Fraunhofer ITMP

Fraunhofer-Institut für Translationale Medizin und Pharmakologie ITMP

Annual report 2022

INVESTING IN IDEAS

Translation in healthcare research

DEAR READERS,

Energy crisis, transformation, turning point — these terms are currently dominating the political debate. Only a few mention health in the same breath.
Yet health is also a constant source of attention, as was the case a few weeks ago when an economist boldly demanded that those with statutory health insurance should pay a co-payment of up to €2,000. So, do we need — in addition to a transformation in energy and security policy — a "health transformation" to keep our healthcare system financially viable? In our opinion, yes.

Innovations are undoubtedly crucial to continuing to provide patients with the best possible yet affordable services. In its recently presented future strategy for research and innovation, the German federal government has therefore defined "Improving health for all" as one of six future missions. One of the central demands is to more closely interlink basic research and applied research in order to translate promising ideas into innovations even more effectively.

A key success factor was also clearly identified: The key players from science, industry and society must cooperate at an early stage and work together to bring innovations to patients quickly and cost-effectively. One of the German federal government's declared goals is therefore to establish new cooperation structures for this purpose.

With its expertise, methods and technologies and its daily work, Fraunhofer ITMP positions itself precisely at the interface between science and industry and is happy to make its contribution to affordable health and the health transformation with innovative ideas, concepts and research projects as a partner of industry.

Prof. Dr. Dr. Gerd Geißlinger

"The institute can look back on a successful 2022, in which many challenges related to the current crises were able to be met."

My special thanks go to all employees whose performance, dedication and commitment have made this success possible. I would also like to thank the executive board of the Fraunhofer-Gesellschaft and the members of our board of trustees for the support they have provided on all sides.

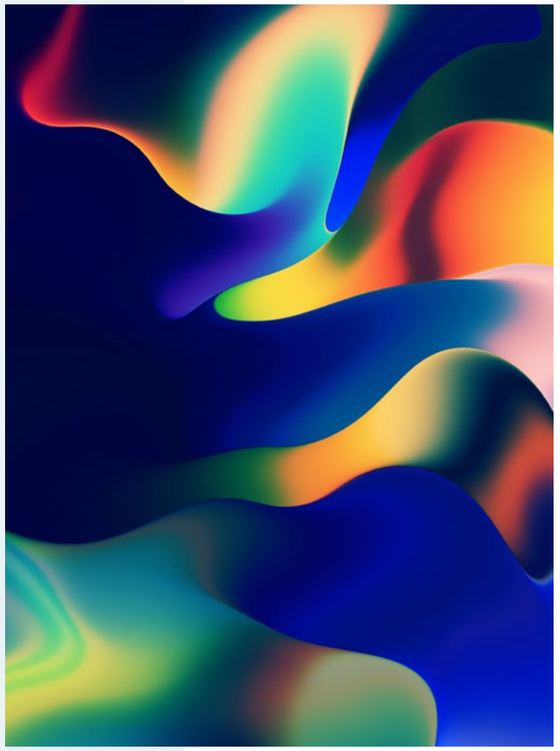
This annual report is intended to give you an overview of the institute's achievements and the portfolio is offers. I would be delighted if you would get in touch with us.

Yours sincerely Prof. Gerd Geißlinger
Executive director of Fraunhofer ITMP

CONTENT

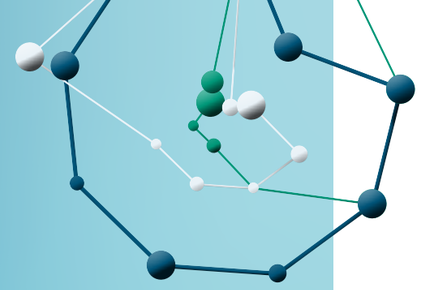
THE INSTITUTE

RESEARCH



IN FOCUS

FACTS



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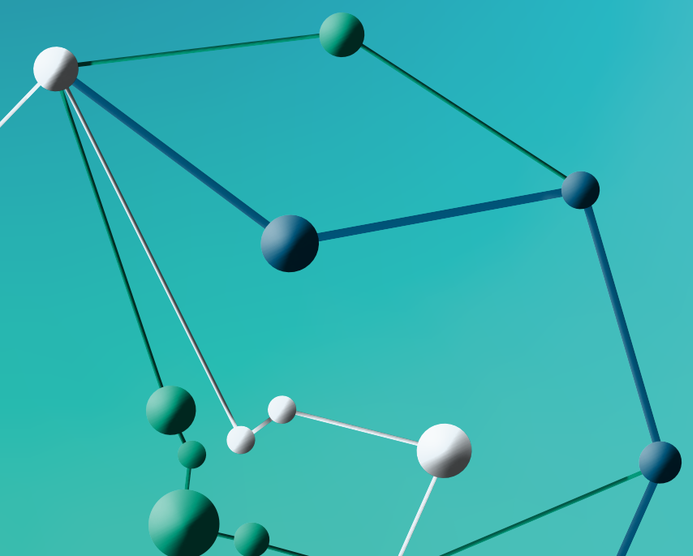
THE INSTITUTE IN PROFILE IN THE GESELLSCHAFT



» Innovation as a connection between vision, research and development.“

FRAUNHOFER ITMP
IN PROFILE

The Fraunhofer Institute for Translational Medicine and Pharmacology ITMP was founded from the Translational Medicine Division 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.

Fraunhofer ITMP's new building at its Frankfurt site, planned completion end of 2024
© wörner traxler richter planungsgesellschaft mbh

“The effective transfer of innovative ideas from biomedical research to medical application and industry is at the core of its scientific objectives.”

The mission statement 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. 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.

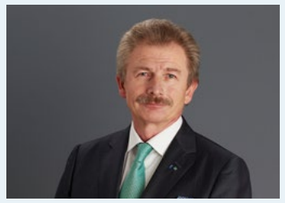
Fraunhofer ITMP currently employs around 237 people at its sites in Frankfurt am Main, Hamburg, Göttingen, Berlin and Penzberg/Munich. The institute is divided into three cross-site research divisions: Drug Discovery, Preclinical Research and Clinical Research. The employees are organized in agile matrix 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 is closely linked scientifically with a large number of institutes and clinics of the University Hospital of the 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.

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.

Institute management:

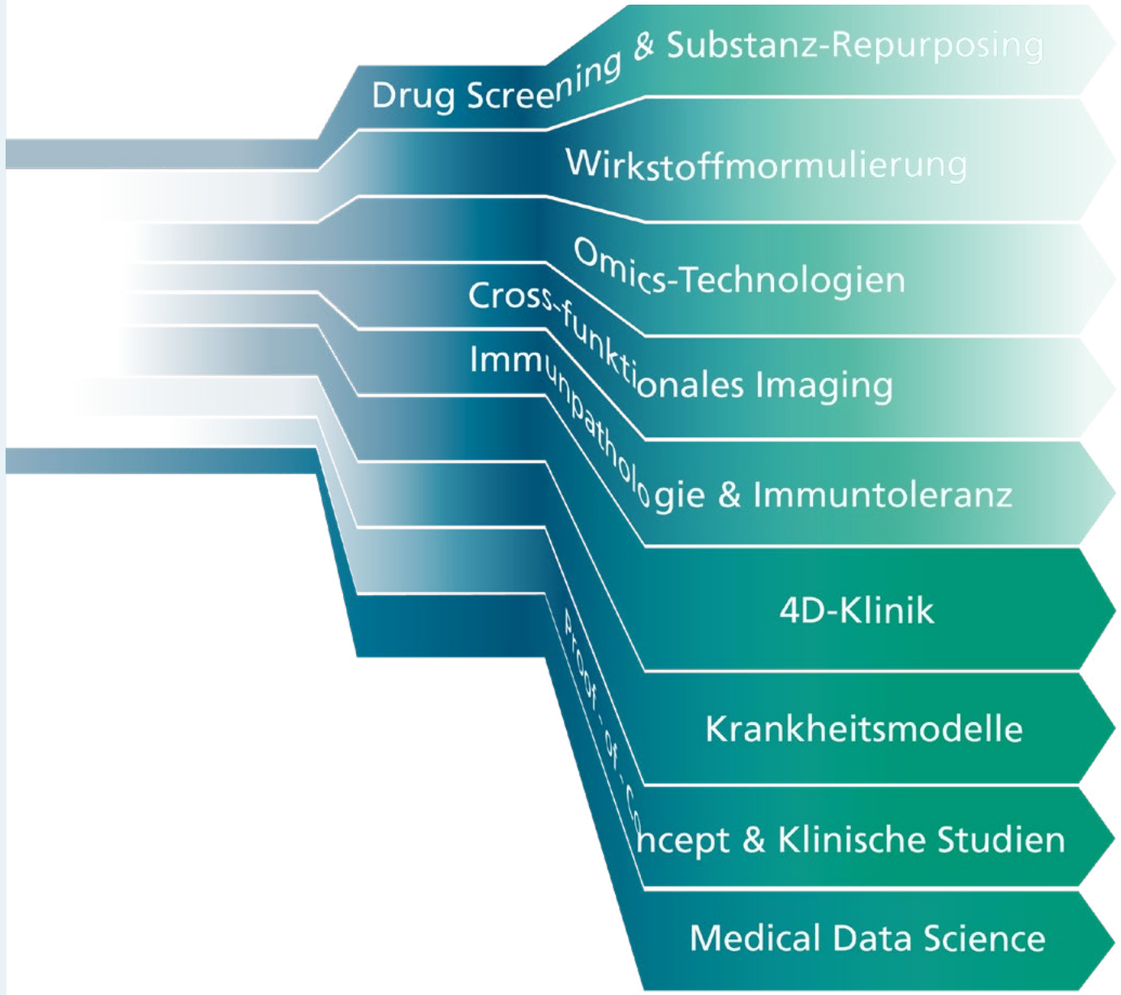


Prof. Dr. Dr. Gerd Geißlinger
Executive director of Fraunhofer ITMP **Frankfurt**

Prof. Dr. Frank Behrens
Deputy director of Fraunhofer ITMP
Frankfurt

RESEARCH DIVISIONS

Drug Discovery — Preclinical Research — Clinical Research



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

Drug Discovery

From the target protein and drug screening to lead optimization and formulation.

The research division covers the spectrum of early drug discovery from the identification and repositioning of pharmacologically active molecules and their characterization in innovative cellular test systems, right the way up to the optimization of their efficacy and physicochemical properties, and the development of suitable formulations to improve bioavailability and stability. The portfolio of therapeutic approaches ranges from small organic molecules to biologics, and research is also being conducted into novel drug entities such as the modulation of intestinal flora or proximity-inducting molecules. In addition, we develop tools and technologies, such as stem cell models or high-resolution and high-throughput imaging techniques for use in pharmaceutical research. An additional focus is the analysis of large data sets, the integration of data from different sources and the processing and storage of data according to the FAIR principles (findable, accessible, interoperable, reusable). In collaboration with the other research divisions at Fraunhofer ITMP, we use findings from clinical research and molecular signatures obtained from patient samples to identify new target proteins and pharmacologically active substances. The main indications are inflammatory diseases, neurodegenerative diseases, bacterial and viral infections, intensive care medicine and rare diseases.

Preclinical Research

Translational cycles and omics analyses for characterization of biological mechanisms and novel targets.

The research division addresses the investigation, identification and validation of disease mechanisms in the context of inflammatory, immune-mediated, neuroinflammatory and neurodegenerative diseases. The retranslational part includes bioanalytical high-throughput-technologies such as omics methods for detection and exploration of biomolecules and pathomechanisms in patient samples that are involved in complex physiological and pathophysiological processes. In the translational part of the division, biological targets and modulators of targets (drugs) are investigated in suitable in vitro, ex vivo and in vivo disease models, which are implemented in different complexities along the pharmaceutical value chain up to models, which are highly predictive for the human and patient situations. In addition, adverse outcome pathways related to (patho-)mechanisms which should not be modulated can also be explored.

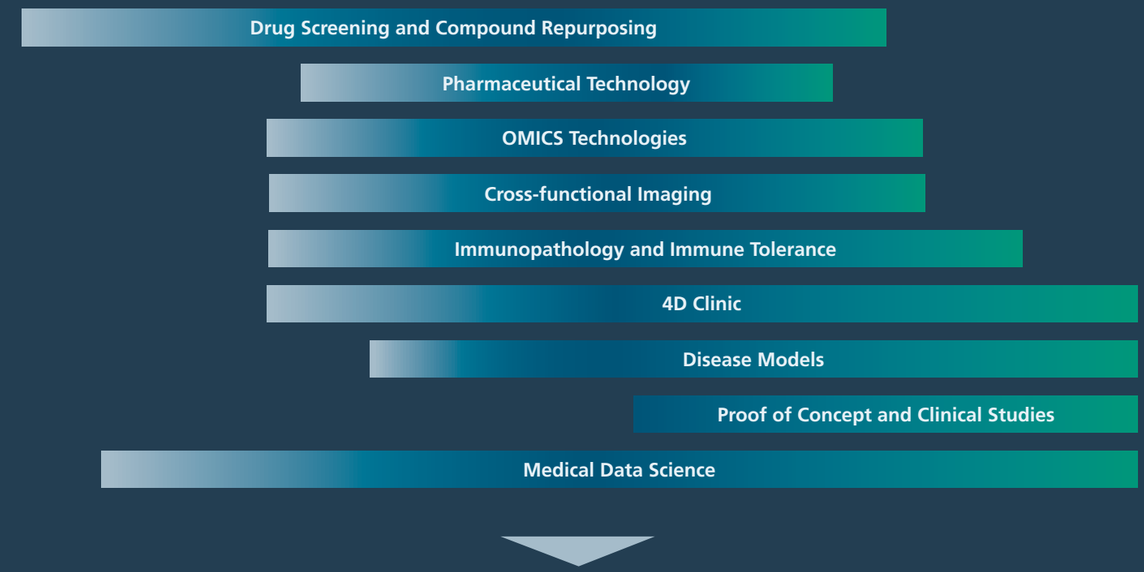
Clinical Research

From proof of concept to the characterization of established products: quality by design for the successful translation of innovative ideas.

The research division deals with the conception, implementation and evaluation of clinical research projects in immune-mediated inflammatory diseases of different organ systems as well as in pain disorders (AMG and non-AMG). In order to meet the challenges of immune-mediated diseases and related disorders such as inflammatory diseases and pain in translational research, innovative clinical projects for early detection, diagnosis, prevention and treatment of these diseases are carried out in the Clinical Research division. In addition to the development of its own drug candidates, proof-of-concept studies as well as investigator-initiated clinical trials are conducted. Innovative study designs are used to sustainably improve patient care and thus address patient needs. In our own phase 1 units at the Frankfurt am Main and Göttingen sites, early drug development of drug candidates in volunteers as well as in patients with corresponding indications is possible due to the direct connection to the university hospitals.

Research divisions

Innovation areas



Expert pool of collaborating universities:

Goethe Universität Frankfurt am Main · LMU Ludwig-Maximilians-Universität München · Charité Universitätsmedizin Berlin · Universitätsklinikum Hamburg-Eppendorf · Universitätsmedizin Göttingen UMG

Heads of research:

PD Dr. Aimo Kannt
Drug Discovery, Preclinical Research — Fraunhofer ITMP **Frankfurt**

Prof. Dr. Frank Behrens
Clinical Research — Fraunhofer ITMP **Frankfurt**

THE FRAUNHOFER ITMP NETWORK

Hamburg
Discovery Research ScreeningPort

Prof. Dr. Carsten Claussen | Dr. Philip Gribbon
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.

Berlin
Immunology and Allergology

Prof. Dr. Torsten Zuberbier | Prof. Dr. Marcus Maurer
The research division addresses the investigation, identification and validation of disease mechanisms in the context of inflammatory, immune-mediated, neuroinflammatory and neurodegenerative diseases. The retranslational part includes bioanalytical high-throughput-technologies such as omics methods for detection and exploration of biomolecules and pathomechanisms in patient samples that are involved in complex physiological and pathophysiological processes. In the translational part of the division, biological targets and modulators of targets (drugs) are investigated in suitable in vitro, ex vivo and in vivo disease models, which are implemented in different complexities along the pharmaceutical value chain up to models, which are highly predictive for the human and patient situations. In addition, adverse outcome pathways related to (patho-)mechanisms which should not be modulated can also be explored.

