Fraunhofer ITMP

Annual Report 2021

The new Fraunhofer Institute: Fraunhofer ITMP Mission - Vision - Strategy

Preface

Dear Readers,

it is not only since the COVID 19 pandemic that medicine has been undergoing an extremely dynamic transformation characterized by new concepts and technologies. The current crisis is a particularly clear manifestation of the high innovation dynamics and demonstrates the enormous potential that rapidly advancing technification of medicine holds for Germany and Europe. In the coming decades, technology-driven innovations for healthcare will offer an outstanding opportunity to sustainably strengthen the German innovation system and tap into effective long-term value creation potential.

On January 1, 2021, the Fraunhofer-Gesellschaft founded its 75th Fraunhofer Institute: the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP. The headquarters of Fraunhofer ITMP, Frankfurt am Main, can look back on a successful and stable development history, which began in 2012 with the establishment of the Fraunhofer Project Group for Translational Medicine and Pharmacology TMP as part of Fraunhofer IME. With the help of the Hessian State Offensive for Economic and Scientific Excellence (LOEWE), structures of the Center for Drug Research, Development and Safety (ZAFES) founded in 2002 at Goethe University Frankfurt am Main, could be institutionalized in the long term. With the Hamburg site »ScreeningPort«, which was initially founded in Hamburg as a public-private partnership with the support of the state government and integrated into the Fraunhofer-Gesellschaft in 2014, the method spectrum was complemented by high-content drug screening processes and medical data science. Thus, Fraunhofer ITMP is one of the driving forces of Fraunhofer health research with the important concepts of the 4D strategy, cost intelligence in medicine, the proof-of-concept platform and the Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD.

The international visibility of the Fraunhofer ITMP in the field of immune-mediated diseases has been increased in recent years due to a high level of expertise in the areas of drug discovery research, pharmaceutical technology, highly differentiated and indication-specific pharmacological models, and clinical research.

The two sites, in Frankfurt am Main and Hamburg, now want to continue this successful path as an independent Fraunhofer ITMP. Together with the University Medical Center Göttingen and financial support from the state of Lower Saxony and the federal government, a new site »Translational Neuroinflammation and Automated Microscopy« was founded on January 1, 2021. Since July 1, 2021, two additional Fraunhofer ITMP sites have also been established with the help of federal and state funding: the Berlin site »Immunology and Allergology« in cooperation with Charité - Universitätsmedizin Berlin and the Penzberg/Munich site »Immunology, Infection and Pandemic Research« in cooperation with the Ludwig-Maximilians-Universität München and Roche Diagnostics GmbH in Penzberg. These strategic site expansions are intended to bring together national competencies in the field of immune diseases and to complement and expand the existing indication areas and technologies of Fraunhofer ITMP in an optimal way in order to be able to address the central goal of our institute with combined forces: The strengthening of the German healthcare industry for the benefit of society and patients.

I would like to express my special thanks to the participating state governments of Hesse, Hamburg, Lower Saxony, Bavaria and Berlin and to the German federal government for their financial support in establishing the sites, without which this institute with its complementary sites could not have been founded.

This annual report is intended to give you an overview of the services and range of services offered by our institute. I would be pleased if you would get in touch with us.

Frankfurt am Main, May 2022

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

Content

The Institute

Fraunhofer ITMP 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 focus is on the research and development of innovative ways for the early detection, diagnosis and therapy of diseases resulting from disturbed functions of the immune system.

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

Institute Management

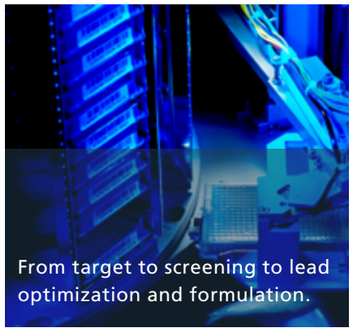
Prof. Dr. Dr. Gerd Geißlinger
gerd.geisslinger@itmp.fraunhofer.de

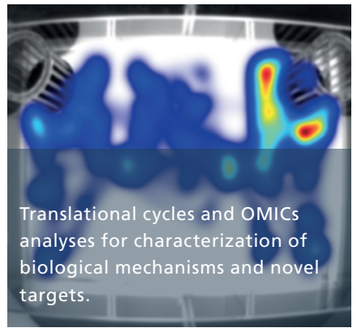
PD Dr. Frank Behrens
frank.behrens@itmp.fraunhofer.de

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. The core of the scientific objective is the effective transfer of innovative ideas from biomedical research to medical application and industry. Based on the 4D concept (linking Drugs, Devices, Diagnostics, 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 about 150 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 in so-called »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 Hospital Hamburg-Eppendorf, the University Medicine Göttingen, the Charité Universitätsmedizin Berlin, the Ludwig-Maximilians-University and the University Clinics of the LMU. In addition, there is a 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. Thus, 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.


From target to screening to lead optimization and formulation.


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


From „Proof-of-Concept“ to the characterization of established products: “Quality by Design” for successful translation of innovative ideas.

Drug Discovery

The research division covers the spectrum of early drug discovery from the identification and repositioning of pharmacologically active molecules to their characterization in innovative cellular test systems, the optimization of their efficacy and physicochemical properties, and the development of suitable formulations to improve bioavailability and stability. 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

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, so-called “adverse outcome pathways” related to (patho-)mechanisms, which should not be modulated, can also be explored.

Clinical Research

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 Unit. In addition to the development of 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.

PD Dr. Aimo Kannt
aimo.kannt@itmp.fraunhofer.de

PD Dr. Frank Behrens
frank.behrens@itmp.fraunhofer.de

The Institute | Fraunhofer ITMP Profile

Locations of Fraunhofer ITMP

Frankfurt am Main

Translational Medicine and Pharmacology

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 immune-mediated diseases and pain.

Hamburg

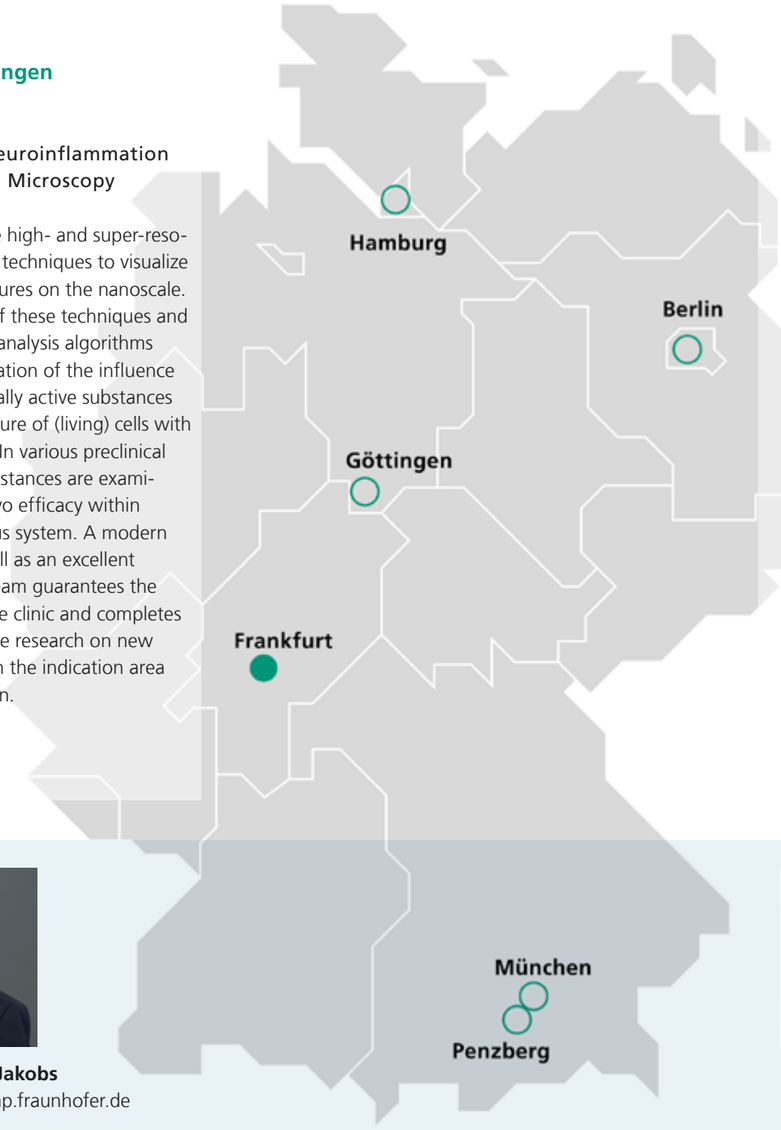
Discovery Research ScreeningPort

Our expertise lies in high-throughput drug discovery using high-quality compound and repurposing 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”.

Göttingen

Translational Neuroinflammation and Automated Microscopy

We use innovative high- and super-resolution microscopy techniques to visualize sub-cellular structures on the nanoscale. The automation of these techniques and innovative image analysis algorithms allow the investigation of the influence of pharmacologically active substances on the nanostructure of (living) cells with high throughput. In various preclinical models, these substances 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 on new drug candidates in the indication area neuroinflammation.



Location map of Fraunhofer ITMP with its headquarters in Frankfurt am Main.

Berlin

Immunology and Allergology

Our expertise lies in the research, validation and testing of new diagnostic and therapeutic approaches of allergic and immunological mast cell-mediated inflammatory diseases of the skin. One focus is the development of a platform of preclinical and prehuman models for the exploration of new therapies. This includes the identification, characterization and validation of novel therapeutic approaches for subsequent preclinical testing, preclinical exploration of novel therapeutic approaches to the translation of these approaches into the clinic. Emphasis is placed on the development of a screening program for new biomarkers and predictors, the identification of previously unknown autoallergens, and the development of detection methods for IgE autoantibodies.

Penzberg/München

Immunology, Infection and Pandemic Research

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.

Prof. Dr. Gerd Geißlinger
gerd.geisslinger@itmp.fraunhofer.de

Dr. Philip Gribbon
philip.gribbon@itmp.fraunhofer.de

Prof. Dr. Stefan Jakobs
stefan.jakobs@itmp.fraunhofer.de

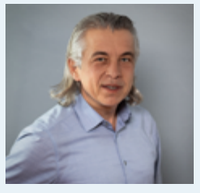
PD Dr. Frank Behrens
frank.behrens@itmp.fraunhofer.de

Prof. Dr. Carsten Claussen
carsten.claussen@itmp.fraunhofer.de

Prof. Dr. Martin Weber
martin.weber@itmp.fraunhofer.de

Prof. Dr. Torsten Zuberbier
torsten.zuberbier@itmp.fraunhofer.de

Prof. Dr. Michael Hoelscher
michael.hoelscher@itmp.fraunhofer.de



Prof. Dr. Marcus Maurer
marcus.maurer@itmp.fraunhofer.de

Prof. Dr. Thomas Gudermann
thomas.gudermann@itmp.fraunhofer.de

Fraunhofer ITMP within the Fraunhofer-Gesellschaft

The Fraunhofer-Gesellschaft is the world's leading applied research organization. Prioritizing key future-relevant technologies and commercializing its findings in business and industry, it plays a major role in the innovation process. A trailblazer and trendsetter in innovative developments and research excellence, it is helping shape our society and our 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. Fraunhofer generates €2.5 billion of this from contract research.

Fraunhofer-Gesellschaft

www.fraunhofer.de/en

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. In these fields, Fraunhofer concentrates excellent upstream research on projects with high potential for exploitation, thus promoting social and cross-industry impact. 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.

FSF Digital Healthcare

www.fraunhofer.de/en/research/fraunhofer-strategic-research-fields/digital-healthcare

In strategic customer segments - so-called **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. As an interdisciplinary organization, the Fraunhofer-Gesellschaft brings together physicians, natural scientists, computer scientists and engineers, creating ideal conditions for innovation and bringing ideas quickly to application.

Lead Market Healthcare Sector

www.fraunhofer.de/de/fuer-kunden-und-partner/gesundheitswirtschaft (German)

The Fraunhofer Institutes are grouped in nine thematically oriented **Fraunhofer Groups**. Their goals are professional coordination within the Fraunhofer-Gesellschaft, the bundling 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 Group for Health

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

The **Fraunhofer Clusters of Excellence** promote the cooperative development and processing of system-relevant topics through a cross-institutional research agenda. 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.

Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

www.cimd.fraunhofer.de/en

The Fraunhofer headquarters in Munich.

Lighthouse Project MED2ICIN

www.fraunhofer.de/en/research/lighthouse-projects-fraunhofer-initiatives/fraunhofer-lighthouse-projects/medicin

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 lighthouse project MED²ICIN. The development of a digital patient model is the basis for personalized and cost-optimized treatment. This enables both, enormous potential for improvement for more effective prevention, diagnostics, therapy and care, as well as a more intelligent use of health care expenditures.

High-Performance Center Innovative Therapeutics TheraNova

Fraunhofer High-Performance Centers organize the close cooperation of university and non-university research with industry. Universities, colleges, Fraunhofer institutes and other players work together on a topic-specific basis at one location in order to bring innovations quickly into application. Together with the Goethe University Frankfurt am Main 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.

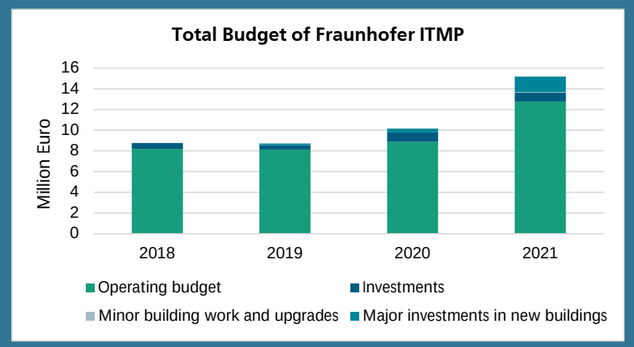
Proof-of-Concept-Initiative

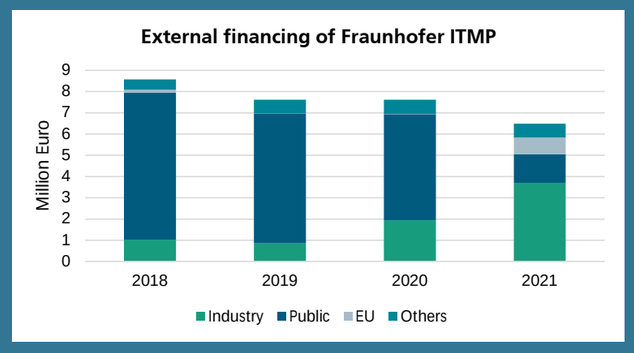
www.fraunhofer.de/de/forschung/fraunhofer-strategische-forschungsfelder/intelligente-medizin/proof-of-concept-initiative.html (German)

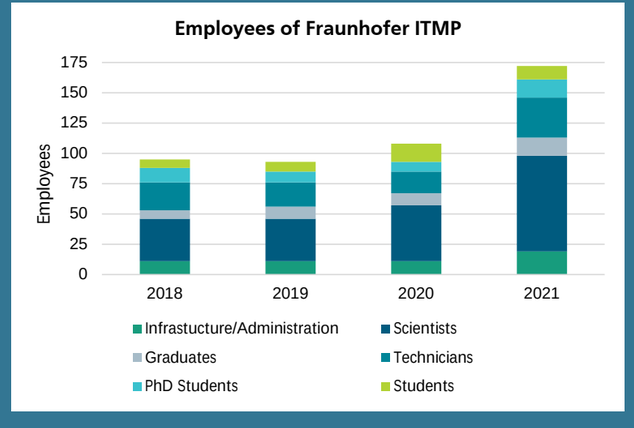
The Proof-of-Concept-Initiative (PoC-Initiative) was initiated by the Fraunhofer-Gesellschaft, the German University Medicine and the Helmholtz Association as a collaborative cross-organizational project to accelerate translation processes of highly innovative approaches from basic research to medical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

The institute directors of Fraunhofer ITMP, Prof. Dr. Dr. Gerd Geißlinger and PD Dr. Frank Behrens, were appointed at the beginning of the Corona pandemic as members of the **Fraunhofer crisis staff for the management of the corona virus SARS-CoV-2 crisis**. In this context, they support the necessary measures, especially from a medical point of view.

Fraunhofer ITMP in numbers







Budget

The operating budget of Fraunhofer ITMP amounted to 12.8 million euros in 2021. In addition, around 860 000 euros were invested for equipment. Expenditure in the area of construction activities for the new institute building in Frankfurt amounted to 1.56 million euros.

The parent institute's budget was financed by 53.1 percent of external income, or 50.8 percent if the predominantly state-funded sites in Göttingen, Berlin and Penzberg/Munich were included.

At 3.71 million euros, the economic income is at a good level. This corresponds to an economic revenue share (Rho Wi) of the core institute of 33.4 percent as the basis for calculating basic funding.

The newly founded Fraunhofer ITMP thus achieved very good values in the decisive key figures of the Fraunhofer-Gesellschaft in 2021.

Personnel

At the end of 2021, a total of 172 people were employed at the Fraunhofer ITMP sites in Frankfurt am Main, Hamburg, Göttingen, Berlin and Penzberg/Munich. 57 percent of the Fraunhofer ITMP personnel were female.

Fraunhofer ITMP Board of Trustees

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.

The first meeting of the Board of Trustees took place on September 16, 2021 in Frankfurt am Main as a hybrid event. The Executive Board of the Fraunhofer-Gesellschaft was represented by Prof. Dr. Raoul Klingner, Director Research of the Fraunhofer-Gesellschaft.

Members of the Board of Trustees in 2021:

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

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

Dr. Rolf Greve
Behörde für Wissenschaft, Forschung, Gleichstellung und Bezirke (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, Berlin

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

Dr. Ulrike Mattig
Hessisches Ministerium für Wissenschaft und Kunst (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 Medical Faculty at the University Medical Center Hamburg-Eppendorf (UKE), Hamburg

Prof. Dr. Angelika Vollmar
Ludwig-Maximilian-Universität München, Munich

Oben:
Prof. Dr. Raoul Klingner at the first meeting of the Fraunhofer ITMP Board of Trustees on September 16, 2021.

Unten:
Group picture of the trustees present.

Our Research

The “e-Pille“: An innovative approach to streamlining formulation of new drugs for oral administration

The new Fraunhofer research project “e-Pille“ is designed to streamline the formulation of new drugs for oral delivery. In this project scientists from three Fraunhofer institutes (Fraunhofer ITMP, EMFT and IZM) are pursuing the goal of developing an electronic capsule roughly the size of a multivitamin capsule by integrating innovative techniques that allow precise, accurate and reproducible dosage and release of a drug.

Diagram of the “e-Pille” showing the its various components..

Oral administration of drugs is preferred by most patients and therefore these account for the majority, more than 80%, of all prescriptions. For this reason, an oral dosage form is often the goal when developing a new drug. To streamline the formulation development process, various factors that are important to drug absorption from the gastrointestinal tract, such as the drug’s solubility and its ability to cross the intestinal wall and enter the bloodstream, must all be evaluated.

In a collaboration among the Fraunhofer institutes ITMP, EMFT and IZM, an innovative electronically controlled capsule, the “e-Pille”, is being developed. With the “e-Pille” it will be possible to trigger the release of a test drug at any pre-selected site in the gastrointestinal tract via an electronic signal. By miniaturizing the components and integrating them with innovative techniques, Fraunhofer scientists plan to reduce the size of the capsule to about the size of a multivitamin capsule and at the same time secure precise, accurate and reproducible dosing of the test drug using a special microfluidics technology. Programming drug release to occur at different sites in the gastrointestinal tract and monitoring the blood plasma levels of the drug that are obtained after release has been initiated provides a topography of the permeability of the drug throughout the gastrointestinal tract. This information can then be used by the formulation scientists to design an oral dosage form that will optimize the release and thus the bioavailability of the drug.

Status quo and project outlook

The current status of the project is that most of the individual components of the “e-Pille” have been designed and are being integrated into a benchtop model. The first prototypes are expected to be ready by the second half of 2022. At this time they will be subjected to intensive testing using in vitro models of the gastrointestinal tract in preparation for pre-clinical proof-of-concept studies in early 2023.

After validating the “e-Pille” for permeability studies, the next phase of the project will be to utilize electronic control of drug release to tailor the release pattern of a drug according to its therapeutic goals and pharmacodynamic properties. Implementation of this phase is expected to usher in a new paradigm of oral drug therapy.

Prof. Dr. Jennifer Dressman

jennifer.dressman@itmp.fraunhofer.de

HIPPOCRATES: Early detection and improved treatment of patients with psoriatic arthritis

The European consortium HIPPOCRATES (Health Initiatives in Psoriasis and PsOriatic arthritis ConsoRTium European States), funded by the Innovative Medicines Initiative (IMI), was established to identify patients at risk for developing PsA and to develop diagnostic methods and personalized approaches for the treatment of patients. Fraunhofer ITMP is involved in the consortium as part of the Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD.

