not until many years later that genotyping studies identified the responsible gene, SLC49A2/FLVCR2, a member of the SLC superfamily, but the function of the transporter remained unclear for a long time.

In another study, specific mutations in the closely related SLC49A1/FLVCR1 transporter were associated with an autosomal recessive neurodegenerative syndrome that begins in childhood and is characterized by sensory ataxia and retinitis pigmentosa (PCARP).

Fig.: © Ella Maru Studio | Ella Maru; Fraunhofer ITMP | Schara Safarian

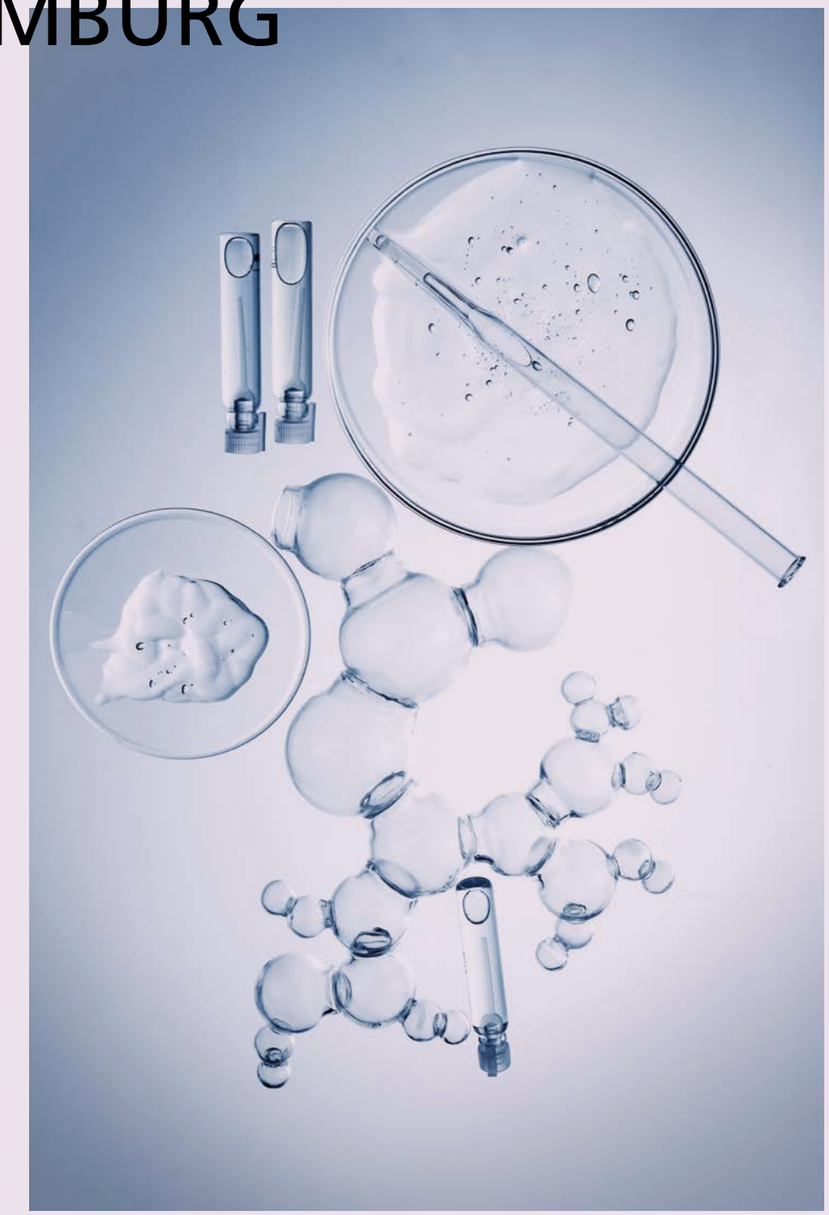


In order to better understand the molecular mechanisms of PVHH and PCARP, our research group led by Dr. Schara Safarian carried out extensive studies in cooperation with international experts. Using cryogenic electron microscopy, MD simulations, in vitro transport assays and mutagenesis studies, we were able to gain detailed insights into the molecular architecture of the two FLVCR transporters for the first time. Our results, published in the Nature journal in 2024, show that the folding of both proteins is almost identical and that the amino acid composition in the substrate binding domain remains particularly conserved. In addition, we identified choline and ethanolamine as the primary transport substrates of FLVCR transporters and confirmed the transport mechanisms in cell-based experiments and MD simulations.

These findings contribute significantly to the understanding of PCARP and PVHH etiology and may point the way for therapeutic approaches — from simple choline/ethanolamine substitutions to SLC49A1/SLC49A2-specific gene therapies.

Publication:
Keiken Ri et al.
Molecular mechanism of choline and ethanolamine transport in humans.
Nature
DOI:10.1038/s41586-024-07444-7

FRAUNHOFER ITMP HAMBURG



Dr. Philip Gribbon
Head of Fraunhofer ITMP Hamburg

Prof. Dr. Carsten Claussen
Head of Fraunhofer ITMP Hamburg

»We use innovative high-throughput methods and complex, cell-based disease models to identify and characterize pharmacologically active substances and rely on advanced data analysis in drug development.«

January 2021 / at Fraunhofer **since 2014**, then as part of the Translational Medicine and Pharmacology project group at Fraunhofer IME. **33** permanent staff (**38** in total).

Close collaboration/cooperation with (local university/university hospital)
- University Medical Center Hamburg-Eppendorf (UKE)
- Bernhard Nocht Institute for Tropical Medicine
- Deutsches Elektronen-Synchrotron DESY
- Screening site of the EU-OPENSCREEN European research infrastructure and the REMEDi4ALL repurposing platformL

Indication area(s)
- Kidney research
- Neuroimmunology and neurodegeneration
- Oncology
- Infectious diseases

Research focus(es)
- High-throughput screening and substance repurposing
- Stem cell biology
- Infection biology
- Medical data science

Particular expertise
- High-throughput drug discovery (in silico, in vitro screening and drug repurposing)
- Development of innovative data analysis workflows in the field of medical data science

Special technologies
- Phenotypic and biochemical assays for drug discovery and toxicity testing
- In vitro disease models and organoid models based on induced pluripotent stem cells (iPSCs)
- Medical data science: development of workflows, algorithms, knowledge graphs and dashboards, cohort analysis, FAIR data management, Fraunhofer Edge Cloud Health

Highlight
Organizer of the »Jugend forscht Hamburg-Volkspark« regional competition for 12 years.

IN FOCUS

Dr Ole Pless
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Translational Kidney Health: Fraunhofer KidMED Unit in Hamburg

The new partnership between the Fraunhofer ITMP Discovery Research ScreeningPort and the III. Department of Medicine of the University Medical Center Hamburg-Eppendorf (UKE) in the nephrology research focus area (headed by Prof. Tobias Huber) strengthens the existing collaboration and individual initiatives between the Fraunhofer-Gesellschaft and the UKE. By combining in-depth expertise in clinical nephrology and basic academic research with extensive proficiency in drug discovery and data analysis, this creates long-term prospects for the future. The aim of the collaboration is to establish a joint translational unit for kidney health at the UKE's Hamburg Center for Kidney Health.

Chronic kidney disease — a challenge for society

Chronic kidney disease (CKD) is a complex and multifactorial disease with a significant impact on patients' quality of life, morbidity and life expectancy. More than 9 million people in Germany and over 850 million worldwide are affected. CKD affects 1 in 10 people worldwide and its prevalence is increasing rapidly. CKD is therefore a global burden for the healthcare system, society and the economy.

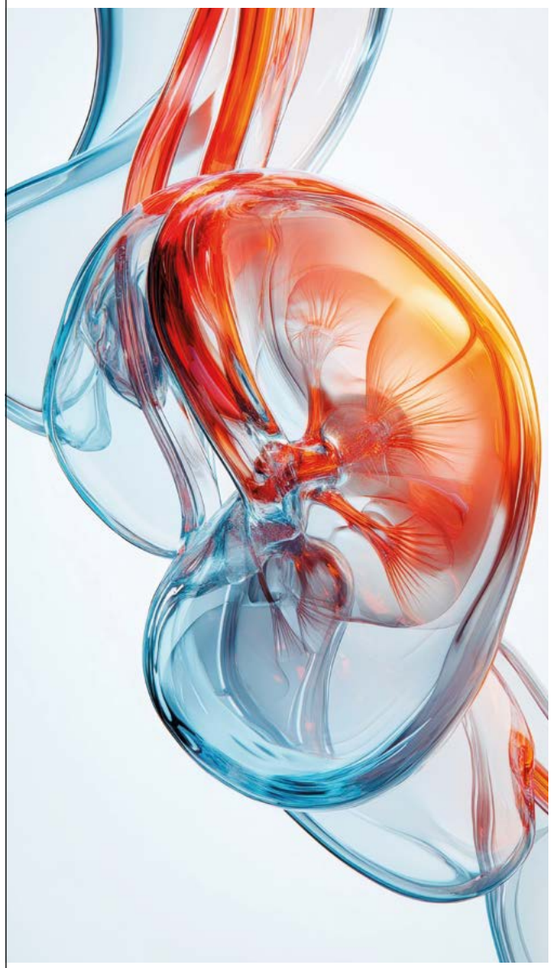
The disease is often progressive and is usually only diagnosed at a late stage. Existing therapies can slow down the progression of the disease, but cannot stop it or have a regenerative effect. Progressive CKD often leads to kidney failure, which means that those affected are dependent on time-consuming and cost-intensive hemodialysis or a kidney transplant. Even with early dialysis, the mortality rate for kidney failure is over 25%. In Germany, the wait for a transplant is around eight years, and many patients do not survive this waiting time.

The translation of scientific findings into successful clinical treatment approaches is particularly difficult in nephrology. Obstacles include the limited understanding of the pathobiology of the kidney, the lack of adequate diagnostic tools to guide precise therapeutic interventions and the lack of individualized therapies. Despite growing demands from science, patient organizations, the medical sector and political decision-makers, the topic remains underrepresented in health policy. In order to sustainably improve the quality of life for CKD patients, an interdisciplinary alliance of experts from universities, non-university research institutions and industry is urgently needed to bring together medical knowledge, innovative ideas, technological advances and an excellent infrastructure.

Goals of Fraunhofer KidMED

The partnership between Fraunhofer ITMP and UKE brings sustainable benefits for both institutions: It strengthens Hamburg as a center of science and integrates the core areas of expertise of the Fraunhofer ITMP Discovery Research ScreeningPort site of small molecule drug discovery and medical data science into (clinical) research at the UKE. In addition, the integration of renal medicine through the partnership with the UKE ideally complements the range of indications of the Fraunhofer ITMP site network, as immune-mediated diseases also play an important role in kidney health.

The Hamburg Center for Kidney Health (HCKH) offers a platform to promote innovative research identifying the disease mechanisms of the kidney end organ and translating them into new therapies. The Fraunhofer KidMED Unit is firmly embedded in the structure of the HCKH, making it an integral part of Campus Research II. The jointly developed research agenda can be divided into four core areas:



»KidMED mechanisms«
Disease-related phenotypes are mapped using suitable model systems (including cell cultures, human tissue, hiPSC-based 2D or 3D organoid systems, murine in vivo models) to verify relevant signaling pathways and molecular features of CKD.

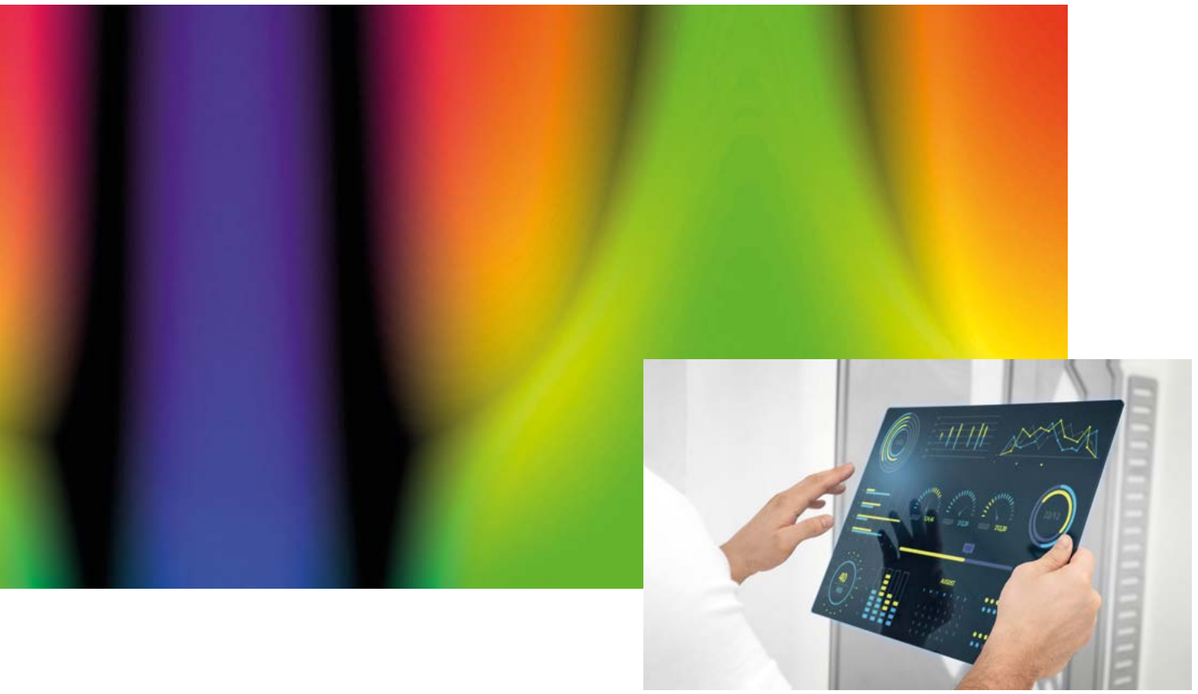
»KidMED Diagnostics«
Nephrology samples and databases are analyzed using advanced bioinformatics approaches to identify and validate the underlying biological processes. The results are used as training sets for subsequent patient stratification and the prognosis of disease progression.

»KidMED translation and therapy«
Once disease-causing characteristics have been identified and validated, screening for derived targets and phenotypic hypotheses is carried out. Active small molecules that have a positive impact on molecular characteristics and phenotypes are combined with histopathological image analysis to close any translational gaps between the different model systems. The following paradigm applies here: »Right destination, right drug, right tissue, right patient.«

»KidMED AI, knowledge graphs and data analysis«
Combining Fraunhofer data science tools with clinical data from kidney patients helps to reveal new correlations. And using knowledge graphs helps to visualize and identify previously unknown patterns in the CKD data.

The Fraunhofer KidMED Unit in Hamburg is a key project for the future of nephrology. The intention is that this interdisciplinary cooperation between basic research and the university medical center will help to develop innovative diagnostic and therapeutic concepts that will provide CKD patients with new treatment prospects and a better quality of life.

RESEARCH



Europe United for Innovation: Synthetic Data as the Key to Joint Progress

The use of medical data in healthcare is often limited by privacy concerns, access permissions, underrepresentation of certain groups and data scarcity. Synthetic data offers a solution: It can be created from patient data, for example, using generative AI models that minimize the patient re-identification risk. At Fraunhofer ITMP, we are creating synthetic data in several projects in order to simulate previously unseen scenarios and to develop algorithms and models for later application to patient data.

Dr. Katja Herzog
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Big data is revolutionizing the healthcare sector. Clinical data from patient records, imaging studies and genome research could help to improve diagnoses and optimize therapeutic approaches. However, data protection, regulatory requirements and statistical significance pose challenges.

Access to real clinical data is essential for the development of new therapeutic approaches, but restricted data sets often limit statistical relevance. Joint initiatives between the EU and the pharmaceutical industry, such as the IDERHA project, are working to overcome these hurdles. They regulate legal and ethical aspects of data access and enable the federated integration of heterogeneous data sets.

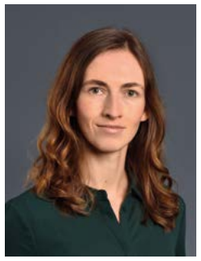
Why synthetic data is essential for clinical research

Synthetic data is generated artificially, but retains the statistical properties of real data. It increases data diversity, improves AI models and ensures data protection. In the IHI-SYNTHIA project, Fraunhofer researchers are developing a platform for generating synthetic patient data. The intention is that digital twins and federated machine learning will close data gaps and drive personalized medicine forward. A key field of application for synthetic data is the reduction of distortions and the improvement of model generalizability. Together with AstraZeneca and various cancer registries and hospitals, we have used synthetic data sets to demonstrate the concrete potential of data sharing in the field of oncological lung diseases. Combining registry data with artificially generated image and survival data could help to answer key research questions. In a project with the clinic for cardiovascular diseases at Charité — Universitätsmedizin Berlin, synthetic data was also used for simulation models to optimize the dosage of heart failure medications, which were then validated in a clinical trial.