Göttingen
Translational Neuroinflammation and Automated Microscopy

Prof. Dr. Stefan Jakobs | Prof. Dr. Martin Weber
We use innovative high- and super-resolution microscopy techniques to visualize sub-cellular structures at the nanoscale. The automation of these techniques and innovative image analysis algorithms allow the investigation of the influence of pharmacologically active compounds on the nano-structure 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 clinic and completes our portfolio in the research into new drug candidates in the neuroinflammation indication area.

Frankfurt am Main
Translational Medicine and Pharmacology

Prof. Dr. Dr. Gerd Geißlinger | Prof Dr. Frank Behrens
Our expertise lies in the research of therapeutic and diagnostic innovations for diseases that are currently untreatable or insufficiently treatable. For this purpose, we use state-of-the-art technologies and multiomics methods for biomarker discovery. We develop predictive disease models for in vitro, ex vivo and in vivo characterization of drugs, as well as innovative, optimized dosage forms. In the field of clinical research, our core expertise lies in the planning and quality-assured execution of clinical studies, as well as in the early clinical development of drug candidates. Our own biomaterial bank enables basic scientific analysis for further characterization of diseases in our indication focus areas of immune-mediated diseases and pain.

Penzberg/Munich
Immunology, Infection and Pandemic Research

Prof. Dr. Michael Hoelscher | PD Dr. Andreas Wieser
We are engaged in the development of interventions to combat the outbreak of new and the spread of existing infectious diseases. In addition, we aim to improve the therapy of infections and their immunological sequelae. We use our expertise to develop and test new multi-parameter diagnostics, novel antiviral and immunomodulatory therapeutics, and active and passive vaccines. We also focus on the development of new devices, which include both technical solutions to interrupt infection pathways and new point-of-need devices for diagnostics. In this context, the use of data science, a topic spanning all fields, is of central importance for our research.

Fraunhofer headquarters in Munich

FRAUNHOFER ITMP WITHIN THE FRAUNHOFER-GESELLSCHAFT

The Fraunhofer-Gesellschaft is the world's leading applied research organization. With its focus on developing key technologies that are vital for the future and enabling the commercial exploitation of this work by business and industry, Fraunhofer plays a central role in the innovation process. As a pioneer and catalyst for groundbreaking developments and scientific excellence, Fraunhofer helps shape society now and in the future. Founded in 1949, the Fraunhofer-Gesellschaft currently operates 76 institutes and research units throughout Germany. Over 30,000 employees, predominantly scientists and engineers, work with an annual research budget of €2.9 billion. Contract research accounts for €2.5 billion of this sum.

Within the Fraunhofer-Gesellschaft, structures, programs and processes have been established to pool the expertise of the independently operating Fraunhofer institutes. In this context, both subject-specific and interdisciplinary networking of the individual Fraunhofer institutes serves to strengthen competitiveness and to open up new, joint fields of business. Within the Fraunhofer-Gesellschaft, Fraunhofer ITMP is involved in various structures and initiatives in the field of health research.

FSF Digital Healthcare

The seven Fraunhofer Strategic Research Fields (FSF) of the Fraunhofer-Gesellschaft form the focus of the research portfolio — especially with a view to the markets and needs of tomorrow. Within these fields, Fraunhofer's outstanding pre-competitive research specifically targets projects that have high potential for exploitation, thereby enhancing its impact on society and across multiple sectors. The FSF Digital Healthcare, in which Fraunhofer ITMP is involved, focuses on digital diagnostics and prevention, cost-intelligent precision therapy, and automation in nursing and care.

Healthcare sector lead market

In strategic customer segments known as lead markets, innovations can give Germany a global competitive edge, secure Germany's and Europe's technological sovereignty and generate sustainable value creation for society. The healthcare sector is of considerable economic importance for Germany as a business location and is characterized by the development of innovative high-tech products in medical technology and pharmaceuticals as well as new treatment and examination methods. Fraunhofer is involved in all four major areas of health research — drugs, diagnostics, devices and data. True to its interdisciplinary principles, the Fraunhofer-Gesellschaft brings together physicians, natural scientists, computer scientists and engineers to create the perfect conditions for innovation and the rapid commercialization of new ideas.

Fraunhofer Group for Health

The Fraunhofer institutes are grouped in nine thematically oriented Fraunhofer groups. Their goals are professional coordination within the Fraunhofer-Gesellschaft, the pooling of core competencies and a joint presence on the market. Fraunhofer ITMP is organized in the Fraunhofer Group for Health, a scientific and technological community of highly qualified experts from key areas of modern life sciences.

Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

The purpose of the Fraunhofer clusters of excellence is to promote a cross-institute research agenda to ensure that systemically important topics are developed and addressed in a collaborative manner. Fraunhofer ITMP is one of the three core institutes of the Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD. The central goal of Fraunhofer CIMD is the efficient translation of innovative ideas and identified targets into individualized therapies for immune diseases.

MED²ICIN lighthouse project

With its lighthouse projects, the Fraunhofer-Gesellschaft sets strategic priorities in order to develop specific solutions for the benefit of Germany as a business location. The goal is to quickly turn original scientific ideas into marketable products. Fraunhofer ITMP contributes its expertise to the MED²ICIN lighthouse project. The development of a digital patient model is the basis for personalized and cost-optimized treatment. This generates enormous potential for improvement with regard to more effective prevention, diagnostics, therapy and care, as well as enabling healthcare expenditure to be deployed more intelligently.

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.

Proof-of-Concept initiative

The Proof-of-Concept initiative (PoC initiative) was initiated by the Fraunhofer-Gesellschaft, German University Medicine and the Helmholtz Association as a collaborative cross-organizational project to accelerate translation processes of highly innovative approaches from basic research to medical practice. Fraunhofer ITMP is leading a project to develop a compound for the treatment of chemotherapy-induced neuropathic pain.

At the beginning of the coronavirus pandemic, the institute directors of Fraunhofer ITMP, Prof. Dr. Dr. Gerd Geißlinger and Prof. Dr. Frank Behrens, were appointed as members of the Fraunhofer crisis management team for the SARS-CoV-2 coronavirus crisis. In this context, they support the necessary measures, especially from a medical point of view.

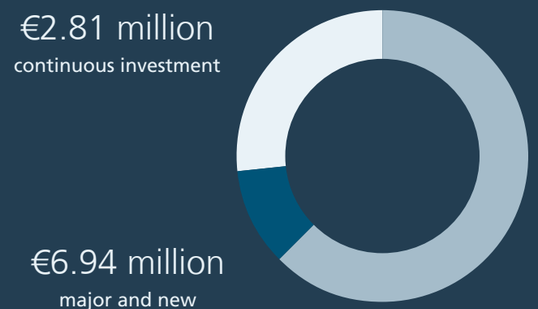
TOTAL BUDGET **2022**

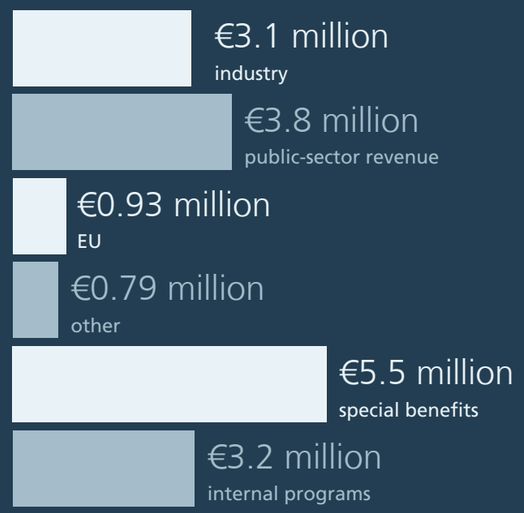
Summary

Fraunhofer ITMP with its sites in Frankfurt am Main, Hamburg, Göttingen, Berlin and Penzberg/Munich recorded considerable growth in 2022 and was thus able to strengthen and expand health research at Fraunhofer in cooperation with excellent university locations.

Budget

The operating budget of Fraunhofer ITMP amounted to €16.4 million in 2022. In addition, around €2.81 million were invested in equipment. Expenditure relating to construction activities for the new institute building in Frankfurt amounted to €6.94 million.





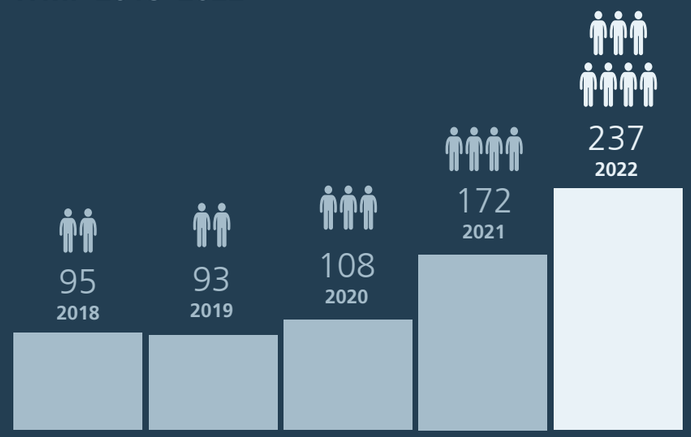
Income

69.9 percent of the operating budget for the contract research area of the parent institute was financed by external income, or 55.1 percent if the predominantly state-financed sites in Göttingen, Berlin and Penzberg/Munich are included.
The industrial revenue of €3.1 million (Rho-Wi:30.3%) is at a good level.

Employees

At the end of 2022, a total of 237 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 59 percent.

Employee development at Fraunhofer ITMP 2018–2022



+237
employees at Fraunhofer ITMP in 2022

105
scientific employees

47
technical employees

25
infrastructure/ administration

24
graduate employees

19
students

17
PhD students

BOARD OF TRUSTEES **2022**

The trustees advise the organs 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.

On June 29, 2022, the second meeting of the board of trustees of Fraunhofer ITMP took place at the Hamburg Chamber of Commerce. Both the current development of the institute and strategic issues were discussed. The broad scientific expertise of the institute was underpinned by lectures from the individual locations.

In his presentation, executive vice president of the Fraunhofer-Gesellschaft, Prof. Dr. Alexander Kurz, assessed the importance of health research for affordable health and securing the future of society as well as the contribution that the Fraunhofer-Gesellschaft, the Fraunhofer Group for Health and, in particular, Fraunhofer ITMP can make to achieving these goals.

The first mayor of the Free and Hanseatic City of Hamburg, Dr. med. Peter Tschentscher, was keen to take the opportunity to make a welcome address to the board of trustees during a break in the meeting of the Hamburg Parliament, in which he emphasized the social importance of innovations and highlighted the innovation strategy of the Free and Hanseatic City of Hamburg, in which Fraunhofer occupies a special place.

l–r: Prof. Dr. Dr. Gerd Geißlinger *executive director of Fraunhofer ITMP,* **Dr. Peter Tschentscher** *first mayor of the Free and Hanseatic City of Hamburg,* **Prof. Dr. Alexander Kurz** *executive vice president of the Fraunhofer-Gesellschaft,* **Prof. Dr. Carsten Claussen** *head of Fraunhofer ITMP Hamburg*
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Fraunhofer ITMP board of trustees meeting, Hamburg Chamber of Commerce. © Fraunhofer ITMP, Mira Grättinger

Fraunhofer ITMP Members of the board of trustees in 2022

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

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

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

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

Dr. Claudia Jentzsch
Novartis Pharma GmbH, Nuremberg

Dr. Joachim Kreuzburg
Chief executive officer Sartorius AG, Göttingen

Prof. Dr. Heyo Kroemer
Chief executive officer Charité Universitätsmedizin, Berlin

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

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

Prof. Dr. Michael Popp
Bionorica SE, Neumarkt in der Oberpfalz

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

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

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

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RESEARCH
INTO THE FUTURE

**» Medical — digital
New technologies in
health research.“**

AIOLOS: DATA INTEGRATION AND AI TO IMPROVE PANDEMIC PREPAREDNESS

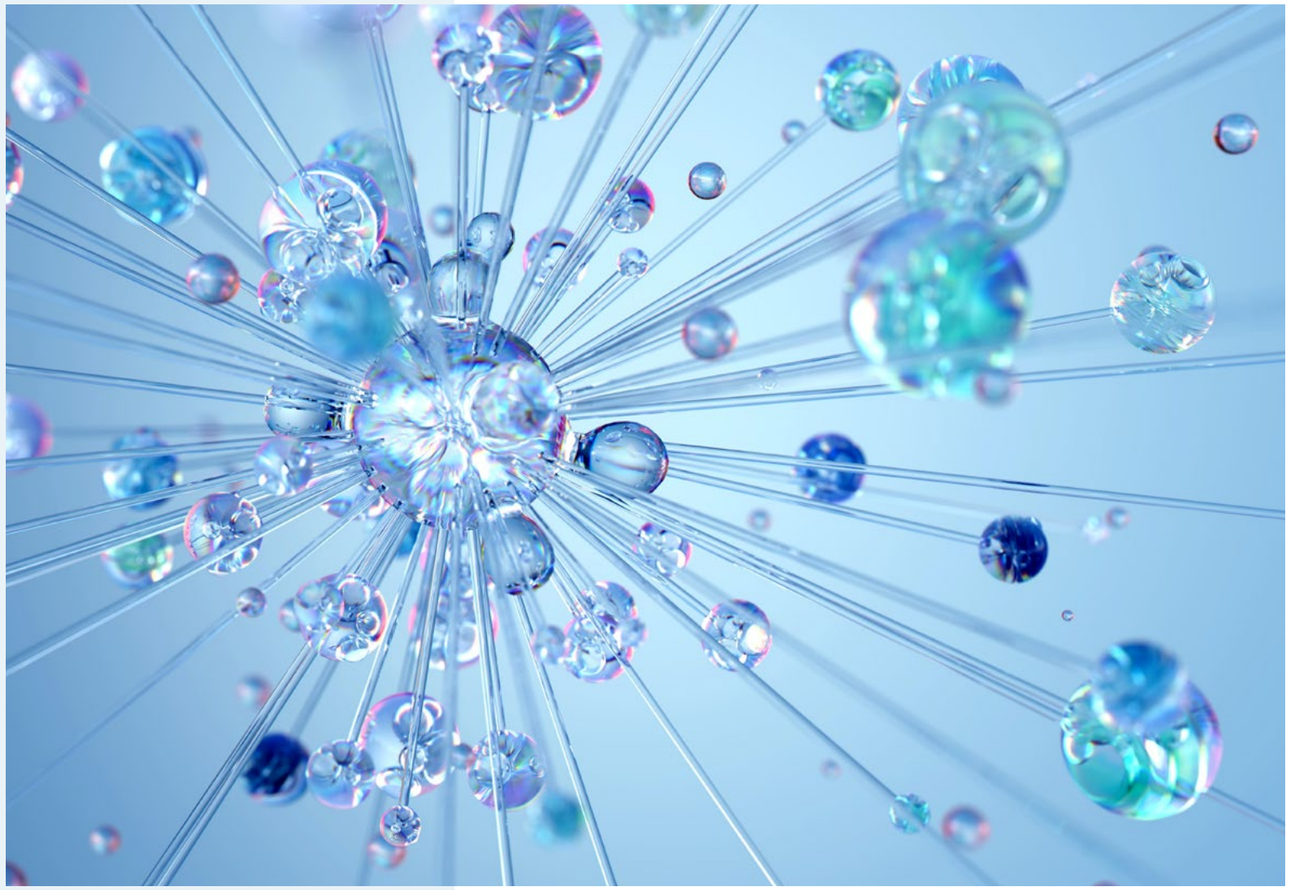
PD Dr. Aimo Kannt
Drug Discovery, Preclinical Research, Fraunhofer ITMP **Frankfurt**
aimo.kannt@itmp.fraunhofer.de

Further contact:
Dr. Mira Grättinger
mira.graettinger@itmp.fraunhofer.de

The AIOLOS (Artificial Intelligence Tools for Outbreak Detection and Response) project aims to detect new outbreaks of infectious respiratory diseases at an early stage, predict and monitor their spread, and support decisions on appropriate countermeasures. For this purpose, data from various sources is combined, analyzed using artificial intelligence methods and predictive modeling, and visualized in a web-based dashboard. AIOLOS is a public-private consortium with the participation of Fraunhofer as well as French and German companies.