In the HIPPOCRATES consortium, Fraunhofer CIMD, together with 25 European partners from research institutes, large pharmaceutical companies, small and medium-sized enterprises and patient organizations, is researching a disease that has been little studied to date but affects millions of people. The 26 European partners in the new HIPPOCRATES research project aim to develop innovative diagnostic and therapeutic options for patients with psoriatic arthritis (PsA) by studying the disease and its mechanisms. By better understanding the complex interplay between clinical and environmental factors, genotype and molecular disease pathways, the team aims to enable earlier diagnosis and more accurate prediction of disease progression. This will revolutionize the treatment for PsA patients.

Research approaches of the consortium

HIPPOCRATES started in July 2021 and will join forces over 60 months to work on 7 work packages to achieve the project goals. These work packages include the reliable diagnosis of PsA, the characterization of the transition from psoriasis to PsA, the identification of predictors of a severe progression with bone loss, and the investigation of factors controlling PsA therapy response. The findings from these clinical work packages are integrated into a further work package using machine learning methods, thus ensuring added value is obtained from the large amounts of data.

Role of Fraunhofer ITMP

In cooperation with the Department of Rheumatology at the University Hospital Frankfurt am Main, Fraunhofer ITMP was involved at an early stage in planning the content and institutional composition of the consortium. Now, together with its Fraunhofer CIMD partner institutes Fraunhofer IAIS and IGD, it will lead 2 of the 7 HIPPOCRATES work packages: »Early Diagnosis of PsA« and »Data Integration and Analysis«. In the former work package, the Fraunhofer team will determine clinical, imaging and molecular disease features and bring them in a combined context in order to derive algorithms for PsA diagnosis. In the latter work package, machine learning will be used to model an AI-based risk score of progression from psoriasis to PsA, to establish a risk score for rapid bone-damaging disease progression, and develop a response score to predict response to a particular treatment.

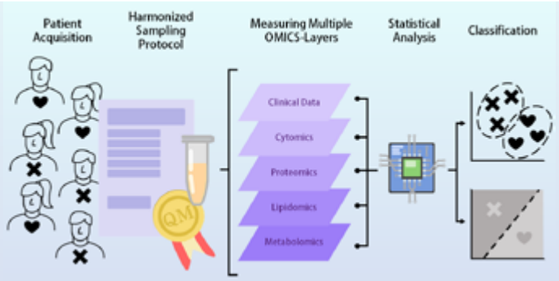
HIPPOCRATES Consortium: Involvement of a network of clinical experts and researchers from all over Europe.

PD Dr. Frank Behrens

frank.behrens@itmp.fraunhofer.de

COVIMMUN: What molecular footprint does COVID-19 leave? Search for tracers in the blood of COVID-19 patients

Severe COVID-19 infections burden intensive care medicine to the extreme, accompanied by negative consequences for all patients requiring medical care. New effective COVID-19 therapies as well as methods that allow better prediction of disease progression could improve the situation. The COVIMMUN project aims to identify prognostic biomarkers for COVID-19 progression in the acute phase of hospitalized treatment, as well as risk biomarkers to support clinical decision making for long-COVID interventions.



COVIMMUN project workflow: patient recruitment, sample collection, multiOMICs sample analysis, computer-assisted data analysis, identification of predictors for disease progression and risk

Dr. Eduard Resch

eduard.resch@itmp.fraunhofer.de

Most COVID-19 patients recover completely from SARS-CoV-2 infection. However, according to a WHO case report, about 10 to 20% of COVID-19 patients continue to suffer from the long-term consequences for weeks to months, which is then referred to as long-COVID or, if symptoms persist for more than 12 weeks, as post-COVID-19 syndrome. The clinical symptoms of long or post-COVID as well as their duration are very heterogeneous, can affect different organ systems, and the quality of life differently.
A holistic understanding of the interplay of the numerous identified COVID-19 pathomechanisms is still missing, which, taking into account all possible factors (including virus variants, risk factors of infected individuals), can explain the enormous diversity of the course of the disease. However, it is obvious that COVID-19 somehow manifests itself at the molecular level in patients during the acute phase. We want to uncover the »molecular footprints« of the disease in order to provide information about the short-term course of the disease as well as the long-term consequences.

Searching for tracers in the blood: targeting the “molecular footprint“

During COVID-19 infection, various organs and tissues can be directly or indirectly affected and damaged (e.g. lungs, heart, kidneys and blood vessels) as well as the blood constitution including its cells becoming significantly altered.

The examination of the blood has several advantages, since it flows through the entire body. In addition to the actual blood components, it also contains chemical messengers molecules from remote organs that would be difficult to directly access for examination. Moreover, blood is comparatively easy to collect and examine at different times during and after COVID-19.

Multidimensional flow cytometry can then be used to characterize the cellular composition of the blood in great detail. Mass spectrometry is used to detect changes in metabolites and signaling molecules in the blood. Proximity Extension Assay, a method that requires only a few microliters of blood, can also be used to investigate the change of hundreds of different proteins. All of this multi-layered data then flow into computer-assisted analyses which apply machine learning to identify molecular patterns indicative of a particular course, whether during or after the acute phase.

Development of a drug candidate for the prevention of Fetal and Neonatal Alloimmune Thrombocytopenia

In collaboration with Fraunhofer ITMP, the biopharmaceutical company Rallybio has initiated the early clinical development of the drug candidate RLYB211 for the prevention of Fetal and Neonatal Alloimmune Thrombocytopenia (FNAIT). This rare but potentially life-threatening condition is triggered by maternal antibodies to fetal platelet traits and can cause severe bleeding in fetuses and neonates. So far, prevention of the disease has not been possible, which could change through therapy with the immunoglobulin RLYB211.

Fetal and Neonatal Alloimmune Thrombocytopenia (FNAIT) occurs in about 1 in 1,500 pregnancies, making it a rare condition, but it can cause severe bleeding in fetuses and neonates. The cause is a mismatch between maternal and fetal platelets - the mother forms antibodies against the fetal platelets so that they are rapidly broken down, which ultimately leads to thrombocytopenia, a deficiency of blood platelets, in the fetus. To develop a drug candidate for the prevention of FNAIT, the »Early Clinical Development« working group of the Clinical Research Unit of the Fraunhofer ITMP in Frankfurt am Main is cooperating with the biopharmaceutical company Rallybio. For this purpose, the drug candidate RLYB211 will be tested in healthy male volunteers in a Phase-1 study.

Active ingredient and mode of action

RLYB211 is a plasma-derived hyperimmunoglobulin that scavenges platelets with the HPA-1a surface protein. HPA-1a is a platelet antigen produced by the mother against the fetus in FNAIT. The administration of RLYB211 is intended to prevent the antibodies produced by the mother from attacking and destroying the platelets of the fetus, resulting in severe bleeding in the fetus, which can cause lifelong severe neurological impairment or death of the child.

The Phase-I-study

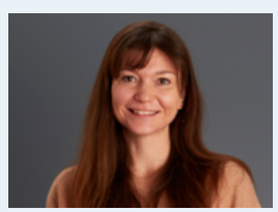
As part of the study conducted at the Fraunhofer ITMP Phase-1 station, platelets from HPA-1a-positive donors are first administered to HPA-1a-negative subjects. This simulates the scenario of HPA-1a-negative mothers into whose bloodstream fetal HPA-1a-positive platelets enter. After administration of RLYB211, it is then possible to quantify the extent to which the agent is able to scavenge the donor’s HPA-1a-positive platelets. This will give a first impression whether the administration of the active substance can actually preven t the development of thrombocytopenia in the fetus.

Fortsetzung der Kooperation des EU-Konsortiums PROFNAIT

The Clinical Research Department of the Fraunhofer ITMP was already involved in the precursor project of the study in the EU consortium PROFNAIT in close cooperation with the German Red Cross Blood Transfusion Service of Baden-Württemberg and Hesse. The first results of the clinical trial, which showed a high efficacy of the drug, were presented at the International Society on Thrombosis and Haemostasis (ISTH) Congress 2021 with the participation of the Fraunhofer ITMP research team. This EU project developed into an ongoing collaboration with the US biotech company Rallybio and a resulting first-in-human study using the drug.

The drug candidate RLYB211 is being tested for efficacy and tolerability in healthy male volunteers in a Phase I study.

Dr. Carmen Walter

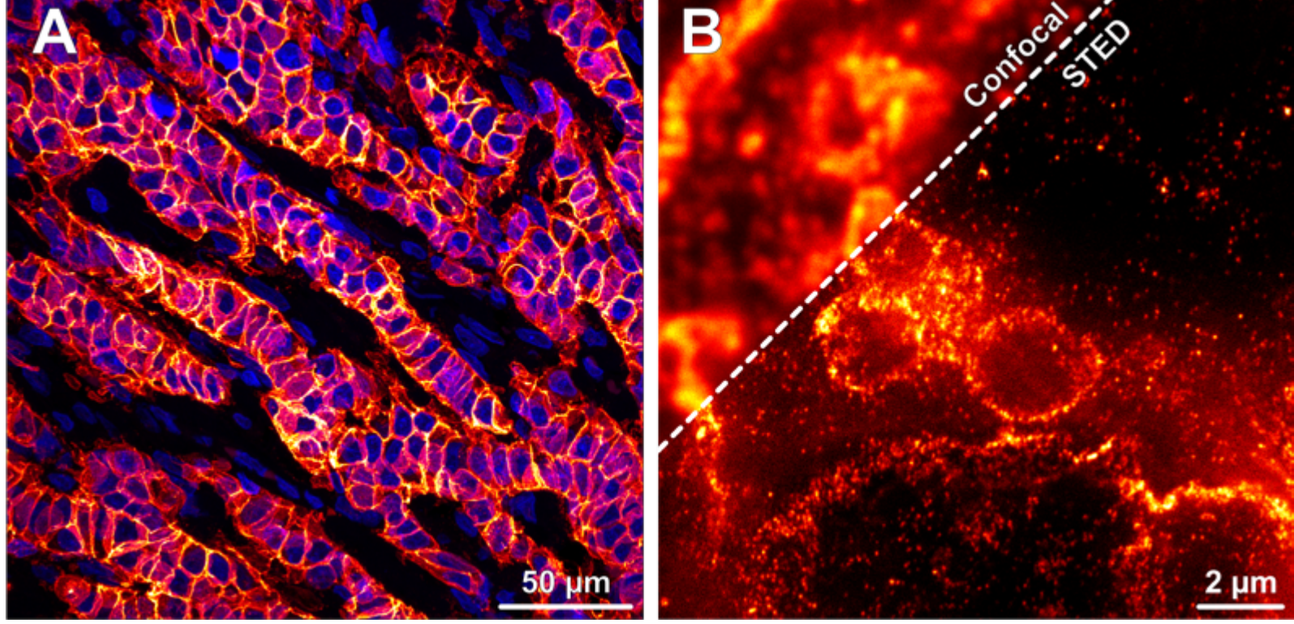


carmen.walter@itmp.fraunhofer.de

In Focus

Nanoscopy at Fraunhofer ITMP: A valuable tool in drug discovery

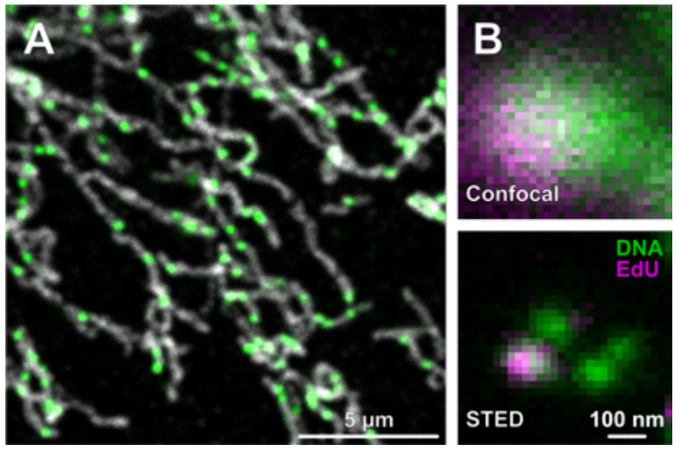
For a long time, light microscopy was governed by Abbe's law: The wavelength of the light used limited the maximum possible optical resolution. However, the invention of super-resolution microscopy, or nanoscopy, opened a window into previously unseen worlds. In particular, basic research in cell biology, such as research on mitochondria, benefited from nanoscopy. The High Resolution and Automated Microscopy department of the Translational Neuroinflammation and Automated Microscopy TNM institute site in Göttingen is making nanoscopy accessible for new applications.



STED microscopy of mitochondrial nucleoids. (A) Confocal overview image of a mitochondrial network (gray) and mitochondrial DNA (mtDNA, nucleoids; green) in a human cell. (B) Comparison of conventional microscopy (confocal) with nanoscopy (STED). STED microscopy allows visualization of single nucleoids and differentiation between replication-active (magenta, EdU) and -inactive nucleoids (green, DNA).

Opening up the nanocosmos

In the 19th century, Ernst Abbe recognized that the resolution of a light microscope is limited due to the wave nature of light. He formulated Abbe's law, named after him, which states that the maximum achievable resolution depends on the wavelength of light used. In the case of the visible spectrum, this is about 200 nm, which corresponds to about one three-hundredth of the thickness of a human hair. In microscopic practice, this means that two fluorescent dots closer together than 200 nm cannot be separated optically and appear as a single light spot in the fluorescence microscope. This law, even carved in stone on a monument by the University of Jena, was considered an immutable principle in light microscopy until the late 1990s. The diffraction limit of light was a barrier whose other side was literally in the dark.



Only the development of super-resolution microscopy, or nanoscopy, for the invention of which Prof. Stefan Hell of the Max Planck Institute for Biophysical Chemistry in Göttingen (now: Multidisciplinary Sciences), among others, was awarded the Nobel Prize in Chemistry in 2014, brought light into the darkness. While the diffraction limit of light recognized by Abbe still holds, it can be circumvented with a trick: Nanoscopy is based on the concept that individual dye molecules in close proximity to each other are excited to fluorescence one after the other, and their emitted photons can therefore be detected independently. In this way, two points can be imaged whose distance from each other is far below the diffraction limit of the light wavelength used.

Another challenge of nanoscopy is the fact that image acquisition times are usually relatively long. Currently, the images are usually also associated with a high personnel effort for sample preparation, acquisition and analysis. An important research goal of Prof. Stefan Jakobs' group at the Göttingen Translational Neuroinflammation and Automated Microscopy TNM site, founded in 2021, is therefore to develop nanoscopy systems that can perform these processes automatically. With their help, researchers will be able to move from the microcosm into the nanocosm more easily than before.

More than just images

The research group led by Prof. Stefan Jakobs uses various nanoscopy techniques, including STED microscopy, which was invented in Göttingen, to study the internal architecture of mitochondria. These cell organelles have a diameter of less than half a micrometer, so their size is close to the classical diffraction limit. Mitochondria are considered the power plants of the cell and are essential for numerous cellular processes. Disorders in mitochondrial function, often associated with alteration of mitochondrial structure, are associated with various serious diseases, such as neurodegenerative diseases or cardiomyopathies.

Mitochondria have their own genetic material, mitochondrial DNA. It encodes some essential proteins of the respiratory chain and is organized into large protein-DNA complexes called nucleoids, which are distributed throughout the mitochondrial network of a cell (Fig. 1A). A single human cell contains hundreds of nucleoids. Recently, the research group of Prof. Stefan Jakobs was able to demonstrate by STED microscopy that only part of the cellular nucleoid population is replication and transcription active, while another part is inactive (Fig. 1B). This surprising finding would not have been possible without nanoscopy.

Great Potential for Clinical Research

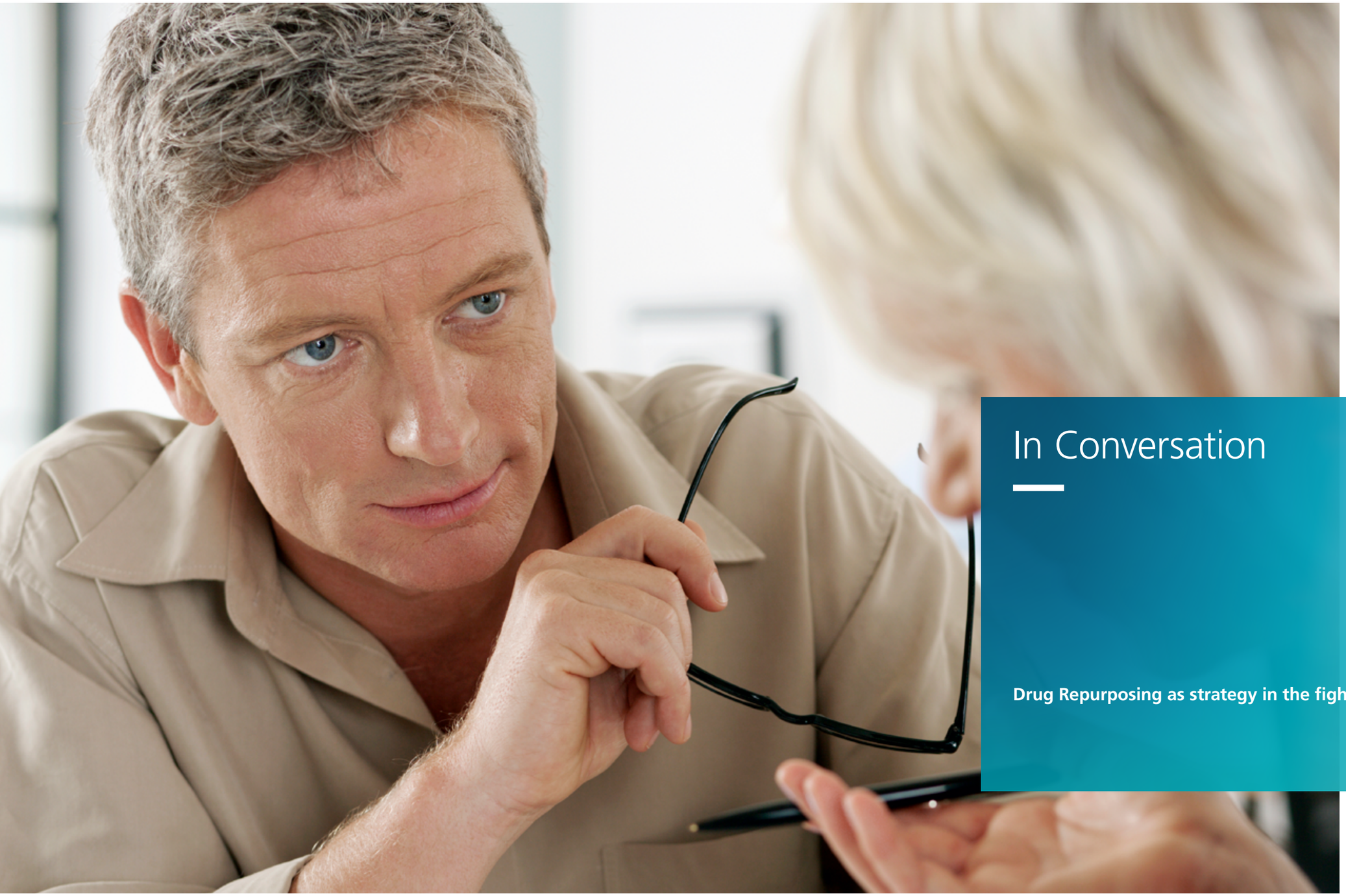
In fact, various nanoscopy techniques are now not uncommon in many cell biology research laboratories, while they have rarely been used in clinical research and diagnostics. The team of Prof. Stefan Jakobs was able to show that nanoscopy is not only possible on fresh but also on archived human tissue sections. Using STED nanoscopy, they were able to resolve the distribution and localization of individual clusters of marker proteins even in decades-old tissue sections embedded in paraffin wax (Fig. 2). Accordingly, a previously inaccessible treasure trove of information may lie dormant in clinical tissue banks that can be brought to light using nanoscopy. The collection of this information could prove to be very important for the development of future personalized medicine.

With various high-resolution microscopes and the necessary application expertise, the High Resolution and Automated Microscopy working group of the Fraunhofer ITMP site TNM will be able to support its customers and cooperation partners from sample preparation to actual image acquisition and data analysis.

STED microscopy of breast cancer cells in paraffin-embedded breast cancer tissue. (A) The overview image shows the cell nuclei (blue) and HER2 proteins detected by immunofluorescence (red). (B) Individual HER2 protein clusters on the cell membrane and on vesicles within the cell only become visible with nanoscopy.

Prof. Dr. Stefan Jakobs

stefan.jakobs@itmp.fraunhofer.de



In Conversation

Drug Repurposing as strategy in the fight against COVID-19

In spring 2019, well before the start of the Corona Pandemic, Fraunhofer ITMP ScreeningPort, the Hamburg site of Fraunhofer ITMP, made an investment in the field of Drug Repurposing and purchased the "Fraunhofer ITMP Repurposing Collection", to position Fraunhofer in this evolving field, especially in the search for treatments addressing neglected and rare diseases. This has been initiated by Dr. Philip Gribbon, Head of the Hamburg site and innovation area Drug Screening & Compound Repurposing, since repurposing of drugs represents an attractive and pragmatic strategy for advancing translational medicine development. Philip Gribbon received his PhD from Imperial College, London, and has a background in early drug discovery including time spent at Pfizer and GSK, before joining Fraunhofer.

Dr. Philip Gribbon,
Head of Hamburg site and innovation area Drug Screening & Compound Repurposing

What is meant by Drug Repurposing?