Ethical boundaries and the future of synthetic data

Despite the potential of synthetic data, ethical aspects must be carefully considered. The EU attaches great importance to regulatory compliance, as demonstrated by projects such as IDERHA and SYNTHIA. These initiatives ensure that the generation of synthetic data complies with strict guidelines while facilitating international research. The combination of real and synthetic data promotes innovation, facilitates access to high-quality data and increases the precision of medical AI technologies. Europe is leading the way here and opening up new avenues for personalized medicine and patient-centered care.

PUBLICATION HIGHLIGHTS



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The TRPM4 Ion Channel as a Target Structure: Innovative Approach to Combating Neurodegenerative Diseases

The activity of neurons is based on an electrochemical gradient that is influenced by the neurotransmitter glutamate, among other things. In Alzheimer's and multiple sclerosis, there is an excessive release of glutamate in the brain, overstimulation and tissue damage. The TRPM4 channel is also activated and amplifies this harmful effect. We have therefore developed new human cell models and potent and selective TRPM4 inhibitors to counteract this effect.

Physiologically relevant models are essential for testing the efficacy and safety of new therapeutic strategies. Traditional animal models and conventional cell lines often do not adequately reflect human physiology and disease patterns. A promising new approach is induced pluripotent stem cells (iPSCs), which are obtained from patients' skin or blood samples and can be differentiated into specific cell types such as neurons.

By combining iPSCs and CRISPR/Cas9 technology, genes can be specifically modified in order to investigate their functions. Examples of this are two recently published iPSC lines developed by us in which the TRPM4 gene is altered and thus turned off. The TRPM4 channel plays an important role in neurodegenerative diseases and enhances the toxic effect of increased glutamate release. Pharmacological inhibition of the TRPM4 channel is therefore considered a promising approach to protect neurons from overstimulation and slow down the progression of the disease.

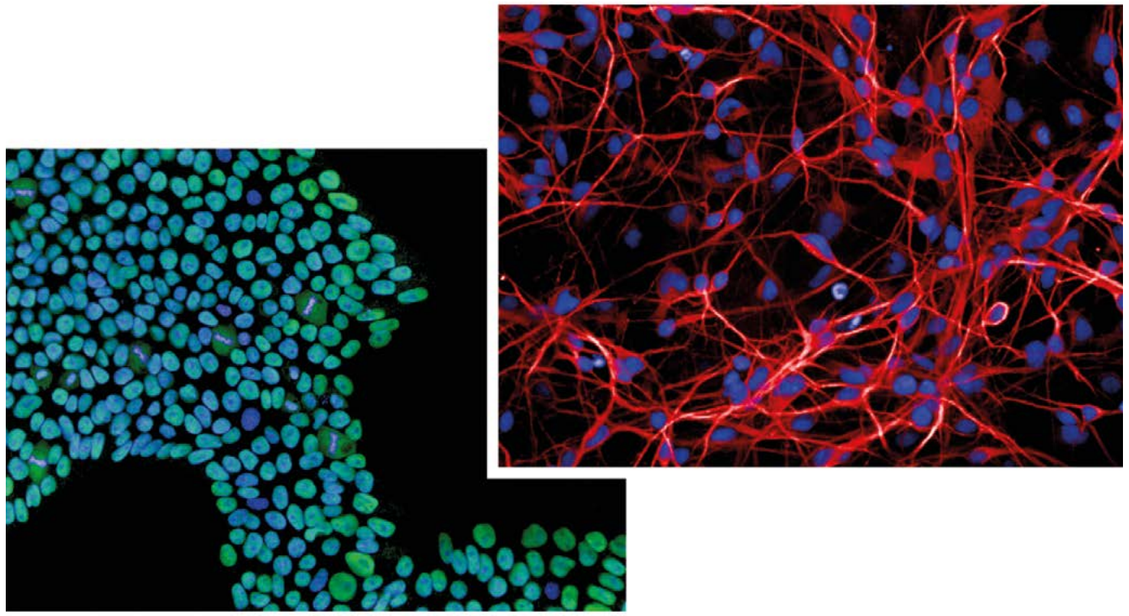
In partnership with the working group led by Prof. Manuel Friese (Institute of Neuroimmunology and Multiple Sclerosis at the University Medical Center Hamburg-Eppendorf) and the biotech company Evotec SE, we have identified novel substances that inhibit the TRPM4 channel and reduce neuronal damage. In a recently published study, we screened over 250,000 molecules for efficacy and prioritized them in terms of their effectiveness, selectivity, metabolism and toxicity. The new iPSC lines now open up the possibility of extensively testing the identified substances in all disease-relevant cell types, such as neurons, and working out their mechanism of action.

Drug development with (patho-)physiologically relevant iPSC models represents a significant advance in translational research. It improves the understanding of human diseases and the transferability of laboratory results to the human body. The example of TRPM4 inhibitors illustrates how these technologies can work together to find innovative solutions to complex health problems.

Publications:

Haferkamp et al.
Generation of two isogenic human iPSC lines (ZIPi013-B-1, ZIPi013-B-2) carrying a CRISPR/Cas9-mediated deletion of TRPM4.
Stem Cell Research
DOI: 10-1016/j.scr.2024.103609

Binkle-Ladisch et al.
Identification and development of TRPM4 antagonists to counteract neuronal excitotoxicity.
iScience
DOI: 10.1016/j.isci.2024.111425



Caption: iPSCs (left, with OCT3/4 expression) and the neurons differentiated from them (right, with MAP2 expression) of the ZIPi013-B-1 cell line in which the TRPM4 gene was inactivated by CRISPR/Cas9. © Fraunhofer ITMP | Dr. Undine Haferkamp

FRAUNHOFER ITMP **GÖTTINGEN**

Prof. Dr. Stefan Jakobs
Executive head of Fraunhofer ITMP Göttingen

Prof. Dr. Martin Weber
Head of Fraunhofer ITMP Göttingen

»We research neuroinflammatory diseases using state-of-the-art automated high-resolution imaging combined with patient-specific model systems to develop innovative approaches for early detection, diagnosis and therapy.«

At Fraunhofer since **2021**. **30** FTE (**49** in total).

Close collaboration/cooperation with (local university/university hospital)
- University of Göttingen
- University Medical Center Göttingen
- Max Planck Institute for Multidisciplinary Sciences

Indication area(s)
- Neuroinflammation
- Chronic diseases of the central nervous system (multiple sclerosis, Alzheimer's, Parkinson's)
- Metabolic diseases

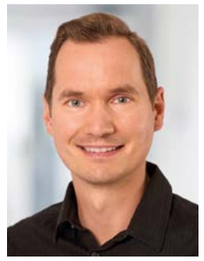
Research focus(es)
- Tailored cellular model systems (patient cells, iPSCs)
- Assay development and biomedical analytics (super-resolution microscopy, automated image analysis, AI)
- Experimental validation platform for inflammatory and degenerative processes in the CNS
- Clinical research and early clinical trials

Particular expertise
- Translational, interdisciplinary research into inflammatory neurodegenerative diseases and rare storage diseases
- Analysis of the function of mitochondria and cellular organelles in ultra-high resolution (STED microscopy)

Special technologies
- Automated super-resolution microscopy
- In vitro and in vivo disease models
- Disease models based on induced pluripotent stem cells (iPSCs) with a focus on neurodegenerative and genetic congenital diseases

Highlight
Date my mate_#_inside cells: With our super-resolution techniques, we observe how proteins in »cells date« each other.

IN FOCUS



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Prof. Dr. Martin Weber
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New Therapeutic Approaches for Difficult-to-Treat CNS Diseases — Models of Efficacy and Toxicity

At the Translational Neuroinflammation and Automated Microscopy TNM site in Göttingen, research is being conducted into new therapeutic approaches for difficult-to-treat diseases of the central nervous system (CNS), such as progressive multiple sclerosis (MS). In order to develop effective therapies, various in vitro and in vivo models are used to investigate both the efficacy and possible neurotoxic effects of potential new drugs. The findings are then transferred to the Early Clinical Trial Unit, where they are further evaluated in clinical trials on patients.

Multiple sclerosis (MS) is one of the most common chronic inflammatory diseases of the CNS. The immune system attacks the myelin coating around the nerve fibers, which leads to impaired signal transmission in the brain and spinal cord. MS is divided into different subtypes depending on its course: relapsing-remitting MS (RRMS), in which the symptoms occur in relapses; secondary progressive MS (SPMS), which in many patients develops into a continuously progressive form after years of RRMS; and primary progressive MS (PPMS), in which the neurological symptoms worsen continuously from the outset. Persistent inflammatory reactions in the CNS play a central role, particularly in progressive forms of the disease. The development of new therapies that stop or slow down this inflammatory process and the resulting damage therefore requires CNS-compatible substance classes. Therefore, in addition to efficacy testing, the analysis of possible neurotoxic side effects is a critical component in the preclinical development phase when identifying potential drug candidates before clinical trials on humans can be carried out.

Preclinical models for testing efficacy

The development of new therapies begins with the characterization of potential drugs in preclinical models. At the Göttingen site, in vitro and in vivo models are used to test the efficacy of potential drugs.

Cell cultures of CNS-resident cells derived from mice or human induced pluripotent stem cells (iPS cells) are used to analyze the mode of action of potential drug candidates in vitro. Various assays can be performed to analyze treatment effects on CNS-resident cells, including measurement of calcium flux, cell activation and differentiation, cytokine and chemokine profiles, phagocytosis, neurite outgrowth, antigen presentation, and neurofilament immunoassays.

Promising candidates are then tested in murine in vivo models. A common model is experimental autoimmune encephalomyelitis (EAE), in which immune cell-mediated demyelination of the nerve cells in the CNS occurs. EAE can be induced by active immunization with CNS antigens, passive immunization after adoptive transfer of myelin-specific T cells or by the use of transgenic models in which spontaneous induction of EAE occurs. This leads to inflammation with focal confluent lesions characterized by pronounced microglial activation, axonal damage and axonal loss. The EAE model is well suited for the analysis of axonal/neuronal protective treatment strategies. Another model is the cuprizone model, in which the copper chelator cuprizone administered via the feed leads to chemical-induced demyelination in the CNS — without involvement of peripheral immunity and with the blood-brain barrier largely intact. The pathophysiology is characterized by oligodendrocyte apoptosis, microglial activation and astrogliosis. Near-complete demyelination is achieved after 5–6 weeks of cuprizone intoxication. When cuprizone is discontinued, spontaneous endogenous remyelination occurs, making the model ideal for studying the therapeutic effects during demyelination and remyelination without peripheral influences.

Preclinical models for testing neurotoxicity

In addition to efficacy, each drug must also be tested for potential toxicity. Neurotoxic effects refer to damage that a drug can cause to the nervous system. Symptoms can range from mild discomfort such as headaches and nausea to severe neurological disorders, indicating temporary and/or permanent damage to the peripheral and/or central nervous system.

Various murine and human neuronal cell culture models as well as a range of analytical methods for the preclinical investigation of neurotoxicity have been established at the Göttingen site. A standardized pipeline enables high-throughput screening for the detection of cell viability, cytotoxicity and neurodegenerative processes. Important indications of neurotoxic effects are provided by morphological analysis of the neurons, which includes morphometric analysis of axons, dendritic branching and the mitochondrial network using high-resolution and super-resolution microscopy techniques.

Summary

The development of new treatment candidates for MS and other CNS diseases requires comprehensive preclinical testing for efficacy and neurotoxicity. The combination of in vitro and in vivo tests enables the targeted evaluation of promising substances before they are tested on humans in clinical trials.

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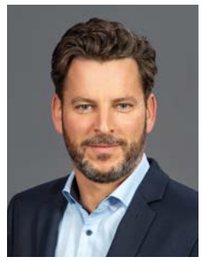

Prof. Dr. Martin Weber
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B-cell Depletion in the Therapy of Neuroinflammatory Diseases

B-cell-depleting therapies have a high therapeutic efficacy in the treatment of multiple sclerosis (MS) and other neuroinflammatory diseases. B-cell-depleting therapies include various anti-CD20 antibodies and an anti-CD19 antibody. In cooperation with partners from the pharmaceutical industry, Fraunhofer ITMP is analyzing the advantages and disadvantages of these antibodies in order to make a disease and patient-specific selection for the best possible therapeutic patient treatment. Neuroinflammatory diseases, such as MS and neuromyelitis optica (NMO), are usually treated with immunomodulatory drugs. Depletion of B cells has established itself as a highly effective therapy, as B cells have numerous functions in inflammatory processes.

Anti-CD19 or anti-CD20 antibodies

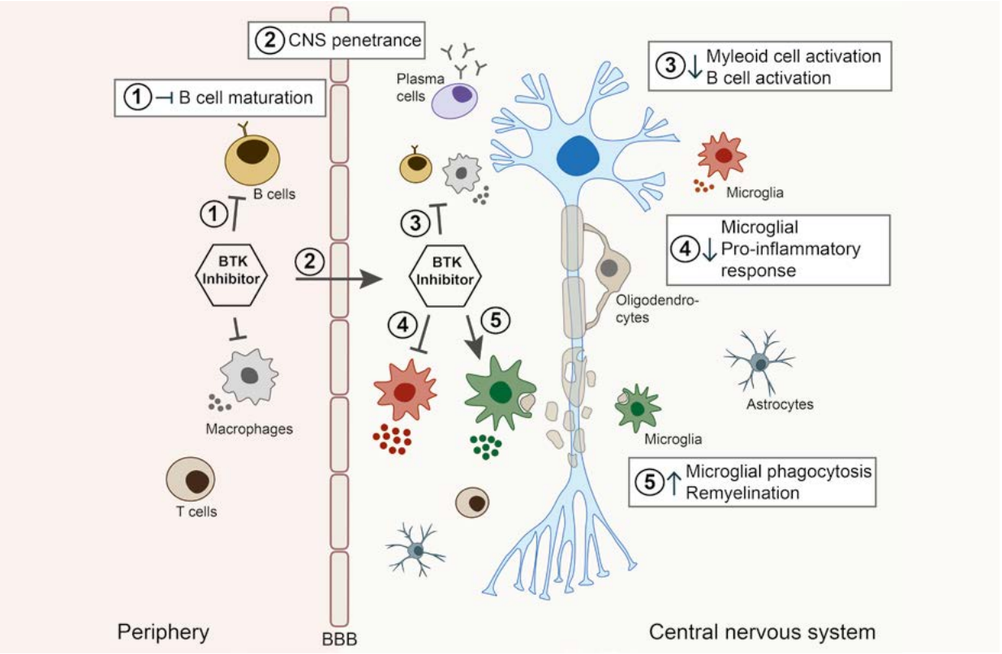
B cells are mainly destroyed with the help of monoclonal antibodies directed against CD20 or CD19. CD19 and CD20 are what are known as cell type markers and are found exclusively on B cells. Both markers play a role in B cell development and are particularly present in stages where B cells are actively involved in inflammatory processes. From a certain stage of maturation,

CD20 is no longer found on the cells. This applies in particular to plasma cells. Plasma cells are mature, antibody-producing B cells whose task is to maintain acquired immunity as an immune memory. Since CD20 is no longer found on plasma cells, only the inflammation-promoting B cells are eliminated with anti-CD20 antibodies, but not the B cells that maintain basic immunity. CD19, on the other hand, remains on the B cell even in the plasma cell stage. Anti-CD19 antibodies thus deplete antibody-producing plasma cells. Anti-CD19 antibodies are therefore preferable in the treatment of diseases where pathogenic antibodies play a role. One example of this is NMO. In this case, the immune system uses pathogenic antibodies to target the body's own aquaporin-4 in the central nervous system. Consequently, the disease defines which B-cell-depleting antibody should be prioritized. It is not only decisive for the individual therapy whether antibodies against CD19 or CD20 are used. Other factors also play a role.

Dose and administration routes can be crucial

There is a broad spectrum of anti-CD20 antibodies. These include the mouse-derived rituximab, the humanized ocrelizumab and the fully human ofatumumab, as well as many others. These antibodies differ not only in the binding site to CD20 and the corresponding receptor-binding domain, but also in the administration method and dosage in which they are used. While high doses of ocrelizumab are administered intravenously in the hospital every six months, ofatumumab can be injected at home subcutaneously once a month in much lower doses using a pre-filled pen. In cooperation with partners from the pharmaceutical industry, Fraunhofer ITMP is currently investigating the extent to which these different administration routes, intervals and dosages affect the treatment of MS.

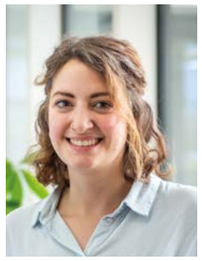
PUBLICATION HIGHLIGHTS



BTK inhibitors as a New Therapeutic Approach Against the Gradual Progression of MS

The gradual progression of multiple sclerosis (MS) represents a major therapeutic challenge. Chronic activation of microglia, which causes inflammatory processes in the central nervous system, plays a key role in this disease. Inhibition of Bruton's tyrosine kinase (BTK) therefore offers a promising approach for influencing these mechanisms and slowing the progression of MS. Our study provides information on the prospects of success of this therapeutic approach.