AIOLOS: a transnational collaborative project

Viruses and other pathogens do not stop at national borders when they spread. When it comes to pandemic preparedness and outbreak containment, it is therefore becoming increasingly important to collaborate across countries. One such translational project is AIOLOS (Artificial Intelligence Tools for Outbreak Detection and Response), which was launched in March 2022. It is supported by the German Federal Ministry for Economic Affairs and Climate Action (BMWK) and the French Ministry for the Economy as part of the Franco-German call for artificial intelligence technologies for risk prevention, crisis management and resilience. AIOLOS is a public-private consortium with the participation of the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP and the Fraunhofer Institute for Algorithms and Scientific Computing SCAI. Other partners include umlaut and CompuGroup Medical on the German side and Sanofi Pasteur, Quinten Health and Impact Healthcare on the French side. The six partners bring complementary expertise in the fields of medicine, data processing, model and technology development, project coordination and public relations. AIOLOS spokespersons are Cedric Mahe of Sanofi Pasteur and Aimo Kannt from Fraunhofer ITMP. Other key organizations, such as the Institut Pasteur, are involved as associated partners, contributing data or providing scientific and technical expertise. The consortium collaborates closely with the WHO Hub for Pandemic and Epidemic Intelligence in Berlin and the Health Emergency Response Authority (HERA) of the European Union.



© Deepmind on Unsplash

Figure below: Goals and approaches of AIOLOS.
© AIOLOS 2022

The goals of AIOLOS

The primary objective of AIOLOS is to detect early signs of an epidemic, monitor its spread, derive appropriate countermeasures and assess their impact. The project focuses on respiratory diseases caused by airborne pathogens. AIOLOS will integrate and combine a variety of data from different sources on a single platform, including healthcare data, demographic data, virus measurements in wastewater, mobility tracking data, and automated text and media analysis. This data is analyzed using AI and various predictive modeling approaches to develop scenarios for the spread and impact of epidemics and to assess the efficiency of countermeasures. AIOLOS has the ambition to develop a prototype of the platform within two years, initially focusing on France and Germany. The platform will then be extended to other European and non-European countries and regions, contributing to a robust global surveillance system for communicable respiratory diseases in collaboration with HERA and WHO.

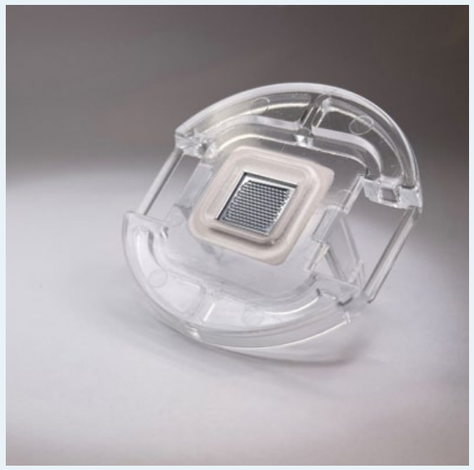
MICRONEEDLE PATCHES: FOR OBTAINING LIQUID BIOPSIES — RESEARCH THAT GOES UNDER THE SKIN

Dr. Jörg Scheffel
Solution Discovery, Fraunhofer ITMP **Berlin**
joerg.scheffel@itmp.fraunhofer.de

Together with the company Ascilion, researchers at Fraunhofer ITMP Berlin are developing microneedle patches to obtain interstitial fluid. This fluid not only mirrors the immune activity in the skin very precisely, but it also represents various signaling molecules of the blood. The potential uses of the device therefore range from molecular characterization of inflammatory skin diseases and the discovery of novel biomarkers right the way up to real-time monitoring of specific disease parameters.

In the skin, a complex interplay of different immune cells and their signaling molecules takes place. However, this is only poorly reflected in peripheral blood, which makes molecular diagnostics and characterization of inflammatory skin diseases difficult. Until now, the only alternative to venous blood sampling has been skin microdialysis, a technically demanding, invasive and painful procedure. Dr. Jörg Scheffel and his team at the Fraunhofer ITMP Berlin site, in collaboration with the Swedish company Ascilion, are therefore testing and developing novel microneedle patches for obtaining interstitial fluid from the skin.

Microneedle patch for obtaining interstitial fluid from the skin.
© Ascilion from Pelle Rangsten



Mode of operation and current application areas

The small silicon chips with their sharp hollow needles (up to 450 µm in length) are applied directly to the skin and the microneedles penetrate the skin almost without being noticed. Using slight negative pressure, interstitial fluid can then be sampled through the tiny holes. The procedure is painless and suitable for all parts of the body as it leaves no marks on the skin. In addition, compared to microdialysis, large biomolecules like albumin, cytokines and immunoglobulins can be recovered more readily and in higher concentration in the collected fluid. Currently, the procedure is successfully used in ex vivo models of allergies and chronic inducible urticaria. Based on the amount of histamine in the interstitial fluid, mast cell activation in the skin in response to various triggers can be determined very accurately. The method is therefore very well suited to contributing to the identification of allergens or (auto) antigens in inflammatory skin diseases. The targeted insights into the micromilieu of the skin also allow for a better understanding of pathomechanisms and the discovery of novel biomarkers. To measure as many markers as possible in the small sample volume, the Olink technology is applied in collaboration with PD Dr. Aimo Kannt from the Fraunhofer ITMP Frankfurt site.

Future potential uses

The microneedle patches are soon set to be used for the first time in patients. Initial studies with a small cohort of patients with dermatological but also cardiovascular diseases are planned for 2023. The latter is possible because different signaling molecules of the peripheral blood are found in comparable amounts in the interstitial fluid of the skin. A combination of the microneedle patches with biosensor technology for real-time measurement of different biomarkers and thus the possibility of monitoring specific disease parameters by patients is also conceivable in the future.

COVEND:
NEW THERAPEUTIC APPROACHES TO FIGHT SARS-COV-2 USING AI AND BIOMARKER ANALYSIS

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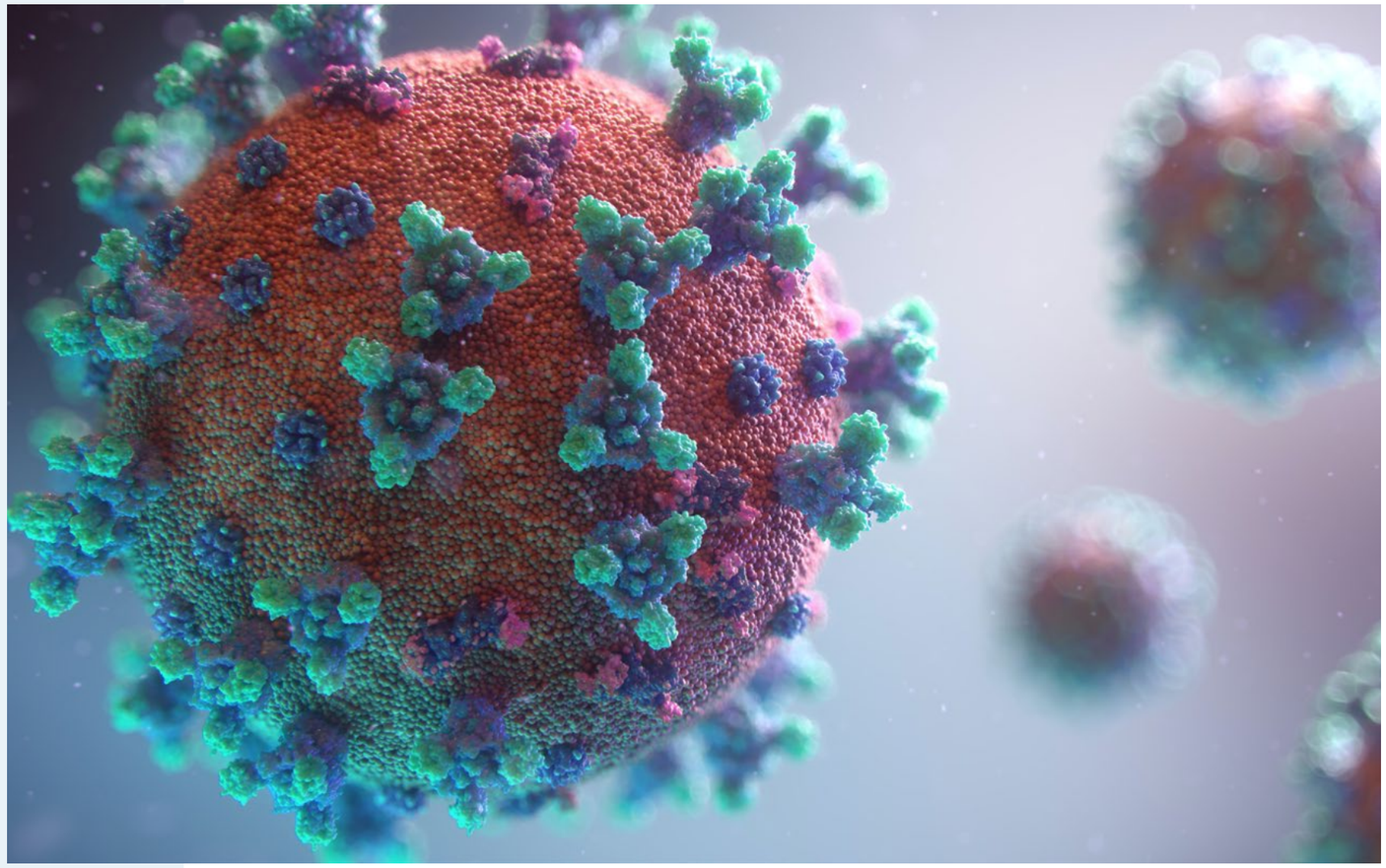
The EU Horizon 2021 funded COVend consortium aims to contribute to the development of a novel therapy against the SARS-CoV-2 coronavirus by conducting a clinical trial, evaluating clinical data using artificial intelligence (AI) and analyzing biomarkers.

To this end, Fraunhofer, Goethe University Frankfurt (GUF) and other cooperation partners from 14 EU countries have joined forces to investigate the novel therapy for mild/moderate to severe COVID in a clinical trial supported by biomarker studies and artificial intelligence (AI). Fraunhofer ITMP is in charge of two work packages within the consortium.

COVend: research approaches of the consortium

The novel coronavirus, referred to as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), has posed an unprecedented challenge to healthcare worldwide. Despite therapeutic options, the treatment of severe (or moderate to severe) COVID remains an unsolved clinical problem. One mechanism discussed is virus-induced endotheliitis, which could explain systemic impairment of microcirculation function and contribute to the clinically catastrophic course of patients with severe COVID-19. The peptide FX06 can reduce endothelial dysfunction by combining interaction with proteins of the endothelium and activation of relevant factors, thus improving the clinical picture of COVID-19 patients. The aim of the consortium is therefore to investigate the efficacy and safety of FX06 and to find a new therapeutic option for the successful treatment of patients severely affected by SARS-CoV-2, as well as to gain further insights into the mechanisms of endothelial dysfunction. In order to further develop



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personalized clinical decisions, the generated study data and omics data will also be analyzed and modeled in the consortium using new algorithms and AI-based tools. In addition, the health economic perspectives of a new therapy will be evaluated.

The role of Fraunhofer ITMP

The heart of the entire project is the phase II clinical trial comparing the FX06 drug to a dummy drug (placebo) and which is being carried out in over 300 patients with moderate to severe COVID at sites of clinical partners within the consortium in 10 different European countries. Fraunhofer ITMP is coordinating this multi-center, multinational clinical trial and is supporting the sponsor of the trial together with GUF. In a further work package, Fraunhofer ITMP will be bringing its expertise in omics technologies to bear by using proteomics and lipidomics to describe the molecular profile in COVID patients treated with FX06 compared to those receiving the placebo. The aim here will be to identify new biomarkers for the characterization of COVID-19. These can serve as support for clinical decisions (precision medicine), leading to a tailor-made therapy for severely affected patients.

COVend

LYCRA:
DEVELOPMENT OF INNOVATIVE BIOTHERAPEUTICS FOR THE TARGETED DEGRADATION OF PATHOGENICITY FACTORS

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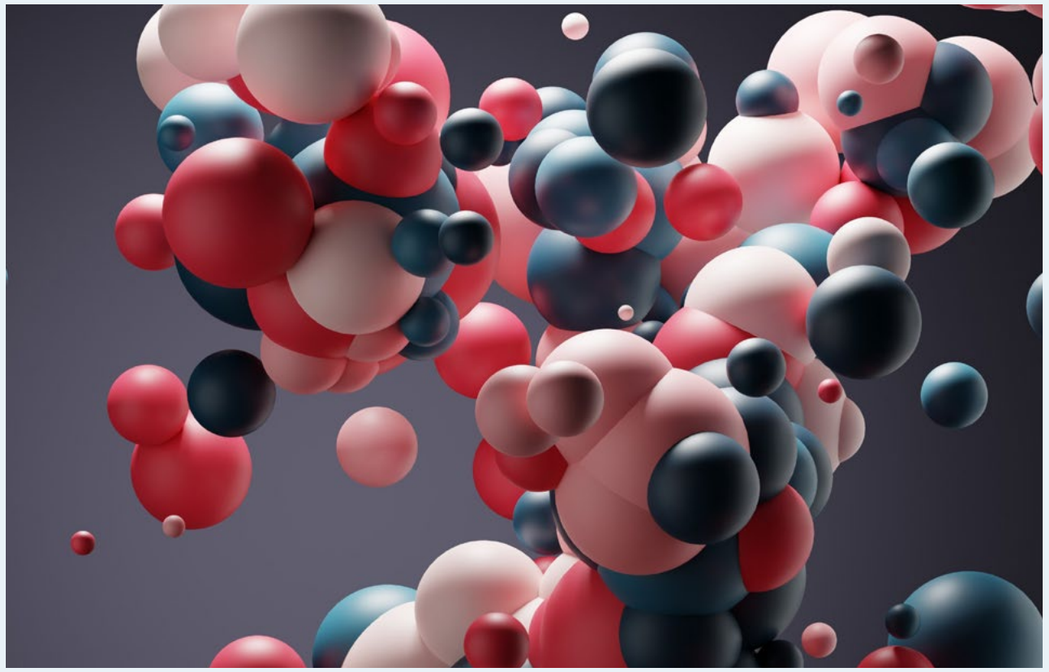
Lycra logo design:
© Christine Schlering

The LYCRA research group, which is funded by the ATTRACT program of the Fraunhofer Gesellschaft, aims to develop new mechanisms of action for biotherapeutic modalities. The basic concept is based on the degradation of target proteins via receptor-mediated delivery to the lysosome — the body's recycling center. Of particular interest here is the targeted recognition and degradation of difficult-to-address pathogenic proteins, which play a central role especially in immune-mediated diseases. In addition, the platform technology behind LYCRA can also represent a therapeutic innovation in other indication areas.

Over the last two decades, biomolecule-based drugs have emerged as the primary therapeutic modality, contributing to remarkable progress in the treatment of many cancers and immune disorders. However, the target space covered by therapeutic antibodies is limited to a small set of human proteins. Around 80% of human proteins are considered undruggable because they lack a defined binding site or catalytic center. This highlights the need for innovative therapeutics with novel mechanisms of action to combat diseases with a high unmet medical need.

One promising new type of therapeutic modality is the molecular degrader (MD). In contrast to conventional small-molecule drugs or therapeutic antibodies, MDs promote the clearance of disease-related proteins by exploiting innate protein homeostasis and quality control systems, and are therefore expected to make a large part of the currently undruggable target space therapeutically accessible. Proteolysis-targeting chimeras (PROTACs) are one such group of small-molecule MDs and have been in development for many years already. However, the therapeutic application of PROTACs is limited to disease-related proteins that accumulate in the intracellular environment.