Drug repurposing, or repositioning involves the reuse of already known bioactive substances for new diseases. Testing already approved or failed drugs - for which drug safety has already been established - for new indications, can quickly bring benefits to patients by significantly reducing the cost and time associated with drug development.

What is the advantage of drug repurposing compared to conventional drug development?

Depending on the indication area, as many of 90% of drugs that enter clinical development phases do not receive approval. Often novel drugs fail at the very end of their development cycles, when drug safety and efficacy are being tested in clinical trials. This extremely high drop-out rate in late development phases turns conventional drug development into a cost intensive and time consuming effort. Therefore, for either approved or failed drugs for which safety has already been established, finding new indications can rapidly bring benefits to patients. Previous drug-repurposing successes span several disease areas; examples include thalidomide to treat multiple myeloma, methotrexate to treat rheumatoid arthritis and Minocyline for Fragile X syndrome.

What distinguishes the „Fraunhofer ITMP Repurposing collection"?

The "Fraunhofer ITMP Repurposing Collection", being one of Europe's largest collections of its kind, is composed of approximately 5600 bioactive compounds, of which over 3000 have found clinical application across 600 different indications. The collection also contains preclinical compounds with

In January 2020 our colleague – Prof. Sandra Ciesek from the Institute for Medical Virology at University Hospital Frankfurt – had access to some of the first clinical isolates of the coronavirus in Europe, and established an assay to screen against the virus on a very short timescale. Working closely with Prof. Ciesek, we then began screening the "Fraunhofer ITMP Repurposing Collection" of over 5500 bioactive compounds, including 3000 clinical stage drugs, for their antiviral activity.«

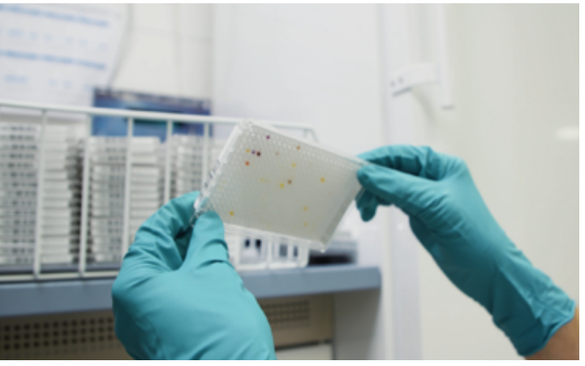
»Fraunhofer ITMP Repurposing Collection«: substance library with approx. 5600 mostly approved drugs.

New treatments and mechanisms

The latest COVID-19 therapeutic, "Paxlovid", recently developed by Pfizer, acts by inhibiting the Main Protease (Mpro) of SARS-CoV-2, demonstrating the validity of targeting protease activity as a therapeutic strategy that we are also following.

www.exscalate4cov.eu

www.itmp.fraunhofer.de/en/drug-repurposing-as-strategy-in-the-fight-against-covid-19



Testing of microtiter plates containing the substances of the »Fraunhofer ITMP Repurposing Collection«

varying degrees of validation. The compound collection is linked to a freely accessible curated database (clue-IO from the BROAD Institute) which contains comprehensive metadata annotation that supports data interpretation and allows new conclusions to be drawn on the likely mechanisms of action of drugs in new disease indications.

How can Drug Repurposing help in the context of COVID-19?

A race was on at the start of the pandemic to develop vaccines and drugs to fight against the SARS-CoV-2 virus. Vaccine development has proven successful, but the need remains to identify therapeutics that can treat the disease for those who have not been vaccinated, for those where the vaccine is not effective enough to prevent disease or for new virus variants which escape the vaccine induced immune response.

When we started to search for drugs against SARS-CoV-2, the precise details of how the viral infection affects tissues and organs, or how this contributes to the development of disease, were not clear. This knowledge of infection and disease-related mechanisms is normally critical to developing medicines, allowing researchers to target key virus replication, or viral:host interactome associated pathways with small molecule compounds or biologicals. At Fraunhofer ITMP in Hamburg, we have been experienced in using high throughput approaches to screen compound libraries for candidate antiviral drugs. We have recognized the opportunity that screening already known drugs and drug analogs against SARS-CoV-2 would allow us to identify candidate compounds with potential to be rapidly analyzed in in vivo efficacy studies, and ultimately clinical trials. Drug repurposing efforts allow candidates to be quickly taken into Phase II and III clinical efficacy trials while potentially reducing the need for the extensive Phase I safety testing normally necessary with novel compounds.

How did you get started with SARS-CoV-2 repurposing projects?

In January 2020 our colleague – Prof. Dr. Sandra Ciesek from the Institute for Medical Virology at University Hospital Frankfurt – had access to some of the first clinical isolates of the coronavirus in Europe, and established an assay to screen against the virus on a very short timescale. Working closely with professor Ciesek, we then began screening the "Fraunhofer ITMP Repurposing collection", for their potential antiviral activities.

As whole virus was used in the screening assay at that point, we sent the plates to professor Ciesek's biosafety level 3 (BSL-3) lab in Frankfurt am Main for testing, Within three months

Project results of the EU-funded project EXSCALATE4CoV.

we had published the first results online,[1] and eventually uploaded the primary data to ChEMBL and the Image Data Repository. All these immediate activities have only been possible due to the enormous efforts of the Fraunhofer-Gesellschaft to fund the research in the frame of the rapidly installed „Fraunhofer versus Corona" program.

Which further projects are you involved in in the meantime?

In the meantime, we have initiated several other collaborative projects to fight COVID-19 in the context of EU- and BMBF-funded initiatives. The most advanced being EXSCALATE4CoV, funded by the European Commission, which brings together high-end computational facilities, drug discovery, and BSL-3 high-throughput screening resources and aims at identifying repurposed candidates for a fast track entrance to in vivo studies and clinical investigations.

As more is known about the viral entry and replication mechanisms, we have also focused on the identification of inhibitors of key enzymes including the viral proteases Mpro and PLpro, as well as the viral helicase. Our data generated on PLpro – as well an outcome of the EXSCALATE4CoV project - has been followed up in a collaboration with the European Lead Factory which resulted in a screen involving a further 550 000 diverse compounds. Many data have already been made available for reuse by the community and deposited at the ChEMBL database.

When will the first patients be able to benefit from your research?

As a result of these efforts in EXSCALATE-4CoV, one compound (Raloxifen) a marketed treatment for osteoporosis, is currently finalizing a Phase II clinical trial in patients at the early stage of SARS-CoV-2 infection.

Dr. Philip Gribbon

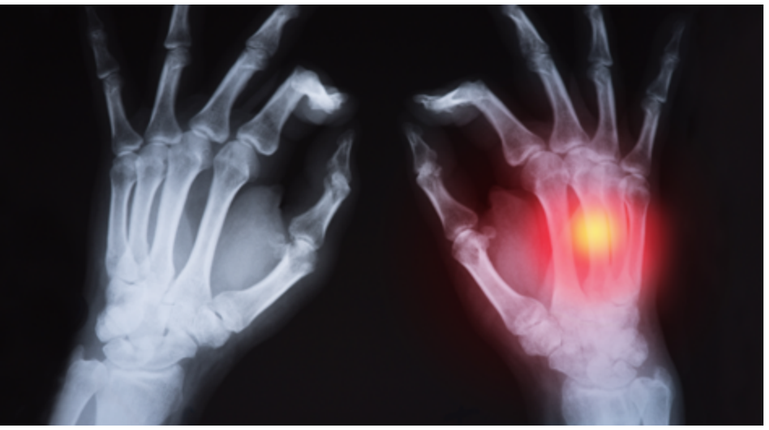
philip.gribbon@itmp.fraunhofer.de

[1] Ellinger, B. et al. A SARS-CoV-2 cytopathicity dataset generated by high-content screning of a large drug repurposing collection. (2021) Sci Data; DOI: 10.1038/s41597-021-00848-4

Publication Highlights

New intracellular mode of action for the treatment of the multiple symptoms of psoriatic arthritis

The oral reversible Janus kinase (JAK) inhibitor upadacitinib is demonstrating efficacy in the multiple disease domains of the cutaneous and musculoskeletal disease psoriatic arthritis.



PsA leads to various inflammations of the musculoskeletal system. In addition to the arthritis itself, tendon attachments and soft tissues are also affected.

Psoriatic arthritis (PsA) is a chronic inflammation of the musculoskeletal system associated with pain, functional limitations and joint deterioration. It affects approximately 30% of patients with psoriasis, one of the most common skin diseases in Europe. To date, drug treatment options are limited. Many oral therapies are insufficiently effective, and most therapies can only be administered as injections or infusions. The development of novel therapeutic approaches is therefore urgently needed for patients with PsA.

This is exactly a research focus at the Fraunhofer ITMP main site in Frankfurt am Main: The research of new diagnostic and therapeutic approaches in PsA. Due to the significant clinical expertise in this field as well as access to patients with PsA for application-related research projects via the interdisciplinary outpatient departments of the cooperating University Hospital Frankfurt, the high clinical research demand in the indication PsA can be adequately addressed with innovative study designs.

In the »SELECT-PsA 1« study, the efficacy of an oral therapy with the JAK inhibitor upadacitinib has now been demonstrated. Due to the innovative design, the study not only allowed the analysis of the differences relative to placebo, but also the direct comparison to a biologics therapy with the TNF inhibitor adalimumab. Thus, it could be shown for the first time that oral therapy with upadacitinib is at least equivalent to adalimumab therapy (15 mg dosage) and even potentially superior at higher dosage (30 mg).

In addition to the good response to therapy with upadacitinib for classic joint inflammation (arthritis), the study also showed that other manifestations of the disease improved significantly with treatment. After 24 weeks of therapy, more than half the patients with tendonitis (enthesitis) were symptom-free, and dactylitis was alleviated in more than 70% of the patients, with more than 60% of patients reporting an improvement in skin symptoms of at least 75% during the course of therapy.

Based partly on this study, which involved more than 1700 patients, the drug has now been approved for the treatment of PsA, enabling patients access to an effective, safe and easy-to-use oral therapy for the treatment of the various symptoms of PsA.

PD Dr. Frank Behrens

frank.behrens@itmp.fraunhofer.de

McInnes *et al.*
Trial of Upadacitinib and Adalimumab for Psoriatic Arthritis.
N Engl J Med. 2021 Apr 1.
DOI: 10.1056/NEJMoa2022516.

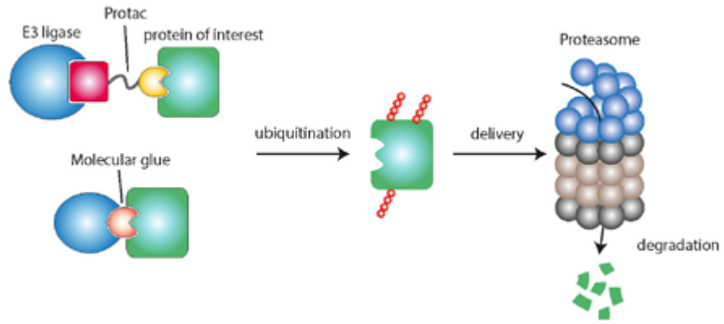
Using the cellular waste disposal system for the treatment of diseases

A new class of drugs aims at the targeted degradation of disease-associated proteins. A specific group of enzymes, so-called E3 ubiquitin ligases, plays a central role in this process.

The ubiquitin-proteasome system (UPS) plays an important role in cellular quality control: A tag consisting of several ubiquitin molecules is attached to misfolded proteins and other proteins destined for degradation, causing them to be transported to the proteasome, the cellular »shredder,« where they are degraded. In this process, ubiquitination is catalyzed by a specific group of enzymes known as E3 ligases.

This process is now also used for the development of novel drugs for the targeted degradation of pathogenic proteins: So-called proximity-inducing drugs bind to both the target protein and an E3 ligase, bringing them into close spatial proximity and thus causing ubiquitination and degradation of the protein of interest. Depending on the structure and size of the drug molecule, a distinction is made between proteolysis-targeting chimeras (PROTACs) and molecular glues as shown in the figure.

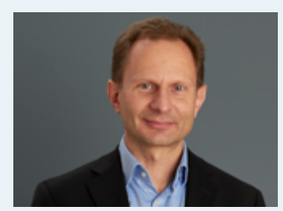
PROTACs are bifunctional molecules with a binding motif for the target protein and a binding motif for the E3 ligase, which are coupled via a suitable linker. While binding motifs for a whole range of target proteins have already been developed, the number of E3 ligases that can be addressed with PROTACs is currently still very limited: only about two percent of the more than 600 known E3 ligases are used for the targeted degradation of proteins by proximity-inducing drugs. By targeting E3 ligases that, for example, only occur in certain cells or tissues or are only expressed under certain conditions, such as specific disease states, the specificity of proximity-inducing drugs can in principal be significantly improved and the risk of unwanted side effects reduced.



Schematic representation of the mechanism of action of PROTACs and molecular glues. Both bring the target protein and an E3 ubiquitin ligase into close spatial proximity, leading to ubiquitination and proteasomal degradation of the target protein.

Our publication in Cell Chemical Biology provides an overview of the major classes of E3 ubiquitin ligases, their expression profiles, and their potential suitability to be recruited for induced protein degradation. It also summarizes the E3 ligases used to date for molecular degradation and highlights the challenges and opportunities for using new E3 ligases for targeted degradation of pathogenic proteins. It also presents technologies that can be used to identify new binding motifs for alternative E3 ligases, thereby significantly expanding the arsenal of proximity-inducing drugs.

PD Dr. Aimo Kannt

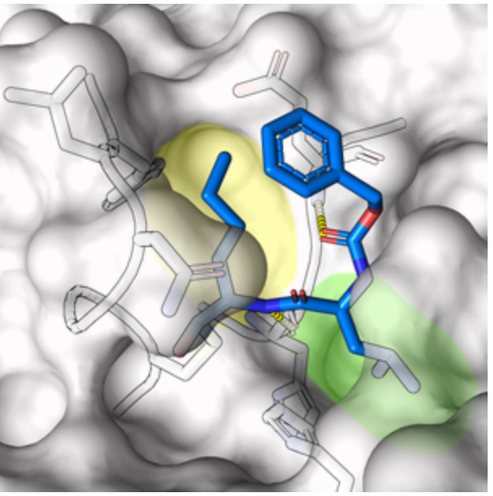


aimo.kannt@itmp.fraunhofer.de

Kannt A, Đikić I.
Expanding the arsenal of E3 ubiquitin ligases for proximity-induced protein degradation.
Cell Chem Biol, 2021 Jul 15, Epub 2021 May 3.
DOI: 10.1016/j.chembiol.2021.04.007.

Local partnership spurs SARS-CoV-2 research at Fraunhofer ITMP in Hamburg

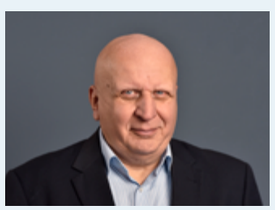
In the search for a drug against COVID-19, a high-throughput x-ray crystallographic screen of repurposing drug libraries has been performed, leading to the identification of active site and allosteric inhibitors of the SARS-CoV-2 main protease.



Close-up view of the active site of SARS-CoV-2 Mpro (PDB 2Q6G) with peptide substrate bound (Calpeptin, blue sticks). The surface of Mpro is shown in gray with selected interacting residues shown as sticks and substrate binding pockets indicated by colored regions. Hydrogen bonds are depicted by dashed lines.

The world has been fighting COVID-19 for the past two years and the enemy is far away from defeating. Meanwhile, the scientific community is working in national and international projects to bring the pandemic to an end. The projects, which are part of the Fraunhofer initiative "Fraunhofer vs. Corona", are prime examples of these endeavors. Next to these large collaborative projects are local cooperations enabling the realization of innovative ideas. One example of a cooperation resulting from a local network is that between Fraunhofer ITMP ScreeningPort in Hamburg, the German Electron Synchrotron (DESY) and the Bernhard Nocht Institute for Tropical Medicine. With their complementary technologies, the three institutes have jointly identified and characterized inhibitors for the SARS-CoV-2 protease (Mpro), an enzyme essential for the replication of the virus. The crystallization team at DESY developed a semi-automated method to record and annotate protein structures with and without bound ligands. In total, more than 8200 data sets were generated. Up to 450 protein structures per day were resolved, producing a total of over 41 terabytes of raw data and its analysis was a major bottleneck in the project. The compounds for this study came from the "Fraunhofer ITMP Repurposing Collection", which is considered one of the largest repurposing compound collections of its kind. In total, this library comprises around 5600 compounds with clinical approval or preclinical validation. From these, 43 were shown to interact with Mpro and the structural data for 29 Mpro/inhibitor complexes was of such high quality that even the binding mode could be determined. All partners worked seamlessly to confirm these results, with the complete data sets available just 6 weeks after the start of the project. In addition to 7 covalently and 9 non-covalently binding inhibitors of the active site of Mpro, two surface regions of the protein could also be identified to which allosterically acting inhibitors bind. The data were published in Science in May 2021.

Andrea Zaliani



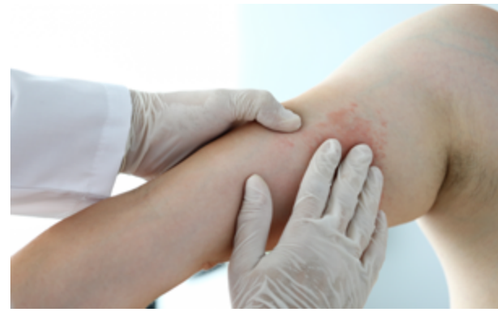
andrea.zaliani@itmp.fraunhofer.de

Günther *et al.*
X-ray screening identifies active site and allosteric inhibitors of SARS-CoV-2 main protease.
Science, 2021 May 7, Epub 2021 Apr 2.
DOI: 10.1126/science.abf7945.

When the body attacks Itself – New drug for the treatment of Chronic Spontaneous Urticaria

A new clinical trial involving the Berlin site of Fraunhofer ITMP shows promising results for the efficacy of a new drug in chronic spontaneous urticaria.

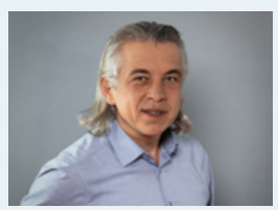
Chronic spontaneous urticaria (CSU) is a condition in which, over a period of at least six weeks, regularly recurring, intensely itchy wheals appear all over the skin for no apparent external reason which are occasionally accompanied by swelling in the facial area (angioedema). The cause of CSU most likely involves the production of so-called autoantibodies. Under normal circumstances, our body produces antibodies against foreign substances for protection, for example, against pathogens such as bacteria or viruses that enter the body. In contrast, in CSU, autoantibodies are not directed against something foreign, but against the body's own proteins resulting in the release of histamine through the activation of mast cells in the skin. Histamine is a chemical that plays a central role in the body's defense against foreign substances, but also in allergic reactions. As a chemical messenger of the inflammatory reaction, it leads to swelling of the tissue via activation of blood vessels and nerve fibers, and thus triggers the symptoms of CSU, the itchy wheals and angioedema. Unfortunately, the current standard therapy, blocking the effect of histamine with antihistamines, is only effective in a small proportion of CSU patients.



Severely itchy wheals all over the skin, sometimes accompanied by angioedema in the facial area - most patients suffer from these complaints for years.

An adequate treatment option for these patients may be on the horizon following the recently conducted clinical study, the results of which have been published in »Nature Medicine«, a premier peer-reviewed journal that has a focus on translational medicine and early-phase clinical research. In this study, patients with CSU who did not respond to standard treatment with antihistamines received the drug fenebrutinib or a placebo. Fenebrutinib is an active ingredient in tablet form that can prevent activation of mast cells and thus the release of histamine. In addition, this drug effects antibody formation, so that it may even be possible to reduce mast cell activation and the production of the autoantibodies responsible for CSU. Following the eight-week study with fenebrutinib, CSU symptoms were well controlled in many patients, whilst some displayed no disease symptoms. Fenebrutinib therefore has the potential to complement existing standard therapies to treat CSU in the future.

Prof. Dr. Marcus Maurer



marcus.maurer@itmp.fraunhofer.de

Metz *et al.*
Fenebrutinib in H1 antihistamine-refractory chronic spontaneous urticaria: a randomized phase 2 trial.
Nat Med., 2021 Nov, Epub 2021 Nov 8.
DOI: 10.1038/s41591-021-01537-w.

People and Events

Brief reports

Employees, encounters, successes, events and new perspectives at Fraunhofer ITMP.

Awards for the »Corona Explainer« Prof. Dr. Sandra Ciesek

Since the end of August 2020, Prof. Dr. Sandra Ciesek, Director of the Institute of Medical Virology at the University Hospital Frankfurt and employee of Fraunhofer ITMP, has been a regular guest on the award-winning NDR podcast series "Coronavirus Update". Alternating weekly with Prof. Dr. Christian Drosten, Head of the Institute of Virology at Berlin's Charité hospital, she educates the public in an easy to understand way about the scientific debates about the Covid-19 pandemic and the latest findings in Corona research.