Fig.: Overview of the mechanism of action of BTK inhibitors
BTK inhibitors inhibit the B cells and macrophages in the periphery (1) and, after crossing the blood-brain barrier (2), also the B cells and macrophages in the CNS (3), as well as the chronically activated microglia (4 and 5).
© Fraunhofer ITMP | Anastasia Geladaris



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Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) that leads to neurological symptoms such as visual impairment or muscle weakness. The disease often progresses in relapses, but can also progress gradually, with the damage to the nerves and the associated impairments increasing continuously — a process known as MS progression. While acute relapses were the focus of MS research early on and are now easily treatable, there is as yet no therapy for gradual progression. However, it is now known that MS mainly progresses independently of relapses. This has also changed the requirements for therapy: Today, the aim is not only to prevent relapses, but also to slow down the gradual progression of MS at an early stage with a highly effective therapy and to prevent the long-term worsening of symptoms.

It is now assumed that inflammatory processes within the CNS are responsible for the progression of MS. Immune cells located in the CNS, the microglia, are thought to play a key role in this process. A promising strategy for controlling MS progression is therefore the inhibition of the enzyme Bruton's tyrosine kinase (BTK), which plays a central role in the activation of both B cells and myeloid cells such as macrophages and microglia.

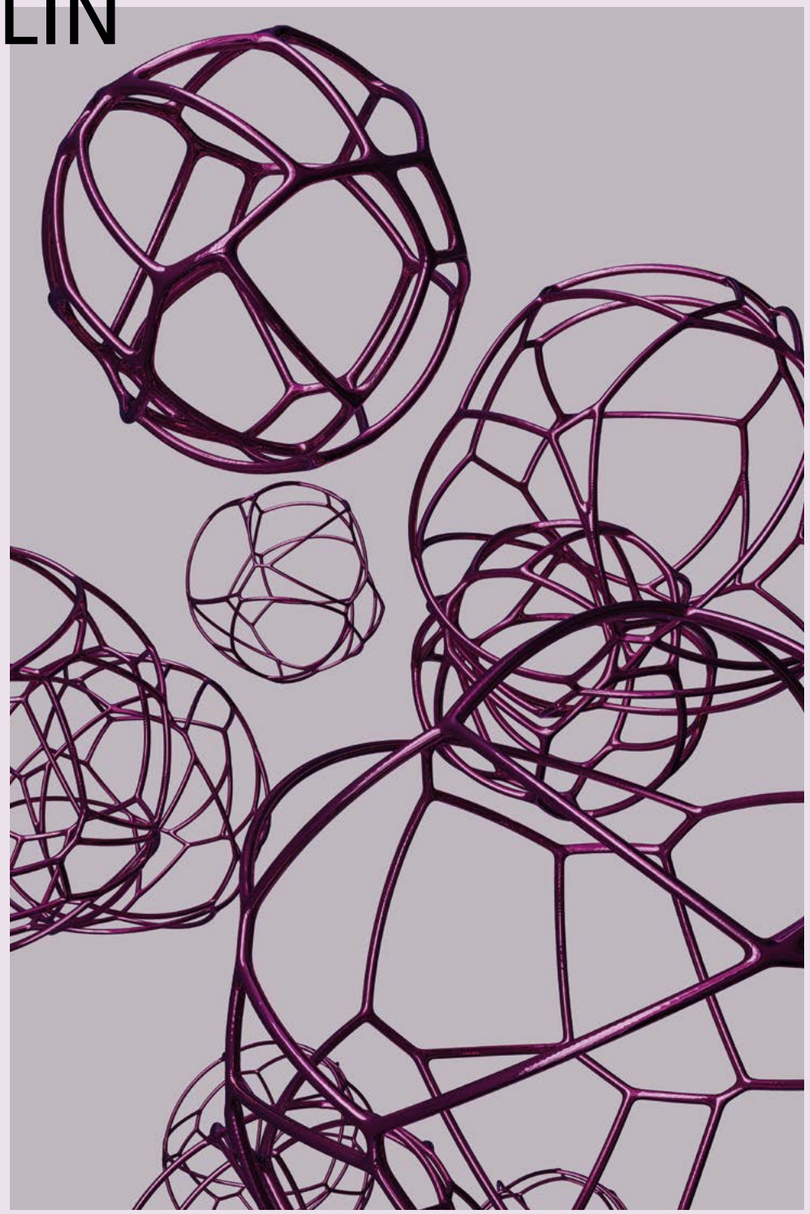
In the present study, we were able to show that BTK is specifically present in microglia in the brains of MS patients. BTK was also upregulated in microglia in an MS mouse model.

We then investigated the potential of BTK inhibition by the BTK inhibitor evobrutinib in various MS mouse models. We were able to demonstrate that evobrutinib can cross the blood-brain barrier and significantly reduce microglial activation in mice with chronic experimental autoimmune encephalomyelitis (EAE) (see Figure 2, 3, 4). In addition, evobrutinib therapy in the cuprizone mouse model of toxic demyelination also induced accelerated remyelination, indicating promising restoration of neuroglial integrity (see Figure 5).

These results emphasize that BTK inhibition has the potential to counteract the underlying chronic progression of MS.

Publication:
Geladaris et al.
BTK inhibition limits microglia-perpetuated CNS inflammation and promotes myelin repair.
Acta Neuropathologica
DOI: 10.1007/s00401-024-02730-0

FRAUNHOFER ITMP BERLIN



Prof. Dr. Torsten Zuberbier
Executive head of Fraunhofer ITMP Berlin

Prof. Dr. Markus Magerl
Head of Fraunhofer ITMP Berlin

»We are researching mast cells and their role in immunology and allergology in order to develop new approaches for diagnostics and therapy.«

At Fraunhofer since **2021**. **69** permanent staff (**73** in total).

Close collaboration/cooperation with (local university/university hospital)
- Charité – Universitätsmedizin Berlin

Indication area(s)
- Mast cell-mediated diseases (urticaria, pruritus, prurigo, (hereditary) angioedema, mastocytosis)
- Asthma, allergy
- Atopic dermatitis

Research focus(es)
- Mast cell biology and mast cell interaction with other immune cells in the skin
- Mast cell-mediated diseases and their differential diagnoses
- Development of experimental and diagnostic tests for early detection and patient stratification
- Characterization of autoreactive antibodies (IgE/IgG) (e.g., specificity)

Particular expertise
- In vitro mast cell skin cell models and ex vivo skin models
- Biobanking of patient samples
- Development of own patient reported outcome measures (PROMs) to measure health status and treatment success
- Execution of clinical trials from phase I to IV

Special technologies
- Spectral flow cytometry for cell analysis
- Microscale thermophoresis and biolayer interferometry for measuring molecular interactions
- High-throughput histology and immunofluorescence microscopy, and AI-assisted analysis
- Microneedle-based collection of interstitial skin fluid for biomarker analysis

Highlight
We are based in an 1980s brutalist building with interesting architecture.

IN FOCUS

Dr. Melba Muñoz
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Chronic inducible urticaria (CIndU)

Chronic inducible urticaria (CIndU) is one of the difficult-to-treat diseases. Symptoms include recurrent wheals and angioedema induced by definite triggers. The only approved and recommended treatment for CIndU is second-generation non-sedating H1-antihistamines (H1-AH). In many cases, however, they remain ineffective. A promising new therapy with barzolvolimab, a monoclonal antibody against KIT, is currently being tested in CIndU patients. Barzolvolimab was the first drug to show high efficacy in chronic inducible urticaria in a large randomized placebo-controlled study.

What is chronic inducible urticaria?

Chronic inducible urticaria (CIndU) is a subset of chronic urticaria (CU) characterized by the occurrence of recurrent itchy wheals, angioedema or both in response to specific, distinct and reproducible triggers. These triggers are physical or chemical in nature and are caused by friction, pressure, cold and heat, solar radiation, vibrations, activities that stimulate sweating, contact with substances and water. CIndU differs from other forms of CU in that the wheals and angioedema only occur after exposure to these triggers and not spontaneously. The incidence of CIndU is estimated at around 0.5% of the population. Pathogenic mechanisms involved in chronic spontaneous urticaria (CSU) also appear to play an important role in CIndU. The activation and degranulation of mast cells and the subsequent release of histamine and other inflammatory mediators are the main causes for the development of CIndU symptoms (Figure 1). The diagnosis of CIndU is based on a thorough medical history and specific provocation tests. For example, symptomatic dermographism can be diagnosed by stroking the patient's skin with a 4-pin comb (FricTest®) to detect the development of wheals and itching after scratching the skin. Cold urticaria can be diagnosed using a temperature test device (TempTest®), which can be used to determine the temperature threshold at which patients develop symptoms due to cold exposure.

Various treatment regimens are currently used in the treatment of CIndU. Avoiding known triggers is recommended for symptom control, which sometimes proves difficult or even impossible. This treatment is also associated with a severe impairment of quality of life. H1-AH are widely used in the treatment of CIndU, however there is a high percentage of sufferers who remain symptomatic despite receiving four times the recommended standard dose. They suffer from severe itching and burning wheals, which can have a dramatic impact on their quality of life.

Fig.: Barzolvolimab inhibits stem cell factor binding on mast cells
The KIT receptor is activated by the binding of stem cell factor, which leads to differentiation, chemotaxis, maturation and survival of mast cells. Barzolvolimab blocks the binding of stem cell factor (SCF) to KIT, which leads to the death of mast cells in the skin.

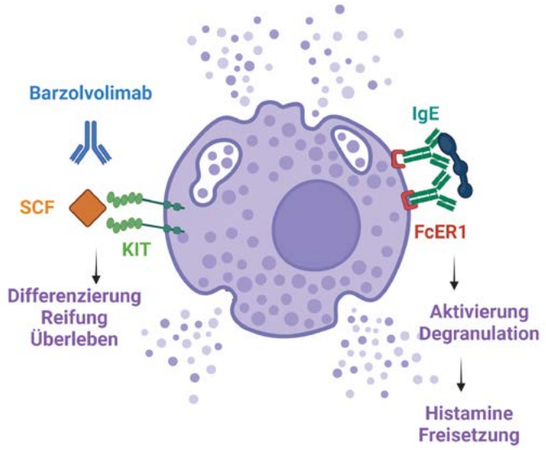
Barzolvolimab, a promising drug for the treatment of CIndU patients

Barzolvolimab (CDX-0159) is a humanized immunoglobulin G1 kappa antibody that binds the extracellular domain of the receptor tyrosine kinase KIT with high specificity (Figure 1). Activation of KIT by its single ligand stem cell factor (SCF) is required for the differentiation, chemotaxis, maturation and survival of mast cells. By inhibiting stem cell factor binding, these die off, which greatly reduces the mast cells in the skin.

The phase 1b study of two of the most common forms of CIndU, symptomatic dermographism and cold urticaria, showed that a single intravenous dose of barzolvolimab rapidly reduced skin mast cells. This resulted in a clear and statistically significant reduction in the disease activity of those affected. This study also highlights the central role of skin mast cells and KIT signaling in symptomatic dermographism and cold urticaria. Apart from changes in hair color (appearance of white hairs) and selective taste changes for umami and salty flavors, barzolvolimab was well tolerated.

In a subsequent randomized, controlled phase 2 study, patients with symptomatic dermographism and cold urticaria were treated with subcutaneous injections of barzolvolimab at a dose of 150 mg every 4 weeks or 300 mg every 8 weeks during a 20-week treatment phase. All primary and secondary endpoints were achieved with high statistical significance. Similarly, all secondary endpoints of the study were met at week 12 of treatment and strongly support the results of the primary endpoint. This includes responder analyses, improvements in critical temperature (for cold urticaria) and changes in critical friction threshold (for symptomatic dermographism) and itching in conjunction with provocation testing and the urticaria control test.

Overall, the results of these studies demonstrate the high efficacy of barzolvolimab in the treatment of CIndU. The symptoms can be much better controlled and the quality of life of those affected can therefore be significantly improved. A planned phase 3 study should now confirm these results. In the near future, this could provide an alternative treatment for CIndU patients for whom there is currently no effective therapy.



Dr. Jörg Scheffel
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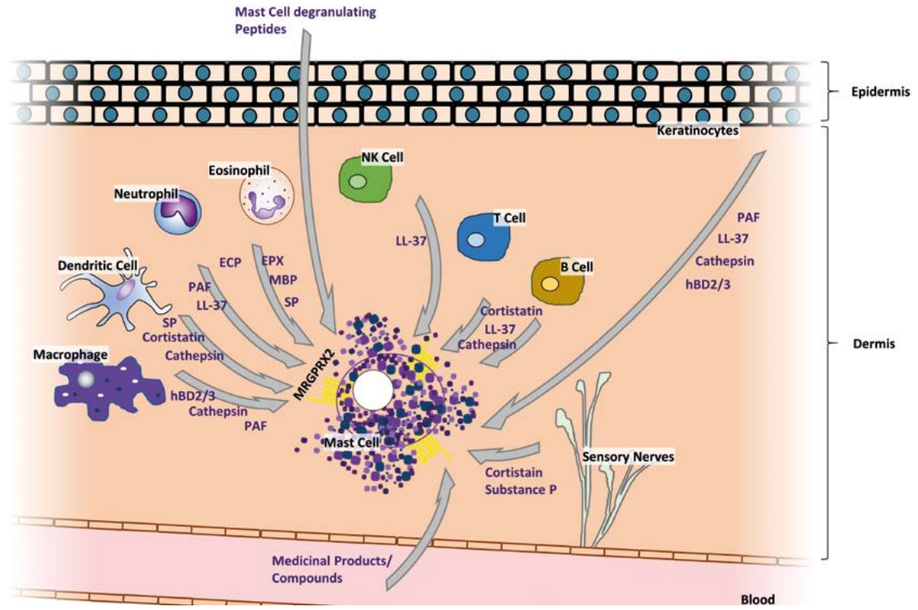
MRGPRX2 — a Promising Therapeutic Target in Mast Cell-Mediated Diseases

The G protein-coupled receptor MRGPRX2 (X2) is a central player in mast cell activation and plays a key role in inflammatory reactions. Its activation by neuropeptides, peptide hormones or certain drugs can trigger allergy-like symptoms. Studies show that X2 antagonists are promising treatment options for patients with chronic spontaneous urticaria. Fraunhofer ITMP in Berlin is conducting intensive research into how X2-mediated mast cell reactions can be specifically influenced in order to develop better diagnostic and therapeutic approaches.

Mas-related G protein-coupled receptor X2 (MRGPRX2, or X2) is a G protein-coupled receptor that is mainly expressed in mast cells, keratinocytes and sensory neurons. In recent years, numerous ligands have been identified that activate X2, including neuropeptides, antimicrobial peptides, peptide hormones and endogenous peptide fragments, but also some FDA-approved drugs such as codeine. The activation of X2 in mast cells leads to degranulation and the release of mediators such as histamine, which promotes inflammatory reactions. Initial studies show that X2 antagonists are effective in patients with chronic spontaneous urticaria (CSU). At Fraunhofer ITMP in Berlin, projects are being carried out to better understand the role of X2 in mast cell-mediated diseases and to develop therapies.

Caption: MRGPRX2 belongs to the family of G-protein-coupled receptors and is expressed on skin mast cells. A large number of ligands that activate this receptor have already been described. Activation of X2 in mast cells leads to an immediate reaction (degranulation) in which the cells release vasoactive and pro-inflammatory mediators, including histamine and proteases. In addition, lipid mediators and cytokines are also secreted, which modulate the inflammatory reaction.



HITME-skin

Study to characterize cytokine profiles in dermal interstitial fluid (dISF) after selective X2 and FcεRI-dependent mast cell provocation.

In healthy test subjects, local mast cell activation is induced by selective application of an X2-agonist or allergen. Using microneedle technology, dISF is extracted from the skin of the test subjects before and after provocation and analyzed for specific biomarkers using a multiplex proximity extension assay (PEA). Initial data suggest that after X2-dependent mast cell activation, individual mediators are selectively and significantly induced and can be detected in dISF. Specific signatures depending on the activation mechanism can help to better stratify patients and optimize treatment decisions.

XMass

Study to identify and characterize X2-agonists in dermal interstitial fluid (dISF) and serum in patients with CSU and chronic inducible urticaria (CIndU).

Can X2-agonists be detected in patients' dISF and serum? This is the subject of the XMass study. In patients with CSU and cold-induced urticaria, both blood and dISF are taken directly from the lesion and analyzed for X2-agonists using mass spectrometry. The serum and dISF are also examined for an X2 signature and other urticaria-associated markers in order to comprehensively characterize the patients. The results from this study will help to identify patients with X2-related mast cell activation at an early stage and distinguish them from patients with type I or type IIb CSU, enabling targeted therapy.

PUBLICATION HIGHLIGHTS

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New Study Results on the Treatment of Chronic Spontaneous Urticaria with Anti-IgE Antibodies

Many people with chronic spontaneous urticaria (CSU) do not respond to the current standard therapy with H1 antihistamines. New phase 3 studies show that the monoclonal anti-IgE antibody ligelizumab is an effective treatment option. Although it does not show superior efficacy compared to omalizumab, another anti-IgE antibody already approved for clinical use, this data confirms the importance of anti-IgE as the main therapy for patients with H1-antihistamine-refractory CSU.