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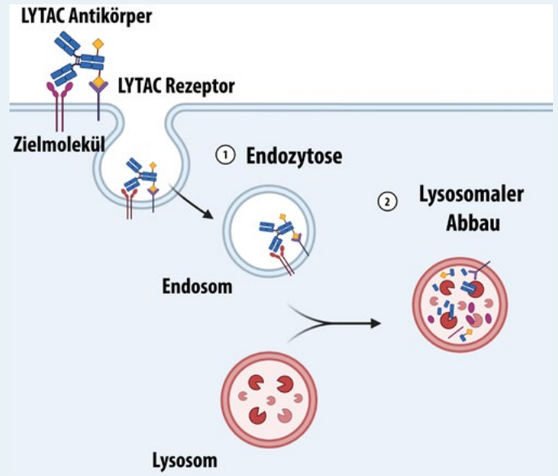
Importantly, almost half of all human proteins are membrane-bound or extracellular, and a significant number of these are involved in autoimmune disorders, cancer and chronic aging-related diseases. A different approach is therefore needed to access these targets. Lysosomes are ubiquitous organelles that help to recycle nucleic acids, polysaccharides and proteins. The regulation of protein levels by lysosomes maintains cellular and systemic homeostasis. Proteins targeted for lysosomal degradation are first taken up by the process of receptor-mediated endocytosis followed by intracellular trafficking and vesicular fusion with the lysosomal membrane (see figure).

The LYCRA project aims to expand the MD tool set by developing lysosome-targeting chimeras (LYTACs). LYTACs are innovative, multi-specific compounds with a biomolecular framework exhibiting the known advantages of this molecule class. In addition, targeted modifications mean LYTACs have specific affinities with membrane receptors, which — when activated — deliver a LYTAC-antigen complex to the lysosome, where target proteins are efficiently degraded. The lysosome-based targeted degradation of proteins is therefore complementary to PROTACs because it can be used as a therapeutic option for the clearance of extracellular and plasma membrane proteins.

LYTAC mechanism of action
© Fraunhofer ITMP, Schara Safarian



PUBLICATION HIGHLIGHTS 2022

Methotrexate plus ustekinumab versus ustekinumab monotherapy in active psoriatic arthritis

In the treatment of psoriatic arthritis, it is unclear whether the combination therapy of biological therapy with methotrexate brings a benefit or is superfluous. This was examined in the MUST study.

" Psoriatic arthritis is a heterogeneous clinical picture that occurs in around 30% of patients with psoriasis. "

In the case of active disease after the use of non-steroidal anti-inflammatory drugs (NSAIDs), basic therapies such as methotrexate are to be proposed before biological drug therapies that inhibit dedicated signaling pathways of systemic inflammation are used. In most cases, therapy with classic basic therapy is supplemented by therapy with biological agents. For rheumatoid arthritis, there is data on this combination therapy that shows an improvement in the effectiveness of the therapy and a lower rate of immunogenicity, i.e., the formation of anti-drug antibodies. This has not yet been studied in a structured manner for the treatment of psoriatic arthritis.

Psoriatic arthritis is a systemic immune disease with a very heterogeneous clinical picture.
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Given this backdrop, the investigator-initiated MUST study was designed by the clinical research team at Fraunhofer ITMP in Frankfurt and carried out throughout Germany. The project was funded by research support from Janssen.

" In addition to the medically relevant question of whether monotherapy using a biologic (ustekinumab) is non inferior to the combination therapy of ustekinumab and methotrexate, an innovative biostatistical method for confirmatory statements was used (van Elteren test) in this non-inferiority design with a realistic and recruitable number of patients. "

The results of the clinical study have now been accepted for publication in The Lancet Rheumatology. For the selected endpoint, the DAS28 as a measure of the arthritis component of psoriatic arthritis, it was possible to demonstrate that both groups, ustekinumab + methotrexate and ustekinumab + placebo, are non inferior and therefore the combination therapy with methotrexate in everyday clinical practice to achieve effectiveness is not necessary. These results can also be reproduced in the other disease characteristics measured for enthesitis, psoriasis of the skin and dactylitis.

In addition to the clinical measurements, determinations of the formation of anti-drug antibodies (ADA) were also carried out from the sera of the patients. Here too, unlike in rheumatoid arthritis, there is no relevant formation of ADA and this is also not influenced by the combination with methotrexate.

" The possibility of omitting the methotrexate dose in the therapy of psoriatic arthritis reduces the rate of side effects and improves the benefit-risk assessment for the patient. This has direct implications for the care of psoriatic arthritis patients. "

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Publication: Koehm M **et al.**
Methotrexate plus ustekinumab versus ustekinumab monotherapy in patients with active psoriatic arthritis (MUST): a randomised, multicentre, placebo-controlled, phase 3b, non-inferiority trial

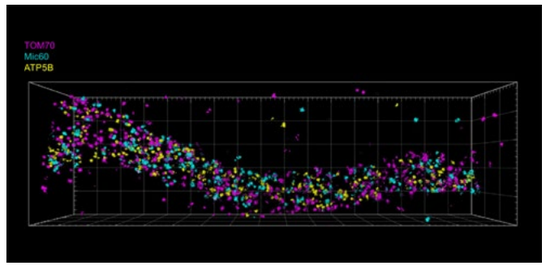
Lancet Rheumatology
DOI: 10.1016/S2665-9913(22)00329-0

Multicolor imaging at the nanoscale

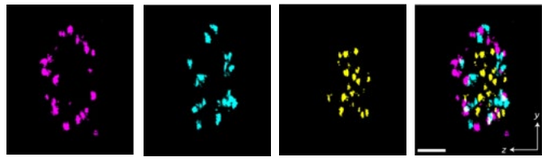
DNA-PAINT MINFLUX super-resolution microscopy enables imaging of multiple molecular targets in three dimensions at the nanoscale.

In the recently developed MINFLUX microscopy (MINimal fluorescence photon FLUXes), the localization of a fluorophore is determined by randomly switching it on and off while simultaneously illuminating it with an excitation light pattern. Initial studies have shown that this method can achieve localization precisions of less than 1 nm in the focal plane and approximately 2 nm in all three dimensions. This impressively demonstrated that MINFLUX is capable of resolving the spatial resolution of target molecules at the molecular level. However, this method places high demands on the properties of the fluorophores used, particularly their ability to switch between a fluorescent "on" and a non-fluorescent "off" state. This makes multicolor imaging challenging, as it requires reconciling the molecular brightness and switching kinetics of different fluorophores in the same sample.
DNA-PAINT (DNA-based point accumulation for imaging in nanotopography) can eliminate the need for on/off switching.

3D PAINT MINFLUX multiplexing. The mitochondrial proteins TOM70, Mic60 and ATP5B were labeled by sequentially adding and washing out specific DNA imager strands and then imaged with MINFLUX super-resolution microscopy.



Overview image of part of a mitochondrion.
© Ostersehlt et al., 2022



Cross-section through the mitochondrion showing the spatial distribution of the proteins. Scale bar 100 nm. © Ostersehlt et al., 2022

" The on/off modulation is realized by temporarily binding imager strands (fluorophore-labeled DNA oligonucleotides) to their corresponding DNA docking strands. "

While the bound imager strands emit photons from a fixed position and can thus be localized, the unbound imager strands contribute less fluorescence and can be considered "off". With DNA-PAINT, therefore, normal bright and stable fluorescent dyes can be used because they no longer need to be switchable or activatable.

By combining DNA-PAINT labeling and MINFLUX imaging, we were able to synergistically combine the advantages of both methods.

" In particular, DNA-PAINT MINFLUX microscopy allows for easy multiplexing, enabling multicolor imaging with unprecedented localization precision. "

By way of example in the present study, we determined the spatial distribution of Mic60 and TOM70 — proteins of the inner and outer mitochondrial membrane respectively, together known as ATP5B — a subunit of F1FO-ATP synthase — in cultured human cells (see figure).

Our study paves the way for widespread application of 3D MINFLUX imaging of cellular compartments at nanometer resolution.

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Publication: Ostersehlt **et al.**
DNA-PAINT MINFLUX nanoscopy

Nature Methods
DOI: 10.1038/s41592-022-01577-1

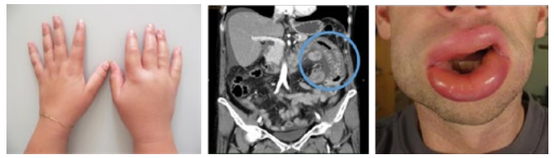
New drug for rapid, on-demand self-medication in hereditary angioedema

In a clinical trial involving the Fraunhofer ITMP Berlin site, an orally available drug for on-demand medication in hereditary angioedema was tested for the first time.

" Hereditary angioedema (HAE) is a rare, potentially life-threatening, genetic disease, which is characterized by unpredictable tissue swelling. "

This can affect the face, extremities, gastrointestinal tract, genitourinary tract as well as the upper airways. The severity and frequency varies greatly both within and between patients. These swellings are caused by an increased vascular permeability due to a disturbance of the bradykinin signaling pathway. During attacks, a genetic malfunction of the C1-inhibitor leads to increased plasma kallikrein (PKa) levels and thus to increased production of the vasoactive factor bradykinin.

" Due to the unpredictability of the attacks, in HAE there is a specific focus on targeted and timely on-demand medication. "



Sudden swelling in various parts of the body causes the high burden of disease in hereditary angioedema and can even become life-threatening. © Marcus Maurer

Until now, this has always involved an injection (subcutaneous or intravenous), which usually results in several hours elapsing between the onset of the attack and medication.

The present study was the first time that a drug available as a tablet for on-demand medication of HAE attacks was tested. In part one of the trial, pharmacokinetics and pharmacodynamics were investigated following one single administration of sebetralstat, a novel small molecule PKa inhibitor. This showed rapid plasma availability and an early, almost complete inhibition of PKa formation. In part two, patients were asked to take a dose of sebetralstat or placebo as early as possible after the onset of an attack.

" The results revealed that sebetralstat had high safety and efficacy. "

In addition, the time before conventional treatment was provided was lengthened significantly. Patients reported significantly faster symptom relief and an overall more frequent improvement of their symptoms following sebetralstat treatment compared to the placebo.

" The mean time to medication was approximately 30 minutes. This was mainly due to the oral availability of the drug and, consequently, the much reduced burden of the treatment. This makes self-medication with sebetralstat an extremely interesting alternative to existing on-demand treatment options. "

Based on the results published in the journal The Lancet, a confirmatory phase III clinical trial on the use of sebetralstat for on-demand medication in HAE is now being prepared.

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Publication: Aygören-Pürsün **et al.**
An investigational oral plasma kallikrein inhibitor for on-demand treatment of hereditary angioedema: a two-part, randomised, double-blind, placebo-controlled, cross-over phase 2 trial

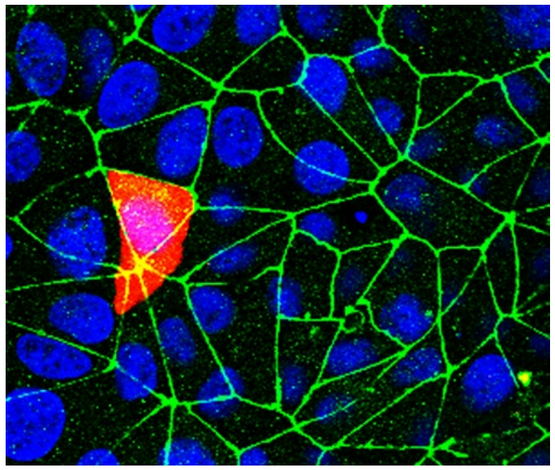
The Lancet
DOI: 10.1016/S0140-6736(22)02406-0

Alternative SARS-CoV-2 infection route via cerebral vessels identified

Researchers from the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP have shown that cells of the blood-brain barrier (BBB) can be infected by the SARS-CoV-2 pathogen.

Fraunhofer scientists have been developing preclinical models and — assisted by them — drug candidates for the treatment of COVID-19 since February 2020.

"The Fraunhofer vs. Corona campaign has enabled us to focus our resources and expertise on the pandemic and bring them into application,"



Immunofluorescence of SARS-CoV-2-infected hiPSC-derived brain capillary endothelial-like cells stained for SARS-CoV-2 N (red) and TJP1 proteins (green) 24 h post-infection; counterstained with DAPI (blue). Scale bar, 50 µm.
© PD Dr. Susanne Krasemann

says Dr. Ole Pless, a senior scientist at Fraunhofer ITMP and also the laboratory head of a guest group at the Center for Molecular Neurobiology Hamburg (ZMNH) at the University Medical Center Hamburg-Eppendorf (UKE). "In addition, we developed the relevant cell models in a project funded by the German Federal Ministry of Education and Research, which we were able to bring directly to application during the pandemic."

"Based on our extensive knowledge of COVID-19 pathology, including central nervous system pathology, we were able to describe precise molecular changes at the blood-brain barrier. These were confirmed in cell models provided by Fraunhofer,"

said the study's first author, PD Dr. Susanne Krasemann from the Institute of Neuropathology at UKE. The study was conducted with the participation of several UKE institutes and other international partners.

COVID-19: Characteristics of brain pathology can be reproduced in cell culture

Extensive analysis of post mortem brain tissue from COVID-19 patients demonstrated upregulation of interferon-gamma signaling pathways, a hallmark of viral defense, in the neurovascular unit of the BBB. By using pluripotent stem cells, the study authors were able to mimic this susceptibility of brain capillary endothelial cells to SARS-CoV-2 infection in the laboratory. In an in vitro test system, they were able to observe the replication of the virus in the cells and its transport across the BBB.

This model was subsequently applied to test compounds that prevent virus entry across the BBB, such as specific protease inhibitors. Thus, a platform was created for testing drugs that could prevent SARS-CoV-2 pathogens from entering the central nervous system and mitigate the resulting neurological consequences.

This publication was selected for the Stem Cell Reports — Best of 2021–2022 collection and was the most downloaded and cited paper from Stem Cell Reports in 2022.

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Publication: Krasemann **et al.**
The blood-brain barrier is dysregulated in COVID-19 and serves as a CNS entry route for SARS-CoV-2.

Stem Cell Reports
DOI: 10.1016/j.stemcr.2021.12.011

Letter to the Editor: Krasemann **et al.**
Stem Cell Reports
DOI: 10.1016/j.stemcr.2022.04.012

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IN FOCUS

PERSPECTIVES LOOKING AHEAD AND LOOKING BACK

» Research as a process between people and development.“

REMEDi4ALL DRIVING FORWARD THE REPURPOSING OF MEDICINES IN EUROPE

Drug repurposing is an increasingly important approach for the identification of new treatments for unmet medical needs, especially in rare and neglected diseases. Fraunhofer ITMP is a key member of the EU-funded REMEDi-4ALL project, which will create a new innovation platform for the sustainable development of reuse strategies for existing drugs in new indications. The project combines practical drug discovery and development workflows along with policy-focused initiatives in order to maximize the chances of success in progressing academic drug repurposing projects along the pathway from idea to market.

Fraunhofer ITMP will use its stem-cell-based in vitro assay technologies to evaluate the efficacy and toxicity of repurposed drugs in new indications.
© Fraunhofer ITMP, Martin Kunze

The process of repurposing of medicinal products commonly called drug repurposing (DR), in which existing drugs with a known efficacy, ADME and safety profiles are tested and validated for use in new therapeutic applications outside of their original indication, has demonstrated high utility to serve unmet patient needs in a broad variety of disease areas.

“ Policy, funding and research attention in this area has been steadily growing in recent years.”

What’s more, systematic computational approaches are augmenting serendipitous successes. Examples such as thalidomide and sildenafil, which were revealed as DR candidates by clinical insight, retrospective clinical analysis and deep understanding of the (poly)-pharmacology, are illustrative of effective repurposing strategies. The rationale behind adopting DR is clear, as development times and costs are estimated to be between 30 and 75% lower than those of developing a new chemical entity from scratch. Analysis of drug development pipelines shows that almost 170 repurposed drugs entered development stages between 2012 and 2017. Of these, some 72% were in phase II clinical development. Of particular interest to Fraunhofer ITMP and its clinical collaborators is that almost 70% of the phase I and II trials for repurposed drugs were sponsored by academia, indicating the key role this sector has in promoting DR as a solution to unmet patient needs. However, DR is a complex endeavor requiring expertise from multiple disciplines to align for success.