This form of public oriented science communication was honored several times in 2021:
On May 31, the German Association of University Professors and Lecturers (DHV) honored Prof. Dr. Sandra Ciesek and Prof. Dr. Christian Drosten as "Germany's Professor of the Year" for their merit as "Corona Enlighteners". The two virologists received the award in particular for their high-profile appearance and their courage to continue to step out of their scientific environment and share the »adventure of research« with a broad public audience despite frequent criticism, thus strengthening society's trust in science in times of crisis.
On September 3, Urania Berlin awarded the two podcast protagonists the traditional Urania Medal for social education on the Corona pandemic.
Furthermore, on November 5, Prof. Dr. Sandra Ciesek and the science journalist Dr. Mai Thi Nguyen-Kim were awarded the Hessian Culture Prize 2021 for their merit in the Corona pandemic.

"Phialogics": innovative biologics to treat autoimmune diseases

In August 2021, after several years of research at Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, a team of scientists has spun-off and created „Phialogics". „Phiylogics – the immune tolerance company" is a preclinical-stage biotechnology company dedicated to the development of innovative biologics to treat autoimmune diseases.

The Fraunhofer ITMP spin-off „Phialogics" utilizes a proprietary protein engineering technology to create and develop immune checkpoint modulators to rebalance the immune response in autoimmune diseases. Phialogics' disruptive approach aims to maximize therapeutic impact while reducing side effects in the treatment of autoimmunity. Among other things, this should prevent tissue and organ damage leading to multi-organ failure in critical care disorders.

The founding team has an extensive background in research and extensive experience gained in industry. The team intends to use this expertise to develop a new generation of immunomodulatory drugs for the benefit of patients.

Webseite: **www.phialogics.com**

»Jugend forscht« defies the pandemic – this time simply different...

Thinking about the future of one's own footprints, taking responsibility and shaping the future - this is what this year's motto »Leave the future behind« of the "Jugend forscht" competition for young researchers was meant to call for, which was not an easy task in the face of the Corona pandemic.

Despite the ongoing lockdown and home schooling, a total of 77 young scientists from Hamburg schools followed this call and presented their research projects at the Hamburg Volkspark regional competition organized by the Fraunhofer ITMP for the first time in the history of Jugend forscht in a virtual format.

The participants unleashed their ideas such as laminating paper with beeswax instead of plastic, developing an app to make life easier with lactose intolerance, creating a fertilizer from organic waste, using essential oils as alternative herbicides, ways to minimize the abrasion of microplastics when washing synthetic fibers, statistically capturing complex cubes and developing a controller of the future. Dr. Mira Grättinger organized the competition for the ninth year in a row, for the third time in shared partnership with the HSV foundation "Der Hamburger Weg", but for the first time in the virtual world. Both pupils and the jury mastered this technical challenge with flying colors.

Clinician Scientist Funding by the Johanna Quandt Foundation

The Johanna Quandt Foundation is funding Dr. Michaela Köhm as a Clinician Scientist. The grant, endowed with 100 000 euros, serves to release Dr. Köhm from her clinical activities in order to enable the establishment of her junior research group on her research project »Development of innovative biomarkers for early diagnosis, prediction and therapy monitoring of immune diseases«.

The research project deals with the characterization (»deep clinical phenotyping«) of early pathological processes in the development of immune diseases.

Special focus is placed on the diseases psoriasis/psoriatic arthritis. These diseases offer the special feature that the presence of psoriasis already identifies a risk group for the development of psoriatic arthritis.

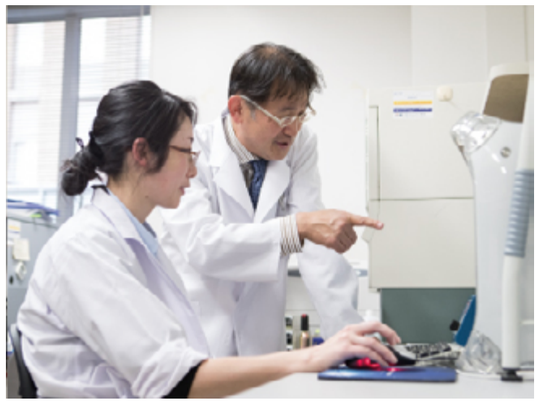
For phenotyping, innovative imaging techniques as well as various OMICS technologies (including lipidomics, metabolomics, proteomics) are used to identify serological biomarkers (»liquid biopsy«). In addition to the search for suitable innovative biomarkers for the early detection and prediction of immune diseases, biomarkers are also sought that can be used to monitor therapy response. Fluorescence optical imaging is considered a promising imaging method for early detection and therapy monitoring of psoriatic arthritis.

SDU awards honorary doctorate to Prof. Jennifer Dressman

Jennifer Dressman, Professor at Fraunhofer ITMP, was presented with the degree of Honorary Doctor at University of Southern Denmark SDU for her work on the pharmaceutical ecosystem in October 2021.

Prof. Dressman's research interests focus principally on predicting the in vivo performance of drugs and dosage forms after oral administration. She is best known for pioneering the use of biorelevant dissolution testing and her contributions to combining dissolution testing with physiologically based pharmacokinetic modelling in order to achieve quantitative predictions of oral drug absorption. This approach saves resources while making it possible to reduce or even eliminate animal or clinical studies in connection with the development of oral formulations for new drugs.

In the Laudatio from the Dean of the Natural Sciences Faculty at the University of Southern Denmark, Professor Marianne Holmer had these words to say about Professor Dressman: "Professor Dressman has made a major impact at all levels of the pharmaceutical ecosystem. Her methods have been picked up by academia and industry and are now also accepted by the regulatory bodies all around the world approving new drug applications. She's bringing basic research from the laboratory all the way to the patient and she's a major inspiration for other researchers and students in Pharmacy."

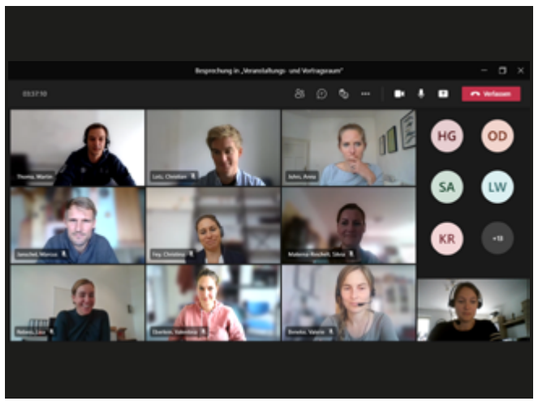


Collaboration with Japan - discovering therapeutics for vascular dementia

Germany and Japan are two industrialized countries with some of the highest life expectancies. As vascular dementia is common in the elderly, urgent action is required to discover drugs to treat this condition.

Dr. Sheraz Gul and his team from the Fraunhofer ITMP are working closely with Prof. Akihiko Taguchi, a clinical researcher at the Institute for Biomedical Research and Innovation at Kobe (FBRI), Japan to understand the processes involved in vascular dementia and discover relevant small molecule therapeutics. The two research teams have used their expertise and identified novel vascular dementia drug targets including Hif-1α, transporters of low molecular weight substances and VEGF. They subsequently developed high-throughput assay systems and screened them against libraries of small molecules to discover chemical starting points for vascular dementia therapies. These molecules are now progressing to in vivo proof-of-concept studies.

This work builds upon previously published results of the researchers showing beneficial effects of cellular therapeutics for transplanted bone marrow mononuclear cells in a Phase1/2a clinical trial for stroke. These types of therapeutics have limited utility in a clinical setting due to their complex nature, variability, and high productions costs. It is anticipated that these drawbacks will be overcome by the small molecule therapeutics which are currently being progressed.



Young Scientists Program: Fraunhofer CIMD Winter School

The first Winter School took place from October 5-8, 2021, as part of Fraunhofer CIMD's support for young researchers. The content was based on the four major topics of Fraunhofer health research: Diagnostics, Data, Drugs and Devices. During the four days, about 30 Fraunhofer PhD students and postdocs listened to numerous excellent presentations by internal and external experts, pitched their own projects and ideas, and discussed the translation into human/patient applications. The 4D topic area was complemented by excursions on vaccine development, innovation management and drug discovery.

To get to know each other better and to strengthen collaboration and communication, despite the digital format, the Winter School was opened with an interactive round of introductions. In smaller groups, divided into four thematic rooms, four questions (1) »What would win you a Nobel Prize?«, (2) »Who is your scientific idol and why?«, (3) »What is your dream destination and why have you never been there?« and (4) »What do you expect from this School?« were discussed in this round of introductions. In addition, the first day was rounded off with an online event (»Animals on Mars«).

The first Winter School was a very successful continuation of Fraunhofer CIMD's support for young scientists for networking and collaboration beyond their current projects and topics.

In times of pandemic: Science and politics in virtual dialog

During the period of virtual conversations, Fraunhofer ITMP employees have actively participated in the public discussion on health, with a focus on the current pandemic events, through a variety of contributions and formats. They actively sought dialogue and informed the public in a factual and fact-driven manner - in order to fulfil their own social responsibility as scientists. In close exchange with politicians, proposals for health research were drawn up at state and federal level, and new health initiatives were launched as a result. The competencies of the Fraunhofer-Gesellschaft in accordance with its 4D approach (Diagnostics, Devices, Drugs, Data) were always brought into play.

One example amongst many is the expert roundtable in the Chancellor's Office at the beginning of June 2021 with Chancellor Dr. Angela Merkel and three of her responsible ministers to discuss R&D needs in the field of antiviral therapies. In the very open discussion between politicians, scientists and industry management, suitable strategies in the field of drug development for a »pandemic preparedness« were discussed and concepts developed to meet the challenges in the development and production of antiviral drugs.

Two of the ten experts, Prof. Carsten Claussen from Fraunhofer ITMP ScreeningPort and Dr. Werner Lanthaler, CEO of Evotec AG, came from Hamburg.

Facts 2021

Publications

A-C

Ali, A., Ellinger, B., Brandt, S.C., Betzel, C., Rühl, M., Wrenger, C., Schlüter, H., Schäfer, W., Brognaro, H., Gand, M.
Genome and Secretome Analysis of Staphylotrichum longicolleum DSM105789 Cultured on Agro-Residual and Chitinous Biomass (2021) Microorganisms, 9 (8).
DOI: 10.3390/microorganisms9081581

Amerikanou, C., Kanoni, S., Kaliora, A.C., Barone, A., Bjelan, M., D'Auria, G., Gioxari, A., Gosalbes, M.J., Mouchti, S., Stathopoulou, M.G., Soriano, B., Stojanoski, S., Banerjee, R., Halabalaki, M., Mikropoulou, E.V., Kannt, A., Lamont, J., Llorens, C., Marascio, F., Marascio, M., Roig, F.J., Smyrnioudis, I., Varlamis, I., Visvikis-Siest, S., Vukic, M., Milic, N., Medic-Stojanoska, M., Cesarini, L., Campolo, J., Gastaldelli, A., Deloukas, P., Trivella, M.G., Francino, M.P., Dedoussis, G.V.
Effect of Mastiha supplementation on NAFLD: The MAST4HEALTH Randomised, Controlled Trial (2021) Molecular nutrition & food research, 65 (10), e2001178.
DOI: 10.1002/mnfr.202001178

Amerikanou, C., Papada, E., Gioxari, A., Smyrnioudis, I., Kleftaki, S.-A., Valsamidou, E., Bruns, V., Banerjee, R., Trivella, M.G., Milic, N., Medić-Stojanoska, M., Gastaldelli, A., Kannt, A., Dedoussis, G.V., Kaliora, A.C.
Mastiha has efficacy in immune-mediated inflammatory diseases through a microRNA-155 Th17 dependent action (2021) Pharmacological research, 171, 105753.
DOI: 10.1016/j.phrs.2021.105753

Behrens, F., Koehm, M., Rossmanith, T., Alten, R., Aringer, M., Backhaus, M., Burmester, G.R., Feist, E., Herrmann, E., Kellner, H., Krueger, K., Lehn, A., Müller-Ladner, U., Rubbert-Roth, A., Tony, H.-P., Wassenberg, S., Burkhardt, H.
Rituximab plus leflunomide in rheumatoid arthritis: a randomized, placebo-controlled, investigator-initiated clinical trial (AMARA study) (2021) Rheumatology (Oxford, England), 60 (11), 5318–5328.
DOI: 10.1093/rheumatology/keab153

Behrens, F., Leage, S.L., Sapin, C., Baou, C.E., La Torre, I. de, Meszaros, G., Schett, G., Combe, B., van den Bosch, F., Gossec, L.
Measuring treatment effect on psoriatic arthritis-related domains: insights from the SPIRIT-H2H study at weeks 24 and 52 (2021) Clinical rheumatology, 40 (12), 4943–4954.
DOI: 10.1007/s10067-021-05891-5

Behrens, F., Leage, S.L., Sapin, C., El Baou, C., La Torre, I. de, Meszaros, G., Schett, G., Combe, B., van den Bosch, F., Gossec, L.
Correction to: Measuring treatment effect on psoriatic arthritis-related domains: insights from the SPIRIT-H2H study at weeks 24 and 52 (2021) Clinical rheumatology, 40 (12), 4955–4956.
DOI: 10.1007/s10067-021-05966-3

Behrens, F., Rech, J., Thaçi, D., Zinke, S., Rothnie, K.J., Daamen, C., Leipe, J.
High rates of therapeutic changes in patients with psoriatic arthritis receiving treatment with disease-modifying antirheumatic drugs: A cross-sectional study (2021) Modern Rheumatology, 32 (1), 87–95.
DOI: 10.1080/14397595.2020.1816597

Bespalov, A., Bernard, R., Gilis, A., Gerlach, B., Guillén, J., Castagné, V., Lefevre, I.A., Ducrey, F., Monk, L., Bongiovanni, S., Altevogt, B., Arroyo-Araujo, M., Bikovski, L., Bruin, N. de, Castaños-Vélez, E., Dityatev, A., Emmerich, C.H., Fares, R., Ferland-Beckham, C., Froger-Colléaux, C., Gailus-Durner, V., Hölter, S.M., Hofmann, M.C., Kabitzke, P., Kas, M.J., Kurreck, C., Moser, P., Pietraszek, M., Popik, P., Potschka, H., Prado Montes de Oca, E., Restivo, L., Riedel, G., Ritskes-Hoitinga, M., Samardzic, J., Schunn, M., Stöger, C., Voikar, V., Vollert, J., Wever, K.E., Wuyts, K., MacLeod, M.R., Dirnagl, U., Steckler, T.
Introduction to the EQIPD quality system (2021) eLife, 10 .
DOI: 10.7554/eLife.63294

Bizjak, M., Košnik, M., Dinevski, D., Thomsen, S.F., Fomina, D., Borzova, E., Kulthanan, K., Meshkova, R., Ahsan, D.M., Al-Ahmad, M., Altrichter, S., Bauer, A., Brockstädt, M., Costa, C., Demir, S., Fachini Criado, R., Ensina, L.F., Gelincik, A., Giménez-Arnau, A.M., Gonçalo, M., Gotua, M., Holm, J.G., Inomata, N., Kasperska-Zajac, A., Khoshkhui, M., Klyucharova, A., Kocatürk, E., Lu, R., Makris, M., Maltseva, N., Miljković, J., Pasali, M., Paulino, M., Pesqué, D., Peter, J., Ramón, G.D., Ritchie, C., Rodrigues Valle, S.O., Rudenko, M., Sikora, A., Souza Lima, E.M. de, Wagner, N., Xepapadaki, P., Xue, X., Zhao, Z., Terhorst-Molawi, D., Maurer, M.
Risk factors for systemic reactions in typical cold urticaria: Results from the COLD-CE study (2021) Allergy .
DOI: 10.1111/all.15194

Blum, L., Ulshöfer, T., Henke, M., Krieg, R., Berneburg, I., Geisslinger, G., Becker, K., Parnham, M.J., Schiffmann, S.
The immunomodulatory potential of the arylmethylaminosteroid sc1o (2021) Journal of molecular medicine (Berlin, Germany), 99 (2), 261–272.
DOI: 10.1007/s00109-020-02024-4

Bojkova, D., Costa, R., Reus, P., Bechtel, M., Jaboreck, M.-C., Olmer, R., Martin, U., Ciesek, S., Michaelis, M., Cinatl, J.
Targeting the Pentose Phosphate Pathway for SARS-CoV-2 Therapy (2021) Metabolites, 11 (10).
DOI: 10.3390/metabo11100699

Bollmann, F., Dohrke, J.-N., Wurm, C.A., Jans, D.C., Jakobs, S.
Mitochondrial Protein Abundance Gradients Require the Distribution of Separated Mitochondria (2021) Biology, 10 (7).
DOI: 10.3390/biology10070572

Brandt, S.C., Brognaro, H., Ali, A., Ellinger, B., Maibach, K., Rühl, M., Wrenger, C., Schlüter, H., Schäfer, W., Betzel, C., Janssen, S., Gand, M.
Insights into the genome and secretome of Fusarium metavorans DSM105788 by cultivation on agro-residual biomass and synthetic nutrient sources (2021) Biotechnology for biofuels, 14 (1), 74.
DOI: 10.1186/s13068-021-01927-9

Brittan, M., Zimmermann, W.-H.
Cell programming to protect the ischemic heart and limb (2021) Molecular therapy : the journal of the American Society of Gene Therapy, 29 (10), 2894–2895.
DOI: 10.1016/j.ymthe.2021.09.007

Brunkhorst-Kanaan, N., Trautmann, S., Schreiber, Y., Thomas, D., Kittel-Schneider, S., Gurke, R., Geisslinger, G., Reif, A., Tegeder, I.
Sphingolipid and Endocannabinoid Profiles in Adult Attention Deficit Hyperactivity Disorder (2021) Biomedicines, 9 (9).
DOI: 10.3390/biomedicines9091173

Brunst, S., Kramer, J.S., Kilu, W., Heering, J., Pollinger, J., Hiesinger, K., George, S., Steinhilber, D., Merk, D., Proschak, E.
Systematic Assessment of Fragment Identification for Multitarget Drug Design (2021) ChemMedChem, 16 (7), 1088–1092.
DOI: 10.1002/cmdc.202000858

Brüser, C., Keller-Findeisen, J., Jakobs, S.
The TFAM-to-mtDNA ratio defines inner-cellular nucleoid populations with distinct activity levels (2021) Cell reports, 37 (8), 110000.
DOI: 10.1016/j.celrep.2021.110000

Cherrez-Ojeda, I., Vanegas, E., Cherrez, A., Felix, M., Weller, K., Magerl, M., Maurer, R.R., Mata, V.L., Kasperska-Zajac, A., Sikora, A., Fomina, D., Kovalkova, E., Godse, K., Rao, N.D., Khoshkhui, M., Rastgoo, S., Criado, R.F.J., Abuzakouk, M., Grandon, D., van Doorn, M.B.A., Rodrigues Valle, S.O., Souza Lima, E.M. de, Thomsen, S.F., Ramón, G.D., Matos Benavides, E.E., Bauer, A., Giménez-Arnau, A.M., Kocatürk, E., Guillet, C., Larco, J.I., Zhao, Z.-T., Makris, M., Ritchie, C., Xepapadaki, P., Ensina, L.F., Cherrez, S., Maurer, M.
Chronic urticaria patients are interested in apps to monitor their disease activity and control: A UCARE CURICT analysis (2021) Clinical and translational allergy, 11 (10), e12089.
DOI: 10.1002/clt2.12089

Costanzi, E., Kuzikov, M., Esposito, F., Albani, S., Demitri, N., Giabbai, B., Camasta, M., Tramontano, E., Rossetti, G., Zaliani, A., Storici, P.
Structural and Biochemical Analysis of the Dual Inhibition of MG-132 against SARS-CoV-2 Main Protease (Mpro/3CLpro) and Human Cathepsin-L (2021) International journal of molecular sciences, 22 (21).
DOI: 10.3390/ijms222111779

D-F

Dennerlein, S., Poerschke, S., Oeljeklaus, S., Wang, C., Richter-Dennerlein, R., Sattmann, J., Bauermeister, D., Hanitsch, E., Stoldt, S., Langer, T., Jakobs, S., Warscheid, B., Rehling, P.
Defining the interactome of the human mitochondrial ribosome identifies SMIM4 and TMEM223 as respiratory chain assembly factors (2021) eLife, 10
DOI: 10.7554/eLife.68213

Dominguez, M., Brüne, B., Namgaladze, D.
Exploring the Role of ATP-Citrate Lyase in the Immune System (2021) Frontiers in immunology, 12, 632526.
DOI: 10.3389/fimmu.2021.632526

Dommel, S., Hoffmann, A., Berger, C., Kern, M., Klöting, N., Kannt, A., Blüher, M.
Effects of Whole-Body Adenylyl Cyclase 5 (Adcy5) Deficiency on Systemic Insulin Sensitivity and Adipose Tissue (2021) International journal of molecular sciences, 22 (9).
DOI: 10.3390/ijms22094353

Ellinger, B., Bojkova, D., Zaliani, A., Cinatl, J., Claussen, C., Westhaus, S., Keminer, O., Reinshagen, J., Kuzikov, M., Wolf, M., Geisslinger, G., Gribbon, P., Ciesek, S.
A SARS-CoV-2 cytopathicity dataset generated by high-content screening of a large drug repurposing collection (2021) Scientific data, 8 (1), 70.
DOI: 10.1038/s41597-021-00848-4