Chronic spontaneous urticaria (CSU) is a mast cell-mediated skin disease characterized by the occurrence of itchy wheals and/or angioedema that last for more than six weeks without a specific trigger. For over 40% of those affected, CSU results in a severe impact on their quality of life. CSU is triggered by an incorrect response of the immune system, which leads to the formation of antibodies against the patient's own body. These IgE and IgG autoantibodies activate mast cells and thus cause the typical symptoms of the disease, as in an allergic reaction.

The international urticaria guidelines recommend non-sedating second-generation H1 antihistamines in approved and increased doses as initial treatment. For patients who do not respond to antihistamines, the only monoclonal anti-IgE antibody omalizumab approved for clinical use to date is to be used as an additional therapy.

The humanized anti-IgE monoclonal antibody ligelizumab showed superior efficacy compared to omalizumab in an in vivo mouse model. In phase 2b dose-finding studies, ligelizumab improved urticaria symptoms in patients with antihistamine-refractory CSU.

The two parallel phase 3 studies PEARL-1 and PEARL-2 have now provided detailed data on the efficacy and safety of ligelizumab. A total of 2,057 patients with moderate to severe H1-antihistamine-refractory CSU were examined. They received either ligelizumab, omalizumab or placebo. The primary endpoint was the change in weekly urticaria activity score from baseline after 12 weeks.

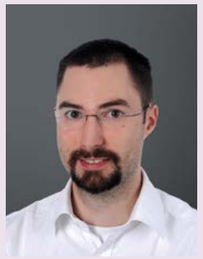
Ligelizumab was clearly superior to placebo, but not more effective than omalizumab. One third of patients in the ligelizumab and omalizumab groups achieved freedom from symptoms, while this was only observed in less than 10% of cases in the placebo group. Ligelizumab was also well tolerated.

The two studies confirm the efficacy and safety of anti-IgE therapies and thus underline their importance for the effective treatment of CSU. Further research is needed to identify biomarkers that can be used to reliably predict and monitor response to treatment with anti-IgE therapies.

Publication
Maurer et al.
Efficacy and safety of ligelizumab in adults and adolescents with chronic spontaneous urticaria: results of two phase 3 randomised controlled trials.
Lancet
DOI: 10.1016/S0140-6736(23)01684-7

FRAUNHOFER ITMP **PENZBERG/ MUNICH**

Prof. Dr. Michael Hoelscher
Executive head of Fraunhofer ITMP Penzberg/Munich



PD Dr. Andreas Wieser
Head of Fraunhofer ITMP Penzberg/Munich

»We are improving infectious healthcare with innovative diagnostic and therapeutic approaches to effectively contain potential pandemic pathogens.«

At Fraunhofer since **2021**. **65** permanent staff (**65** in total).

Close collaboration/cooperation with (local university/university hospital)
- Ludwig-Maximilians-Universität München
- LMU Medical Center Munich
- Roche Diagnostics GmbH

Indication area(s)
- Infectious diseases (e.g., tuberculosis, sepsis, yellow fever, Clostridioides difficile, diseases of the upper respiratory tract, TBE, Lyme disease)
- Immune-mediated diseases
- Neurodegenerative diseases (e.g., Alzheimer's)

Research focus(es)
- Microbiological analyses and pandemic research
- Immunology and infection research
- Aerosol research
- Drug research for neurodegenerative diseases

Particular expertise
- Execution of decentralized clinical trials to develop and evaluate new diagnostic procedures and therapies for tuberculosis in children and adults and to research the long-term consequences of tuberculosis
- Development of phage-based diagnostic and therapeutic methods against bacterial pathogens (e.g., Bacillus anthracis)
- Electrophysiological characterization of intracellular ion channels for drug discovery
- Diagnostic detection and monitoring of pathogens in wastewater samples
- Development and characterization of measurement technologies for the detection of microorganisms in aerosols

Special technologies
- Olink Proximity Extension Assay (PEA) technology
- Neuronal lysosomal patch-clamp electrophysiology
- Opera Phenix® Plus High Content Confocal Imaging
- Epidemiological statistical analyses and mathematical modeling
- Interaction measurements with MST
- Cloning and expression of antibodies from human B cells

Highlight
The mountain is calling! 72 steps of varying heights await employees who come to our offices in Schwabing. A free fitness program for your next mountain hike.

IN FOCUS

Dr. Lidia Chitimia-Dobler
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The Silent Tick Pandemic: Increasing Threat From Native and Tropical Ticks

Like mosquitoes, fleas, lice, etc., ticks are vectors that can transmit pathogens between animals and humans. After mosquitoes, ticks are the second most important species in human medicine worldwide and are responsible for the transmission and spread of infections such as Lyme disease and tick-borne encephalitis (TBE), particularly in temperate latitudes. A worrying trend has emerged in recent years: The number of infections transmitted by ticks is constantly increasing. Despite effective vaccines against TBE, the number of cases continues to rise. This silent tick pandemic could have far-reaching health consequences.

Ticks are the most important vectors of pathogens in Central Europe and play a significant role in the spread of infections. They are responsible for more than 90 percent of vector-borne infections in Germany. Of the 20 native tick species, the castor bean tick (Ixodes ricinus) plays a particularly significant role in Germany. In recent years, the number of TBE cases in Germany has risen steadily, with a record level of more than 300 TBE cases in Bavaria in 2024. Europe and North America are experiencing similar developments, which can be described as a silent global tick pandemic. However, the exact causes of this situation, which is particularly being observed in the northern hemisphere, are largely unclear.

In connection with this, research in Germany is currently focusing on two key aspects of the increase in tick-borne infections: the increase in TBE cases and the introduction of tropical tick species and their pathogens.

Why is the number of infectious diseases transmitted by ticks increasing in Germany?

This raises the question of whether the increase in TBE cases is caused by an increase in the tick population or an increase in tick activity. A globally unique data set is available to help answer this question: Since 2009, ticks have been collected and tested for the TBE virus in a natural TBE focus in eastern Bavaria on a monthly basis in a standardized process. Since 2024, this data set has been continued with the support of the Fraunhofer ITMP site for Immunology, Infection and Pandemic Research in Penzberg/Munich.

The evaluation of this data set shows that the number of nymphs, an important developmental stage of ticks for virus transmission, has not increased over the 15-year observation period. The number of adult ticks collected has not increased either but instead has decreased. The proportion of infected ticks and the amount of TBE virus in the ticks have also remained unchanged over the years. However, there is a noticeable increase in nymphs from 2016 onwards when the data is analyzed month by month. This corresponds exactly to the time when TBE cases also increased. The constant number of adult ticks indicates that the nymphs have increasingly failed to survive the summers due to excessively dry or hot weather or a lack of hosts. In addition, the results indicate that due to the mild winters, more ticks overwinter in the larval and nymph stage and then search for hosts in spring and early summer — precisely when people move their leisure activities outside in spring-like temperatures, which then increases the chances of contact with ticks and the transmission of pathogens.

Tropical ticks in Germany — a new threat?

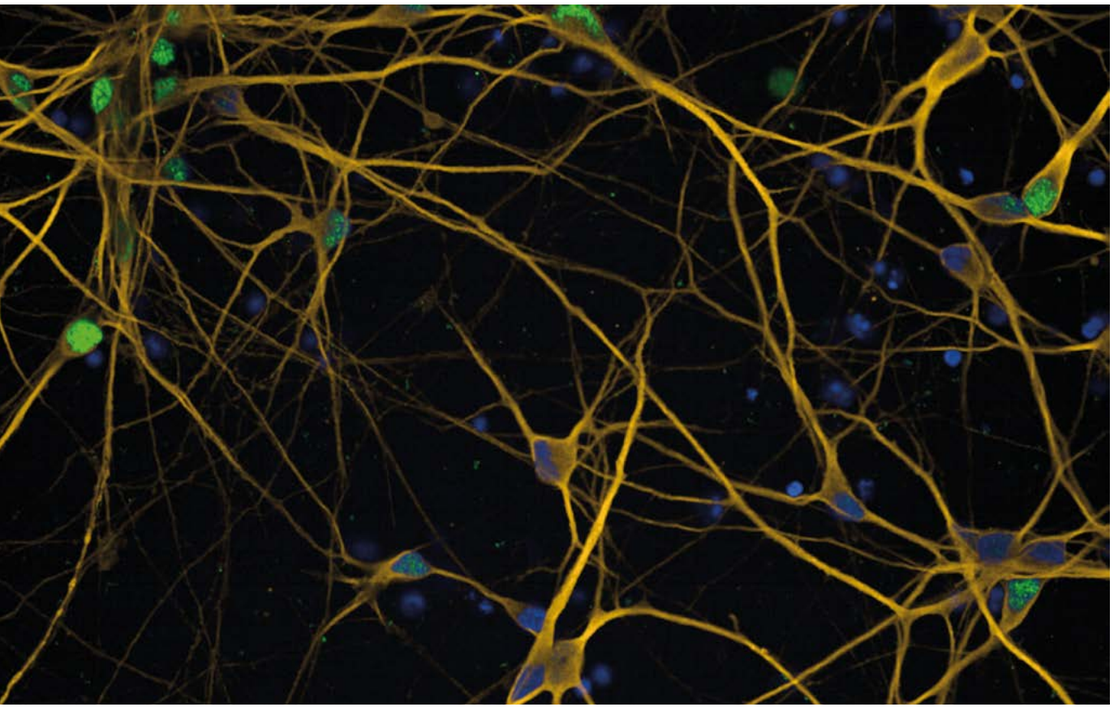
In recent years, an increasing number of tropical ticks have been sighted in Germany, especially Hyalomma marginatum and Hyalomma rufipes. These tick species, which originally come from the Mediterranean region and Africa, are known carriers of the highly contagious Crimean-Congo hemorrhagic fever.

Current research work is therefore investigating the significance of the introduction of tropical tick species and the tropical pathogens transmitted by them, as well as the conditions under which these tick species can become established in Germany and result in a continuing threat. These results should provide clues to classify and explain the silent tick pandemic on a global level.

Analyses conducted with the involvement the Fraunhofer ITMP site IIP for Immunology, Infection and Pandemic Research have shown that these ticks have probably been introduced to Europe via migratory birds from southern regions for many years. However, these steppe ticks were unable to develop into the adult stage due to the damp soil in early summer. Humid early summers thus prevented the development of permanent populations. However, in the last few years with little precipitation, soil moisture levels have fallen sharply, meaning that these ticks can now develop into the adult stage here too and are therefore increasingly being spotted on animals and humans. The reduction in rainfall in Germany therefore offers these ticks ideal conditions to establish themselves permanently in Germany and transmit potentially dangerous infectious diseases. This is already underway in Spain, with an increasing number of cases of Crimean-Congo hemorrhagic fever occurring in humans in recent years.

The two research projects involving the Fraunhofer ITMP site for Immunology, Infection and Pandemic Research IIP therefore identify different aspects of the current climate changes as contributory causes of the trend towards an increase in tick-borne infectious diseases, particularly in the northern hemisphere.

RESEARCH



New High-Throughput Imaging for Research Into Lysosomal Storage Disorders and Neurodegenerative Diseases

DThe Opera Phenix® Plus High-Content Imaging System provides a highly effective platform to research diseases and discover new potential drugs. Multiwell plates make it possible to analyze various conditions simultaneously in a single assay. The Opera Phenix® Plus enables the automated recording of multiple data points in these multiwell plates within a remarkably short space of time. At the Fraunhofer ITMP site for Immunology, Infection and Pandemic

Caption: Cells differentiated into neurons are used in high-throughput screening in 96-well plates and then visualized and evaluated on the Opera Phenix® Plus extremely quickly. © Fraunhofer ITMP | Yvonne E. Klingl

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Research in Penzberg/Munich, this technology is used to analyze new drug candidates for various diseases.

There is still a great need to develop better and more targeted therapies for numerous diseases and to discover and therapeutically exploit new disease mechanisms. Target structures in intracellular organelles such as lysosomes are a completely new approach. Lysosomes play a role, for example, in neurodegenerative lysosomal storage diseases, which often develop in early childhood, but also in classic neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. Endolysosomal transport pathways also play an important role in numerous infectious diseases. For example, individuals with mutations in the Niemann-Pick-C1 protein (NPC1) are protected against Ebola and numerous other viral diseases because the corresponding viruses use lysosomal proteins such as NPC1 to escape lysosomal degradation in order to replicate effectively in the cell. The findings from this project should therefore also prove useful in the future to better understand infection pathways of various pathogens and possibly discover new therapeutic approaches.

Ion channels:

Targets for potential drugs in neurodegeneration, lysosomal storage diseases and infectious diseases.

Lysosomes are therefore becoming an increasing focus for research in the fight against neurodegenerative diseases, lysosomal storage diseases and infectious diseases as well as cancer, kidney and liver diseases. The pH value and the ion concentration are particularly important for their efficient function. This delicate balance is regulated by ion channels, which are therefore currently of particular interest as new drug target structures.

High-throughput screening with Opera Phenix® Plus: fast drug analysis on multiwell plates

The Opera Phenix® Plus High-Content Imaging System can be used to test the effectiveness of various different cell lines or numerous potential drugs simultaneously. This means that up to 384 or 1,536 different conditions can be analyzed in parallel. For example, new ion channel modulators for therapy can be tested quickly and efficiently.

At the Fraunhofer ITMP site for Immunology, Infection and Pandemic Research in Penzberg/Munich, this new platform is currently being used, for example, to examine cells from patients and test the effectiveness of these ion channel modulators. These substances, which were developed in partnership with industry, are being tested for their effectiveness against the symptoms of lysosomal storage diseases, for example. There are plans for this analysis to be extended to other diseases in the future, particularly infectious diseases.

PUBLICATION HIGHLIGHTS

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Clinical Study Demonstrates Potential of BTZ-043 as a New Antituberculosis Drug Candidate

The clinical trial investigating BTZ-043, a novel active substance for antituberculosis treatment, shows promising results. The safety, bactericidal activity and pharmacokinetic properties of the drug were comprehensively analyzed in two specialized centers in South Africa. BTZ-043 could represent an important alternative to the current treatment of tuberculosis and be particularly effective against resistant strains of the pathogen.

Mit weltweit 10,8 Millionen Neuinfektionen und 1,25 Millionen Todesfällen im Jahr With 10.8 million new infections worldwide and 1.25 million deaths in 2023, tuberculosis (TB) remains a major challenge.1 Resistance is steadily increasing. The Fraunhofer ITMP site for Immunology, Infection and Pandemic Research in Penzberg/Munich has extensive expertise in the field of TB research and is involved in the development of the active substance BTZ-043 through our employees, Dr. Heinrich and Prof. Michael Hoelscher, Head of Fraunhofer ITMP Penzberg/Munich.

BTZ-043, one of the class of benzothiazinones, inhibits an enzyme that is responsible for the synthesis of important cell wall components of the pathogen Mycobacterium tuberculosis. The active substance was discovered at the Leibniz Institute for Natural Product Research and Infection Biology — Hans Knöll Institute (Leibniz-HKI) in Jena, Germany, and has been undergoing further development since 2014 in a collaboration between the Leibniz-HKI and the Institute of Infectious Diseases and Tropical Medicine at LMU Medical Center Munich under the direction of Prof. Michael Hoelscher. BTZ-043 is the first anti-TB agent to be developed exclusively by scientific research institutions in Germany in decades.

[1]Source on the number of new TB cases and deaths per year:
https://www.who.int/teams/global-tuberculosis-programme/tb-reports, p. 2

Caption: Molecular structure of the active substance BTZ-043. © Fraunhofer ITMP | Florian Kloß

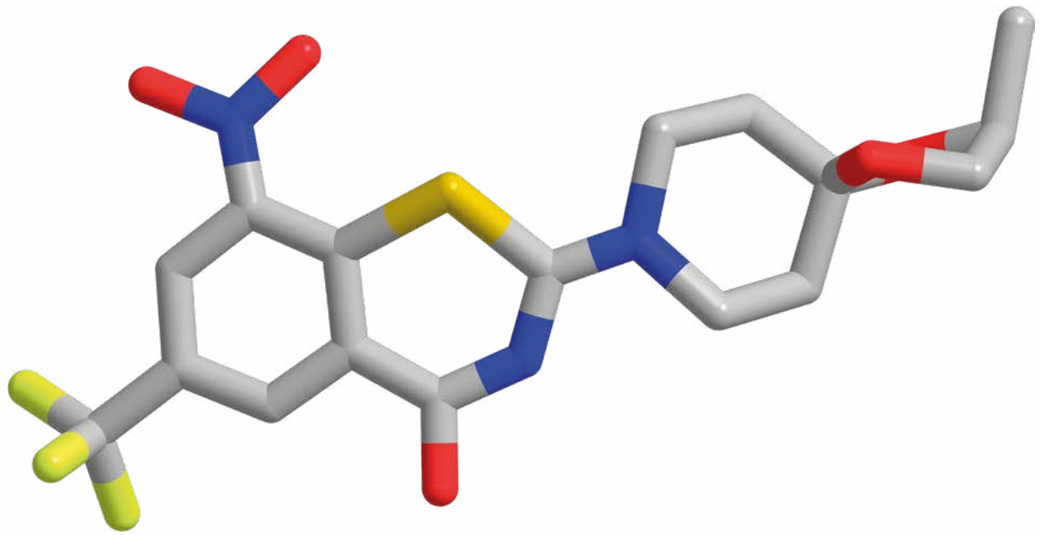
A phase 1b/2a study with a novel design, led by Dr. Norbert Heinrich of the Institute of Infectious Diseases and Tropical Medicine at the LMU Medical Center Munich, comprised a stepwise dose escalation up to 1,750 mg with 24 participants (phase 1b) followed by a randomized, controlled phase 2a study with 54 patients who received doses of 250 mg, 500 mg and 1,000 mg BTZ-043 over 14 days. A control group received a standard combination therapy against TB with rifampicin.