“ Currently, the European DR ecosystem remains at an early stage of development, with several systemic inefficiencies that hamper the pace and effectiveness of DR.”

These include a fragmented and siloed DR research and development environment and a healthcare landscape that lacks a framework for true co-creation with patients and without an easily identifiable value chain. This results in substantial inefficiencies as DR researchers struggle to find competent partners outside of their own specialized domains, and projects lack the momentum and drive provided by patient champions. A recent and worrying example of this has been in DR efforts seeking COVID-19 therapeutics, where highly fragmented repurposing activities — in some cases with minimal quality control — have led to premature use of therapeutics. Other shortcomings include the varying availability and quality of computational tools, a lack of standardized datasets and other resources to support effective, rational DR utilizing machine learning (ML) and artificial intelligence (AI) methods. DR researchers also have only limited access to reliable infrastructures (chemical libraries, screening technologies) for hit finding, while later preclinical projects are often advanced with little evidence of the mechanism of action. In many cases, the underlying environment in relation to reimbursement and the assessment of health technologies impedes the efficient introduction of repurposed drugs, and there is no financially viable path to market for repurposed generic medicines. Both the European regulatory landscape and funding ecosystems are not yet fully aligned with the specific needs of the DR process, which leads to unwelcome duplication, funding gaps and large variation across European countries.

To address these challenges, the European Union recently sort to establish sustainable European innovation platforms for DR to generate system-wide improvement in the efficiency and effectiveness of the DR process and support harmonization in the EU.

“ Two projects received funding under the Horizon Europe program to implement these platforms.”

These are REPO4EU (https://repo4.eu/), which will focus on mechanism-based repurposing and, REMEDi4ALL (https://remedi4all.org/), where Fraunhofer is a key partner and which will implement a patient-informed approach to create a sustainable open DR platform. The REMEDi4ALL project started in September 2022 and will run for five years. Fraunhofer ITMP leads the in vitro biology and screening aspects of the project as well as supporting the preclinical development of drugs in terms of pharmacokinetic profiling and reformulation of existing drugs for new indications. An essential part of the project is the application of in-silico-based rational repurposing using ML methods trained using newly generated as well as historical data. Here, Fraunhofer ITMP works with colleagues at Fraunhofer SCAI to develop networked pharmacology representations of marketed drugs, therapeutic targets and disease pathways. In further collaboration with Uppsala University and the informatics company Chemotargets, Fraunhofer ITMP will apply AI methods to cell painting (phenotype to chemotype) and omics data to elucidate the mechanism of action and off-target/safety-related properties of repurposed drugs.

The setup and performance of the REMEDi4ALL platform will be refined through the completion of four demonstrators representing different indications and phases of the DR development process. One of the demonstrator projects, which involves repurposing the psoriasis drug tazarotene for the treatment of the inherited genetic disorder multiple sulfatase deficiency, originates from Dr. Lars Schlotawa of University Medical Center Göttingen and his colleagues located at the Fraunhofer ITMP Göttingen site. REMEDi4ALL, therefore, will provide an excellent opportunity for further practical collaboration between the Hamburg, Frankfurt and Göttingen sites of Fraunhofer ITMP.

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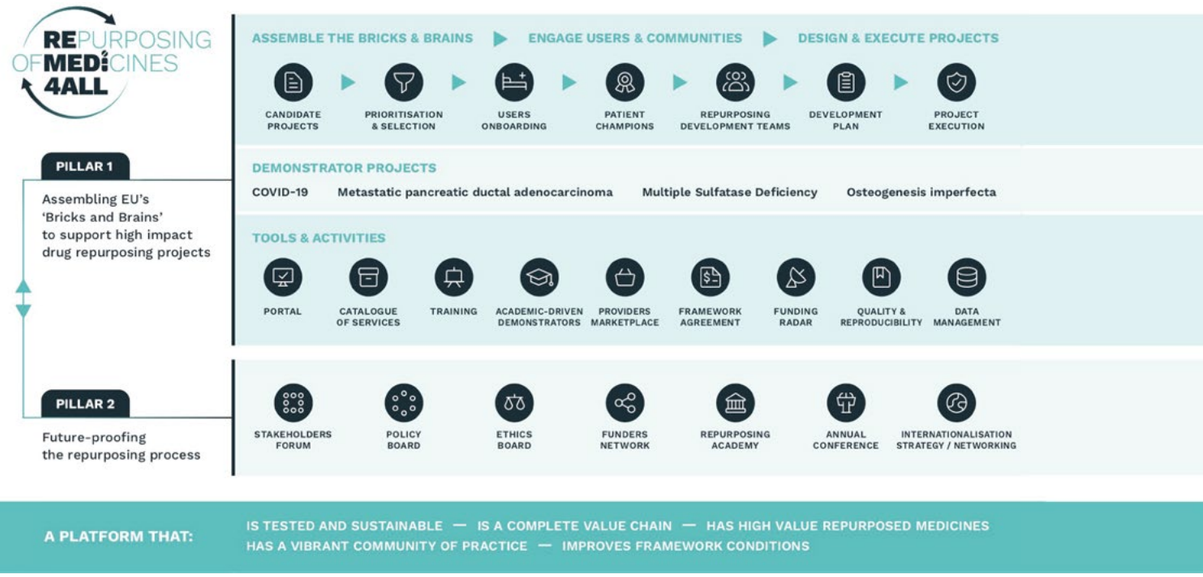
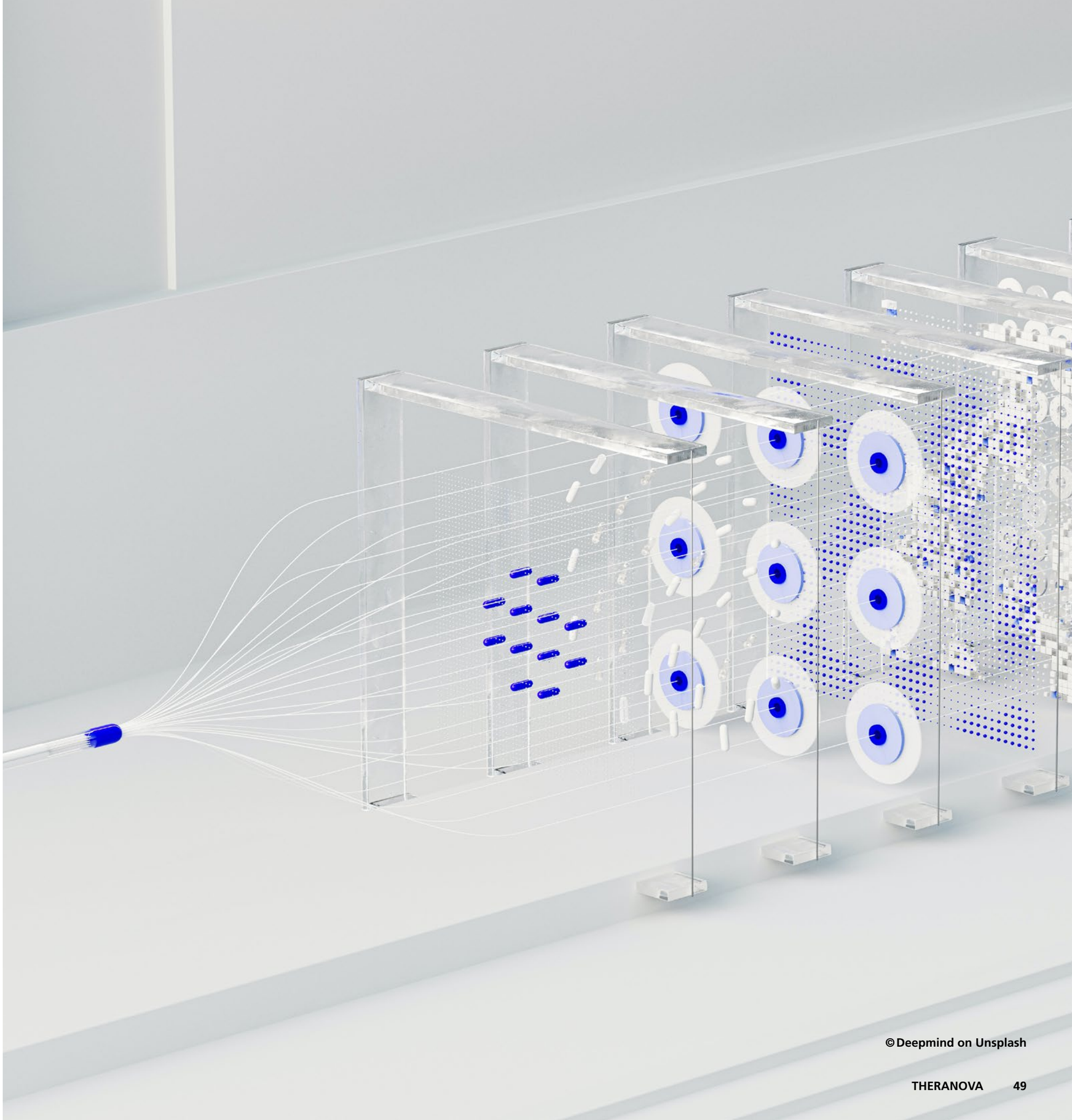


THERANOVA

RAPID TRANSFER OF INNOVATIVE THERAPIES INTO CLINICAL APPLICATION

The development of novel therapies and their rapid transfer into clinical practice require interdisciplinary collaboration between the areas of basic and applied research, medicine and (bio)informatics, as well as close cooperation with biotechnological and pharmaceutical companies. The Fraunhofer High-Performance Center Innovative Therapeutics TheraNova unites all relevant expertise and partners under one roof in order to decipher pathological mechanisms, develop innovative therapeutic approaches and accelerate their transfer into products and medical applications.



"A regional science-industry cluster to develop new treatment modalities."

High-Performance Center TheraNova started its work in January 2022. Headed by the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP and in cooperation with the Fraunhofer Institute for Computer Graphics Research IGD, the high-performance center combines the expertise of various working groups of the Goethe University Frankfurt am Main, the University Hospital Frankfurt and the Max Planck Institute for Heart and Lung Research in Bad Nauheim. The focus of the high-performance center is to establish a joint innovative research and development portfolio specifically supporting and focusing on projects with a particularly high transfer potential. Research activities aim at developing novel therapeutic entities such as proximity-inducing molecules, multi-specific biotherapeutics, innovative fusion proteins and customized microbiota for the treatment of diseases with a high unmet medical need. The close collaboration between basic and applied research as well as the hospital should enable rapid identification of promising early projects and subsequently provide a critical mass of resources and capabilities for their realization. The high-performance center regards itself as a bridge in this process to facilitate the transition from drug research to clinical testing, where currently many drug candidates fail.

The Rhine-Main region is an ideal location for establishing such a regional science-industry cluster in the field of innovative therapeutics, as it has a high density of biopharmaceutical companies and the Goethe University Frankfurt is the only German university with a special focus on drug research. These circumstances allow the development of new strategic partnerships and collaboration models with industry partners.

"Transfer-oriented research in close cooperation with the hospital."

To identify and optimize innovative active compounds and the associated technologies up to a level of maturity that enables commercial exploitation, patient-oriented research in close cooperation with University Hospital Frankfurt and access to biomaterials are of vital importance. This approach allows target structures and mechanisms of action identified in research laboratories to be rapidly verified using patient-derived materials and by conducting clinical trials. In this environment, the Fraunhofer 4D Inflammation Clinic is an important interface between research and clinical applications.

In addition to scientific doctoral theses in various biomedical fields, the high-performance center also supports clinician scientists in order to facilitate the integration of patient data and results of medical care in different indications. This strong focus on translation and transfer is essential to accelerate the transition to clinical trials and the acquisition of industrial partners. An integral part of the research and transfer strategy of the high-performance center is the development of innovative cooperation models such as joint laboratories or job rotations with industry partners. Furthermore, the ability to perform clinical studies or screening campaigns to identify novel active compounds provides additional opportunities for contract research or partnerships.

"Promoting young scientists."

The education and advanced training of young scientists is another important goal of TheraNova. Funding from the Hessian Ministry of Science and the Arts (HMWK) and the Fraunhofer-Gesellschaft enables the implementation of doctoral and medical research projects as well as a comprehensive continuing education program for young scientists within the framework of the high-performance center. For example, all participants have access to the offers of the GRADE Graduate Academy of the Goethe University for further interdisciplinary and career-oriented qualifications. The high-performance center develops new modules for GRADE on topics dealing with drug research and transfer as well as patents, licensing and spin-offs. Regular meetings offer doctoral candidates, researchers and project leaders the opportunity to exchange ideas and to network.

The high-performance center builds on existing networks and structures of the participating partners: Numerous collaborative research centers, joint projects, the Proxidrugs Cluster4Future as well as the EUbOpen and HIPPOCRATES Innovative Medicines Initiatives, and the Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD are located at the Goethe University Frankfurt am Main and Fraunhofer ITMP. Additional joint projects funded by private or public sponsors have already been acquired via the high-performance center — for example, the MACROVIR project, funded by the Volkswagen Foundation, which is working to identify new broad-spectrum antiviral agents.

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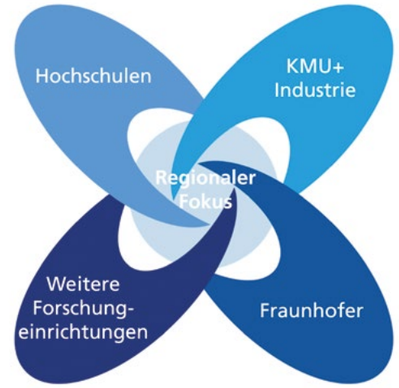
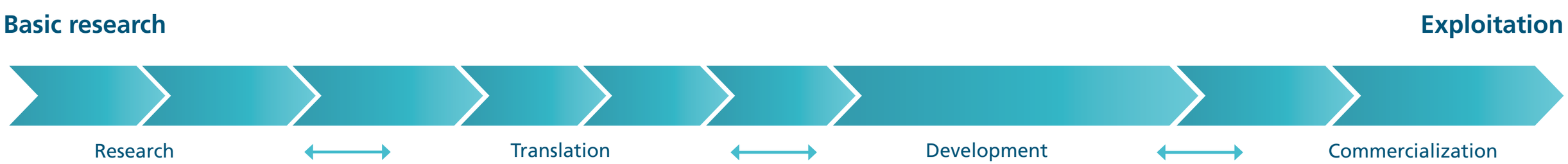
High-Performance Center TheraNova science-industry cluster. © Fraunhofer-Gesellschaft





UNDER DISCUSSION

PREPARING FOR THE NEXT PANDEMIC

Prof. Dr. med. Michael Hoelscher, storing and cooling laboratory samples for SARS-CoV-2 research in a biobank at -80 °C. © LMU, Christoph Olesinksi

How can we protect ourselves from new pandemics in the future? In 2022, the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP opened a new site for Immunology, Infection and Pandemic Research IIP in Penzberg/Munich. Working together with Roche Diagnostics GmbH, Ludwig-Maximilians-Universität (LMU) and the LMU Medical Center in Munich, the goal of the new facility is to identify and characterize pandemic pathogens, develop new diagnostics and therapies, and better understand the role of the immune system in infectious diseases. Prof. Dr. med. Michael Hoelscher, site head, and PD Dr. med. Andreas Wieser, head of research, bring not only their expertise as specialists in infectious diseases and tropical medicine to the Fraunhofer ITMP site in Penzberg/Munich, but also their formative experience in outbreak management of the COVID-19 pandemic.

"What was the most important learning experience for you personally over the past three years of the COVID-19 pandemic?"

Hoelscher: " This was probably the experience that, when it really matters, it is possible — even in Germany — to act flexibly and quickly, without being thwarted by bureaucracy. We now need to build on this experience. At the same time, we need to ask ourselves and critically reflect as a scientific community on why we did not manage to combine and coordinate our efforts more effectively — especially at the beginning of the pandemic. But there were also challenges in logistical terms — for example, it became apparent that centralized testing can reach capacity limits. At Fraunhofer ITMP's IIP site, we will develop patient-centered laboratory diagnostics for decentralized and mobile use in view of possible future pandemics. "

" What is your prognosis, will research soon be able to defeat or at least push the viral opponent SARS-CoV-2 aside?"