Emmerich, C.H., Gamboa, L.M., Hofmann, M.C.J., Bonin-Andresen, M., Arbach, O., Schendel, P., Gerlach, B., Hempel, K., Bespalov, A., Dirnagl, U., Parnham, M.J.
Improving target assessment in biomedical research: the GOT-IT recommendations (2021) Nature reviews. Drug discovery, 20 (1), 64–81.
DOI: 10.1038/s41573-020-0087-3

Erkoc, P., Schmitt, M., Ingelfinger, R., Bischoff-Kont, I., Kopp, L., Bode, H.B., Schiffmann, S., Fürst, R.
Xenocoumacin 2 reduces protein biosynthesis and inhibits inflammatory and angiogenesis-related processes in endothelial cells (2021) Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie, 140, 111765.
DOI: 10.1016/j.biopha.2021.111765

Faudone, G., Bischoff-Kont, I., Rachor, L., Willems, S., Zhubi, R., Kaiser, A., Chaikuad, A., Knapp, S., Fürst, R., Heering, J., Merk, D.
Propranolol Activates the Orphan Nuclear Receptor TLX to Counteract Proliferation and Migration of Glioblastoma Cells (2021) Journal of medicinal chemistry, 64 (12), 8727–8738.
DOI: 10.1021/acs.jmedchem.1c00733

Faudone, G., Kilu, W., Ni, X., Chaikuad, A., Sreeramulu, S., Heitel, P., Schwalbe, H., Knapp, S., Schubert-Zsilavecz, M., Heering, J., Merk, D.
The Transcriptional Repressor Orphan Nuclear Receptor TLX Is Responsive to Xanthines (2021) ACS pharmacology & translational science, 4 (6), 1794–1807.
DOI: 10.1021/acsptsci.1c00195

Fischer, C., Wilken-Schmitz, A., Hernandez-Olmos, V., Proschak, E., Stark, H., Fleming, I., Weigert, A., Thurn, M., Hofmann, M., Werner, E.R., Geisslinger, G., Niederberger, E., Watschinger, K., Tegeder, I.
AGMO Inhibitor Reduces 3T3-L1 Adipogenesis (2021) Cells, 10 (5).
DOI: 10.3390/cells10051081

Frank, A.-C., Raue, R., Fuhrmann, D.C., Sirait-Fischer, E., Reuse, C., Weigert, A., Lütjohann, D., Hiller, K., Syed, S.N., Brüne, B.
Lactate dehydrogenase B regulates macrophage metabolism in the tumor microenvironment (2021) Theranostics, 11 (15), 7570–7588.
DOI: 10.7150/THNO.58380

G-I

Gao, G.F., Ashtikar, M., Kojima, R., Yoshida, T., Kaihara, M., Tajiri, T., Shanehsazzadeh, S., Modh, H., Wacker, M.G.
Predicting drug release and degradation kinetics of long-acting microsphere formulations of tacrolimus for subcutaneous injection (2021) Journal of controlled release : official journal of the Controlled Release Society, 329, 372–384.
DOI: 10.1016/j.jconrel.2020.11.055

García, M.A., Cristofoletti, R., Abrahamsson, B., Groot, D.W., Parr, A., Polli, J.E., Mehta, M., Shah, V.P., Tomakazu, T., Dressman, J.B., Langguth, P.
Biowaiver Monograph for Immediate-Release Solid Oral Dosage Forms: Carbamazepine (2021) Journal of pharmaceutical sciences, 110 (5), 1935–1947.
DOI: 10.1016/j.xphs.2021.02.019

Gossen, J., Albani, S., Hanke, A., Joseph, B.P., Bergh, C., Kuzikov, M., Costanzi, E., Manelfi, C., Storici, P., Gribbon, P., Beccari, A.R., Talarico, C., Spyrakis, F., Lindahl, E., Zaliani, A., Carloni, P., Wade, R.C., Musiani, F., Kokh, D.B., Rossetti, G.
A Blueprint for High Affinity SARS-CoV-2 Mpro Inhibitors from Activity-Based Compound Library Screening Guided by Analysis of Protein Dynamics (2021) ACS pharmacology & translational science, 4 (3), 1079–1095.
DOI: 10.1021/acsptsci.0c00215

Gottlieb, A.B., Merola, J.F., Reich, K., Behrens, F., Nash, P., Griffiths, C.E.M., Bao, W., Pellet, P., Pricop, L., McInnes, I.B.
Efficacy of secukinumab and adalimumab in patients with psoriatic arthritis and concomitant moderate-to-severe plaque psoriasis: results from EXCEED, a randomized, double-blind head-to-head monotherapy study (2021) The British journal of dermatology, 185 (6), 1124–1134.
DOI: 10.1111/bjd.20413

Gray, V.A., Diaz, D.A., Dressman, J., Tsume, Y., Fotaki, N.
Highlights from the 2020 AAPS 360 Annual Meeting (2021) Dissolution Technologies, 28 (2), 36–40.
DOI: 10.14227/DT280221P36

Günther, S., Reinke, P.Y.A., Fernández-García, Y., Lieske, J., Lane, T.J., Ginn, H.M., Koua, F.H.M., Ehrt, C., Ewert, W., Oberthuer, D., Yefanov, O., Meier, S., Lorenzen, K., Krichel, B., Kopicki, J.-D., Gelisio, L., Brehm, W., Dunkel, I., Seychell, B., Gieseler, H., Norton-Baker, B., Escudero-Pérez, B., Domaracky, M., Saouane, S., Tolstikova, A., White, T.A., Hänle, A., Groessler, M., Fleckenstein, H., Trost, F., Galchenkova, M., Gevorkov, Y., Li, C., Awel, S., Peck, A., Barthelmess, M.,

Schlünzen, F., Lourdu Xavier, P., Werner, N., Andaleeb, H., Ullah, N., Falke, S., Srinivasan, V., França, B.A., Schwinzer, M., Brognaro, H., Rogers, C., Melo, D., Zaitseva-Doyle, J.J., Knoska, J., Peña-Murillo, G.E., Mashhour, A.R., Hennicke, V., Fischer, P., Hakanpää, J., Meyer, J., Gribbon, P., Ellinger, B., Kuzikov, M., Wolf, M., Beccari, A.R., Bourenkov, G., Stetten, D. von, Pompidor, G., Bento, I., Panneerselvam, S., Karpics, I., Schneider, T.R., Garcia-Alai, M.M., Niebling, S., Günther, C., Schmidt, C., Schubert, R., Han, H., Boger, J., Monteiro, D.C.F., Zhang, L., Sun, X., Pletzer-Zelgert, J., Wollenhaupt, J., Feiler, C.G., Weiss, M.S., Schulz, E.-C., Mehrabi, P., Karničar, K., Usenik, A., Loboda, J., Tidow, H., Chari, A., Hilgenfeld, R., Uetrecht, C., Cox, R., Zaliani, A., Beck, T., Rarey, M., Günther, S., Turk, D., Hinrichs, W., Chapman, H.N., Pearson, A.R., Betzel, C., Meents, A.
X-ray screening identifies active site and allosteric inhibitors of SARS-CoV-2 main protease (2021) Science (New York, N.Y.), 372 (6542), 642–646.
DOI: 10.1126/science.abf7945

Hahnefeld, L., Kornstädt, L., Kratz, D., Ferreirós, N., Geisslinger, G., Pierre, S., Scholich, K.
Lipidomic analysis of local inflammation models shows a specific systemic acute phase response to lipopolysaccharides (2021) Biochimica et biophysica acta. Molecular and cell biology of lipids, 1866 (1), 158822.
DOI: 10.1016/j.bbalip.2020.158822

Harberts, J., Bours, K., Siegmund, M., Hedrich, C., Glatza, M., Schöler, H.R., Haferkamp, U., Pless, O., Zierold, R., Blick, R.H.
Culturing human iPSC-derived neural progenitor cells on nanowire arrays: mapping the impact of nanowire length and array pitch on proliferation, viability, and membrane deformation (2021) Nanoscale, 13 (47), 20052–20066.
DOI: 10.1039/d1nr04352h

Hartmann, M., Bibli, S.-I., Tews, D., Ni, X., Kircher, T., Kramer, J.S., Kilu, W., Heering, J., Hernandez-Olmos, V., Weizel, L., Scriba, G.K.E., Krait, S., Knapp, S., Chaikuad, A., Merk, D., Fleming, I., Fischer-Posovszky, P., Proschak, E.
Combined Cardioprotective and Adipocyte Browning Effects Promoted by the Eutomer of Dual sEH/PPARγ Modulator (2021) Journal of medicinal chemistry, 64 (5), 2815–2828.
DOI: 10.1021/acs.jmedchem.0c02063

Hartmann, M., Huber, J., Kramer, J.S., Heering, J., Pietsch, L., Stark, H., Odadzic, D., Bischoff, I., Fürst, R., Schröder, M., Akutsu, M., Chaikuad, A., Dötsch, V., Knapp, S., Biondi, R.M., Rogov, V.V., Proschak, E.
Demonstrating Ligandability of the LC3A and LC3B Adapter Interface (2021) Journal of medicinal chemistry, 64 (7), 3720–3746.
DOI: 10.1021/acs.jmedchem.0c01564

Hernandez-Olmos, V., Heering, J., Bischoff-Kont, I., Kaps, A., Rajkumar, R., Liu, T., Fürst, R., Steinhilber, D., Proschak, E.
Discovery of Irbesartan Derivatives as BLT2 Agonists by Virtual Screening (2021) ACS medicinal chemistry letters, 12 (8), 1261–1266.
DOI: 10.1021/acsmedchemlett.1c00240

Holz-Müller, J., Dauth, S., Behrens, F., Köhm, M.
Spondyloarthritis (2021) Arthritis und Rheuma, 41 (02), 106–122.
DOI: 10.1055/a-1352-9692

Hu, J., Sisignano, M., Brecht, R., Perumal, N., Angioni, C., Bibli, I.-S., Fisslthaler, B., Kleinert, H., Pfeiffer, N., Fleming, I., Manicam, C.
Cyp2c44 epoxygenase-derived epoxyeicosatrienoic acids in vascular smooth muscle cells elicit vasoconstriction of the murine ophthalmic artery (2021) Scientific reports, 11 (1), 18764.
DOI: 10.1038/s41598-021-98236-w

Huard, A., Do, H.N., Frank, A.-C., Sirait-Fischer, E., Fuhrmann, D., Hofmann, M.C.J., Raue, R., Palmer, G., Brüne, B., Bruin, N. de, Weigert, A.
IL-38 Ablation Reduces Local Inflammation and Disease Severity in Experimental Autoimmune Encephalomyelitis (2021) Journal of immunology (Baltimore, Md. : 1950), 206 (5), 1058–1066.
DOI: 10.4049/jimmunol.2000923

J-L

Janczi, T., Meier, F., Fehrl, Y., Kinne, R.W., Böhm, B., Burkhardt, H.
A Novel Pro-Inflammatory Mechanosensing Pathway Orchestrated by the Disintegrin Metalloproteinase ADAM15 in Synovial Fibroblasts (2021) Cells, 10 (10).
DOI: 10.3390/cells10102705

Jung, F., Thurn, M., Krollik, K., Li, D., Dressman, J., Alig, E., Fink, L., Schmidt, M.U., Wacker, M.G.
Sustained-release hot melt extrudates of the weak acid TMP-001: A case study using PBB modelling (2021) European journal of pharmaceutics and biopharmaceutics : official journal of Arbeitsgemeinschaft fur Pharmazeutische Verfahrenstechnik e.V, 160, 23–34.
DOI: 10.1016/j.ejpb.2021.01.007

Kannt, A., Đikić, I.
Expanding the arsenal of E3 ubiquitin ligases for proximity-induced protein degradation (2021) Cell chemical biology, 28 (7), 1014–1031.
DOI: 10.1016/j.chembiol.2021.04.007

Kannt, A., Rajagopal, S., Hallur, M.S., Swamy, I., Kristam, R., Dhakshinamoorthy, S., Czech, J., Zech, G., Schreuder, H., Ruf, S.
Novel Inhibitors of Nicotinamide-N-Methyltransferase for the Treatment of Metabolic Disorders (2021) Molecules (Basel, Switzerland), 26 (4).
DOI: 10.3390/molecules26040991

Kannt, A., Wohlfart, P., Madsen, A.N., Veidal, S.S., Feigh, M., Schmoll, D.
Activation of thyroid hormone receptor-β improved disease activity and metabolism independent of body weight in a mouse model of non-alcoholic steatohepatitis and fibrosis (2021) British journal of pharmacology, 178 (12), 2412–2423.
DOI: 10.1111/bph.15427

Kanoni, S., Kumar, S., Amerikanou, C., Kurth, M.J., Stathopoulou, M.G., Bourgeois, S., Masson, C., Kannt, A., Cesarini, L., Kontoe, M.-S., Milanović, M., Roig, F.J., Beribaka, M., Campolo, J., Jiménez-Hernández, N., Milošević, N., Llorens, C., Smyrnioudis, I., Francino, M.P., Milić, N., Kaliora, A.C., Trivella, M.G., Ruddock, M.W., Medić-Stojanoska, M., Gastaldelli, A., Lamont, J., Deloukas, P., Dedoussis, G.V., Visvikis-Siest, S.
Nutrigenetic Interactions Might Modulate the Antioxidant and Anti-Inflammatory Status in Mastiha-Supplemented Patients With NAFLD (2021) Frontiers in immunology, 12, 683028.
DOI: 10.3389/fimmu.2021.683028

Khodzhaeva, V., Schreiber, Y., Geisslinger, G., Brandes, R.P., Brüne, B., Namgaladze, D.
Mitofusin 2 Deficiency Causes Pro-Inflammatory Effects in Human Primary Macrophages (2021) Frontiers in immunology, 12, 723683.
DOI: 10.3389/fimmu.2021.723683

Kienzl, M., Hasenoehrl, C., Maitz, K., Sarsembayeva, A., Taschler, U., Valadez-Cosmes, P., Kindler, O., Ristic, D., Raftopoulou, S., Santiso, A., Bärnthaler, T., Brcic, L., Hahnefeld, L., Gurke, R., Thomas, D., Geisslinger, G., Kargl, J., Schicho, R.
Monoacylglycerol lipase deficiency in the tumor microenvironment slows tumor growth in non-small cell lung cancer (2021) Oncoimmunology, 10 (1), 1965319.
DOI: 10.1080/2162402X.2021.1965319

Kikuchi-Taura, A., Okinaka, Y., Saino, O., Takeuchi, Y., Ogawa, Y., Kimura, T., Gul, S., Claussen, C., Boltze, J., Taguchi, A.
Gap junction-mediated cell-cell interaction between transplanted mesenchymal stem cells and vascular endothelium in stroke (2021) Stem cells (Dayton, Ohio), 39 (7), 904–912.
DOI: 10.1002/stem.3360

Kilu, W., Merk, D., Steinhilber, D., Proschak, E., Heering, J.
Heterodimer formation with retinoic acid receptor RXRα modulates coactivator recruitment by peroxisome proliferator-activated receptor PPARγ (2021) The Journal of biological chemistry, 297 (1), 100814.
DOI: 10.1016/j.jbc.2021.100814

Knethen, A. von, Rodriguez-Barbosa, J.-I.
Editorial: The Roles of Checkpoint Inhibitors in Inflammatory Diseases (2021) Frontiers in immunology, 12, 795495.
DOI: 10.3389/fimmu.2021.795495

Kocak, M., Ezazi Erdi, S., Jorba, G., Maestro, I., Farrés, J., Kirkin, V., Martinez, A., Pless, O.
Targeting autophagy in disease: established and new strategies (2021) Autophagy, 1–23.
DOI: 10.1080/15548627.2021.1936359

Köhm, M., Burkhardt, H., Behrens, F.
Therapiestrategien der Psoriasisarthritis (2021) Aktuelle Dermatologie, 47 (12), 544–551.
DOI: 10.1055/a-1676-9290

Kolkhir, P., Elieh-Ali-Komi, D., Metz, M., Siebenhaar, F., Maurer, M.
Understanding human mast cells: lesson from therapies for allergic and non-allergic diseases (2021) Nature reviews. Immunology .
DOI: 10.1038/s41577-021-00622-y

Kolkhir, P., Kovalkova, E., Chernov, A., Danilycheva, I., Krause, K., Sauer, M., Shulzhenko, A., Fomina, D., Maurer, M.
Autoimmune Chronic Spontaneous Urticaria Detection with IgG Anti-TPO and Total IgE (2021) The journal of allergy and clinical immunology. In practice, 9 (11), 4138-4146.e8.
DOI: 10.1016/j.jaip.2021.07.043

Komasaka, T., Dressman, J.
Simulation of oral absorption from non-bioequivalent dosage forms of the salt of raltegravir, a poorly soluble acidic drug, using a physiologically based biopharmaceutical modeling (PBBM) approach (2021) European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences, 157, 105630.
DOI: 10.1016/j.ejps.2020.105630

Kornstädt, L., Pierre, S., Weigert, A., Ebersberger, S., Schäufele, T.J., Kolbinger, A., Schmid, T., Cohnen, J., Thomas, D., Ferreirós, N., Brüne, B., Ebersberger, I., Scholich, K.
Bacterial and Fungal Toll-Like Receptor Activation Elicits Type I IFN Responses in Mast Cells (2020) Frontiers in immunology, 11, 607048.
DOI: 10.3389/fimmu.2020.607048

Kraft, V., Schmitz, K., Wilken-Schmitz, A., Geisslinger, G., Sisignano, M., Tegeder, I.
Trehalose Reduces Nerve Injury Induced Nociception in Mice but Negatively Affects Alertness (2021) Nutrients, 13 (9).
DOI: 10.3390/nu13092953

Kratz, D., Thomas, D., Gurke, R.
Endocannabinoids as potential biomarkers: It's all about pre-analytics (2021) Journal of mass spectrometry and advances in the clinical lab, 22, 56–63.
DOI: 10.1016/j.jmsacl.2021.11.001

Krause, T., Bonnekoh, H., Dilling, A., Nast, A., Metz, M.
A distinctive bullous skin reaction associated with enfortumab vedotin-ejfv treatment for metastatic urothelial cancer: A case report (2021) Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology : JDDG, 19 (12), 1781–1783.
DOI: 10.1111/ddg.14617

Krause, T., Bonnekoh, H., Dilling, A., Nast, A., Metz, M.
Ausgeprägte bullöse Hautreaktion bei metastasiertem Urothelkarzinom unter der Behandlung mit Enfortumab Vedotin: Ein Fallbericht (2021) Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology : JDDG, 19 (12), 1781–1783.
DOI: 10.1111/ddg.14617_g

Kringel, D., Malkusch, S., Kalso, E., Lötsch, J.
Computational Functional Genomics-Based AmpliSeq™ Panel for Next-Generation Sequencing of Key Genes of Pain (2021) International journal of molecular sciences, 22 (2).
DOI: 10.3390/ijms22020878

Kringel, D., Malkusch, S., Lötsch, J.
Drugs and Epigenetic Molecular Functions. A Pharmacological Data Scientometric Analysis (2021) International journal of molecular sciences, 22 (14).
DOI: 10.3390/ijms22147250

Kuzikov, M., Costanzi, E., Reinshagen, J., Esposito, F., Vangeel, L., Wolf, M., Ellinger, B., Claussen, C., Geisslinger, G., Corona, A., Iaconis, D., Talarico, C., Manelfi, C., Cannalire, R., Rossetti, G., Gossen, J., Albani, S., Musiani, F., Herzog, K., Ye, Y., Giabbai, B., Demitri, N., Jochmans, D., Jonghe, S. de, Rymenants, J., Summa, V., Tramontano, E., Beccari, A.R., Leyssen, P., Storici, P., Neyts, J., Gribbon, P., Zaliani, A.
Identification of Inhibitors of SARS-CoV-2 3CL-Pro Enzymatic Activity Using a Small Molecule in Vitro Repurposing Screen (2021) ACS Pharmacology & Translational Science, 4 (3), 1096–1110.
DOI: 10.1021/acsptsci.0c00216

Lillich, F.F., Willems, S., Ni, X., Kilu, W., Borkowsky, C., Brodsky, M., Kramer, J.S., Brunst, S., Hernandez-Olmos, V., Heering, J., Schierle, S., Kestner, R.-I., Mayser, F.M., Helmstädter, M., Göbel, T., Weizel, L., Namgaladze, D., Kaiser, A., Steinhilber, D., Pfeilschifter, W., Kahnt, A.S., Proschak, A., Chaikuad, A., Knapp, S., Merk, D., Proschak, E.
Structure-Based Design of Dual Partial Peroxisome Proliferator-Activated Receptor γ Agonists/Soluble Epoxide Hydrolase Inhibitors (2021) Journal of medicinal chemistry, 64 (23), 17259–17276.
DOI: 10.1021/acs.jmedchem.1c01331

Loisios-Konstantinidis, I., Dressman, J.
Physiologically Based Pharmacokinetic/Pharmacodynamic Modeling to Support Waivers of In Vivo Clinical Studies: Current Status, Challenges, and Opportunities (2021) Molecular pharmaceutics, 18 (1), 1–17.
DOI: 10.1021/acs.molpharmaceut.0c00903