BTZ-043 proved to be safe, well-tolerated and effective, as demonstrated by the decrease in colony-forming units (CFU) in sputum, the secretion of the deep respiratory tract. Bactericidal activity was high and corresponded to that of rifampicin in the standard dosage.

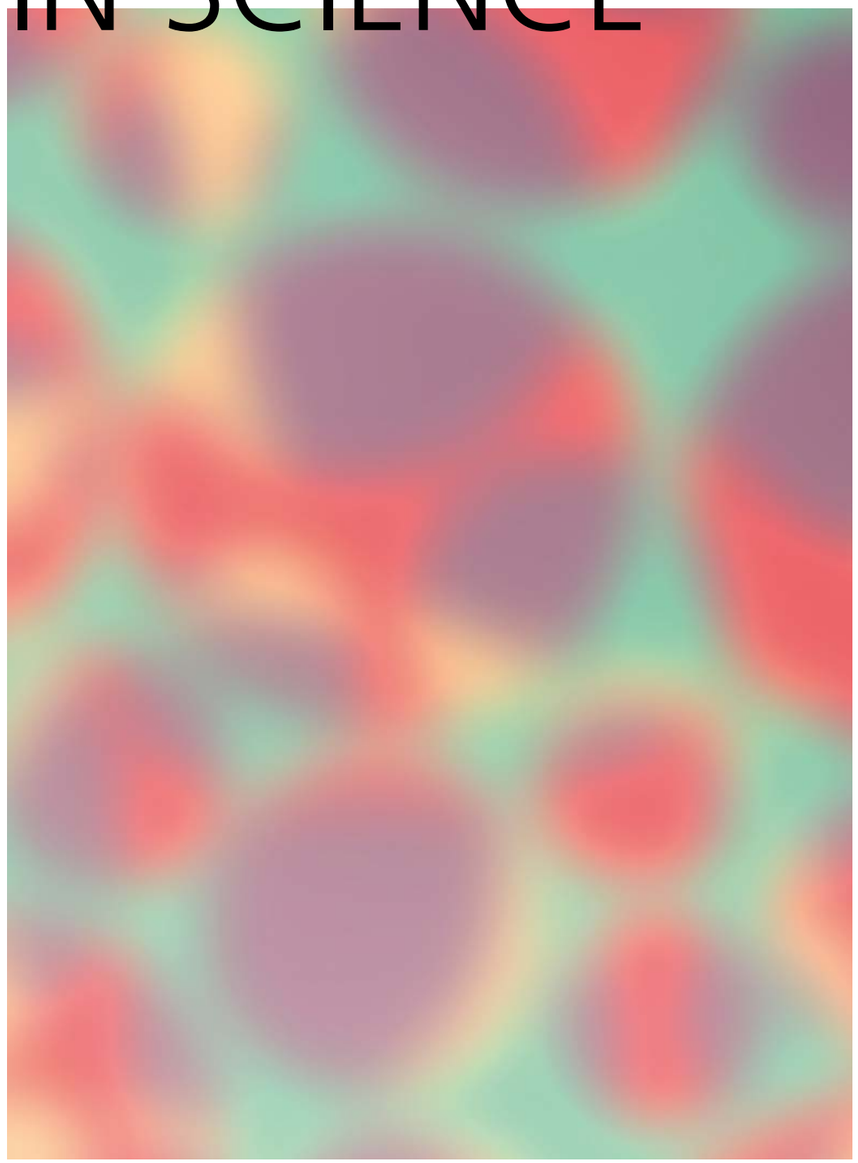
Since TB is usually treated with rifampicin in combination with two to three other drugs, possible interactions with other drugs were investigated. No clinically relevant interactions with the tested substances, including the antiretroviral agent dolutegravir, were identified, so this means BTZ-043 can potentially be combined with other TB and HIV drugs without any complications.

These results highlight the potential of BTZ-043 as an effective adjunct or alternative to existing TB therapies.

Publication:
Heinrich N et al.
Safety, bactericidal activity, and pharmacokinetics of the antituberculosis drug candidate BTZ-043 in South Africa (PanACEA-BTZ-043-02): an open-label, dose-expansion, randomised, controlled, phase 1b/2a trial.
Lancet Microbe
DOI: 10.1016/j.lanmic.2024.07.015



WOMEN IN SCIENCE



The Women in Science interview series shines a spotlight on women involved in research at Fraunhofer ITMP. In these sessions, we pose five questions to each of five female interviewees from five sites, report on projects in various areas of health research from different perspectives and discuss what motivates these women.

PD Dr. Lena M. Biehl
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Dr. Lena M. Biehl has been working at Fraunhofer ITMP in Frankfurt in the Clinical Research department since the beginning of January 2025. Here, she is setting up her own working group on microbiota-based therapies as part of an Attract funding. As an infectious disease specialist with many years of research experience, including in fecal microbiota transfer, she brings the necessary clinical and technical expertise to the project.

What exactly are you currently researching at Fraunhofer ITMP and how do you think research into the immune system influences the development of innovative treatments?

We are currently focusing on building up two areas of the working group: The first of these is bioinformatic expertise to enable us to identify potential candidates for microbiota-based therapies from existing in-house and external research on specific indications. Clinical data and multi-omics data sets from clinical trials, and models and preclinical data on nutrient competition need to be integrated here. Secondly, we are dedicated to setting up a manufacturing laboratory for microbiota-based therapies. In specific terms, we are currently planning initial validation trials for the optimization of production steps such as lyophilization and encapsulation.

What challenges have you faced as a woman in health research and how did you overcome them?

Some of the challenges have been more subtle and can't be described explicitly. But one thing I have repeatedly encountered is people having reservations and false expectations about me. Particularly since having children, I have found that I have sometimes been seen in a different light in my work. This became evident in the way I was no longer trusted to do as much as before and in the way people were surprised by my ambitions and goals. On the other hand, I was fortunate to receive a lot of positive support from my superiors and colleagues right from the start of my academic career and to have successful women in my immediate environment as positive role models.

In your opinion, what are the key steps that need to be taken to promote equality in health research in the long term?

In my opinion, we would be a lot further forward if we didn't always have to think about family-friendly policies at the same time as promoting women. After all, it should be men as well (and not predominantly women) who are pushing for a better work-life balance for their career and professional development. Women are still effectively doing more of the childcare. What is needed here is more macro-social processes to establish and normalize modern partnership models. Employers and colleagues should set out their expectations here and change how they communicate about this. This would promote a more equal distribution of women and men.

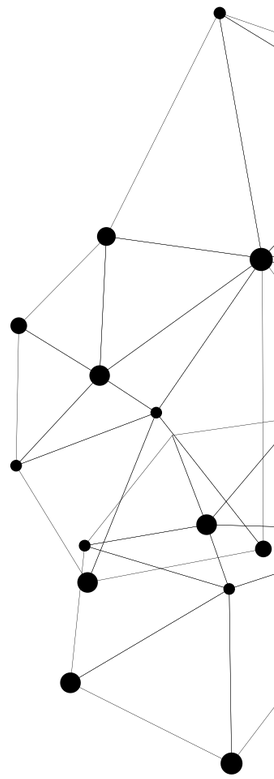
I believe that further promoting gender equality is an important issue in the wider context, away from the subject of parenthood. I also believe that, given the large number of female health science graduates, management positions should generally be filled equally.

What does success in research mean to you? Is it scientific progress, social recognition or something else?

For me, success in research means, on the one hand, gaining new insights that are clinically relevant and therefore have the potential to bring about improvements in healthcare. On the other hand, I also find it really inspiring to be able to present and discuss these research results at scientific conferences or in small groups with our cooperation partners. The opportunity to discuss them with other experts brings new approaches and critical points to light or shows transfer possibilities for further issues that you haven't yet considered.

How can networks and mentoring programs support women in health research and what experiences have you had in this area?

Networks are important for sharing experiences and tips. At the same time, they provide the opportunity to get to know role models and women in similar professional positions personally. Networks can also highlight grievances and inequality with greater emphasis and impact. I had many positive experiences when I took part in a mentoring program for female doctors with a Habilitation (postdoctoral degree). Through this program and through various networks, I became much more aware of the topics of visibility and external presentation, as well as their relevance for my own positioning and prospects.



Pict.: © Lena Biehl

Fatima-Zahra Rachad
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Born in Morocco, Fatima-Zahra Rachad came to Germany for her bachelor's degree in biotechnology at HAW Hamburg where she mastered the linguistic and administrative challenges of an international study program. She also completed her practical semester and her bachelor's thesis at Fraunhofer ITMP. She has been working there as a technical employee since 2024. She carries out biophysical measurements and is active in the stem cell laboratory, especially in the TRR 305 collaborative research center project funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation).

What exactly are you currently researching at Fraunhofer ITMP and how do you think research into the immune system influences the development of innovative treatments?

I am currently researching new active substances for cancer patients with brain metastases at Fraunhofer ITMP Hamburg. To this end, we are using human in vitro models, which we are developing in higher throughput for drug testing.

The long-term goal is to modulate and investigate the tumor-associated microenvironment, which includes immune cells. We also want to address these metastases in their niche tissue with new active substances, which should inhibit tumor progression. This enables us to exclude potential side effects in the sensitive nerve tissue. With our research, we also hope that our complex organoid models derived from human cells will contribute to identifying new drugs in a much more relevant way in the future.

What challenges have you faced as a woman in health research and how did you overcome them?

I have been lucky enough to be surrounded by many women in health research right from the beginning of my career. But I noticed that there are fewer women in senior positions. This also raises questions with regard to my own career. I would still like to work in an open environment.

As a fresh bachelor's graduate, I found it particularly challenging to translate complex procedures — as they are used in research — from theory into practice with all the guidelines. To master this, I had to ask many questions and go through manual "trial-and-error" exercises. .

In your opinion, what are the key steps that need to be taken to promote equality in health research in the long term?

One key step is to increase the number of women in senior positions. From my personal perspective, equality is not only made more difficult by the lack of gender equality, but also by the fact that, as a foreign employee, I have to go through a much more complicated recruitment process. The knowledge about what I am and am not allowed to do with my residence status varies immensely. There are also many hurdles involved in hiring someone with a permanent employment contract. In addition, more permanent contracts should be offered in research professions in general. Many women are put off by this — especially women who wish to have children. Fixed-term contracts offer no security whatsoever that they will be able to take up their old position again. That is why many of them make the move to industry.

What does success in research mean to you? Is it scientific progress, social recognition or something else?

Scientific progress is my benchmark for success. My goal is to find solutions for various diseases and malfunctions in the body to treat or even cure them. I love working in a field that can help other people. But I'm just at the beginning of my career. My next step is to complete my master's degree.

I do not see success in research as a factual result, but as a path, with all the opportunities that come with it. I am proud that — even as a young professional — I am given a lot of trust and responsibility in my work in the screening and stem cell laboratories. That is very motivating.

How can networks and mentoring programs support women in health research and what experiences have you had in this area?

Networks and mentoring programs help you to think outside the box. Networking and exchanging ideas are very important factors when it comes to supporting one another. Women should be encouraged to exchange more information and share their experiences with each other. And I don't just mean that in professional terms — but also about opportunities and best practice examples for career paths.

Personally, I have learned a lot through academic supervision, both in terms of the discipline and in terms of processes and etiquette. This was only touched on superficially during my studies. Mentoring programs can be very useful here. At Fraunhofer ITMP in Hamburg, we work in an international team. This greatly motivates the exchange of ideas during our Visiting Scientists program, which lasts several months.

Pict.: © Fatima-Zahra Rachad

PD Dr. Hanna Bonnekoh
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Dr. Hanna Bonnekoh is a specialist in dermatology and venereology with an additional focus on allergology and has been working at the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP in the Immunology and Allergology IA since January 2024. The Fraunhofer ITMP site in Berlin conducts research in cooperation with the Institute of Allergology at Charité — Universitätsmedizin Berlin. Hanna Bonnekoh is Head of Preclinical Research there. Her research focuses on the disease urticaria and its differential diagnoses.

What exactly are you currently researching at Fraunhofer ITMP and how do you think research into the immune system influences the development of innovative treatments?

Our current research projects focus on the pathomechanisms of urticaria, a common mast cell-mediated disease that often causes itchy wheals and/or swelling on a daily basis. Autoallergy and autoimmunity play an important role in chronic spontaneous urticaria. We want to find out whether these concepts are also relevant for other forms of urticaria. Research into these mechanisms is fundamental for the development of new therapeutic approaches for urticaria. We also test new substances in cell models and on material from patients. And we conduct clinical studies.

What challenges have you faced as a woman in health research and how did you overcome them?

I became pregnant at the end of the COVID-19 pandemic. Due to the regulations in force at the time, I was subject to a partial employment ban, which meant that I was no longer allowed to work directly with patients. That was a blow for me, as I wasn't expecting it and I really enjoy my clinical work. I then focused more on non-clinical scientific work, which enabled me to complete several projects with successful publications. Looking back, this intensive writing period had lots of benefits for me.

In your opinion, what are the key steps that need to be taken to promote equality in health research in the long term?

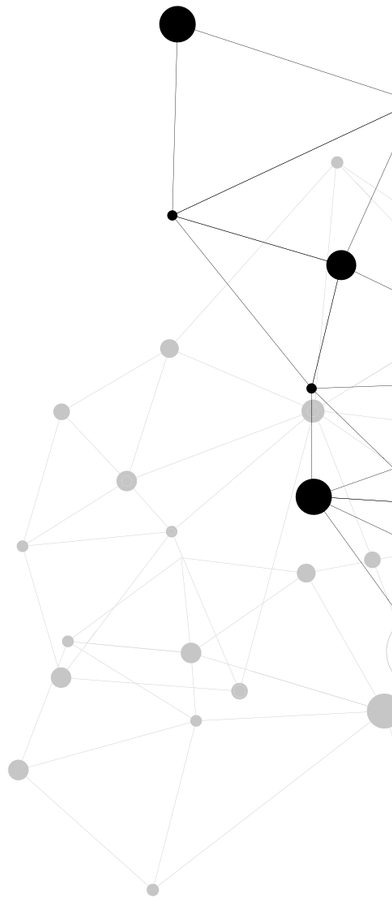
When does unbalanced participation of women, men and gender-diverse people occur in the labor market, in this case in health research? I believe that this happens when you start a family, or just after. Sharing parental leave equally between both parents is the key to equality in my view. I also believe that we need Germany-wide, non-contributory childcare. The option of flexible working hours in health research makes it much easier to combine work and family life.

What does success in research mean to you? Is it scientific progress, social recognition or something else?

For me personally, success in research means working intensively on projects, generating results and then making them available. But for me, success in research is also when we succeed in raising awareness of urticaria and its differential diagnoses in areas such as the public, the media, industry and, last but not least, the medical profession. I will consider our research to have been successful if it helps to improve the care situation for these patients. These successes are only possible as a team!

How can networks and mentoring programs support women in health research and what experiences have you had in this area?

The discussion opportunities provided by networks and mentoring programs for women in health research can help women to overcome their own challenges and find role models. Through discussions in network meetings, I have become more aware of the different needs and challenges of other women.



Pict.: © Sarah Hahn

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Dr. Anastasia Geladaris is a scientist in the Translational Neuroinflammation working group. She has been working at the Fraunhofer ITMP site in Göttingen since its foundation in January 2021. In addition to her passion for science, she is also an advocate for women's rights and regularly practices Thai yoga.

What exactly are you currently researching at Fraunhofer ITMP and how do you think research into the immune system influences the development of innovative treatments?

My research focuses on the progression of multiple sclerosis (MS). While the focus used to be on MS relapses, it is now known that MS mainly progresses independently of relapses. This process is called progression. The progression predominantly takes place within the central nervous system (CNS) and is caused by chronic inflammation in the CNS. Microglia are one of the driving forces behind the underlying mechanisms of progression. Microglia are innate immune cells in the CNS. There are currently no drugs approved for the treatment of MS progression. There are various reasons for this: On the one hand, the exact mechanisms that lead to progression need to be better understood, and on the other, biomarkers are needed that enable early detection of the progression of MS.

It is therefore important to better understand the mechanisms that take place in the CNS and lead to the progression of MS. This is the only way to discover biomarkers and new innovative targets in order to develop a therapeutic strategy against the progression of MS.