Wieser: " SARS-CoV-2 has brought many new insights in the field of virological research. The virus will probably remain as an endemic pathogen; however, our efforts in vaccine development, diagnostics, prevention and therapy research have produced and proven many new techniques and approaches. This will benefit us with respect to other diseases, too, to the extent that the results can be applied in those areas as well. Unless a new virus variant of concern emerges, SARS-CoV-2 has lost much of its terror. "

"What knowledge gained in the last three years could be crucial in preventing a possible next pandemic or at least mitigating its course?"

Hoelscher: " We have seen for the first time how rapidly effective vaccines can be produced with mRNA technology and be deployed worldwide. This could also prove very effective in other outbreaks. Adequate provision of protective equipment and disinfectants, as well as infection control measures such as social distancing, have also proven to be effective ways to bridge the time until effective therapeutics or vaccines are available. In addition, it has been shown that more therapeutic and diagnostic reserves should be kept available overall. "

"There has been controversy about the available vaccines. How effective were the COVID-19 vaccinations and what do you expect for the future?"

Wieser: " The vaccines led to a significant reduction in deaths, especially in the vulnerable patient groups, which was very good. However, the anticipated protective effect against infection and further transmission was not as high; this effect was exacerbated by the newer SARS-CoV-2 variants. Presumably, we will nevertheless continue to vaccinate vulnerable individuals in particular. How useful this is in young healthy individuals will depend on the pathogenicity of the dominant viral variants. "

"What other challenges do you anticipate with SARS-CoV-2?"

Hoelscher: " Presumably, like influenza, RSV infections and other respiratory diseases, SARS-CoV-2 will establish itself as another differential diagnosis in patients. The biggest challenge will probably be to find a good balance between allowing natural chains of infection, recommending vaccines in vulnerable patient populations and protective measures. We must remain vigilant to rapidly detect the development of possible more aggressive variants. "

" How is the new Fraunhofer ITMP IIP site preparing for a possible next pandemic?"

Wieser: " We are working on various model pathogens in a modular system that will enable us to quickly develop and provide adapted diagnostics and therapeutics in the event of an outbreak. At the same time, we are building a global network with countries from Asia, Africa and South America so that we can react quickly in the event of an outbreak, no matter where it is in the world, and provide good support for coordinated responses by the international community. Pandemics can only be fought together. "

" How quickly can these findings be incorporated into the work of the new IIP site?"

Hoelscher: " Scientists from the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP and partner institutions moved into the rented research laboratories on the Roche Diagnostics GmbH site in Penzberg in May 2022. The laboratories will be fully operational in a few months. The pandemic research site is currently still under construction and is set to be transferred to its own building in around 2026. In a few years, around a hundred researchers working on projects related to immunology, infection and pandemic research will be based at the newly established Fraunhofer site in Nonnenwald in Penzberg and in Munich. "

"To what extent does Future Made in Bavaria take place at the Fraunhofer ITMP IIP site?"

Hoelscher: " The Penzberg/Munich site is ideal for the new Fraunhofer institute. With its partners Roche, LMU as well as the campus of the LMU Medical Center in Munich-Großhadern, the Fraunhofer ITMP's IIP site offers enormous potential for scientific progress and translational research through its proximity to Europe's largest biotech location around the state capital in Munich. The local network will also play a central role: A next step will be to build a network with other important research institutions in Munich, especially with our sister university the Technical University of Munich (TUM) and the Helmholtz Association in Munich. "

PD Dr. med. Andreas Wieser, blood samples for SARS-CoV-2 antibody research: separation of blood components, blood cells and plasma, after centrifugation.
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Fraunhofer ITMP IIP site in Penzberg/Munich

The new Fraunhofer ITMP site for Immunology, Infection and Pandemic Research IIP in Penzberg/Munich is one of the five institute sites of Fraunhofer ITMP. The institute has its headquarters in Frankfurt am Main plus sites in Hamburg, Göttingen and Berlin.

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PEOPLE AND EVENTS

Brief reports on staff, encounters, successes, events and new perspectives at Fraunhofer ITMP.

Opening of the Early Clinical Trial Unit ECTU in Göttingen

The Fraunhofer Institute for Translational Medicine and Pharmacology ITMP opened the Early Clinical Trial Unit ECTU for early clinical phase I studies on September 15, 2022.

The focus of the ECTU is on the first-time clinical testing of active substances for the treatment of difficult-to-treat (autoimmune) diseases of the central nervous system (CNS), such as multiple sclerosis or Parkinson's disease. The aim is to obtain information on tolerability, safety and pharmacokinetics. The ECTU, which is located in the University Medical Center Göttingen (UMG), has all the necessary and prescribed personnel and structural requirements for the implementation of early phase I studies. The new Early Clinical Trial Unit is integrated into the Fraunhofer site for Translational Neuroinflammation and Automated Microscopy TNM of Fraunhofer ITMP and also works closely with the UMG study center. Under the leadership of Prof. Dr. Martin Weber, deputy director of the Department of Neurology at UMG, an excellent interdisciplinary team supports translation into the clinical department as well as research into new drug candidates in neuroinflammation at UMG.
The institute heads of the Fraunhofer ITMP sites in Göttingen and Frankfurt as well as Dr. Sabine Johannsen, state secretary in the Lower Saxony Ministry of Science and Culture (MWK), were in attendance to mark the inauguration of the new ECTU at UMG.

Inauguration of the new ECTU at UMG; l–r: Prof. Dr. Frank Behrens (head of division Clinical Research Fraunhofer ITMP), Prof. Dr. Martin Weber (head of ECTU at Fraunhofer ITMP, Translational Neuroinflammation and Automated Microscopy TNM), Prof. Dr. Stefan Jakobs (head of Fraunhofer ITMP site for Translational Neuroinflammation and Automated Microscopy TNM), Prof. Dr. Wolfgang Brück (chairman of the executive board of UMG), Dr. Sabine Johannsen (state secretary in the MWK), Prof. Dr. Dr. Gerd Geißlinger (executive director of Fraunhofer ITMP).
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Networking event: Allergology Workshop with Fraunhofer ITEM

On July 8, 2022, the ITEM Allergology Workshop took place in the special ambiance of the Fraunhofer Forum Berlin as a networking event between the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM (Hannover) and the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP site for Immunology and Allergology (Berlin). A total number of 25 scientists from both institutes took part.

The first part of the event dealt with current findings in research into the pathomechanisms of mast cell-mediated diseases (PD Dr. Frank Siebenhaar, ITMP) and asthma (Dr. Katherina Sewald and Prof. Dr. Armin Braun, ITEM) as well as their interfaces. In the second part, Dr. Magda Babina, ITMP, provided insights into the methodology and advances in mast cell biology research. Clinical research projects to improve the understanding of mast cell-mediated diseases as well as approaches for targeted modulation of immune cells in allergies were presented by Prof. Dr. Martin Metz, ITMP, and Prof. Dr. Jens Hohlfeld and Dr. Meike Müller, ITEM, respectively. Following the scientific presentations, there was also time for the attendees to hold in-depth discussions and share experiences. New contacts were made and opportunities for collaboration between both institutes were explored.

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Fraunhofer ITMP Young Talent Class and Journal Club

With the Fraunhofer ITMP Young Talent Class, Fraunhofer ITMP is supporting the education and training of young scientists, especially female scientists. The initiative aims to strengthen communication and exchange between the locations. Through a Visiting Scientist Program, laboratories can be used and expertise tapped into across locations. What's more, the program facilitates travel and provides reagents and software tools for pilot projects and master's theses.

The Journal Club, meanwhile, is organized by Ann C. Foldenauer, a mathematician at Fraunhofer ITMP, and can be attended by all employees via Teams. The presentations cover a wide range of scientific topics and are suitable for all levels of knowledge. These regular events typically attract up to 50 participants and provide an opportunity for speakers to present their work in a friendly "safe space". A recent example was "The 1-permille study: the sensation of pain in the EEG under the influence of alcohol. "

A cooperative pilot project that emerged from the Journal Club is the combination of experimental Olink analyses and pharmacological interpretation in Frankfurt am Main. It results in statistical bioinformatics for biomarker signatures in Hamburg, on samples from COVID-19 intensive care patients, which originate from a clinical study in Erlangen. This shows the potential of developing talented Fraunhofer ITMP offerings for the future.

Opening of the Fraunhofer laboratories at the Roche Biotechnology Center in Penzberg/Munich

On May 6, 2022, the laboratories for Immunology, Infection and Pandemic Research IIP in Penzberg/Munich were officially opened. The aim of the research at the site is to identify and characterize pandemic pathogens, to develop new diagnostics and therapies and to better understand the role of the immune system in infectious diseases.

The new Fraunhofer ITMP site in Penzberg/Munich is the result of a strategic partnership between Roche, LMU, the LMU Medical Center in Munich and the Fraunhofer-Gesellschaft. It is part of a network for immune-mediated diseases, which in future will ensure that relevant forces in the German research landscape are pooled together in a targeted way.

To permanently accommodate the new research capacities, a new building is built in the immediate vicinity of the Roche site. For the time being, research will begin in rented premises at Roche's Life Sciences Competence Center in Penzberg.

Among the guests and speakers at the opening ceremony were the heads of Roche Diagnostics GmbH, LMU and the Fraunhofer ITMP sites in Frankfurt and Penzberg, as well as Hubert Aiwanger, Bavarian state minister for economic affairs, regional development and energy, Alexander Dobrindt, chairman of the CSU in the German Federal Parliament and Stefan Korpan, first mayor of the City of Penzberg.

Inauguration of the Fraunhofer laboratories at Roche Diagnostics GmbH on the Penzberg site; l–r: Stefan Korpan, Ullrich Opitz, Alexander Dobrindt, Raoul Klingner, Hubert Aiwanger, Klaus Haberda, Thomas Gudermann, Gerd Geißlinger, Michael Hölscher **© Bernhard Huber Fotografie**

Fraunhofer spin-off Phialogics wins Sanofi's Golden Ticket

Phialogics AG, a 2021 spin-off of Fraunhofer ITMP, develops immune-modulating agents for patients with autoimmune diseases. The most advanced of these drug candidates are known as checkpoint agonists, which are designed to dampen immune reactions and prevent the rejection of transplanted organs. With this innovative approach, the company won Sanofi's Golden Ticket Competition in 2022. The prize includes free residence at the Heidelberg BioLabs and access to the network of industry partners and investors there.

The experienced team of founders at Phialogics AG, which includes former Fraunhofer scientists Andreas Ernst and Michael Parnham as well as two other professors from Goethe University Frankfurt am Main, is building its research on a proprietary phage display technology for the rapid identification of high-affinity ligands for receptors that play an important role in controlling the immune response.

BioLabs Heidelberg is an incubator for young companies from the life science sector that want to translate the results of their academic research into applications and products. BioLabs provides them with the necessary laboratory and administrative infrastructure for this purpose. In addition, the start-ups receive intensive mentoring and the opportunity to exchange ideas with other start-ups as well as with investors and companies in the biotechnology and pharmaceutical industries.

© Phialogics, www.phialogics.com

Phialogics
The immune tolerance company

Fraunhofer ITMP opening — awarding of the Fraunhofer Medal to Volker Bouffier, former state premier of Hesse

On September 21, 2022, the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP was officially opened at its headquarters in Frankfurt am Main. The occasion was the transfer of the Fraunhofer Institute Branch for Translational Medicine and Pharmacology TMP of the Fraunhofer Institute for Molecular Biology and Applied Ecology IME into the independent Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, which formally took place on January 1, 2021. An important success factor is the cooperation with local partners, including Goethe University and the University Hospital Frankfurt. In addition, Fraunhofer ITMP is located at four other sites in Hamburg, Göttingen, Penzberg/Munich and Berlin. Through innovative ways for the early detection, diagnosis and therapy of immune diseases, Fraunhofer ITMP is an important part of Fraunhofer health research. Excellent preparatory work and years of expertise in the field of drug research lay the foundation of Fraunhofer ITMP for sustainably strengthening the German healthcare industry for the benefit of patients. ►

In addition, former State Premier of Hesse Volker Bouffier was honored with the Fraunhofer Medal for his many years of determined commitment to science, research and innovation. The Fraunhofer Medal was designed on March 6, 1987 on the occasion of the 200th birthday of Joseph v. Fraunhofer and has since honored people who have rendered outstanding services to the Fraunhofer-Gesellschaft.

During the opening ceremony of Fraunhofer ITMP, Prof. Dr. Reimund Neugebauer, president of the Fraunhofer-Gesellschaft, awarded the Fraunhofer Medal to former State Premier Volker Bouffier. **© Fraunhofer ITMP, Jürgen Lecher**

Welcome, Professor Behrens!

On October 1, 2022, Prof. Dr. med. Frank Behrens was appointed to the professorship (W2) of Translational Rheumatology, Immunology — Inflammation Medicine (Medical Clinic 2), at the Centre for Internal Medicine of the University Hospital Frankfurt. Since 2013, Professor Behrens has been involved in the establishment of the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP and is deputy director alongside Prof. Dr. Dr. Gerd Geißlinger. Since 2017, he has been a member of the steering committee of the Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD.

The focus of the new professorship is to guarantee the optimal care of patients with various inflammatory and IMID (immune-mediated inflammatory diseases) in one unit (care clinic). Working together with the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, the professorship will facilitate applied research and the rapid transfer of newly gained findings to diagnostics and therapy for these disease groups.

The clinical work of Prof. Behrens also includes the interdisciplinary care of patients with IMIDs that affect several organ systems (including the musculoskeletal system, skin and gastrointestinal tract). This work will be carried out in close cooperation with the Zentrum der Dermatologie und Venerologie (center for dermatology and venereology; ZDV) and the Medical Clinic 1. Professor Behrens is dedicated to university teaching and interdisciplinary cooperation in order to jointly achieve innovative progress in understanding, diagnosis and therapy of corresponding clinical diseases.

BMBF-funded Fraunhofer CIMD summer school 2022 in Berlin

The four-day summer school which took place in June 2022 in Berlin at the Fraunhofer Forum, was oriented around the four major topics of Fraunhofer health research — diagnostics, data, drugs and devices, the 4D. The field of participants consisted of PhD students and young post-docs from research institutions, university hospitals, universities, federal authorities and industry. Over the course of the four days, the participants listened to numerous excellent presentations by internal and external experts, pitched their own projects, discussed existing problems, and developed ideas in interdisciplinary groups. During the summer school, the four interdisciplinary working groups had time to discuss challenges and problems of interdisciplinary collaboration and to develop their own requests and suggestions for improvement as well as project experiences and new ideas.

They presented their work on the last day of the summer school. With regard to interdisciplinary collaboration, communication, expectations, appreciation of the other disciplines and regular interdisciplinary exchange were identified as areas in need of improvement. New project ideas were developed, for example, by transferring existing techniques/methods from one participant's project to the disciplines of the other participants and adapting them theoretically. Overall, the summer school was a successful continuation of Fraunhofer CIMD's promotion of young talent with regard to networking and collaboration beyond their own projects and topics. Further information can be found on the Fraunhofer CIMD website.

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A quantum leap for the industry

The Hamburg sites of Fraunhofer CML, ITMP, IAP-CAN and IAPT are bringing together their expertise across industries in the Fraunhofer Industrial Application Center Quantum Computing Hamburg IQHH. The IQHH will provide industry with an application-oriented portfolio for the development and optimization of products, materials and processes through quantum computing.

The initiative was launched at the Hamburg Innovation Summit in June 2022 by Prof. Carlos Jahn (Fraunhofer CML), Prof. Carsten Claussen (Fraunhofer ITMP), Dr. Christoph Gimmler (IAP-CAN) and Prof. Ingomar Kelbassa (Fraunhofer IAPT) together with Katharina Fegebank, second mayor of the Free and Hanseatic City of Hamburg. In a first round of financing, funding for two pilot projects in each of the four application fields and the establishment of a virtual organization including employee training was acquired.

The use of quantum computers and their suitability is being analyzed and driven forward by the four Fraunhofer institutes, in the four application fields of maritime logistics, health, nanotechnology and additive manufacturing, corresponding to their expertise and areas of focus.