Lötsch, J., Hähner, A., Schwarz, P.E.H., Tselmin, S., Hummel, T.
Machine Learning Refutes Loss of Smell as a Risk Indicator of Diabetes Mellitus (2021) Journal of clinical medicine, 10 (21).
DOI: 10.3390/jcm10214971

Lötsch, J., Hintschich, C.A., Petridis, P., Pade, J., Hummel, T.
Machine-Learning Points at Endoscopic, Quality of Life, and Olfactory Parameters as Outcome Criteria for Endoscopic Paranasal Sinus Surgery in Chronic Rhinosinusitis (2021) Journal of clinical medicine, 10 (18).
DOI: 10.3390/jcm10184245

Lötsch, J., Hintschich, C.A., Petridis, P., Pade, J., Hummel, T.
Self-Ratings of Olfactory Function and Their Relation to Olfactory Test Scores. A Data Science-Based Analysis in Patients with Nasal Polyposis (2021) Applied Sciences, 11 (16), 7279.
DOI: 10.3390/app11167279

Lötsch, J., Hummel, T.
Data Science-Based Analysis of Patient Subgroup Structures Suggest Effects of Rhinitis on All Chemosensory Perceptions in the Upper Airways (2021) Chemical senses, 46 .
DOI: 10.1093/chemse/bjab001

Lötsch, J., Malkusch, S.
Interpretation of cluster structures in pain-related phenotype data using explainable artificial intelligence (XAI) (2021) European journal of pain (London, England), 25 (2), 442–465.
DOI: 10.1002/ejp.1683

Lötsch, J., Malkusch, S., Ultsch, A.
Optimal distribution-preserving downsampling of large biomedical data sets (opdisDownsampling) (2021) PloS one, 16 (8), e0255838.
DOI: 10.1371/journal.pone.0255838

Lötsch, J., Ultsch, A., Hähner, A., Willgeroth, V., Bensafi, M., Zaliani, A., Hummel, T.
Data-science based analysis of perceptual spaces of odors in olfactory loss (2021) Scientific reports, 11 (1), 10595.
DOI: 10.1038/s41598-021-89969-9

Luciano, V., Proschak, E., Langer, J.D., Knapp, S., Heering, J., Marschalek, R.
Closantel is an allosteric inhibitor of human Taspase1 (2021) iScience, 24 (12), 103524.
DOI: 10.1016/j.isci.2021.103524

Luo, Y., Fernandez Vallone, V., He, J., Frischbutter, S., Kolkhir, P., Moñino-Romero, S., Stachelscheid, H., Streu-Haddad, V., Maurer, M., Siebenhaar, F., Scheffel, J.
A novel approach for studying mast cell-driven disorders: Mast cells derived from induced pluripotent stem cells (2021) The Journal of allergy and clinical immunology
DOI: 10.1016/j.jaci.2021.07.027

Lütjohann, D., Stellaard, F., Kerksiek, A., Lötsch, J., Oertel, B.G.
Serum 4β-hydroxycholesterol increases during fluconazole treatment (2021) European journal of clinical pharmacology, 77 (5), 659–669.
DOI: 10.1007/s00228-020-03041-5

M-O

Magoulas, G.E., Afroudakis, P., Georgikopoulou, K., Roussaki, M., Borsari, C., Fotopoulou, T., Santarem, N., Barrias, E., Tejera Nevado, P., Hachenberg, J., Bifeld, E., Ellinger, B., Kuzikov, M., Fragiadaki, I., Scoulica, E., Clos, J., Gul, S., Costi, M.P., Souza, W. de, Prousis, K.C., Da Cordeiro Silva, A., Calogeropoulou, T.
Design, Synthesis and Antiparasitic Evaluation of Click Phospholipids (2021) Molecules (Basel, Switzerland), 26 (14).
DOI: 10.3390/molecules26144204

Malkusch, S., Hahnefeld, L., Gurke, R., Lötsch, J.
Visually guided preprocessing of bioanalytical laboratory data using an interactive R notebook (pguIMP) (2021) CPT: pharmacometrics & systems pharmacology, 10 (11), 1371–1381.
DOI: 10.1002/psp4.12704

Marcelino, J., Baumann, K., Skov, P.S., Pereira Santos, M.C., Wyroslak, I., Scheffel, J., Altrichter, S., Woetmann, A., Pereira-Barbosa, M., Costa, C., Maurer, M.
What Basophil Testing Tells Us About CSU Patients - Results of the CORSA Study (2021) Frontiers in immunology, 12, 742470.
DOI: 10.3389/fimmu.2021.742470

Mast, M.-P., Modh, H., Champanhac, C., Wang, J.-W., Storm, G., Krämer, J., Mailänder, V., Pastorin, G., Wacker, M.G.
Nanomedicine at the crossroads - A quick guide for IVIVC (2021) Advanced drug delivery reviews, 179, 113829.
DOI: 10.1016/j.addr.2021.113829

Mast, M.-P., Modh, H., Knoll, J., Fecioru, E., Wacker, M.G.
An Update to Dialysis-Based Drug Release Testing-Data Analysis and Validation Using the Pharma Test Dispersion Releaser (2021) Pharmaceutics, 13 (12).
DOI: 10.3390/pharmaceutics13122007

Maurer, M., Caballero, T., Aberer, W., Zanichelli, A., Bouillet, L., Bygum, A., Grumach, A.S., Botha, J., Andresen, I., Longhurst, H.J.
Variability of disease activity in patients with hereditary angioedema type 1/2: longitudinal data from the Icatibant Outcome Survey (2021) Journal of the European Academy of Dermatology and Venereology : JEADV, 35 (12), 2421–2430.
DOI: 10.1111/jdv.17654

McInnes, I.B., Kato, K., Magrey, M., Merola, J.F., Kishimoto, M., Pacheco-Tena, C., Haaland, D., Chen, L., Duan, Y., Zueger, P., Liu, J., Lippe, R., Pangan, A.L., Behrens, F.
Upadacitinib in patients with psoriatic arthritis and an inadequate response to non-biological therapy: 56-week data from the phase 3 SELECT-PsA 1 study (2021) RMD open, 7 (3).
DOI: 10.1136/rmdopen-2021-001838

Meier, K., Thorkelsson, S.R., Quemin, E.R.J., Rosenthal, M.
Hantavirus Replication Cycle-An Updated Structural Virology Perspective (2021) Viruses, 13 (8).
DOI: 10.3390/v13081561

Meiser, I., Majer, J., Katsen-Globa, A., Schulz, A., Schmidt, K., Stracke, F., Koutsouraki, E., Witt, G., Keminer, O., Pless, O., Gardner, J., Claussen, C., Gribbon, P., Neubauer, J.C., Zimmermann, H.
Droplet-based vitrification of adherent human induced pluripotent stem cells on alginate microcarrier influenced by adhesion time and matrix elasticity (2021) Cryobiology, 103, 57–69.
DOI: 10.1016/j.cryobiol.2021.09.010

Mergenthal, K., Schulz-Rothe, S., Siebenhofer, A., Gerlach, F.M., Dauth, S., Petersen, J.J.
Aufgabenteilung im hausärztlichen Praxisteam bei der Durchführung von Versorgungsstudien (2021) Zeitschrift für Allgemeinmedizin (97 (6), 281–285.
DOI: 10.3238/zfa.2021.0281-0285

Mertens, C., Schnetz, M., Rehwald, C., Grein, S., Elwakeel, E., Weigert, A., Brüne, B., Jung, M.
Iron-Bound Lipocalin-2 from Tumor-Associated Macrophages Drives Breast Cancer Progression Independent of Ferroportin (2021) Metabolites, 11 (3).
DOI: 10.3390/metabo11030180

Metry, M., Shu, Y., Abrahamsson, B., Cristofoletti, R., Dressman, J.B., Groot, D.W., Parr, A., Langguth, P., Shah, V.P., Tajiri, T., Mehta, M.U., Polli, J.E.
Biowaiver Monographs for Immediate Release Solid Oral Dosage Forms: Metformin Hydrochloride (2021) Journal of pharmaceutical sciences, 110 (4), 1513–1526.
DOI: 10.1016/j.xphs.2021.01.011

Metz, M., Sussman, G., Gagnon, R., Staubach, P., Tanus, T., Yang, W.H., Lim, J.J., Clarke, H.J., Galanter, J., Chinn, L.W., Chu, T., Teterina, A., Burgess, T., Haddon, D.J., Lu, T.T., Maurer, M.
Fenebrutinib in H1 antihistamine-refractory chronic spontaneous urticaria: a randomized phase 2 trial (2021) Nature medicine, 27 (11), 1961–1969.
DOI: 10.1038/s41591-021-01537-w

Miettinen, T., Mäntyselkä, P., Hagelberg, N., Mustola, S., Kalso, E., Lötsch, J.
Machine learning suggests sleep as a core factor in chronic pain (2021) Pain, 162 (1), 109–123.
DOI: 10.1097/j.pain.0000000000002002

Mitra, A., Suarez-Sharp, S., Pepin, X.J.H., Flanagan, T., Zhao, Y., Kotzagiorgis, E., Parrott, N., Sharan, S., Tistaert, C., Heimbach, T., Zolnik, B., Sjögren, E., Wu, F., Anand, O., Kakar, S., Li, M., Veerasingham, S., Kijima, S., Lima Santos, G.M., Ning, B., Raines, K., Rullo, G., Mandula, H., Delvadia, P., Dressman, J., Dickinson, P.A., Babiskin, A.
Applications of Physiologically Based Biopharmaceutics Modeling (PBBM) to Support Drug Product Quality: A Workshop Summary Report (2021) Journal of pharmaceutical sciences, 110 (2), 594–609.
DOI: 10.1016/j.xphs.2020.10.059

Mota, A.C., Dominguez, M., Weigert, A., Snodgrass, R.G., Namgaladze, D., Brüne, B.
Lysosome-Dependent LXR and PPARγ Activation Upon Efferocytosis in Human Macrophages (2021) Frontiers in immunology, 12, 637778.
DOI: 10.3389/fimmu.2021.637778

Namgaladze, D., Brüne, B.
Pharmacological Activation of p53 during Human Monocyte to Macrophage Differentiation Attenuates Their Pro-Inflammatory Activation by TLR4, TLR7 and TLR8 Agonists (2021) Cancers, 13 (5).
DOI: 10.3390/cancers13050958

Nash, P., Mease, P.J., Fleishaker, D., Wu, J., Coates, L.C., Behrens, F., Gladman, D.D., Kivitz, A.J., Wei, J.C., Shirinsky, I., Menon, S., Romero, A.B., Fallon, L., Hsu, M.-A., Wang, C., Kanik, K.S.
Tofacitinib as monotherapy following methotrexate withdrawal in patients with psoriatic arthritis previously treated with open-label tofacitinib plus methotrexate: a randomised, placebo-controlled substudy of OPAL Balance (2021) The Lancet Rheumatology, 3 (1), e28-e39.
DOI: 10.1016/S2665-9913(20)30339-8

Nelson, N., Razeto, A., Gilardi, A., Grättinger, M., Kirchmair, J., Jücker, M.
AKT1 and PTEN show the highest affinities among phosphoinositide binding proteins for the second messengers PtdIns(3,4,5)P3 and PtdIns(3,4)P2 (2021) Biochemical and biophysical research communications, 568, 110–115.
DOI: 10.1016/j.bbrc.2021.06.027

Ni, X., Schröder, M., Olieric, V., Sharpe, M.E., Hernandez-Olmos, V., Proschak, E., Merk, D., Knapp, S., Chaikuad, A.
Structural Insights into Plasticity and Discovery of Remdesivir Metabolite GS-441524 Binding in SARS-CoV-2 Macrodomain (2021) ACS medicinal chemistry letters, 12 (4), 603–609.
DOI: 10.1021/acsmedchemlett.0c00684

Niederberger, E., Parnham, M.J.
The Impact of Diet and Exercise on Drug Responses (2021) International journal of molecular sciences, 22 (14).
DOI: 10.3390/ijms22147692

Nieraad, H., Bruin, N. de, Arne, O., Hofmann, M.C.J., Gurke, R., Schmidt, D., Ritter, M., Parnham, M.J., Geisslinger, G.
Effects of Alzheimer-Like Pathology on Homocysteine and Homocysteic Acid Levels-An Exploratory In Vivo Kinetic Study (2021) International journal of molecular sciences, 22 (2).
DOI: 10.3390/ijms22020927

Nieraad, H., Pannwitz, N., Bruin, N. de, Geisslinger, G., Till, U.
Hyperhomocysteinemia: Metabolic Role and Animal Studies with a Focus on Cognitive Performance and Decline-A Review (2021) Biomolecules, 11 (10).
DOI: 10.3390/biom11101546

Niesel, K., Schulz, M., Anthes, J., Alekseeva, T., Macas, J., Salamero-Boix, A., Möckl, A., Oberwahrenbrock, T., Lolies, M., Stein, S., Plate, K.H., Reiss, Y., Rödel, F., Sevenich, L.
The immune suppressive microenvironment affects efficacy of radio-immunotherapy in brain metastasis (2021) EMBO molecular medicine, 13 (5), e13412.
DOI: 10.15252/emmm.202013412

Ntari, L., Nikolaou, C., Kranidioti, K., Papadopoulou, D., Christodoulou-Vafeiadou, E., Chouvardas, P., Meier, F., Geka, C., Denis, M.C., Karagianni, N., Kollias, G.
Combination of subtherapeutic anti-TNF dose with dasatinib restores clinical and molecular arthritogenic profiles better than standard anti-TNF treatment (2021) Journal of translational medicine, 19 (1), 165.
DOI: 10.1186/s12967-021-02764-y

O'Dwyer, P.J., Box, K.J., Dressman, J., Griffin, B.T., Henze, L.J., Litou, C., Pentafragka, C., Statelova, M., Vertzoni, M., Reppas, C.
Oral biopharmaceutics tools: recent progress from partnership through the Pharmaceutical Education and Research with Regulatory Links collaboration (2021) The Journal of pharmacy and pharmacology, 73 (4), 437–446.
DOI: 10.1093/jpp/rgaa055

P-R

Parrott, N., Suarez-Sharp, S., Kesisoglou, F., Pathak, S.M., Good, D., Wagner, C., Dallmann, A., Mullin, J., Patel, N., Riedmaier, A.E., Mitra, A., Raines, K., Butler, J., Kakhi, M., Li, M., Zhao, Y., Tsakalozou, E., Flanagan, T., Dressman, J., Pepin, X.
Best Practices in the Development and Validation of Physiologically Based Biopharmaceutics Modeling. A Workshop Summary Report (2021) Journal of pharmaceutical sciences, 110 (2), 584–593.
DOI: 10.1016/j.xphs.2020.09.058

Pepin, X.J.H., Dressman, J., Parrott, N., Delvadia, P., Mitra, A., Zhang, X., Babiskin, A., Kolhatkar, V., Seo, P., Taylor, L.S., Sjögren, E., Butler, J.M., Kostewicz, E., Tannergren, C., Koziolek, M., Kesisoglou, F., Dallmann, A., Zhao, Y., Suarez-Sharp, S.
In Vitro Biopredictive Methods: A Workshop Summary Report (2021) Journal of pharmaceutical sciences, 110 (2), 567–583.
DOI: 10.1016/j.xphs.2020.09.021

Pepin, X.J.H., Parrott, N., Dressman, J., Delvadia, P., Mitra, A., Zhang, X., Babiskin, A., Kolhatkar, V., Suarez-Sharp, S.
Current State and Future Expectations of Translational Modeling Strategies to Support Drug Product Development, Manufacturing Changes and Controls: A Workshop Summary Report (2021) Journal of pharmaceutical sciences, 110 (2), 555–566.
DOI: 10.1016/j.xphs.2020.04.021

Quendt, C., Ochs, J., Häusser-Kinzel, S., Häusler, D., Weber, M.S.
Proinflammatory CD20+ T Cells are Differentially Affected by Multiple Sclerosis Therapeutics (2021) Annals of neurology, 90 (5), 834–839.
DOI: 10.1002/ana.26216

Raad, F.S., Khan, T.A., Esser, T.U., Hudson, J.E., Seth, B.I., Fujita, B., Gandamala, R., Tietze, L.F., Zimmermann, W.
Chalcone-Supported Cardiac Mesoderm Induction in Human Pluripotent Stem Cells for Heart Muscle Engineering (2021) ChemMedChem, 16 (21), 3300–3305.
DOI: 10.1002/cmdc.202100222

Rappl, P., Brüne, B., Schmid, T.
Role of Tristetraprolin in the Resolution of Inflammation (2021) Biology, 10 (1).
DOI: 10.3390/biology10010066

Rappl, P., Rösser, S., Maul, P., Bauer, R., Huard, A., Schreiber, Y., Thomas, D., Geisslinger, G., Jakobsson, P.-J., Weigert, A., Brüne, B., Schmid, T.
Inhibition of mPGES-1 attenuates efficient resolution of acute inflammation by enhancing CX3CL1 expression (2021) Cell death & disease, 12 (2), 135.
DOI: 10.1038/s41419-021-03423-2

Raue, R., Frank, A.-C., Syed, S.N., Brüne, B.
Therapeutic Targeting of MicroRNAs in the Tumor Microenvironment (2021) International journal of molecular sciences, 22 (4).
DOI: 10.3390/ijms22042210

Reus, P., Schneider, A.-K., Ulshöfer, T., Henke, M., Bojkova, D., Cinatl, J., Ciesek, S., Geisslinger, G., Laux, V., Grättinger, M., Gribbon, P., Schiffmann, S.
Characterization of ACE Inhibitors and AT1R Antagonists with Regard to Their Effect on ACE2 Expression and Infection with SARS-CoV-2 Using a Caco-2 Cell Model (2021) Life (Basel, Switzerland), 11 (8).
DOI: 10.3390/life11080810

Rimola, V., Osthues, T., Königs, V., Geißlinger, G., Sisignano, M.
Oxaliplatin Causes Transient Changes in TRPM8 Channel Activity (2021) International journal of molecular sciences, 22 (9).
DOI: 10.3390/ijms22094962

Robinson, W.J., Taylor, A.E., Lauga-Cami, S., Weaver, G.W., Arroo, R.R.J., Kaiser, M., Gul, S., Kuzikov, M., Ellinger, B., Singh, K., Schirmeister, T., Botana, A., Eurtivong, C., Bhambra, A.S.
The discovery of novel antitrypanosomal 4-phenyl-6-(pyridin-3-yl)pyrimidines (2021) European journal of medicinal chemistry, 209, 112871.
DOI: 10.1016/j.ejmech.2020.112871

Rosenkranz, S.C., Shaposhnykov, A.A., Träger, S., Engler, J.B., Witte, M.E., Roth, V., Vieira, V., Paauw, N., Bauer, S., Schwencke-Westphal, C., Schubert, C., Bal, L.C., Schattling, B.,

Pless, O., van Horssen, J., Freichel, M., Friese, M.A.
Enhancing mitochondrial activity in neurons protects against neurodegeneration in a mouse model of multiple sclerosis (2021) eLife, 10
DOI: 10.7554/eLife.61798

Rothenburger, T., Thomas, D., Schreiber, Y., Wratil, P.R., Pflantz, T., Knecht, K., Digianantonio, K., Temple, J., Schneider, C., Baldauf, H.-M., McLaughlin, K.-M., Rothweiler, F., Bilen, B., Farmand, S., Bojkova, D., Costa, R., Ferreirós, N., Geisslinger, G., Oellerich, T., Xiong, Y., Keppler, O.T., Wass, M.N., Michaelis, M., Cinatl, J.
Differences between intrinsic and acquired nucleoside analogue resistance in acute myeloid leukaemia cells (2021) Journal of experimental & clinical cancer research : CR, 40 (1), 317.
DOI: 10.1186/s13046-021-02093-4

Runfola, M., Perni, M., Yang, X., Marchese, M., Bacci, A., Mero, S., Santorelli, F.M., Polini, B., Chiellini, G., Giuliani, D., Vilella, A., Bodria, M., Daini, E., Vandini, E., Rudge, S., Gul, S., Wakelam, M.O.J., Vendruscolo, M., Rapposelli, S.
Identification of a Thyroid Hormone Derivative as a Pleiotropic Agent for the Treatment of Alzheimer's Disease (2021) Pharmaceuticals (Basel, Switzerland), 14 (12).
DOI: 10.3390/ph14121330

S-U

Santos, G.L., Meyer, T., Tiburcy, M., DeGrave, A., Zimmermann, W.-H., Lutz, S.
Fibroblast Derived Human Engineered Connective Tissue for Screening Applications (2021) Journal of visualized experiments : JoVE (174).
DOI: 10.3791/62700

Schiffmann, S., Gunne, S., Henke, M., Ulshöfer, T., Steinhilber, D., Sethmann, A., Parnham, M.J.
Sodium Bituminosulfonate Used to Treat Rosacea Modulates Generation of Inflammatory Mediators by Primary Human Neutrophils (2021) Journal of inflammation research, 14, 2569–2582.
DOI: 10.2147/JIR.S313636

Schmid, T., Brüne, B.
Prostanoids and Resolution of Inflammation - Beyond the Lipid-Mediator Class Switch (2021) Frontiers in immunology, 12, 714042.
DOI: 10.3389/fimmu.2021.714042