What challenges have you faced as a woman in health research and how did you overcome them?

In my opinion, as in many areas, one of the biggest challenges is still the underrepresentation of women, especially in management positions.

Fraunhofer ITMP in Göttingen was founded in December 2020. The head of site and all the working group managers are male. This begs the question of why there is such a gender imbalance in a young company.

Pict.: © Neuropathologie, Universitätsmedizin Göttingen

This is a challenge, not only for me as a researcher, but also as a woman. That is why I am committed to equal rights and to improving conditions for women in science in the future.

In your opinion, what are the key steps that need to be taken to promote equality in health research in the long term?

The first step is to raise awareness of the fact that gender inequality no longer has a place in today's society. This starts with the application process, where gender shouldn't play any part. People in management positions in particular need to recognize and question their own internalized stereotypes. Subjects like maternity protection and parental leave management need to be reinforced and promoted in the work culture. Splitting childcare equally between parents and raising awareness of both in equal parts in the work environment would also help to make things easier for women.

What does success in research mean to you? Is it scientific progress, social recognition or something else?

For me, success in research means contributing to a better understanding of the mechanisms of MS progression and finding a possible therapy to ultimately help people with MS.

How can networks and mentoring programs support women in health research and what experiences have you had in this area?

I took part in a mentoring program for women in science in Göttingen as a mentee during my doctorate and can fully recommend it! I found the opportunities it provided for discussions with women from different fields and stages in their careers extremely empowering and energizing. The opportunity to learn from other women's experiences and gain insights into their processes and lives was a real gift and something for which I am very grateful. Networks are important for campaigning for important issues such as equal rights in science.

Dr. Kathrin Held
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Dr. Kathrin Held is an immunologist and head of the Working Group on Infection and Immunology at the Fraunhofer ITMP site for Immunology, Infection and Pandemic Research in Penzberg/Munich and at the Institute of Infectious Diseases and Tropical Medicine at the LMU Medical Center in Munich. Following her degree in biology and research into neuroimmunology, her current research focus is on the systematic analysis of the immune response in infections such as HIV, tuberculosis and HPV in order to improve the prevention, diagnosis and treatment of infectious diseases.

What exactly are you currently researching at Fraunhofer ITMP and how do you think research into the immune system influences the development of innovative treatments?

We are investigating the human immune response to infections and vaccinations at the cellular and molecular level. By analyzing samples from international clinical trials, we can identify immunological mechanisms that protect against infectious diseases such as tuberculosis, HIV, respiratory infections and HPV. This enables a better understanding of the development of the disease and can help to prevent it in a targeted manner. At the same time, these mechanisms can serve as diagnostic or prognostic biomarkers for rapid and reliable diagnoses, for evaluating the success of therapy and for developing new treatment strategies.

One central research project is focusing on the development of personalized medical approaches for tuberculosis. For this project, we are analyzing specific immune responses to enable early diagnosis, more precise therapy monitoring and host-specific therapies. This not only improves individual treatment, but also makes a significant contribution to the global fight against infectious diseases such as tuberculosis, one of the most common causes of death worldwide.

In the long term, a deeper understanding of protective immune mechanisms can promote innovative therapies by identifying new therapeutic target structures and advancing personalized therapeutic approaches.

What challenges have you faced as a woman in health research and how did you overcome them?

As a woman in research, you are often publicly recognized not only for your own scientific work, but also for the fact that you are doing it "despite" everything — despite being a woman, despite being a mother. While for my male colleagues it's quite natural for them to talk about their research in public, for women the focus is more often on your role as a woman. Topics such as Women in Science are important, but they take time away from the actual research. I have learned to create space for my scientific work and not to allow myself to be reduced to attributes. It's also important to me to challenge these patterns and speak about them openly in order to actively combat them — because excellence should not be dependent on gender roles.

In your opinion, what are the key steps that need to be taken to promote equality in health research in the long term?

It's not enough to promote individual women — there needs to be a fundamental change in thinking. The ability to accomplish scientific achievements must be assessed on an equal basis regardless of gender or appearance. Often, external perceptions count more than content: People who appear dominant are considered competent, while others who remain objective are considered reserved. The solution can't just be for women to adapt their communication — all of us need to learn to recognize competence beyond traditional stereotypes.

For women, scientific careers are also often associated with bigger workloads: Invisible additional tasks, a lack of support when raising a family or stereotypical expectations make them more challenging. This leads many women to deliberately decide against a long-term research career. This means we don't just need structural changes, such as equal parental leave models and a fairer distribution of administrative tasks, but also a general change in thinking — not only to achieve equal opportunities, but also to keep brilliant female scientists in the system.

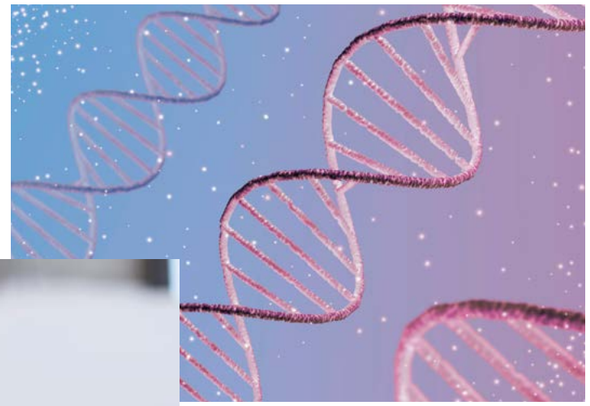
What does success in research mean to you? Is it scientific progress, social recognition or something else?

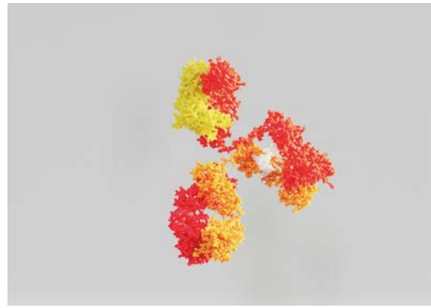
For me, success in research is the moment when various small pieces of the puzzle and seemingly unrelated data suddenly come together to create a bigger picture. The pleasure I gain from generating new knowledge after a lengthy period of work and, through this, contributing in a small way to mankind's overall knowledge is one of my greatest motivations as a scientist.

How can networks and mentoring programs support women in health research and what experiences have you had in this area?

Networks have a vital role in science — they provide a forum in which to share ideas and develop partnerships. Programs and meetings for women should do just that: encourage scientific debate and spark new research. For example, a conversation with a colleague at a conference for women in infection research gave me the idea for a potential joint project. These types of networks not only provide support, but they also act as catalysts for scientific progress.

PEOPLE AND **EVENTS**





TheraNova High-Performance Center Successful in Second Funding Phase

Within the Fraunhofer High-Performance Center Innovative Therapeutics (TheraNova), scientists from Fraunhofer ITMP and Fraunhofer IGD, Goethe University Frankfurt am Main and the Max Planck Institute for Heart and Lung Research work closely with pharmaceutical and biotechnology companies. The aim of the high-performance center is to find novel therapeutic approaches and drug classes, and to develop them for the treatment of diseases with a high medical need. Projects include research into proximity-inducing molecules, multispecific biotherapeutics, innovative fusion proteins and tailored microbiota.
In 2024, all high-performance centers were evaluated by an independent panel of experts with regard to their transfer success and strategic direction for the future. TheraNova has successfully secured a place in the top group and will continue to be funded by the Fraunhofer-Gesellschaft over the next three years.
Together with the PROXIDRUGS Cluster4Future and the EnABLE cluster project, TheraNova organized the international Advances in Therapeutic Approaches symposium for the first time in December 2024. Over two days, the latest findings on the development of novel drugs and other innovative approaches to the treatment of diseases were presented and discussed. The symposium also offered young researchers from the region the opportunity to present their research work and network with each other. .

Symposium Advances in Therapeutic Approaches.

Patient Participation in the 4D Inflammation Clinic

Taking patients' perspectives into account has great potential to make medical research and care more up-to-date, innovative and relevant. In addition, the active involvement of patients as co-researchers also has a positive effect in terms of empowerment.
The 4D Inflammation Clinic team has therefore set itself the goal of promoting the active participation of those affected in inflammation medicine in the long term. The Inflammation Medicine Patients Active in Research (IMPACT) initiative was launched for this purpose.
The kick-off event "Active patient participation in inflammation medicine at Frankfurt University Hospital" took place on October 25, 2024. Through presentations by Dr. Michaela Köhm (4D Inflammation Clinic, Fraunhofer ITMP and Translational Rheumatology, Immunology and Inflammation Medicine, University Medical Center Frankfurt), Dr. Alica Kubesch-Grün (4D Inflammation Clinic, Fraunhofer ITMP and Medical Clinic 1, University Medical Center Frankfurt), Dr. Jennifer Engler (Institute of General Medicine, Goethe University Frankfurt), Ute Keller (ForN Patient Advisory Board) and Corinna-Elling Audersch (German Rheumatism League), interested patients, clinicians and scientists were given insights into the 4D Inflammation Clinic and various participation formats for patients. The content and perspectives presented as well as the subsequent discussions and talks form a promising basis for the concrete implementation of participation formats in the 4D Inflammation Clinic in 2025.

PROXIDRUGS Cluster-4Future Enters the Next Round

Following the successful evaluation by an independent jury, the German Federal Ministry of Education and Research (BMBF) has decided to fund the PROXIDRUGS Cluster4Future with 15 million euros for a further three years as part of the Clusters4Future initiative. PROXIDRUGS, one of seven clusters initially successful in the first round of tenders, is thus entering the second implementation phase. One of the main objectives of the Clusters4Future initiative is to accelerate the transfer from basic research to application.
Proxidrugs are active substances that bring proteins into close proximity to each other. In the therapeutic context, one of these proteins is involved in the development of a disease, while the other protein is an enzyme, an E3 ubiquitin ligase. This leads the disease-relevant protein to the cellular waste disposal system, the degradation via the proteasome. The PROXIDRUGS consortium is dedicated to researching this innovative class of active substances and developing the necessary technologies.
In the second implementation phase, 21 partners, including 13 companies from industry, will work together on 10 interdisciplinary projects. Fraunhofer ITMP is significantly involved in five of these projects, is providing the project management for two projects and is also providing the vice spokesperson for the consortium in the shape of Aimo Kannt. Researchers at the institute will be working on developing test systems to identify new proxidrugs and on improving their bioavailability. Fraunhofer ITMP is also involved in the development of AI prediction tools to help design new types of proxidrugs and in the data and innovation management of the PROXIDRUGS cluster.

The Proxidrugs principle: combination of two proteins

The Proxidrugs principle: combination of two proteins

The first Science Festival organized by the Frankfurt Alliance was held at Frankfurt's Rossmarkt on September 28, 2024. The Frankfurt Alliance brings together several research institutions from the Rhine-Main region, including Fraunhofer ITMP, with the aim of making research and science visible and engaging in a direct dialogue with the public. Interactive exhibits offered visitors insights into various areas of research, from basic research to application in clinical practice. A mobile laboratory showcased current Fraunhofer ITMP research methods, while an ultrasound stand provided an introduction to human anatomy. The juice detective experiment was particularly popular with younger visitors. In addition to talks on subjects such as climate change and artificial intelligence, the organizers also held science slams.
Frankfurt plays a central role as a location for science and, together with the Frankfurt Alliance, provides an important boost for future scientific cooperation and involving the public in the conversation around science.

The Fraunhofer ITMP stand at the Frankfurt Science Festival: visitors talking to our scientists about innovative technologies and applications.

Dr. Philip Gribbon appointed Director General of EU-OPENSCREEN

Dr. Philip Gribbon has been working as the Director General of the EU OPENSCREEN research infrastructure for chemical biology and screening based in Berlin alongside his work at Fraunhofer ITMP since January 2024. Many researchers lack access to the necessary technologies, expertise and resources for bioactivity screening of substances and medicinal chemistry optimization of drugs. EU-OPENSCREEN (EU-OS) closes this gap by providing access to state-of-the-art infrastructure, training and expertise through its more than 30 European partner sites. Current services include: 1) hit identification through drug screening; 2) hit-to-lead optimization and medicinal chemistry; 3) fragment-based drug discovery; 4) compound management and quality control; 5) open access database, 6) bioprofiling and cell painting.
A central resource is the EU-OS substance collection with >100,000 commercial small molecules, >5,000 (constantly growing) academic substances and the European Fragment Screening Library (EFSL, >1,000 substances) developed by EU-OS.

Caption. f.l.t.r.: © Fraunhofer ITMP | Jürgen Lecher; Modified according to Irina Bezsonova © Irina Bezsonova; © Fraunhofer ITMP | Michelle Schönbein

Researchers can use these libraries at screening partner sites such as Fraunhofer ITMP to identify potential biological effectors against their target molecules or in phenotypic in vitro disease models. Primary screening data from EU-OS projects is made available for reuse in the European Chemical Biology Database (ECBD). A recent publication by Philip Gribbon describes the structure of ECBD and its role in modern AI-assisted drug discovery

In-person EU-OS training workshop in Cape Town for young researchers in the field of drug discovery, 2024, supported by the Volkswagen Foundation with tutors from EU-OS partner sites, including Fraunhofer ITMP.

Farewell to Jugend forscht (Youth Research) in Hamburg After 12 Years of Sponsorship

In 2024, we held the Jugend forscht regional competition in Hamburg Volkspark, where 88 students presented 38 research projects at the Fraunhofer ITMP ScreeningPort. Jugend forscht is Germany's best-known competition for young researchers. The aim of this joint initiative by the German federal government, Stern magazine, industry and schools is to get young people interested in science, technology, engineering and mathematics (STEM) in the long term, to encourage talented students and to support them with career guidance beyond the competition.

The Fraunhofer ITMP Discovery Research ScreeningPort site in Hamburg has sponsored the regional competition since 2013, acting as joint sponsor with the HSV-Stiftung foundation Der Hamburger Weg for the past six years. During this time, a total of 1,390 school students have presented a total of 659 projects. Of these, 121 were awarded a first prize, 49 in the Schüler experimentieren (School Students Experiment) category and 72 in the Jugend forscht (Youth Research) category. Of the first-placed Jugend forscht projects, 11 were successful at federal state level, qualifying them for the national competition — and one even won the national competition. It is worth mentioning that the proportion of girls has risen from 44% to 50% during this period, which is a welcome development. In 2024, Fraunhofer ITMP opened its doors to Hamburg's STEM talent for the last time. After twelve successful competitions, Dr. Mira Grättinger relinquished her sponsorship of the Hamburg Volkspark regional competition and was bid farewell with great applause.

Chair of the Stiftung Jugend forscht e. V. foundation thanks Prof. Carsten Claussen (left) and Dr. Mira Grättinger (center) for 12 years of sponsorship and presents Dr. Mira Grättinger with the foundation's golden badge of honor.

Dr. Maria Kuzikov receives Doctoral Prize from the Paul Ehrlich Foundation

The coronavirus pandemic brought with it numerous challenges: uncertainty about the health risks of the new virus, restrictions on social contact, economic consequences and the closure of public institutions. At the same time, it demonstrated the progress that can be achieved in a very short space of time through targeted, global research. Free access to research results, data and publications, and the willingness of public and private institutions to invest in research played a particularly crucial role in enabling a rapid and in-depth understanding of SARS-CoV-2 and possible therapeutic approaches.
Numerous research projects at Fraunhofer ITMP have also been dedicated to this topic. The exceptional work carried out by Dr. Maria Kuzikov, whose dissertation focused on strategies for containing SARS-CoV-2 and new therapeutic approaches, is particularly worth mentioning here. Her work was awarded the Paul Ehrlich Foundation's doctoral prize in 2024. This prestigious award recognizes outstanding achievements in scientific research and honors doctoral theses that provide important new insights in the fields of microbiology, pharmacology, genetics, immunology and host-pathogen interaction.
We congratulate Dr. Maria Kuzikov on this well-deserved award, which is not only a recognition of her achievements to date, but also a great motivation for future groundbreaking research work.

Experts at Global Congress on Stem Cell Research in Hamburg

In July 2024, numerous researchers came together at the annual meeting of the International Society for Stem Cell Research (ISSCR), the leading global congress for stem cell research, for a week of outstanding science and networking. With almost 4,000 members from all over the world, a wide range of ideas, thoughts and perspectives were exchanged in the recently opened Congress Center Hamburg (CCH) in Germany. Groundbreaking developments in stem cell research and the resulting applications for human health were presented in more than 350 lectures and almost 1,400 posters.
The conference, which had been in the planning since 2016, was made possible by the active participation of the Free and Hanseatic City of Hamburg, the Life Science Nord cluster, the German Stem Cell Network (GSCN) and the Fraunhofer ITMP Discovery Research ScreeningPort site in Hamburg. The congress was opened by the Second Mayor and Senator for Science, Research and Equality Katharina Fegebank and ISSCR President Prof. Amander Clark (UCLA). Senator Melanie Schlotzhauer (Authority for Labor, Health, Social Affairs, Family and Integration) hosted the Senate reception in the large ballroom of the town hall on the second day of the congress. Hamburg was able to showcase itself to visitors as a cosmopolitan city and the congress will have numerous positive repercussions.