For Fraunhofer ITMP, quantum computing opens new dimensions for drug discovery. The technical focus is on identifying novel hypotheses about disease causes, conducting time-resolved protein structure studies, understanding molecular interactions and preparing data for quantum readiness in these applications.

l-r: Prof. Dr. Ingomar Kelbassa, Fraunhofer IAPT, Prof. Dr. Carlos Jahn, Fraunhofer CML, Katharina Fegebank, second mayor and senator for science of the Free and Hanseatic City of Hamburg, Prof. Dr. Carsten Claussen, Fraunhofer ITMP ScreeningPort, Dr. Christoph Gimmler, Fraunhofer IAP-CAN **© Fraunhofer ITMP, Mira Grättinger**

Philip Gribbon named to the SLAS board of directors

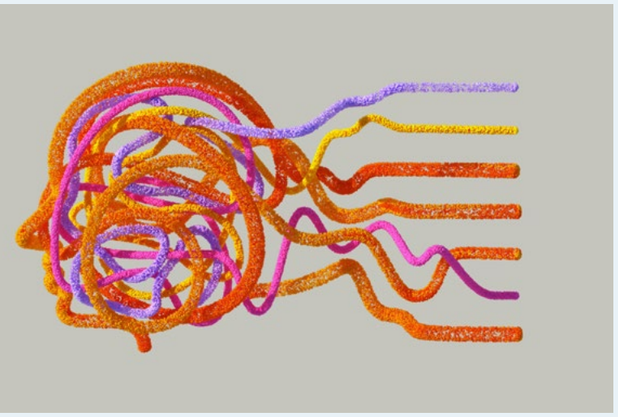
Dr. Philip Gribbon from the Fraunhofer ITMP Hamburg site was recently elected to the board of directors of the Society for Laboratory Automation and Screening (SLAS; https://www.slas.org/) for a three-year term. The current plan is that in 2023 Dr. Gribbon will serve as secretary to the board, in 2024 as vice president and in 2025 as president.

SLAS is an international professional society of academic and industry researchers as well as developers and providers of laboratory automation technology. SLAS supports its members by providing tangible resources such as its international conferences and symposia, scientific publications, opportunities for continuing education, grants and scholarships, professional collaboration, networking and career advancement. Dr. Gribbon joined the Society of Biomolecular Screening (SBS), a predecessor of SLAS, back in 2000 just after starting his first job in the discovery group of a large pharmaceutical company. Back then, this field was experiencing a period of furious activity. Many of the findings of fundamental scientific and technical advances in laboratory automation, human genome sequencing and chemical syntheses were being applied to search for ligands against every conceivable therapeutic target. The international SBS meetings were the industry meeting of the screening community and involved suppliers of instruments, reagents and software as well as the users from industry and academia. The motivation of the new SLAS board is to bring in the application-oriented offerings of the Fraunhofer-Gesellschaft and to promote exchange between industry and academia in today's SLAS community.

" TALENTA speed up "

Fraunhofer TALENTA offers a comprehensive development program that is also used at Fraunhofer ITMP to strengthen the career advancement of young female scientists. Dr. Undine Haferkamp has been evaluating human induced pluripotent stem cells (iPS cells) and their use in pharmaceutical drug development. In the case of multiple sclerosis, COVID-19 and Alzheimer's disease, she has developed human brain models ►

based on iPS cells to investigate disease mechanisms in vitro and to test new therapeutic strategies and potential drug candidates. In 2021, she also completed her doctorate at the University of Lübeck under the supervision of Prof. Dr. Jeanette Erdmann and Dr. Ole Pless at the Fraunhofer ITMP Screening-Port in Hamburg.
Following her doctorate, Dr. Undine Haferkamp successfully applied for the "TALENTA speed up" funding program, which provides tailored opportunities to support and accelerate careers in managerial and specialist positions.
With the recent birth of her daughter, a new focus has also entered her life alongside her scientific career. The temporary pause in her career due to parental leave in combination with the "TALENTA speed up" funding enables her to reposition herself and further develop her role at Fraunhofer ITMP in a targeted manner. It is precisely this flexibility and the response to individual life situations that she describes as valuable. As a role model for her young daughter, she wants to continue working on interesting research projects while also devoting enough time to her family.



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Value creation appraisal of the economic benefits of the institute

Using a value creation appraisal of the LOEWE Centre TMP (until the end of 2020)/Fraunhofer Institute for Translational Medicine and Pharmacology ITMP (from 2021), the economic and pre-economic benefits of the last three years were to be determined on a scientific basis. What's more, a forecast of the development of Fraunhofer ITMP for the period from 2022 to 2026 was to be created. In essence, this was a continuation of the development of the LOEWE Centre TMP/the Fraunhofer TMP project group of Fraunhofer IME as shown in the appraisal from 2014.
The value creation appraisal prepared by the Research Group Corporate Management and Marketing (FGMU) at the Technische Universität Dresden concluded that Fraunhofer ITMP has developed into a strong partner at the interface between university research and industry with supra-regional and international visibility. With innovative solution approaches such as the 4D Clinic or joint labs as new forms of cooperation with industry, Fraunhofer ITMP is driving translation and acting as a bridge builder at interfaces.
In the years 2019 to 2021, the LOEWE Centre TMP/Fraunhofer ITMP has generated a total value added of €28.7 million. Of this, only €8.2 million can be attributed to LOEWE funds from the state of Hesse. According to the appraisal, this leverage effect of 1:3.5 can increase significantly to 1:41.5 by 2026. For the LOEWE Centre TMP/Fraunhofer ITMP as a pure research institution, the determined economic leverage effects are to be assessed as very high.

aidCURE — from a vision of tolerance induction to a real treatment option

Rheumatoid arthritis is the most common inflammatory rheumatic disease. All current treatment options are based on the principle of inhibiting specific pro-inflammatory cytokines or the proliferation of immune cells, i.e., immunosuppression to a greater or lesser degree. This means that there is always a risk of adverse effects, for example on the ability to fight infections. Furthermore, although these drugs do a good job in suppressing the inflammation to some extent, they do not change anything about the disturbed immune reaction as the cause of this very inflammation.
aidCURE is a drug and technology platform project that takes the excellent basic research of its partners — the Goethe University Frankfurt am Main and the Karolinska Institutet Stockholm — and translates it into human application. With a completely new fusion protein (first in its class), it is possible to restore the disturbed self-tolerance in all representative models of rheumatoid arthritis, thus "turning off" the disease and restoring the physiological immune response.
Following initial funding from the highly competitive GO-Bio program of the German Federal Ministry of Education and Research (BMBF) and now that this innovation project has been developed to application maturity at Fraunhofer ITMP, the next logical step is now being taken, namely the spin-off of aidCURE AG, based in Frankfurt am Main. Financed by venture capitalists and family offices and supported by a professional business team and Fraunhofer expertise, the new company will go on to manufacture the drug and test its tolerability and efficacy in humans for the first time.

Fourth Day of Immune Research 2022

On September 27, 2022 Fraunhofer CIMD's fourth Day of Immune Research took place in Frankfurt am Main. After two years in a virtual format, the event could be held in person again this year. The field of participants consisted of employees from 19 Fraunhofer
institutes, 11 universities and university hospitals, one federal authority (BfArM) and 15 companies.
Prof. Dr. Dr. Geißlinger, head of
Fraunhofer ITMP and spokesperson of Fraunhofer CIMD, opened the event with an overview of the current status and the further goals and tasks of Fraunhofer CIMD. Prof. Dr. Behrens, deputy director of Fraunhofer ITMP and scientific coordinator of Fraunhofer CIMD, guided the audience through the event as moderator. The first part of the event was dedicated to the topics of clinical research and data sovereignty. Before and after the lunch break, some of Fraunhofer CIMD's work was presented. During the lunch break, participants were able to enjoy a generous buffet and had time to look at and be introduced to the 40 posters on display. During the coffee break in the afternoon, there was also plenty of time to talk about the posters. The third and fourth parts of the event were dedicated to the topics of digital medicine and perspectives in immunology. The event was a successful continuation of networking, collaboration and cooperation opportunities along the 4D within the entire Fraunhofer-Gesellschaft and beyond. Further information can be found on the Fraunhofer CIMD website.

Poster presentation at the Day of Immune Research 2022
© Fraunhofer CIMD, Jürgen Lecher

PATENTS 2022

Patent registrations 2022

Geißlinger, Gerd; Zaliani, Andrea; Kuzikov, Maria; Gribbon, Philip
Compounds for the treatment of covid-19

Holmdahl, Rikard; Burkhardt, Harald; Do, Nhu Nguyen; Edinger-Jakobi, Katja; Turgay, Ninorta
VISTA as a biomarker for therapeutic stratification and monitoring of T cell receptor targeted tolerogenic therapies of immune-mediated diseases

Patents granted 2022

Brüne, Bernhard; Ernst, Andreas; Mora, Javier; Parnham, Michael John; Putyrski, Mateusz; Weigert, Andreas
Inhibitors of IL-38 for use in treating and/or preventing cancer in a subject
US 2020/0165334 A1

Christen, Urs; Parnham, Michael John; Sweeney-Lasch, Stanley
Combination therapy for the treatment of autoimmune diseases
2,944,811

Parnham, Michael John; Sha, Lisa Katharina; von Knethen, Andreas
B7-H1 fusion polypeptides for treating and preventing organ failure
CN 107921093 A

Baumann, Isabell; Jakobsson, Per-Johan; Saul, Meike Julia; Steinhilber, Dieter; Süß, Beatrix
MiRNA-574-5p as a biomarker for stratification of prostaglandin E-dependent tumors
18728664.6

BACHELOR'S, MASTER'S, AND DOCTORAL THESES **2022**

Doctoral Theses

Saba Ezazi
Validation and characterization of small molecule modulators of autophagy
Johann Wolfgang Goethe-Universität Frankfurt am Main

Issa Sabi Masenza
Evaluation of new diagnostics for Tuberculosis in Children
Ludwig-Maximilians-Universität München

Jia Bainga Kangbai
Treatment outcome and survival analysis of Ebola patients receiving treatment in Sierra Leone
Ludwig-Maximilians-Universität München

Nur Baibaktyevna Tukhanova
Serological and molecular investigations of Orthohantaviruses in the Republic of Kazakhstan
Ludwig-Maximilians-Universität München

Sadia Abdul Remane Amade Ali Pereira
Epidemiological analysis of emerging and re-emerginf virus infections in Mozambique: from arbovirus to SARS-CoV-2
Ludwig-Maximilians-Universität München

Cugota Canals, Roger
Crosstalk between lung microenvironment and CNS autoimmunity
Georg-August Universität Göttingen

Jasemin Dannheim
Analysis of teriflunomide therapy on EAE
Georg-August Universität Göttingen

Bartsch, Lydia
Identification and characterization of novel disease genes related to early onset neurodegeneration in childhood and adolescence.
Georg-August-Universität Göttingen

Rösch, Axel
Mitochondrial nucleoid distribution and its relation to presynaptic activity investigated by correlative light microscopy, Georg-August-Universität Göttingen

Stumpf, Daniel
Engineering of a bacteriophytochrome-derived reversibly switchable fluorescent protein for the application in super-resolution microscopy in the near-infrared window
Georg-August-Universität Göttingen

Bierbaum, Sebastian
Automated STED microscopy for cell-biological high-throuput assays
Georg-August-Universität Göttingen

Yousefi, Roya
Monitoring mitochondrial translation with spatial resolution and high throughput strategies
Georg-August-Universität Göttingen

Susvirkar, Vivek
Biochemical characterization of human shieldin complex
Georg-August-Universität Göttingen

Driehorst, Til
Development of a Novel Fluorescence Indicator System for the Characterization of Sacomere Organization and Function in Human Cardiomyocytes
Universitätsmedizin Göttingen

Balfanz, Paul
Über die Herstellung von humanem Makro-Herzgewebe zur Therapie der Herzinsuffizienz
Universitätsmedizin Göttingen

Freier, Marie
Investigating how peripheral myelin-specific antibodies contribute to central nervous system demyelination – implications for future therapeutical approaches
Georg-August-Universität Göttingen - Universitätsmedizin

Haberl, Michael
Characterization of the invasion of hematopoietic myeloid cells into the CNS during EAE
Georg-August Universität Göttingen

Segregur, Domagoj
Development of biorelevant media and dissolution tests for gastrointestinal diseases
Johann Wolfgang Goethe-Universität Frankfurt am Main

Loisios-Konstantinidis, Ioannis
Physiologically based population pharmacokinetic/ pharmacodynamic modelling and simulation approaches to support waiver of in vivo clinical pharmacology studies
Johann Wolfgang Goethe-Universität Frankfurt am Main

Gao, Ge (Fiona)
Study on pharmacokinetics of subcutaneously injected depot formulations with biorelevant release tests and translational modelling strategies
Johann Wolfgang Goethe-Universität Frankfurt am Main

Nieraad, Hendrik
Effekte von chronischer Hyperhomocysteinämie und spezifischen Mikronährstoff-Interventionen auf die kognitive Leistungsfähigkeit im AppNL-G-F knock-in Mausmodell der Alzheimer-Erkrankung
Johann Wolfgang Goethe-Universität Frankfurt am Main

Klatt-Schreiner, Katharina
Endocannabinoide und andere Lipidmediatoren bei Morbus Parkinson-assoziierten Schmerzen
Johann Wolfgang Goethe-Universität Frankfurt am Main

Ngoc Tran, Bao
Nucleoredoxin's interaction with Camk2a and the behavioral characterization of neuronal nucleoredoxin knockout mice
Johann Wolfgang Goethe-Universität Frankfurt am Main

Hahn, Marcel
Salmonella induced cell-autonomous immunity
Johann Wolfgang Goethe-Universität Frankfurt am Main

Brunst, Steffen
Biochemische Untersuchung von Substanzbibliotheken hinsichtlich Selektivität und dualer Aktivität
Johann Wolfgang Goethe-Universität Frankfurt am Main

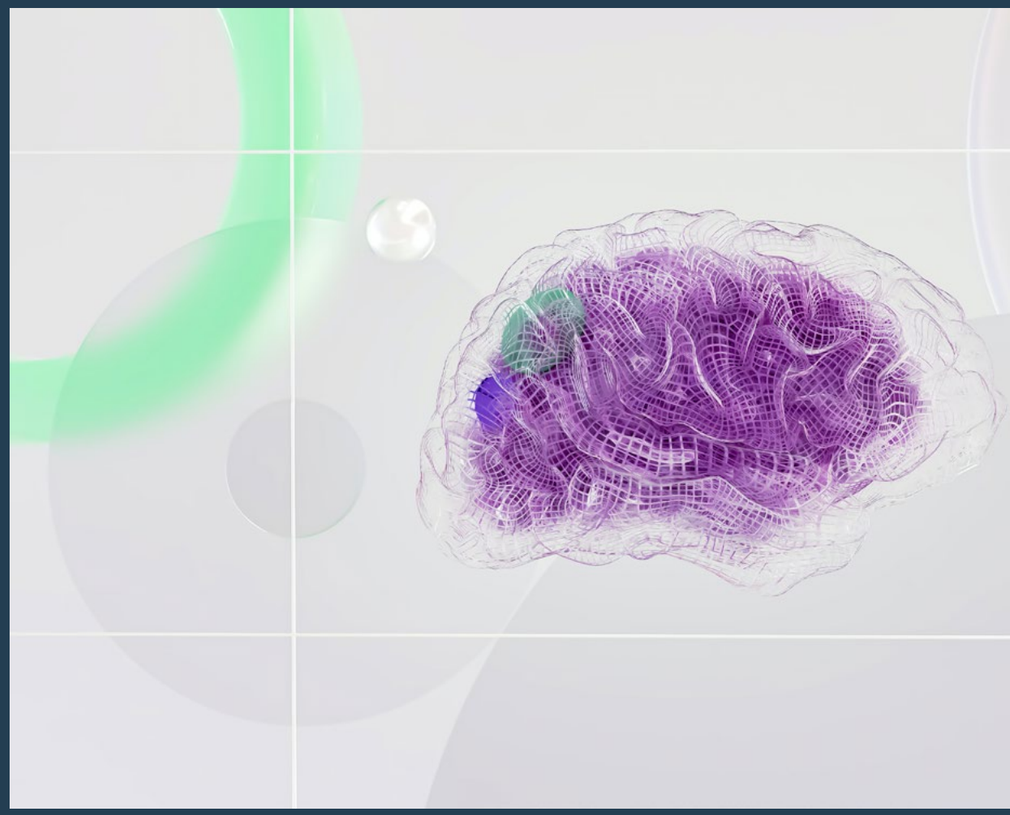
Holländer, Christian
M&A Function and M&A Performance: A Capability-based Analysis
Johann Wolfgang Goethe-Universität Frankfurt am Main

Wang, Jean
Empirical Examination of Communication Practices During Chinese Cross-border Mergers & Acquisitions Integration
Johann Wolfgang Goethe-Universität Frankfurt am Main

Theses 2022 overview

Overview of the number of theses whose experimental part was supervised by Fraunhofer ITMP staff.