Schmitz, K., Trautmann, S., Hahnefeld, L., Fischer, C., Schreiber, Y., Wilken-Schmitz, A., Gurke, R., Brunkhorst, R., Werner, E.R., Watschinger, K., Wicker, S., Thomas, D., Geisslinger, G., Tegeder, I.
Sapropterin (BH4) Aggravates Autoimmune Encephalomyelitis in Mice (2021) Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics, 18 (3), 1862–1879.
DOI: 10.1007/s13311-021-01043-4

Schneider, E., Petersen, J.J., Schulz-Rothe, S., Gerlach, F.M., Rossmanith, T., Siebenhofer, A., Mergenthal, K.
Interprofessionelle Versorgung von Patienten mit rheumatoider Arthritis aus hausärztlicher Sicht: Ergebnisse einer Querschnittserhebung (2021) Gesundheitswesen (Bundesverband der Arzte des Offentlichen Gesundheitsdienstes (Germany), 83 (2), e1-e8.
DOI: 10.1055/a-1152-4576

Schoger, E., Zimmermann, W.-H., Cyganek, L., Zelarayán, L.C.
Establishment of a second generation homozygous CRISPRa human induced pluripotent stem cell (hiPSC) line for enhanced levels of endogenous gene activation (2021) Stem cell research, 56, 102518.
DOI: 10.1016/j.scr.2021.102518

Schoger, E., Zimmermann, W.-H., Cyganek, L., Zelarayán, L.C.
Establishment of two homozygous CRISPR interference (CRISPRi) knock-in human induced pluripotent stem cell (hiPSC) lines for titratable endogenous gene repression (2021) Stem cell research, 55, 102473.
DOI: 10.1016/j.scr.2021.102473

Schultz, B., Zaliani, A., Ebeling, C., Reinshagen, J., Bojkova, D., Lage-Rupprecht, V., Karki, R., Lukassen, S., Gadiya, Y., Ravindra, N.G., Das, S., Baksi, S., Domingo-Fernández, D., Lentzen, M., Strivens, M., Raschka, T., Cinatl, J., DeLong, L.N., Gribbon, P., Geisslinger, G., Ciesek, S., van Dijk, D., Gardner, S., Kodamullil, A.T., Fröhlich, H., Peitsch, M., Jacobs, M., Hoeng, J., Eils, R., Claussen, C., Hofmann-Apitius, M.
A method for the rational selection of drug repurposing candidates from multimodal knowledge harmonization (2021) Scientific reports, 11 (1), 11049.
DOI: 10.1038/s41598-021-90296-2

Schumann, L., Wilken-Schmitz, A., Trautmann, S., Vogel, A., Schreiber, Y., Hahnefeld, L., Gurke, R., Geisslinger, G., Tegeder, I.
Increased Fat Taste Preference in Progranulin-Deficient Mice (2021) Nutrients, 13 (11).
DOI: 10.3390/nu13114125

Segregur, D., Mann, J., Moir, A., Karlsson, E.M., Dressman, J.
Prediction of plasma profiles of a weakly basic drug after administration of omeprazole using PBPK modeling (2021) European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences, 158, 105656.
DOI: 10.1016/j.ejps.2020.105656

Sisignano, M., Fischer, M.J.M., Geisslinger, G.
Proton-Sensing GPCRs in Health and Disease (2021) Cells, 10 (8).
DOI: 10.3390/cells10082050

Ullmann, T., Luckhardt, S., Wolf, M., Parnham, M.J., Resch, E.
High-Throughput Screening for CEBPD-Modulating Compounds in THP-1-Derived Reporter Macrophages Identifies Anti-Inflammatory HDAC and BET Inhibitors (2021) International journal of molecular sciences, 22 (6).
DOI: 10.3390/ijms22063022

V-W

Valek, L., Tran, B., Wilken-Schmitz, A., Trautmann, S., Heidler, J., Schmid, T., Brüne, B., Thomas, D., Deller, T., Geisslinger, G., Auburger, G., Tegeder, I.
Prodromal sensory neuropathy in Pink1-/- SNCAA53T double mutant Parkinson mice (2021) Neuropathology and applied neurobiology, 47 (7), 1060–1079.
DOI: 10.1111/nan.12734

Wegner, M.-S., Schömel, N., Olzomer, E.M., Trautmann, S., Olesch, C., Byrne, F.L., Brüne, B., Gurke, R., Ferreirós, N., Weigert, A., Geisslinger, G., Hoehn, K.L.
Increased glucosylceramide production leads to decreased cell energy metabolism and lowered tumor marker expression in non-cancerous liver cells (2021) Cellular and molecular life sciences : CMLS, 78 (21-22), 7025–7041.
DOI: 10.1007/s00018-021-03958-9

Willems, S., Gellrich, L., Chaikuad, A., Kluge, S., Werz, O., Heering, J., Knapp, S., Lorkowski, S., Schubert-Zsilavecz, M., Merk, D.
Endogenous vitamin E metabolites mediate allosteric PPARγ activation with unprecedented co-regulatory interactions (2021) Cell chemical biology, 28 (10), 1489-1500.e8.
DOI: 10.1016/j.chembiol.2021.04.019

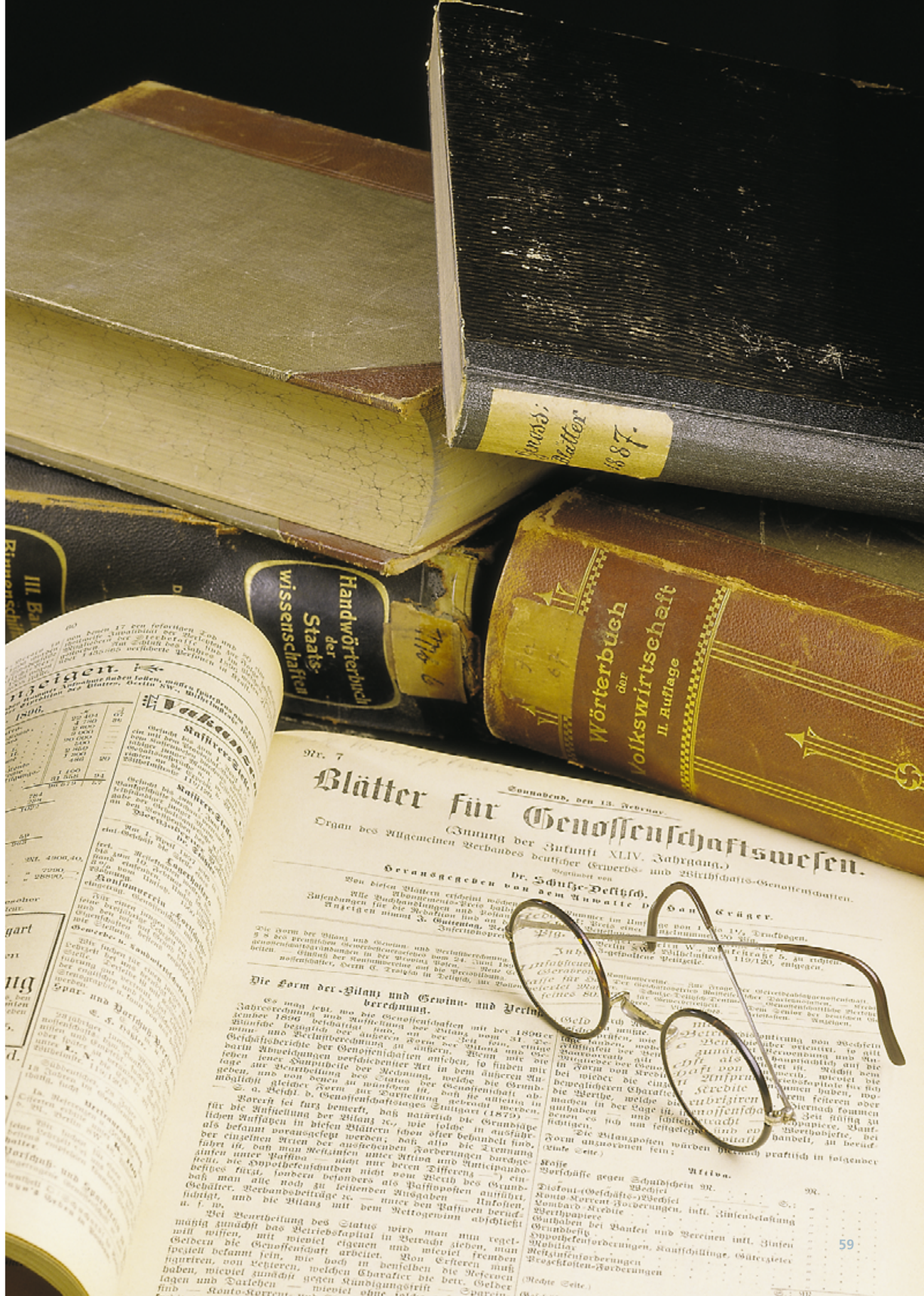
Willems, S., Ohrndorf, J., Kilu, W., Heering, J., Merk, D.
Fragment-like Chloroquinolineamines Activate the Orphan Nuclear Receptor Nurr1 and Elucidate Activation Mechanisms (2021) Journal of medicinal chemistry, 64 (5), 2659–2668.
DOI: 10.1021/acs.jmedchem.0c01779

Witkowski, M., Tizian, C., Ferreira-Gomes, M., Niemeyer, D., Jones, T.C., Heinrich, F., Frischbutter, S., Angermair, S., Hohnstein, T., Mattiola, I., Nawrath, P., McEwen, S., Zocche, S., Viviano, E., Heinz, G.A., Maurer, M., Kölsch, U., Chua, R.L., Aschman, T., Meisel, C., Radke, J., Sawitzki, B., Roehmel, J., Allers, K., Moos, V., Schneider, T., Hanitsch, L., Mall, M.A., Conrad, C., Radbruch, H., Duerr, C.U., Trapani, J.A., Marcenaro, E., Kallinich, T., Corman, V.M., Kurth, F., Sander, L.E., Drosten, C., Treskatsch, S., Durek, P., Kruglov, A., Radbruch, A., Mashreghi, M.-F., Diefenbach, A.
Untimely TGFβ responses in COVID-19 limit antiviral functions of NK cells (2021) Nature, 600 (7888), 295–301.
DOI: 10.1038/s41586-021-04142-6

Zaienne, D., Willems, S., Schierle, S., Heering, J., Merk, D.
Development and Profiling of Inverse Agonist Tools for the Neuroprotective Transcription Factor Nurr1 (2021) Journal of medicinal chemistry, 64 (20), 15126–15140.
DOI: 10.1021/acs.jmedchem.1c01077

Zimmermann, W.-H.
Organs-on-chip models for cardiovascular drug development (2021) Cardiovascular research, 117 (12), e164-e165.
DOI: 10.1093/cvr/cvab229

Zuberbier, T., Abdul Latiff, A.H., Abuzakouk, M., Aquilina, S., Asero, R., Baker, D., Ballmer-Weber, B., Bangert, C., Ben-Shoshan, M., Bernstein, J.A., Bindslev-Jensen, C., Brockow, K., Brzoza, Z., Chong Neto, H.J., Church, M.K., Criado, P.R., Danilycheva, I.V., Dressler, C., Ensina, L.F., Fonacier, L., Gaskins, M., Gáspár, K., Gelincik, A., Giménez-Arnau, A., Godse, K., Gonçalo, M., Grattan, C., Grosber, M., Hamelmann, E., Hébert, J., Hide, M., Kaplan, A., Kapp, A., Kessel, A., Kocatürk, E., Kulthanan, K., Larenas-Linnemann, D., Lauerma, A., Leslie, T.A., Magerl, M., Makris, M., Meshkova, R.Y., Metz, M., Micallef, D., Mortz, C.G., Nast, A., Oude-Elberink, H., Pawankar, R., Pigatto, P.D., Ratti Sisa, H., Rojo Gutiérrez, M.I., Saini, S.S., Schmid-Grendelmeier, P., Sekerel, B.E., Siebenhaar, F., Siiskonen, H., Soria, A., Staubach-Renz, P., Stingeni, L., Sussman, G., Szegedi, A., Thomsen, S.F., Vadasz, Z., Vestergaard, C., Wedi, B., Zhao, Z., Maurer, M.
The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria (2021) Allergy, 77 (3), 734–766.
DOI: 10.1111/all.15090



Patents

Patent applications

There were no new patent applications at Fraunhofer ITMP in 2021.

Patents issued

Brüne, Bernhard; Dillmann, Christina; Geisslinger, Gerd; Mora, Javier; Parnham, Michael John; Weigert, Andreas
N-terminally truncated interleukin-38
CN 106661095 A

Brenneis, Christian; Geisslinger, Gerd; Parnham, Michael John; Scholich, Klaus; Sisignano, Marco; Zinn, Sebastian
CYP2J2-hemmende Substanzen als Therapeutika bei Chemotherapie-induzierten neuropathischen Schmerzen
2020-111595; 3632469

Geisslinger, Gerd; Parnham, Michael John; Sisignano, Marco
Oxidized lipids in the treatment of chronic or neuropathic pain
EP 3 207 926 A1

Parnham, Michael John; Sha, Lisa Katharina; von Knethen, Andreas
Rekombinantes B7-H1-Fusionsprotein als Therapiekonzept des multiplen Organversagens bei Sepsis
2018-523483

Beyer, Susanne; Kirsamer, Li; Mäntele, Werner; Parnham, Michael John; Vogel, Vitali; Wacker, Matthias
Composition comprising a biocompatible and biodegradable polymer, nanocarriers and a drug and methods of making and using the same
15/773,696

Geisslinger, Gerd; Hohmann, Stephan; Schiffmann, Susanne; Scholich, Klaus; Sisignano, Marco
Inhibitors of GPR132 for use in preventing and/or treating chemotheraphy-induced neuropathic pain
3515498

Geisslinger, Gerd; Scholich, Klaus; Zinn, Sebastian; de Bruin, Natasja
BLT2 Agonists for the treatment of pain
EP 3 215 146 A1

Bachelor‘s, Master‘s and Doctoral Theses

Doctoral Theses

Khalil Ahmad
Regulation der 5-Lypoxygenase-Genexpression durch MLL, AF4 sowie deren Fusionsproteine MLL•AF4 und AF4•MLL
Johann Wolfgang Goethe-Universität Frankfurt am Main

Moritz Belling
Familiness: A Millstone Around the Firm’s Neck Or a Catalyst for Change?
Technische Universität Berlin

Camilla Brat
Untersuchungen zum Einfluss von Nitrofettsäuren auf das Ubiquitin-Proteasom-System in Tumorzellen
Johann Wolfgang Goethe-Universität Frankfurt am Main

Jennifer Cohnen
The role of lipids in the development of tumor-induced neuropathic pain
Johann Wolfgang Goethe-Universität Frankfurt am Main

Roland Ebert
5-/15-Lipoxigenase interaction as regulatory principle in the lipoxin synthesis during resolution of inflammation
Johann Wolfgang Goethe-Universität Frankfurt am Main

Tom Fiolka
Biorelevant two-stage in vitro tools to evaluate supersaturation and precipitation of weakly basic drugs
Johann Wolfgang Goethe-Universität Frankfurt am Main

Anastasia Geladaris
Exploring the potential of BTKi in models of chronic CNS demyelinating disease
Georg-August-Universität Göttingen

Yana Hackler
Interaktionen von Mastzellen und CD8+ T-Zellen während einer viralen Infektion
Charité - Universitätsmedizin Berlin

Undine Haferkamp
Human iPSC-derived models for central nervous system drug discovery
Universität zu Lübeck

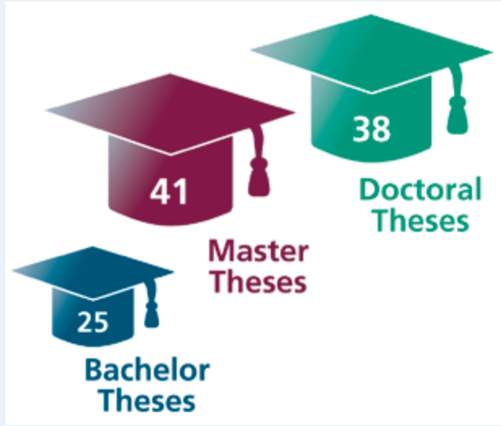
Markus Hartmann
Synthese und biochemische Charakterisierung selektiver Modulatoren der beiden Atg8-Homologen LC3A und LC3B
Johann Wolfgang Goethe-Universität Frankfurt am Main

Nadine Hellmuth
Studies on anti-bacterial and anti-inflammatory effects of endogenous nitro fatty acids and derivatives
Johann Wolfgang Goethe-Universität Frankfurt am Main

Martin Hofsäss
In vitro Release Testing as an Alternative to Establishing Bioequivalence of Drug Products in vivo
Johann Wolfgang Goethe-Universität Frankfurt am Main

Theses 2021 at a glance

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



Bettina Homberg
Regulation of Respiratory Chain Supercomplex Formation and the Involvement of Rcf-proteins
Georg-August-Universität Göttingen

Arnaud Huard
IL-38 as a new regulator of the resolution of inflammation
Johann Wolfgang Goethe-Universität Frankfurt am Main

Whitney Kilu
Establishment of fluorescence based affinity assay systems for the investigation of nuclear receptor dimerization and ligand modulated coregulator recruitment
Johann Wolfgang Goethe-Universität Frankfurt am Main

Lisa Kornstädt
Anti-inflammatory and pro-resolving role of mast cells during resolution of local inflammation
Johann Wolfgang Goethe-Universität Frankfurt am Main

Arne Benjamin Krahn
Über die Differenzierung und Charakterisierung von Kardiomyozyten aus induzierten pluripotenten Stammzellen aus Rhesusmakaken in 2D- und 3D-Kulturen
Georg-August-Universität Göttingen

Felix Lange
Mitochondrial Adaptation at the Neuronal Presynapse
Georg-August-Universität Göttingen

Felix Lillich
Design und Synthese von Multitarget-Lipid-Modulatoren
Johann Wolfgang Goethe-Universität Frankfurt am Main

Yaobin Liu
Function and regulation of novel phospgoribosyl ubiquitination catalyzed by Legionella pneumophila effectors
Johann Wolfgang Goethe-Universität Frankfurt am Main

Arianna Merlini
Characterization of immune responses in the meninges
Georg-August-Universität Göttingen

Jasmin Ochs
Proinflammatory CD20+ T cells: Their origin and therapeutic depletion in CNS-directed autoimmunity
Georg-August-Universität Göttingen

Tabea Osthues
Oxidized lipids and signaling pathways of G2A receptor involved in nerve-injury induced neuropathic pain
Johann Wolfgang Goethe-Universität Frankfurt am Main

Rafael Leal Monteiro Paraiso
A physiologically based biopharmaceutical analysis of zolpidem
Johann Wolfgang Goethe-Universität Frankfurt am Main

Gerlinde Plöger
Optimization of solubility studies performed in the context of BCS biowaiver monographs
Johann Wolfgang Goethe-Universität Frankfurt am Main

Sabine Poerschke
Investigation of mitochondrial ribosome regulators at the inner membrane
Georg-August-Universität Göttingen

Daniel Price
Novel in vitro and in silico tools for the development of mesoporous silica formulations with optimal precipitation inhibitors
Johann Wolfgang Goethe-Universität Frankfurt am Main

Peter Rappl
The role of mPGES-1 in macrophages during resolution of inflammation
Johann Wolfgang Goethe-Universität Frankfurt am Main

Vittoria Rimola
Neuronal Changes in Oxaliplatin-Induced Acute Peripheral Pain
Johann Wolfgang Goethe-Universität Frankfurt am Main

Christian Ringel
S1PR4-dependent CCL2 production promotes macrophage recruitment in psoriasis
Johann Wolfgang Goethe-Universität Frankfurt am Main

Nina Ariane Schröter
Identification and mitigation of novel reactive organic chemicals during processing of viopharmaceuticals
Johann Wolfgang Goethe-Universität Frankfurt am Main

Mina Shahriyari
Engineered skeletal muscle from human pluripotent stem cells to model muscle disease and regeneration
Georg-August-Universität Göttingen

Evelyn Sirait
Strategies for Sensitizing Tumors to Anti-PD1 Immune Checkpoint Blockade
Johann Wolfgang Goethe-Universität Frankfurt am Main

Jannik Stemler
Einfluss von Einzelzimmer-Kontaktisolierungsmaßnahmen auf nosokomiale Übertragung von Vancomycin-resistenten Enterokokken
Universität zu Köln

Elisabeth Strack
Characterization of myeloid cell populations in human mammary carcinoma
Johann Wolfgang Goethe-Universität Frankfurt am Main

Tatjana Ullmann
Screening for CEBPD-Modulating Compounds Using a THP-1-Derived Reporter Cell Line in the Context of Rheumatoid Arthritis
Johann Wolfgang Goethe-Universität Frankfurt am Main

Zhao Wang
The MRGPRX2-dependent pseudo-allergic/neurogenic route in human skin mast cells: functional programs, signal transduction, and regulation by cytokines
Charité - Universitätsmedizin Berlin

Xin You
The role of interleukin 38 (IL-38) in inflammatory colon carcinogenesis
Johann Wolfgang Goethe-Universität Frankfurt am Main

Networks in Science and Industry

International activities and cooperations 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 2021, 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, and the Senckenberg Biodiversity and Climate Research Center.