Fraunhofer Researcher Receives Julius Springer Prize for Rheumatology

Since 2016, Springer Medizin Verlag has awarded the Julius Springer Prize for Rheumatology every two years for the best continuing medical education (CME) article in the Zeitschrift für Rheumatologie (Journal for Rheumatology). The prize is endowed with 2,500 euros and is awarded for groundbreaking work that has been transferred from science to practice in an outstanding way.
Fraunhofer scientist Hanna Bonnekoh and an interdisciplinary group of authors published the prize-winning article "Autoinflammatorische Syndrome" (Autoinflammatory Syndromes) (DOI: 10.1007/s00108-023-01505-1), which appeared in the Zeitschrift für Rheumatologie in May 2023.
As the title suggests, the article deals with autoinflammatory syndromes. These include rare hereditary and acquired diseases characterized by excessive activation of the innate immune system without evidence of antigen-specific T cells or autoantibody formation. Due to the rarity and the associated lack of awareness of these diseases, diagnosis is often delayed, which leads to a long period of suffering for those affected. Knowledge of autoinflammatory diseases is also limited among doctors and healthcare professionals, meaning that further knowledge transfer and training measures are required.
The award ceremony was held in September 2024 as part of the 52nd Congress of the German Society for Rheumatology (DGRh) in Düsseldorf, Germany.

AI: Knowledge as the Key to Modern Guideline Development

The 7th Global Allergy and Asthma Excellence Network Global Urticaria Forum (GUF) was held in Berlin in December 2024. In addition to an outstanding program on the subject of urticaria, the forum also provided an important platform for contacts to be made and strengthened between medicine, science, industry and those affected.
This was followed by a meeting of the 7th Consensus Conference on the Update and Revision of the International Guideline for Urticaria 2024 with the participation of international experts from more than 110 specialist organizations.
The previous guidelines on the pathophysiology, diagnosis and treatment of urticaria were based on scientific studies, in particular double-blind, placebo-controlled and head-to-head studies. However, these only cover a small proportion of patients treated in everyday clinical practice, as comorbidities and concomitant medications are often excluded at the time of study inclusion.

Caption. f.l.t.r.: © EU-OPENSCREEN | Bahne Stechmann; © Fraunhofer ITMP | Pia Kauven

By using advanced AI technologies, real-world experience and patient preferences can now also be taken into account. AI-assisted analysis makes it possible to systematically evaluate patient forums, search engine queries and chats to obtain a more comprehensive picture of the actual care situation. Under the direction of Prof. Torsten Zuberbier, Head of the Fraunhofer ITMP Immunology and Allergology IA site in Berlin, and Prof. Martin Metz, the findings were discussed and agreed upon in order to update the international guideline for urticaria.

Global Urticaria Forum and 7th Consensus Conference on Urticaria 2024 in Berlin.

The DZKJ: Research for Children and Young People — for a Healthy Life

The German Center for Child and Adolescent Health (DZKJ) is a new partner of the German Centers for Health Research. The German Federal Ministry of Education and Research (BMBF) is providing 30 million euros in funding for the two-year start-up phase. The DZKJ brings together university hospitals, universities and non-university research institutions at seven locations. The University Medical Center Göttingen, the German Primate Center, the Max Planck Institute for Multidisciplinary Natural Sciences and Fraunhofer ITMP are involved in the DZKJ at its location in Göttingen.
The DZKJ Göttingen site focuses on the development of personalized medicine specifically for the needs of children and adolescents with neurological and developmental diseases — from basic research to clinical application. Children and young people are also actively involved in the research structures and activities. Prof. Jutta Gärtner, spokesperson of the DZKJ and director of the Göttingen site as well as Fraunhofer ITMP scientist, explains: "The close networking of the site-specific infrastructures, including disease models of the central nervous system, real-time MRI, innovative technological developments such as STED microscopy at the Fraunhofer ITMP site TNM, as well as the integrative research data infrastructure enable the development and use of novel diagnostic procedures and therapies." The Fraunhofer ITMP site TNM in Göttingen is carrying out work for the DZKJ on projects to identify pathomechanisms and develop therapies for childhood neurological diseases using high-resolution microscopy and human stem cell models.

First Phase I Study Started in the Early Clinical Trial Unit in Göttingen

The newly founded Early Clinical Trial Unit (ECTU) at the Fraunhofer ITMP Translational Neuroinflammation and Automated Microscopy TNM site in Göttingen enables early clinical trials to be conducted in cooperation with the University Medical Center Göttingen (UMG). As part of the RED4MS multicenter phase I study conducted by the sponsor Cellerys, the first person in the ECTU has now been treated with a novel therapeutic approach for relapsing-remitting multiple sclerosis. Red blood cells were first removed from the patient, coupled with 12 different disease-specific antigens and then reintroduced. Due to the natural cell death of the red blood cells, the antigens are presented to the immune system as the body's own substances, so that an immune tolerance is built up. Compared to conventional immunosuppressive methods, this represents an innovative therapy concept that specifically addresses the defective immune response.
The participation of patients in clinical trials is essential for medical progress. It provides insights for optimizing therapies and thus contributes to improving the quality of life of future patients. The first patient of the ECTU in Göttingen also shares this motivation: »On my very first visit to the multiple sclerosis outpatient clinic at the UMG, I asked if there was a study I could take part in. When the opportunity arose with RED4MS, I leaped at this chance. I hope that many people will benefit from this research work.«

Possible Active Substances Discovered for Rare Childhood Disease

Researchers from the Fraunhofer ITMP sites in Hamburg, Frankfurt and Göttingen have jointly achieved initial partial successes in a project to develop a drug therapy for the rare metabolic disease multiple sulfatase deficiency (MSD), which occurs in children.
MSD is characterized by various neurological symptoms and also affects other organs at a later stage. Children with MSD initially develop more slowly than normal children and then, similar to dementia, lose motor and cognitive skills that they have already acquired. There is no cure and most affected children die in the second decade of life.
Supported by an Irish patient organization for MSD (MSD Action Foundation, Dublin) and the Health Research Board (HRB) Ireland, the Fraunhofer ITMP sites tested 5,600 existing drugs and substances in a high-throughput process for their ability to normalize the reduced enzyme activity seen in MSD in patient cells in laboratory tests. Drugs identified in this way were then examined in more detail in further experiments in the laboratory.
Around 50 drugs and substances showed positive effects on the patient cells in this detailed laboratory testing. A selection of these will now be investigated further and will be tested in preclinical and clinical trials in the future for their potential to become the first therapy for MSD and further developed accordingly.

2024 bioMérieux Diagnostics Award for Dr. Peter Braun

Dr. Peter Braun from the Fraunhofer ITMP site for Immunology, Infection and Pandemic Research IIP in Penzberg/Munich was awarded the 2024 bioMérieux Diagnostics Award. The German Society for Hygiene and Microbiology (DGHM) presented him with the award at its annual conference in Würzburg, Germany, on June 2, 2024.
The award recognizes his research on bacteriophages and their receptor binding proteins (RBPs), as well as the resulting development of innovative diagnostic methods for bacterial pathogens. From 2016 to 2023, his research as a scientist and officer at the Bundeswehr Institute of Microbiology focused on the development of innovative diagnostic methods for the rapid detection of highly pathogenic bacteria such as Yersinia pestis, Bacillus anthracis and Burkholderia pseudomallei. His research group focused primarily on the use of recombinant RBPs from bacteriophages, i.e., viruses that exclusively infect bacteria — often only one specific species. This high specificity of bacteriophages is driven by their RBPs, which are responsible for the initial binding to the bacterial host cell. Produced recombinantly, RBPs can be used as an alternative to antibodies both for targeted pathogen detection and for therapeutic purposes.

Since 2023, Dr. Braun has headed up a research group at the Fraunhofer ITMP site for Immunology, Infection and Pandemic Research IIP, where he contributes his extensive expertise in developing innovative diagnostic and therapeutic approaches to combat bacterial infections.

Caption p.79: © GA2LEN Global Allergy and Asthma Excellence Network | nilo – Agentur für Fotografie GbR, Alexander Labrentz; p. 80 © PCO Conventus;

Dr. Laura Olbrich is the LMU Clinician Scientist of the Year 2024

Dr. Laura Olbrich from the Institute of Infectious Diseases and Tropical Medicine at LMU Medical Center Munich was awarded the LMU Clinician Scientist of the Year 2024 prize for her paper "Diagnostic accuracy of a three-gene Mycobacterium tuberculosis host response cartridge using fingerstick blood for childhood tuberculosis: a multicentre prospective study in low-income and middle-income countries." At the Fraunhofer ITMP site for Immunology, Infection and Pandemic Research IIP in Penzberg/Munich, she is also developing and testing new methods that can detect tuberculosis (TB) in children more easily and quickly than the sputum tests currently used.
As part of an international research consortium, the RaPaed-TB study was conducted in five countries under the leadership of the LMU Medical Center Munich. The aim was to test a new diagnostic tool that facilitates the diagnosis of TB in children. This innovative, semi-automated test procedure only requires a blood sample from the fingertip instead of a sputum sample in order to make a quick and reliable diagnosis. This method analyzes the activity of three specific genes in capillary blood and creates a transcriptional signature of these genes that can quickly and easily identify TB. The test result is available after just over an hour.
This study shows promising approaches that could also improve TB diagnostics in adults in the future through the use of biomarker tests.

ABOUT PERSON

Foto: © Jörg Distler

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New Fraunhofer ITMP Group in Düsseldorf: Research for Innovative Therapies for Tissue Remodeling and End-Organ Damage

Prof. Jörg Distler and members of his team at Heinrich Heine University Düsseldorf have been part of Fraunhofer ITMP since the end of 2024. Jörg Distler is Director of the Clinic for Rheumatology at Düsseldorf University Hospital and Director of the Hiller Research Center. He has founded two biotechnology companies, which he supports as CEO and scientific director. His work focuses on the development of new diagnostic and therapeutic approaches for the treatment of pathological tissue remodeling processes and the resulting end-organ damage, particularly in chronic inflammatory diseases.

Pathological tissue remodeling as a central medical problem

Inflammatory processes trigger tissue reactions that aim to eliminate the inflammation, repair the damage and thus maintain organ function. However, chronic inflammation often leads to excessive tissue reactions that result in scarring and fibrotic tissue remodeling. This pathological tissue remodeling, which occurs in the context of many common diseases, leads to progressive end-organ damage and is a major cause of death in industrialized nations. Effective, targeted therapies are largely lacking. There is therefore a great medical need for effective therapies to treat this scarring fibrotic tissue remodeling.

Translational, application-oriented research

Jörg Distler and his team at Düsseldorf University Hospital have been researching the pathophysiological basis of this scarring fibrotic tissue remodeling for many years. As a doctor who regularly treats affected patients, he is keen to translate these findings into new diagnostic and, in particular, therapeutic approaches for use in patients with scarring fibrotic tissue remodeling. His research groups and companies provided the basis for several clinical intervention studies with new drug treatment approaches and new diagnostic procedures.

This research and its clinical translation is based on large patient cohorts, standardized biobanking, a comprehensive portfolio of disease models (murine, human, in vitro, in vivo, ex vivo) and molecular technologies (including various spatial proeomics and spatial transcriptomics methods), as well as a broad network of cooperation partners. Jörg Distler will contribute this portfolio and expertise to translational research at Fraunhofer ITMP in his role as the head of the new Tissue Response to Chronic Inflammation Fraunhofer ITMP group. Jörg Distler and his team are looking forward to further expanding this work as a new member of the Fraunhofer ITMP family and helping to improve the prognosis for affected patients.

IN MEMORY

Prof. Marcus Maurer

In Memory of Prof. Marcus Maurer

Last year, we lost Marcus Maurer, our esteemed colleague and the head of our Berlin site. We were profoundly shaken by his loss.

In Marcus, we have lost an extraordinary person, an exceptional scientist and an inspiring mentor. He was an inexhaustible source of ideas and smart advice, and an inspiring speaker, with a gift for organization and a passion for networking. His ability to bring people together and inspire them to achieve common goals significantly shaped and developed the institute's team.

His management style was characterized by trust, openness and great respect for each individual. He created a friendly working atmosphere based on respect and with a family feel, where everyone feels welcome — regardless of position, qualifications or experience. Despite his busy schedule, he always made time for conversations, listened to people attentively and treated everyone with respect and without prejudice.

Marcus's tireless commitment, his optimism and his famous motto "Never give up!" always inspired us and still serve as the guiding principle for our team to this day. In situations where others had already given up, Marcus found solutions. When challenges arose, he always looked for ways to overcome them together. With his energy and charisma, he motivated us all and created an environment in which we enjoyed working and were fully committed.

Alongside all his scientific successes and achievements, his greatest legacy remains the community he built and the spirit of cohesion he inspired in us all. We are infinitely grateful for the moments we shared with him, for his support, his humor, his generosity and his trust.

We miss Marcus dearly, but will preserve and carry on his legacy. His ideals, his values and his unshakable confidence will continue to guide and accompany us.

PATENTS 2024

Patent registrations

Rösch, Axel
Beschichtung von Objektträgern zur Aufrechterhaltung von Immersionen in der Mikroskopie
(Fraunhofer ITMP-Standort TNM)

Hamed, Mostafa; Willocx, Daan; Lillich, Felix; Kany, Andreas; Haupenthal, Jörg; Proschak, Eugen; Hirsch, Anna K. H
Targeting the Energy Coupling Factor (ECF) Transporters as novel antimicrobial target

Holmdahl, Rikard; Kihlberg, Jan; Romero Castillo, Laura; Linusson Jonsson, Anna
Vaccination with a modified type II collagen peptide to protect against arthritis

Safarian, Schara; Köllner, Sarah; Kannt, Aimo
Sortilin-specific biological degrader molecules

Held, Kathrin Anne; Ahmed, Mohamed; Geldmacher, Jan Christof; von Both, Ulrich; Heinrich, Norbert; Höelscher, Michael; Baranov, Olga
Method for diagnosis, prediction of progression, and therapy monitoring of latent Mycobacterium tuberculosis infection and active tuberculosis disease
(Fraunhofer ITMP-Standort IIP)

Safarian, Schara; Rasoulinejad, Samaneh; Kannt, Aimo
A method for enzymatic bioconjugation of biomolecules

Patents granted

Schiederig, Tim; Zaliani, Andrea; Gul, Sheraz; Chachulski, Laura; Claussen, Carsten
Development of algorithms to predict age
WE-EU, WE-CH, WE-GB 19779946.3

Weigert, Andreas; Mora, Javier; Brüne, Bernhard; Dillmann, Christina; Parnham, Michael; Geisslinger, Gerd
N-terminally truncated interleukin-38
WO-CA 2,951,840

Brenneis, Christian; Geisslinger, Gerd; Parnham, Michael; Scholich, Klaus; Sisignano, Marco; Zinn, Sebastian
CYP2J2-hemmende Substanzen als Therapeutika bei Chemotherapie-induzierten neuropathischen Schmerzen
US 16/594,790

Baumann, Isabell; Jakobsson, Per-Johan; Saul, Meike; Steinhilber, Dieter; Süs, Beatrix
MiRNA-574-5p as a biomarker for stratification of prostaglandin E-dependent tumors
WO-KR 10-2019-7038690

BACHELOR'S, MASTER'S, AND DOCTORAL THESES **2024**

Theses 2024 overview

A total of 107 academic theses were successfully completed in 2024 where the experimental part was prepared or supervised by Fraunhofer ITMP employees. The proportion of female graduates was 56%. The breakdown of theses by type was:

5 Habilitations (postdoctoral degree)
43 Doctoral theses
30 Master's theses
19 Bachelor's theses

Habilitations (postdoctoral degree)

Bonnekoh, Hanna: Pathomechanismen, **Klinik und Therapie chronischer urtikarieller Hauterkrankungen.** Charité - Universitätsmedizin Berlin

Buttgereit, Thomas: **Pathomechanismen, klinisches Management und Therapie von mastzell-vermittelten Erkrankungen der Haut und deren Differentialdiagnosen**. Charité - Universitätsmedizin Berlin

Castelletti, Noemi: **Surveillance of novel infectious diseases: from the development of diagnostic methods to biological-based statistical and mathematical modelling of SARS CoV-2.** Ludwig-Maximilians-Universität München

Köhm, Michaela: **Identifizierung, Entwicklung und Anwendung innovativer Messinstrumente zum Nachweis der Wirksamkeit medikamentöser Therapien immunvermittelter entzündlicher Erkrankungen.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Kolkhir, Pavel: **Endotypische Klassifikation der chronischen spontanen Urtikaria auf der Grundlage der Untersuchung eines Komplexes von Biomarkern mit einem personalisierten Therapieansatz.** Charité - Universitätsmedizin Berlin

Doctoral theses

Ablorde, Aikins: **Does household use of mosquito coil influence insecticide susceptibility in vector mosquitoes? A laboratory investigation with Aedes aegypti population.** Ludwig-Maximilians-Universität München