27 Doctoral Theses
22 Master´s Theses



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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 2022, 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 has close cooperations with a large number of institutes and clinics of the University Hospital of the Goethe University Frankfurt am Main, the University Medical Center Hamburg-Eppendorf, the University Medical Center Göttingen, the Charité - Universitätsmedizin Berlin, the Ludwig-Maximilians-Universität München LMU and the LMU Medical Center. There is also close cooperation with national universities such as the Philipps-Universität Marburg, the Justus Liebig University Giessen, the Jacobs University Bremen, the Hannover Medical School, the Senckenberg Biodiversity and Climate Research Center, the Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology IKP Stuttgart and the BNITM in Hamburg.
In addition, there are cooperations with several international universities such as the University of Florida, the University of Maryland, the University of Cork, the University of Southern Denmark, the National and Kapodistrian University of Athens and the National University of Ireland, Galway.

Teaching activities

Prof. Dr. Frank Behrens is Head of the Division translational Rheumatology, Immunology – Inflammation medicine at the University Hospital Frankfurt am Main and Professor and lecturer for Internal Medicine/Rheumatology and holds courses, seminars and lectures in Internal Medicine, Rheumatology and Clinical Pharmacology at the University Hospital of Goethe-University Frankfurt am Main and at Goethe-Business school.

Prof. Dr. Harald Burkhardt is Head of the Division of Rheumatology at Goethe University Hospital Frankfurt am Main and Professor of Internal Medicine/Rheumatology at Goethe University Frankfurt am Main. He holds lectures in Internal Medicine at the University Hospital Frankfurt am Main.

Prof. Dr. Bernhard Brüne is Professor and Director of the Institute for Biochemistry I at the Faculty of Medicine at Goethe University Frankfurt am Main. He lectures within the framework of GRK AVE »Resolution of Inflammation«, in biochemistry for medical students, as well as in the master program in Molecular Medicine.

Demetrios Christou holds seminars and lectures for students in the New Revised Medical Curriculum at the Charité – Universitätsmedizin Berlin.

Prof. Dr. Sandra Ciesek is Director of the Institute of Medical Virology at the University Hospital Frankfurt am Main and lectures for students of human and dental medicine.

Prof. Dr. Carsten Claussen is Honorary Professor for Information Systems at the Heinz-Nixdorf Institute of the University of Paderborn and holds lectures, seminars and internships at the Faculty of Medicine of the University Hamburg UKE).

Prof. Dr. Jennifer Dressman retired from her position as Professor of Pharmaceutical Technology in the Department of Biochemistry, Chemistry and Pharmacy at the Goethe University Frankfurt am Main in March, 2021.

Dr. Bernhard Ellinger Bernhard Ellinger holds seminars and internships in the model course in Medicine the model course in dentistry at the University Medical Center Hamburg-Eppendorf.

Prof. Dr. Prof. Alexander Flügel is Director of the Institute for Neuroimmunology und Multiple Sclerosis Research at the University Medical Center Göttingen UMG. He gives lectures in Neuroimmunology for the educational programs Development, Neuronal & Behavioral Biology, Molecular Medicine and Neuroscience at the University of Göttingen.

Prof. Dr. Jutta Gärtner is University Professor and Director of the Clinic for Pediatrics and Adolescent Medicine at the University Hospital Göttingen. She holds seminars and courses at the Medical Faculty of the Georg-August University Göttingen.

Prof. Dr. Dr. Gerd Geißlinger is Professor and Director of the Institute for Clinical Pharmacology of the University Medical Center Frankfurt am Main. He lectures in clinical pharmacology and therapy for medical students.

Dr. Philip Gribbon has been appointed as a visiting professor at the University of Cagliari. He has lectured at the: EU-OPENSCREEN 2022 Autumn school, on the topic of FAIR data; FEBS Practical/Lecture Course 2022 Biomolecules in Action III, on the topic of compound screening and probe development.

Prof. Dr. Dr. Christian Grimm is a university Professor at the Walther Straub Institute for Pharmacology and Toxicology at the University Medical Centre of the LMU München. He gives lectures in pharmacology and toxicology for medical and natural science students.

Prof. Dr. Sabine Grösch is extraordinary Professor at the Institute for Clinical Pharmacology at the Goethe-University Frankfurt am Main. She holds lectures in clinical pharmacology and molecular medicine.

Dr. Sheraz Gul is Adjunct Lecturer at the NUI Galway, College of Medicine, Nursing & Health Sciences, Ireland and was an invited instructor at »MSc Toxicology – Screening Molecular Libraries Module«.

Dr. Robert Gurke supervises practical courses in the Department of Medicine and Pharmacy and gives lectures in the master program Molecular Medicine at Goethe University Frankfurt am Main.

Dr. Jan Heering supervises internships and gives lectures in assay development (part of lecture series on drug design) in the Faculty of Biochemistry, Chemistry and Pharmacy at Goethe University Frankfurt am Main.

Prof. Dr. Michael Hoelscher is Director of the Department of Infectious Diseases & Tropical Medicine at the University Medical Center of LMU. He is holding lectures in Infectious and Tropical Diseases and International Health. He is the chair of the PHD Program of LMU.

Prof. Dr. Stefan Jakobs is Professor of High Resolution Microscopy of the Cell at the Department of Neurology, University Medical Center Göttingen and research group leader at the MPI for Multidisciplinary Sciences. He holds seminars and practical courses on cell biology and high-resolution microscopy.

PD Dr. Aimo Kannt is a lecturer at Goethe University and Heidelberg University Medical Schools. In addition, he gives seminars for the International Master Programs in Translational Medicine at the Universities of Heidelberg and Groningen. At Goethe Business School, he is responsible for the R&D module of the Pharma MBA program for which he received the Best Teaching Award in 2022.

Prof. Dr. Andreas von Knethen is the head of the experimental research unit of the Department of Anesthesiology, Intensive Care and Pain Therapy and contributes to teaching in biochemistry at Goethe University Frankfurt am Main.

Dr. Michaela Köhm is Adjunct Lecturer of the Division of Rheumatology at University Hospital Frankfurt am Main and holds seminars and courses in Internal Medicine and Rheumatology.

Dr. Edmund Kostewicz holds lectures at the Goethe Business School, Frankfurt University, at the Master of Pharma Business Administration Program.

Prof. Dr. Ellen Niederberger is an APL professor at the Institute of Clinical Pharmacology of the Goethe University Frankfurt am Main. She is involved in lectures and courses of the study program human medicine, the master program Molecular Medicine and the master program Neuroscience.

Dr. Ole Pless holds lectures, seminars and practical courses at the Faculty of Medicine of the University Hamburg (UKE) as well as seminars at Goethe University Frankfurt am Main.

Prof. Dr. Eugen Proschak is Professor of Drug Design in the Department of Biochemistry, Chemistry and Pharmacy at Goethe University Frankfurt am Main.

Prof. Dr. Peter Rehling is University Professor and Director of the Institute of Cell Biochemistry at the University Medical Center Göttingen. He gives lectures, seminars and practical courses in biochemistry and molecular biology for students of human and dental medicine, molecular medicine and cardiovascular science.

Dr. Maria Rosenthal holds lectures, seminars and exercises in biochemistry and virology at the faculty of mathematics, informatics and natural sciences of the University Hamburg as well as the German Academy for public health on the topic of viral hemorrhagic fevers.

Dr. Otto Quintus Russe is the academic director of the Master of Pharma Business Administration and the Data Science in Health Program at Goethe University Frankfurt am Main.

Dr. Stephan Schäfer is Adjunct lecturer at the medical faculty at the University Hospital in Frankfurt, where he holds seminars in Clinical Pharmacology.

PD Dr. Susanne Schiffmann holds seminars and lectures for medical, molecular medicine and medical technology students at Goethe University Frankfurt am Main.

Prof. Dr. Klaus Scholich holds seminars, practical courses and lectures at the University Hospital Frankfurt am Main.

Prof. Dr. Lars Schweizer is Professor for Strategic Management at the Faculty of Business and Economics at Goethe-University Frankfurt am Main. In addition, he is academic Director for Master of Pharma Business Administration at Goethe Business School.

PD Dr. Frank Siebenhaar holds seminars and courses in allergology and is a lecturer in the teaching format »Problem-based Learning« POL for students in the New Revised Medical Curriculum at the Charité – Universitätsmedizin Berlin.

PD Dr. Marco Sisignano holds lectures in Clinical Pharmacology for medical students and seminars for students in the master program Molecular Medicine at the University Hospital Frankfurt am Main.

Prof. Dr. Dieter Steinhilber is Professor for Pharmaceutical Chemistry at the Faculty of Biochemistry, Chemistry and Pharmacy at Goethe University Frankfurt am Main.

Dr. Dominique Thomas supervises practical courses for pharmacy students and molecular medicine students and holds seminars in Clinical Pharmacology at Goethe University Frankfurt am Main.

Prof. Dr. Maria Vehreschild holds lectures in Internal Medicine at Goethe University Frankfurt am Main and leads a series of in-service training courses of physicians with recognition by the Landesärztekammer LÄK.

Dr. Carmen Walter holds seminars and lectures at the University Hospital Frankfurt am Main.

Prof. Dr. Martin Weber is associate Professor for Translational Neuroinflammation at the University Medical Center Göttingen. He holds lectures seminars and courses on the field of Neurology for medical students. He leads the PhD program VorSPrUNG.

PD Dr. Andreas Wieser is a private lecturer at LMU and gives lectures, seminars and practical courses for medical and pharmaceutical students, as well as lecturing nurses at the clinic. Additionally he is teaching at the Centre for International Health CIH of the LMU. In a joint program with the CIH he is also lecturing on vector biology and control at the University of Cape Coast in Ghana.

Prof. Dr. Björn Windshügel is Honorary Professor for Computational Drug Discovery at Jacobs University Bremen and holds lectures in the MCCB program.

Prof. Dr. Wolfram-Hubertus Zimmermann is University Professor and Director at the Institute of Pharmacology and Toxicology at the University Medical Center Göttingen. He lectures in pharmacology and toxicology for medical students and students of molecular medicine.

Prof. Dr. Torsten Zuberbier is University Professor and Director at the Institute of Allergology at the Charité – Universitätsmedizin Berlin. He holds seminars and lectures for students in the Standard Medical Curriculum at the Charité – Universitätsmedizin Berlin.

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International Journal of Molecular Sciences
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Journal of the German Society of Dermatology (JDDG)
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Journal of Mass Spectrometry & Advances in the Clinical Lab
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Direktorium (Wissenschafts-koordinator): PD Dr. Frank Behrens

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Fachberater für das Portfolio der Arzneimittelentdeckung: Dr. Philip Gribbon

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Nationale Akademie der Wissenschaften Leopoldina
Mitglied und gewähltes Mitglied der Präsidiumsklasse III (Medizin): Prof. Dr. Jutta Gärtner

Novartis
Mitglied des Beirats »Siponimod«: Prof. Martin S. Weber

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Ehrenmitglied: Prof. Dr. Torsten Zuberbier

Paul Ehrlich Gesellschaft (PEG)
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Pharmadialog der Bundesregierung
Mitglied: Prof. Dr. Dr. Gerd Geißlinger

Roche
Mitglied des Beirats »Ocrelizumab«; Mitglied des Lenkungsausschusses »Fenebrutinib phase III«: Prof. Martin S. Weber

Senatskommission für Forschung und Transfer
Prof. Dr. Bernhard Brüne

Senatskommission für Third Mission
Prof. Dr. Bernhard Brüne

Society for Laboratory Automation and Screening
Gewähltes Mitglied des Exekutivausschusses. Seine Amtszeit beträgt drei Jahre, wobei er zunächst die Rolle des Sekretärs und anschließend die des Präsidenten der Gesellschaft übernimmt.: Dr. Philip Gribbon

Mitglied des Rates für strategische Beziehungen: Dr. Sheraz Gul

Stiftung für Unternehmensrecht an der Heinrich Heine Universität Düsseldorf
Kuratoriumsmitglied: Prof. Dr. Carsten Claussen

Stiftungsrat der Dr. Robert Pfleger Stiftung
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urticaria network e.V.
Schatzmeister: PD Dr. Frank Siebenhaar

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Mitglied des Beirats: Dr. Sheraz Gul

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Organization of Scientific Meetings and Courses

Journal Club des Fraunhofer ITMP zu Immunerkrankungen, Datenanalyse, Datenmodellierung, regulatorischen Richtlinien in Studien, und mehr
Virtuell, 20. Januar, 24. Februar, 25. Februar, 10. März 5. Mai, 2. Juni, 23. Juni, 13. Oktober, 17. November, 24. November und 1. Dezember 2022; Organisator: Ann C. Foldenauer

Regionalwettbewerb Jugend forscht Hamburg Volkspark
Hamburg, 16.-17. Februar 2022; Patenbeauftragte: Dr. Mira Grättinger

Fraunhofer CIMD 4D-Workshop »In-vitro Testsysteme als Alternative für Tierversuche«
Virtuell, 18. März 2022; organisiert durch das Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD und das Fraunhofer-Institut für Silicatforschung ISC

Screening Molecular Libraries – NUI Galway, MSC toxicology
Galway, 28.-31. März 2022
Co-organisator: Dr. Sheraz Gul

Vortragsreihe und Expertenaustausch zum Thema Alternativen zum Tierversuch
Virtuell, 31. März, 28. April, 25. Mai, 30. Juni, 25. August und 27. Oktober 2022; organisiert im Rahmen der Fraunhofer CIMD Kompetenzplattform »Alternativmethoden für Tierversuche«

Workshop zu FAIR Data Management in Antibiotic Drug Discovery
durchgeführt während der 6th AMR Conference
Basel, 7.-8. April 2022; Organisator: Dr. Philip Gribbon

Fraunhofer CIMD 4D-Workshop »Zell- und Gentherapie«
Virtuell, 9. Mai 2022; organisiert durch das Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD und das Fraunhofer-Institut für Zelltherapie und Immunologie IZI

Fraunhofer CIMD Summer School
Berlin, 7.-10. Juni 2022; organisiert durch das Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD und gefördert durch das BMBF

ITEM-ITMP Allergology Workshop
Berlin, 8. Juli 2022; organisiert durch den Fraunhofer ITMP Standort Immunologie und Allergologie IA in Berlin

Tag der Immunforschung 2022
Frankfurt am Main, 27. September 2022; organisiert durch das Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

AMR »Drug Discovery Bootcamp«
durchgeführt während der **annual ESCMID/ASM Conference on Drug Development to Meet the Challenge of Antimicrobial Resistance**,
Dublin, 4.-7. Oktober 2022; Co-Organisator: Dr. Philip Gribbon

TheraNova Summer School
Mainz, 13.-14. Oktober 2022; organisiert durch das Leistungszentrum Innovative Therapeutika (TheraNova)

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PUBLICATIONS FRAUNHOFER ITMP **2022**

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Abuzakouk, M., Ghorab, O., Al-Hameli, H., Salvo, F., Grandon, D., Maurer, M.
Using an extended treatment regimen of lanadelumab in the prophylaxis of hereditary angioedema: a single-centre experience (2022) The World Allergy Organization journal, 15 (7), 100664. DOI: 10.1016/j.waojou.2022.100664

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