In addition, there are cooperations with several international universities such as the University of Florida, the University of Maryland, the Universities of Cork, the University of Southern Denmark, the National and Kapodistrian University of Athens and the National University of Ireland, Galway.

Teaching activities

PD Dr. Frank Behrens is Assistant Professor and lecturer for Internal Medicine 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.

Dr. Natasja de Bruin holds seminars at the University Hospital Frankfurt am Main, the Frankfurt International Research School for Translational Biomedicine (FIRST) and the “Donders Institute for Brain, Cognition and Behaviour” at the Radboud University (Nijmegen, Netherlands).

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 holds seminars and internships in the model course in Medicine 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.

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.

Dr. Martine Hofmann gives lectures for the graduate academy of the Goethe University and teaches in the FELASA module of Molecular Medicine at Goethe University Frankfurt am Main.

Prof. Dr. Stefan Jakobs iis 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 gives lectures and holds seminars in general and clinical pharmacology at Goethe University Frankfurt am Main and the University of Heidelberg, and in translational medical research at the Medical Faculty Mannheim, University of Heidelberg. He is a private lecturer at the Goethe University Frankfurt am Main (transfer of Habilitation in 2021).

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 at University Hospital Frankfurt am Main and holds seminars and courses in Internal Medicine.

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.

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.

Dr. Otto Quintus Russe is the academic director of the Master of Pharma Business Administration at Goethe University Frankfurt am Main.

Dr. Stephan Schäfer holds seminars in Clinical Pharmacology at the Faculty of Medicine at the University Hospital Frankfurt am Main.

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. 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 at Goethe University Frankfurt am Main and leads a series of training courses for in-service training of doctors with recognition by the LÄK (Landesärztekammer). LÄK (Landesärztekammer).

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.

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.

Memberships in Editorial Boards and Committees

Scientific Journals

Amino Acids
Editorial Board: Dr. Robert Gurke

Antioxidants
Editorial Board: Prof. Dr. Andreas von Knethen

Basic Research in Cardiology
Editorial Board: Prof. Dr. Wolfram-Hubertus Zimmermann

Biological Chemistry
Editorial Board: Prof. Dr. Bernhard Brüne

Cancers
Editorial Board: Prof. Dr. Sabine Grösch

Cardiovascular Research
Associate Editor: Prof. Dr. Wolfram-Hubertus Zimmermann

Circulation Research
Editorial Board: Prof. Dr. Wolfram-Hubertus Zimmermann

Cells
Guest Editors: Prof. Dr. Ellen Niederberger, Prof. Dr. Björn Windshügel

Current Research in Drug Discovery
Editorial Board: Dr. Sheraz Gul

Clinical Trials in Degenerative Diseases (CTDD)
Editorial Board: Dr. Stephanie Dauth

Dissolution Technologies
Editorial Board: Prof. Dr. Jennifer Dressman

Drug Target Review
Scientific Contributing Editor: Dr. Sheraz Gul

European Journal of Pharmaceutical Sciences
Editorial Board: Prof. Dr. Jennifer Dressman

European Journal of Pharmaceutics and Biopharmaceutics
Editorial Board: Prof. Dr. Jennifer Dressman

European Pharmaceutical Review
Editorial Board: Dr. Sheraz Gul

Frontiers in Chemistry
Guest Associate Editor: Dr. Sheraz Gul

Frontiers in Immunology
Guest Associate Editor: Prof. Dr. Andreas von Knethen

Frontiers in Pharmacology
Editor in Chief: Prof. Dr. Dieter Steinhilber
Editorial Board: Prof. Dr. Sabine Grösch
Review Editor: Prof. Dr. Andreas von Knethen

International Journal of Molecular Sciences
Editorial Board: Prof. Dr. Andreas von Knethen

Journal of Mass Spectrometry & Advances in the Clinical Lab
Editorial Board: Dr. Robert Gurke

Journal of Medicinal Chemistry
Editorial Advisory Board: Prof. Dr. Eugen Proschak

Journal of Molecular and Cellular Cardiology
Associate Editor: Prof. Dr. Wolfram-Hubertus Zimmermann

Journal of Pharmaceutical Sciences
Editorial Board: Prof. Dr. Jennifer Dressman

Journal of Pharmacy and Pharmacology
Associate Editor: Prof. Dr. Jennifer Dressman

Methods and Applications in Fluorescence
Editorial Board: Prof. Dr. Stefan Jakobs

Neuropediatrics
Editorial Board: Prof. Dr. Jutta Gärtner

Nutrients
Guest Editor: Dr. Natasja de Bruin

Pharmacological Research
Editorial Board: Prof. Dr. Bernhard Brüne

PLoS ONE, Public Library of Science
Editorial Board: Prof. Dr. Dieter Steinhilber

Regenerative Therapy
Editorial Board: Prof. Dr. Wolfram-Hubertus Zimmermann

Scientific Report
Editorial Board: PD Dr. Susanne Schiffmann

Zeitschrift für Rheumatologie
Editorial Board: Prof. Dr. Harald Burkhardt

Committees

Altmetric
Ambassador: Dr. Sheraz Gul

Ausschuss Bewertungsverfahren der Deutschen Gesellschaft für Kardiologie (DGK)
Prof. Dr. Wolfram-Hubertus Zimmermann

Ausschuss für Innovation, Handelskammer Hamburg
Prof. Dr. Carsten Claussen

Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)
Member "Kommission für Arzneimittel für Kinder und Jugendliche (KAKJ)": Prof. Jutta Gärtner

Bundesvereinigung Deutscher Apothekerverbände e. V
Member of the ABDA Digital Hub: Dr. Otto Quintus Russee

Certara L.P.
Scientific Advisory Board of Simcyp: Prof. Dr. Jennifer Dressman

Deutsche Gesellschaft für Infektiologie (DGI)
Board member: Prof. Dr. Maria Vehreschild

Deutsche Gesellschaft für Kinder- und Jugendmedizin (DGKJ)
Chair of the University Commission: Prof. Jutta Gärtner

Deutsche Gesellschaft für Rheumatologie
Speaker Working Group NIS PAS: PD Dr. Frank Behrens

Deutsches Zentrum für Herzkreislaufforschung (DZHK)
Speaker Göttingen site and member Research Coordinating Committee: Prof. Dr. Wolfram-Hubertus Zimmermann

DFG, Fachkollegium, Medizin, Sektion Entzündungsforschung
Prof. Dr. Dr. Gerd Geißlinger

DFG Programm »Clinician Scientist«
Spokesperson for the focus neuroscience: Prof. Dr. Martin Weber

Dutch NeuroFederation
Dr. Natasja de Bruin

EARTO European Association of Research & Technology Organizations
Member of WG Healthtech: Dr. Mira Grättinger

ECNP, European College of Neuropsychopharmacology & Preclinical Data Forum Network
Dr. Natasja de Bruin

ESGHAMI Studiengruppe für Wirts- und Mikrobiotain-teraktionen der ESCMID (European Society of Infectious Diseases)
Treasurer: Prof. Dr. Maria Vehreschild

ETH Review Panel (Department of Chemistry and Applied Biosciences)
Prof. Dr. Jennifer Dressman

Ethikkommission Universitätsmedizin Göttingen
Member: Prof. Dr. Martin Weber

EU COST Actions CM1406 and CA15135 German Management Committee
Substitute: Dr. Sheraz Gul

EU OPENSCREEN Operational Management Board
Member: Dr Philip Gribbon

EU OPENSCREEN Partner Site Forum
Chair: Dr Philip Gribbon

European Federation for Pharmaceutical Sciences
President: Prof. Dr. Dieter Steinhilber

Fakultätsrat der Universitätsmedizin Göttingen
Prof. Dr. Wolfram-Hubertus Zimmermann

FENS Federation of European Neuroscience Societies
Dr. Natasja de Bruin

Forschungskommission der Universitätsmedizin Göttingen
Prof. Dr. Wolfram-Hubertus Zimmermann, Prof. Dr. Stefan Jakobs

Forschungskommission des Fachbereichs Medizin der Goethe-Universität
Prof. Dr. Dr. Gerd Geißlinger

Forschungsrat der Goethe-Universität
Prof. Dr. Dr. Gerd Geißlinger

Forum »Gesundheitsforschung« des BMBF
Prof. Dr. Dr. Gerd Geißlinger

Frankfurt Rhein Main GmbH
Advisory Board: Dr. Otto Quintus Russe

Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD
Board of Directors (Spokesperson):
Prof. Dr. Dr. Gerd Geißlinger
Board of Directors (Scientific Coordinator):
PD Dr. Frank Behrens

Fraunhofer Strategie-Kommission Gesundheitsforschung
Prof. Dr. Dr. Gerd Geißlinger

Freundlich-Stiftung
Board of Trustees: Prof. Dr. Bernhard Brüne

Gesellschaft für Virologie e.V.
Board member: Prof. Dr. Sandra Ciesek

Gesundheitsforschungsbeauftragter der Fraunhofer-Gesellschaft
Prof. Dr. Dr. Gerd Geißlinger

GRADE-Vorstand der Goethe-Universität Frankfurt
Board member: Prof. Dr. Bernhard Brüne

Hochschulforum der Hamburger Wirtschaft
Prof. Dr. Carsten Claussen

House of Pharma and Healthcare
Board members: Prof. Dr. Dr. Gerd Geißlinger, PD Dr. Frank Behrens

IBWF (Institut Für Biotechnologie und Wirkstofffor-schung), Mainz
Chair of the Board of Trustees: Prof. Dr. Bernhard Brüne

Industrial Quality and Productivity Centre (IQPC)
Pharmaceutical Advisory Board: Dr. Sheraz Gul

Initiative Gesundheitsindustrie Hessen
Member of the Steering Committee: Prof. Dr. Dr. Gerd Geißlinger

International Lipidomics Society
Dr. Robert Gurke

International Society for Stem Cell Research (ISSCR)
Vice Chairman of the International Committee: Dr. Ole Pless

Kaertor Foundation, Galicia Spain
Expert Advisor for the Drug Discovery portfolio: Dr. Philip Gribbon

Kompetenznetz Multiple Sclerose (KKNMS)
Mitglied Fachausschuss Daten-, Biomaterialverwertung, Ethik und Datenschutz (FaBIO): Prof. Martin S. Weber

Ksilink
Board of Directors: Prof. Dr. Wolfram-Hubertus Zimmermann

Landesapothekerkammer Hessen
Board and delegate: Dr. Otto Quintus Russe

Leadership Committee of the Basic Cardiovascular Research Council, American Heart Association (AHA)
European Liaison: Prof. Dr. Wolfram-Hubertus Zimmermann

Life Science Nord e.V.
Authorized representative member: Dr. Mira Grättinger

LOEWE-Zentrum TBG
Member of the Steering Committee: Prof. Dr. Dr. Gerd Geißlinger

Merck
Advisory Board Member "Cladribine" and "Evobrutinib"; Steering Committee Member "Evobrutinib Phase II + III": Prof. Martin S. Weber

Nationale Akademie der Wissenschaften Leopoldina
Member and elected member of Presidium Class III (Medicine): Prof. Dr. Jutta Gärtner

Novartis
Advisory Board Member "Siponimod": Prof. Martin S. Weber

Paul Ehrlich Gesellschaft (PEG)
Advisory Board Member: Prof. Dr. Maria Vehreschild

Pharmadialog der Bundesregierung
Member: Prof. Dr. Dr. Gerd Geißlinger

Roche
Advisory Board Member "Ocrelizumab"; Steering Committee Member "Fenebrutinib phase III": Prof. Martin S. Weber

Science Fund of the Republic of Serbia
Project Peer Reviewer, Dr. Sheraz Gul

Senatskommission für Forschung und Transfer
Prof. Dr. Bernhard Brüne

Senatskommission für Third Mission
Prof. Dr. Bernhard Brüne

Society for Laboratory Automation and Screening
Elected fellow and member of the "Advocacy Committee": Dr. Philip Gribbon
Member of the Strategic Relations Council: Dr. Sheraz Gul

Stiftung für Unternehmensrecht an der Heinrich Heine Universität Düsseldorf
Member of the Board of Trustees: Prof. Dr. Carsten Claussen

Stiftungsrat der Dr. Robert Pfleger Stiftung
Prof. Dr. Dr. Gerd Geißlinger

Stiftungsrat der Freundlich-Stiftung
Prof. Dr. Dr. Gerd Geißlinger

The Chemical Probes Portal
Scientific Advisory Board Member: Dr. Sheraz Gul

Tierethikkommission Regierungspräsidium Darmstadt
Dr. Martine Hofmann

Transcriptogen Ltd.
Scientific Co-Founder: Dr. Sheraz Gul

VIB Screening Core, Belgium
Advisory Board Member: Dr. Sheraz Gul

Von-Behring-Röntgen-Stiftung
Member and Scientific Advisory Board: Prof. Dr. Jutta Gärtner

Zentrale Ethik-Kommission für Stammzellforschung (ZES)
Prof. Dr. Wolfram-Hubertus Zimmermann

Organization of Scientific Meetings and Courses

Strategic Entrepreneurship and Innovation Research Seminar - Goethe University Frankfurt & TU Darmstadt
January 2021 and May 2021; Member of the Organization Committee: Prof. Dr. Lars Schweizer

Regional Contest Jugend forscht Hamburg Volkspark
Hamburg, February10-11, 2021; Organisational representative: Dr. Mira Grättinger

Drug Discovery Workshop Series – ITN-DRIVE
Virtual, lectures on March 26, April 2, April 9, and April 16,2021; organized by Dr. Sheraz Gul

Fraunhofer CIMD 4D-Workshop "Visual Computing in Medicine"
Virtual, May 10-11, 2021; organized by Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD and Fraunhofer Institute for Computer Graphics Research IGD

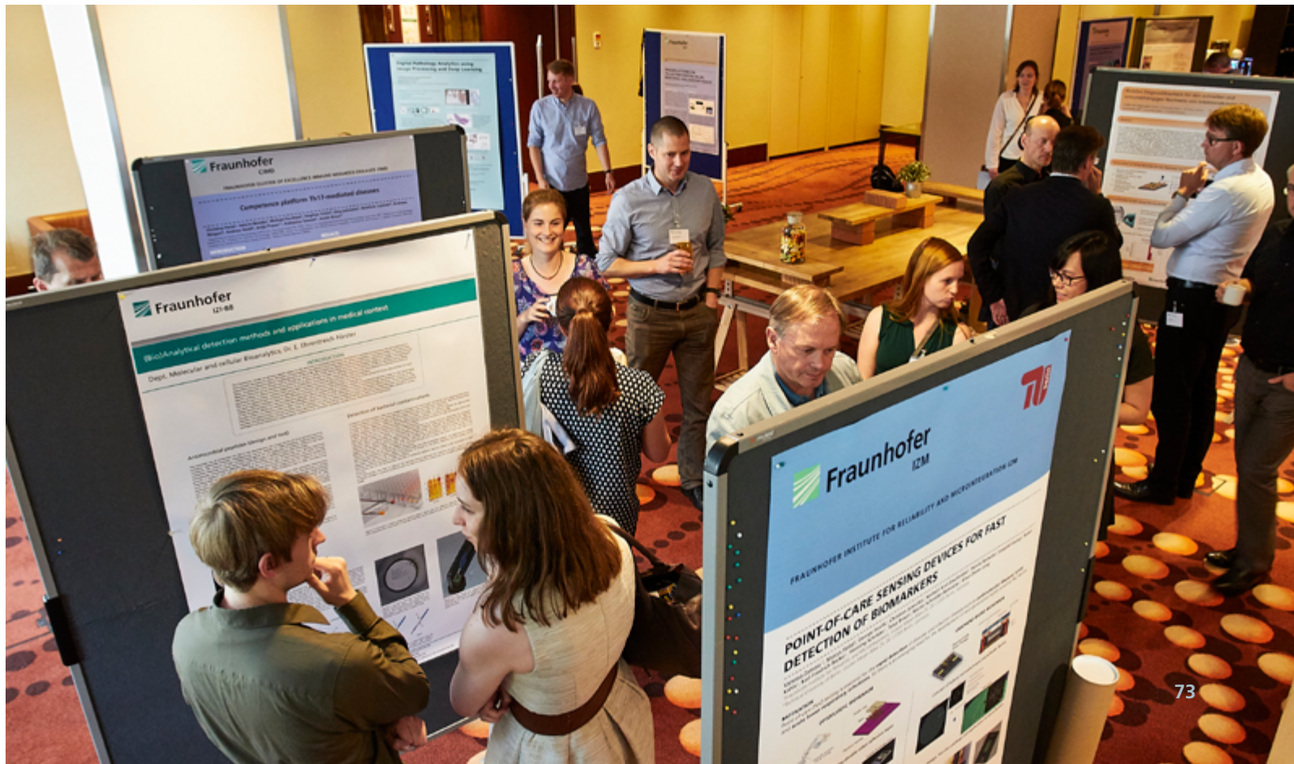
Basic Cardiovascular Research Conference, American Heart Association (AHA)
Virtuel, May 17-20, 2021; member of the organization committee: Prof. Dr. Wolfram-Hubertus Zimmermann

Fraunhofer CIMD Winter School
Virtual, October 5-8, 2021; organized by Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

Excellence Course SPA Psoriasis Arthritis and Axial Spondlyoarthritis
Rhein-Main Lufthansa Trainingscenter, October 7-9, 2021; organization: PD Dr. Frank Behrens and Dr. Michaela Köhm

Day of Immune Research 2021
Virtual, November 12, 202; organized by Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

Fraunhofer CIMD 4D-Workshop "Drug Discovery"
Virtual, December 14, 2021; organized by Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD and Fraunhofer Institute for Translational Medicine and Pharmacology ITMP



Editorial Notes

Publisher

Fraunhofer Institute for Translational Medicine and Pharmacology ITMP

Prof. Dr. Dr. Gerd Geisslinger

Theodor-Stern-Kai 7
60596 Frankfurt am Main
Germany

Editorial Team
Dr. Alena Wötzel
Dr. Mira Grättinger

Translation proofreading
Katarina Stevanovic
Dr. Sheraz Gul

Coordination and Design
Dr. Alena Wötzel

Reporting Period
January 1 to December 31, 2021

Further information on projects, technologies and competencies as well as contact details of our institute can be found in German and English on the internet at:
www.itmp.fraunhofer.de/en.html

Photo acknowledgements

Cover: wörner traxler richter planungsgesellschaft mbh

p. 4/5: MEV-Verlag

p. 6/7: wörner traxler richter planungsgesellschaft mbh

p. 8: Fraunhofer ITMP | Alena Wötzel

p. 9 l.: Fraunhofer ITMP | Bernd Müller

p. 9 m. : Fraunhofer ITMP | Mike Schmidt

p. 9 r.: iStock | ipopba

p. 10/11: Fraunhofer ITMP | Alena Wötzel

p. 13: Fraunhofer | Markus Jürgens

p. 15: both Fraunhofer ITMP | Jürgen Lecher

p. 16/17: MEV-Verlag

p. 18: Fraunhofer IZM | Manuel Seckel

p. 19: iStock | sefa ozel

p. 20: Fraunhofer ITMP | Samuel Rischke

p. 21: Fraunhofer ITMP | Bernd Müller

p. 22/23: MEV-Verlag

p. 24: Fraunhofer ITMP | Christian Brüser

p. 25: Fraunhofer ITMP | Peter Ilgen

p. 26/27: MEV-Verlag

p. 28: both Fraunhofer ITMP | Martin Kunze

p. 29: Fraunhofer ITMP | Perspektive Media

p. 30: both Fraunhofer ITMP | Perspektive Media

p. 28: Source: www.exscalate-4cov.eu/index.html

p. 32/33: iStock | pinkomolet

p. 34: iStock | herraez

p. 35: Cell Press, Elsevier Ltd. 2021

p. 36: DESY | Sebastian Günther

p. 37: iStock | Ivan-balvan

p. 38/39: Fraunhofer CIMD | Jürgen Lecher

p. 40 l.: Universitätsklinikum Frankfurt | Ellen Lewis

p. 40 r.: Fraunhofer ITMP

p. 41 l.: Fraunhofer ITMP | Lea Komm

p. 41 r.: Fraunhofer ITMP | Jürgen Lecher

p. 42 l.: Fraunhofer ITMP

p. 42 r.: FBRI

p. 43 l.: Fraunhofer CIMD | Stephanie Dauth

p. 43 r.: Fraunhofer ITMP | Martin Kunze

p. 44/45: MEV-Verlag

p. 46: Fraunhofer ITMP | Alena Wötzel

p. 51: MEV-Verlag

p. 54: MEV-Verlag

p. 59: MEV-Verlag

p. 60: Fraunhofer ITMP | Alena Wötzel

p. 62: Fraunhofer ITMP | Alena Wötzel

p. 64: MEV-Verlag

p. 65: MEV-Verlag

p. 66: Fraunhofer ITMP | Alena Wötzel

p. 69: iStock | pinkomolet

p. 73: Fraunhofer CIMD | Jürgen Lecher