Abrahamian, Carla: **Unraveling the Potential and Complex Interplay of Endolysosomal Proteins TRPML1, TPC2, and Rab7a: Implications for Cancer and Neurodegenerative Disorders.** Ludwig-Maximilians-Universität München

Adbaru, Mulatu Gashaw: **Characterization of microbial resistome in bacteria isolated from Human, Environmental and Animal sources using DNA Microarray technique and Whole Genome Sequencing.** Ludwig-Maximilians-Universität München

Appel, Tobias: **Empfindlichkeit und molekulare Resistenzmechanismen gegenüber Ceftazidim/ Avibactam in gramnegativen Mikroorganismen aus fünf lateinamerikanischen Ländern.**
Johann Wolfgang Goethe-Universität Frankfurt am Main

Bauer, Rebekka: **Changes in RNA dynamics in the course of hypoxia in myeloid cells**.
Johann Wolfgang Goethe-Universität Frankfurt am Main

Bhatta, Arjun: **Structural basis of human mitochondrial RNA processing.** Georg-August-Universität Göttingen

Boshnakovska, Angela: **Elucidating the Molecular Pathologies in Mouse Models for Mitochondrial Diseases.**
Georg-August-Universität Göttingen

Burger, Alexandra: **Linezolid and BTZ043 Combined Activity against M. smegmatis as a Precursor Model for New Combined Antimicrobial Treatment of M. tuberculosis.**
Ludwig-Maximilians-Universität München

Dohrke, Jan-Niklas: **PUCK: Primer Utilised CRISPR/Cas Knock-Ins for High Throughput Super-Resolution Microscopy.**
Georg-August-Universität Göttingen

Dybowski, Sarah: **Characterizing immunomodulatory properties of a novel therapeutic approach for multiple sclerosis - Inhibition of Bruton's tyrosine kinase.**
Georg-August-Universität Göttingen

Fell, Jakob: **The Melody of Miscommunication in the Heart - Decoding LZTR1 deficiency with a Multicellular Focus.**
Georg-August-Universität Göttingen

Göbel, Tamara: **5-Lipoxygenase (5-LO) regulation and activity in colorectal cancer cell lines.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Goebel, Bjarne: **Synthesis and biological characterization of esterified lipid mediators.**
Johann Wolfgang Goethe-Universität Frankfurt am Main

Kargaran, Soghra: **T-cell-mediated ocular autoimmunity.**
Georg-August Universität Göttinigen

Kolbinger, Anja: **Organization of microenvironments by eosinophil granulocytes and macrophages during local inflammation.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Kratz, Daniel: **Lipidmediatoren als Biomarker: Relevanz der Präanalytik am Beispiel der Prostanoide und Endocannabinoide.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Kreiss, Marius: **Die nicht-kanonische Funktion humaner 5-Lipoxygenase - Regulation der Genexpression durch Bindung an Euchromatin.**
Johann Wolfgang Goethe-Universität Frankfurt am Main

Mansuroglu, Yaser: **Formulation and quality control of anti-inflammatory drugs.**
Johann Wolfgang Goethe-Universität Frankfurt am Main

Matkovic, Vigor: **Regulatory Roles of TRIM28 and USP39 in mRNA Splicing.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Müller-Kirschbaum, Lukas Christoph: **Mechanisms of T-cell-mediated inflammatory neurodegeneration.** Georg-August Universität Göttinigen

Pieroth, Nora: **Complete absence of linear immunodominant epitope regions recognized by IgG after flavivirus infection and vaccination in whole proteome analyses.** Ludwig-Maximilians-Universität München

Plano, David: **Elektronische Pille für die Bemessung der Wirkstoffpermeabilität im Magen-Darm-Trakt.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Raue, Rebecca: **Macrophage miRNA profile and their polarization.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Roos, Lennart: **Functional CRISPR repair of induced pluripotent stem cells from patients with Noonan syndrome-associated cardiac hypertrophy.** Georg-August-Universität Göttingen

Rubik, Nina: **Generation of human innervated engineered skeletal muscle.** Georg-August-Universität Göttingen

Saleem, Nosheen: **Sarcomere signaling in a patient-specific iPSC model of hypertrophic cardiomyopathy.** Georg-August-Universität Göttingen

Sänger, Lennart: **Characterization of interactions between Lassa virus nucleoprotein, matrix protein and RNA essential for RNP assembly and recruitment.** Universität Hamburg

Schäufele, Tim: **The role of lipids in the development of tumor-induced neuropathic pain.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Scherf, Janna: **Bunyavirus L protein as an inhibitor target.** Universität Bremen

Schreiber, Marie: Investigating Myelination in Bioengineered Neuronal Organoids (BENOs). Georg-August-Universität Göttingen

Schwieren, Bill: **Die intestinale Mikrobiota bei hämatologisch-onkologischen Hochrisiko-patient:innen – Diversität und 3-IS als progn. Marker bei allogenen Stammzell-transplantationen?** Universität zu Köln

Seitz, Bianca: **Stoffwechselbeeinflussung vom BCG Modellorganismus durch antimycobakterielle Substanzen in der massenspektrometrischen Analyse von Proteinextrakten nach stabiler Isotopenmarkierung.** Ludwig-Maximilians-Universität München

Sitoe, Nádia Elisa Safira: **Inflammatory and prognostic biomarkers associated with pulmonary tuberculosis long-term sequelae after TB treatment in relation to HIV status and lung impairment.** Ludwig-Maximilians-Universität München

Stuut, Christiaan: **Investigation of OPA1 in Mitochondrial Dynamics and Ultrastructure.** Georg-August-Universität Göttingen

Tang, Rachel: T**argeting endolysosomal ion channels and their interaction partners as potential treatment for rare disorders and cancer.** Ludwig-Maximilians-Universität München

Tomaskovic, Ines: **New insights into unconventional serine PR-ubiquitination mediated by SidE effector family of Legionella pneumophila.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Tsakmaklis, Anastasia: **The Microbial Mediators: Investigating Microbiome-Driven Responses in Cancer Therapy.** Universität zu Köln

Wallenwein, Chantal: **Entwicklung und Charakterisierung topsicher Nanoformulierungen unter Berücksichtigung biorelevanter in vitro Freisetzungstests.** Johann Wolfgang Goethe-Universität Frankfurt am Main

Wittek, Anna Laura: I**nvestigation of the Mitochondria-ER axis and its interconnection with the MICOS complex.** Georg-August-Universität Göttingen

Yarova, Kateryna: **Depletion of respiratory chain complexes modulates CRISTAE architecture via MIC10 in human cells.** Georg-August-Universität Göttingen

Zaremba, Nina: **Phospholamban – Characterization of the Potential Interaction Partner SLMAP.** Georg-August-Universität Göttingen

Zerweck, Lukas: **Using AI for an objective detection and evaluation of psoriatic arthritis in fluorescence optical imaging.** TU Darmstad und Johann Wolfgang Goethe-Universität Frankfurt am Main

Zhu, Wenxin Felix: **Sythese Bioaktiver Tricyclen.** Johann Wolfgang Goethe-Universität Frankfurt am Main

NETWORKS IN SCIENCE AND INDUSTRY

International activities and cooperation's with industry

Fraunhofer ITMP cooperates with many international research partners and remains in close contact with universities and other research organizations. The aim is to recognize trends and developments as they emerge, and to develop and implement novel research strategies and technologies. In 2024, Fraunhofer ITMP cooperated with around 40 national and international industrial clients and carried out confidential projects for several international industrial associations.

Cooperation with universities

Fraunhofer ITMP maintains close links with local universities and university hospitals at its five institute sites:

- Goethe University Frankfurt am Main
- University Hospital of the Goethe University
- University Medical Center Hamburg-Eppendorf (UKE)
- University of Göttingen
- University Medical Center Göttingen
- Charité — Universitätsmedizin Berlin
- Ludwig-Maximilians-Universität München (LMU)
- LMU Medical Center Munich

Fraunhofer ITMP also works together with a large number of other national and international universities and research institutions to drive forward joint research projects and harness synergies in science and application.

Below is a selection of important national and international academic cooperation partners for Fraunhofer ITMP:

National universities and research institutions

- University of Marburg
- Justus Liebig University Giessen
- Constructor University Bremen
- Hannover Medical School
- Senckenberg Biodiversity and Climate Research Centre
- Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology Stuttgart
- Bernhard Nocht Institute for Tropical Medicine in Hamburg
- and many more

International universities

- University of Florida
- University of Maryland
- University of Cork
- University of Southern Denmark
- National and Kapodistrian University of Athens
- National University of Ireland, Galway
- and many more

Teaching activities

Our employees are involved in academic teaching at various universities. They deliver teaching activities in the form of lectures, courses, seminars and internships in various bachelor's, master's and PhD programs. These teaching activities cover a wide range of disciplines, including medicine, human medicine, molecular medicine, pharmacy, biochemistry, clinical pharmacology, immunology, neuroimmunology, inflammation medicine, neurology, infectiology, tropical medicine, cell biology, allergology, drug design, data science and health management. In addition, some of our employees also hold management positions, heading up university institutes, clinics or specialized research areas. In 2024, a total of 45 lecturers were working at the following prestigious universities:

- Goethe University Frankfurt am Main
- Goethe Business School
- University Medical Center Hamburg-Eppendorf (UKE)
- University of Göttingen
- Charité — Universitätsmedizin Berlin
- Ludwig-Maximilians-Universität München (LMU)
- Technical University of Munich (TUM)
- Heinrich Heine University Düsseldorf
- Heidelberg University, Medical Faculty Mannheim
- Heinz Nixdorf Institute Paderborn University
- Constructor University Bremen
- and many more

Memberships of scientific journals and committees

Our employees are involved in numerous scientific journals as well as national and international specialist committees.

Scientific journals

Many of our scientists are members of editorial boards and, through this work, help to ensure the quality and develop the content of leading journals. They also take on other roles, including associate editor, review editor, guest editor or editorial advisory board member. A few of our employees also serve as editors in chief or scientific contributing editors.

Scientific committees

Our employees are involved in a large number of scientific committees. They serve as members of scientific advisory boards, steering committees and technical, working and ethics committees, as well as executive and management bodies. They also hold senior leadership positions as board members, spokespersons and presidents of specialist organizations or chairs of scientific commissions. Other key roles held by our employees include acting as members of advisory boards and as treasurers.

Organisation of scientific events and courses

Jugendforschungswettbewerb
»Regionalwettbewerb Jugend forscht Hamburg Volkspark«
Hamburg, 1. - 2. März 2024
Patenbeauftragte: Dr. Mira Grättinger

Fachtagung
»5. Tag der Immunforschung«
Frankfurt, 12. März 2024
Organisation: Fraunhofer CIMD, Dr. Stephanie Dauth

Internationaler Kurs
»Inflammation and Lipid Signaling in Disease Pathogenesis«
Erice, Italien, 25. - 28. März 2024
Kursleiter: Prof. Dr. Dieter Steinhilber
Outreach-Aktivität
»IDERHA Public Forum«
Berlin, 15. April 2024
Organisation: Dr. Philip Gribbon

Symposium
»Klinisches Tuberkulose Symposium 2024«
(2. klinisches Tuberkulose-Symposium der Sektion Mykobakteriosen der DGI)
Frankfurt, 3. - 4. Mai 2024
Organisation: Prof. Dr. Maria Vehreschild

Workshop
»Cryo-EM: Advancing Drug Discovery through Structural Insights«
Frankfurt, 16. Mai 2024
Organisation: Dr. Schara Safarian

Co-Creation Innovation Day
»Fraunhofer CIMD Co-Creation Day 2024«
Frankfurt, 16. - 17. Mai 2024
Organisation: Fraunhofer CIMD, Dr. Kevin Frank

Wissenschaft zum Anfassen
im Rahmen des Science City Day in Hamburg
»Fraunhofer Mobiles Stammzelllabor«
Hamburg, 1. Juni 2024
Organisation: Fraunhofer ITMP und Fraunhofer IBMT, Prof. Dr. Carsten Claussen und Markus Michel

Science Slam
im Rahmen des Science City Day in Hamburg
»Fraunhofer Science Slam«
Hamburg, 1. Juni 2024
Organisation und Moderation: Dr. Mira Grättinger

Workshop
»Alternativen zu Tierversuchen«
Hannover, 11. Juni 2024
Organisation: Fraunhofer CIMD und Fraunhofer ITEM, Dr. Katherina Sewald

Fachkonferenz
»17th Seeon Conference: Microbiota–Probiotics–Host«
Kloster Seeon, 27. - 29. Juni 2024
Organisation: Prof. Dr. Maria Vehreschild

Fachtagung
»Bunyavirus 2024«
Leeds, UK, 15. - 16. Juli 2024
Organisation und Moderation: Dr. Maria Rosenthal

Seminar
»Vom Campus zur Karriere«
Online, 11. September 2024
Organisation: Fraunhofer CIMD, Dr. Christina Gehbauer

Fachkurs
»Exzellenzkurs Spondyloarthritiden«
Lufthansa Trainingszentrum Seeheim, 12. – 14. September 2024
Organisation: Prof. Frank Behrens, Dr. Michaela Köhm, Yixin Wang

Symposium
»RNA-basierte Therapeutika«
Hannover, 30. September 2024
Organisation: Fraunhofer CIMD und Fraunhofer ITEM, Dr. Sabine Kafert-Kasting

Akademische Weiterbildung für Nachwuchswissenschaftler
»Fraunhofer CIMD und TheraNova Winter School 2024«
Bad Nauheim, 9. – 11. Oktober 2024
Organisation: Fraunhofer CIMD und Fraunhofer-Leistungszentrum TheraNova, Katrin Donde und Dr. Christiane Schönfeld

Patientenveranstaltung
»Aktive Patient/innenbeteiligung in der Entzündungsmedizin«
Frankfurt, 25. Oktober 2024
Organisation: Fraunhofer ITMP, J Janssen-Cilag GmbH und Universitätsmedizin Frankfurt

Wissenschaftliche Tagung der Gesellschaft für Biochemie und Molekularbiologie GBM
»GBM Compact: Focus on Imaging«
Frankfurt, 26. - 27. September 2024
Mitglied des Organisationskommitees: Prof. Dr. Stefan Jakobs

Wissenschaftsfestival der Frankfurt Alliance
»Science Festival Frankfurt 2024«
Frankfurt, 28. Oktober 2024
Organisation: Yixin Wang

Symposium
»Dietary and Therapeutic Microbiome Modulation: State of the Art and Perspectives«
Frankfurt, 13. - 14. November 2024
Maria Vehreschild, TheraNova

Öffentliche Film-Veranstaltung mit Podiumsdiskussion
»Unser Bauch, die wunderbare Welt des Mikrobioms«
Frankfurt, 13. - 14. November 2024
Organisation: Prof. Dr. Maria Vehreschild

Fachworkshop
»IDERHA and EU-DataSpaces Stakeholder Meeting«
Wien, Österreich, 28. November 2024
Organisation: Dr. Philip Gribbon

Symposium
»Advances in Therapeutic Approaches«
Frankfurt, 5. - 6. Dezember 2024
Organisation: Fraunhofer-Leistungszentrum TheraNova, ProxiDRUGs und EnABLE, Dr. Christiane Schönfeld
Fortbildungsreihe für Ärzte mit LÄK Anerkennung
»Frankfurter Forum Infektionsmedizin«
Frankfurt, ganzjährig mit monatlichen Fortbildungen
Organisator: Maria Vehreschild, TheraNova und Fraunhofer ITMP

Journal Club
»Journal Club des Fraunhofer ITMP – Immunerkrankungen, Datenanalyse, Datenmodellierung, optische Bildgebungsverfahren und mehr«
Hybrid, 3 Termine in 2024
Organisatation: Yixin Wang

PUBLICATIONS 2024

A

Ablorde, A., et al.
Impact of the exposure of sublethal dose of mosquito coil on the development of insecticide resistance in Aedes aegypti (L.) (Diptera: Culicidae)
Medical and Veterinary Entomology, 2024
DOI: 10.1111/mve.12721

Abrahamian, C., et al.
TPC2: From Blond Hair to Melanoma?
Cancers, 2024
DOI: 10.3390/cancers16234065

Abrahamian, C., et al.
Rab7a is an enhancer of TPC2 activity regulating melanoma progression through modulation of the GSK3β/β-Catenin/MITF-axis
Nature Communications, 2024
DOI: 10.1038/s41467-024-54324-9

Abrahams, A.B., et al.
Exploring the incidence of inadequate response to antidepressants in the primary care of depression
European Neuropsychopharmacology, 2024
DOI: 10.1016/j.euroneuro.2024.04.005

Abreu, M., et al.
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Publisher
Fraunhofer-Institut für Translationale Medizin
und Pharmakologie ITMP
Theodor-Stern-Kai 7
60596 Frankfurt am Main

Editors
Nicole Landwehrs, Dr. Alena Wötzel

Translation proofreading
Transline Deutschland
Am Heilbrunnen 47
72766 Reutlingen
www.transline.de

Coordination and design
Nicole Landwehrs, Dr. Alena Wötzel

Print
Saxoprint
https://www.saxoprint.de

Reporting period
January 1 to December 31, 2024

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