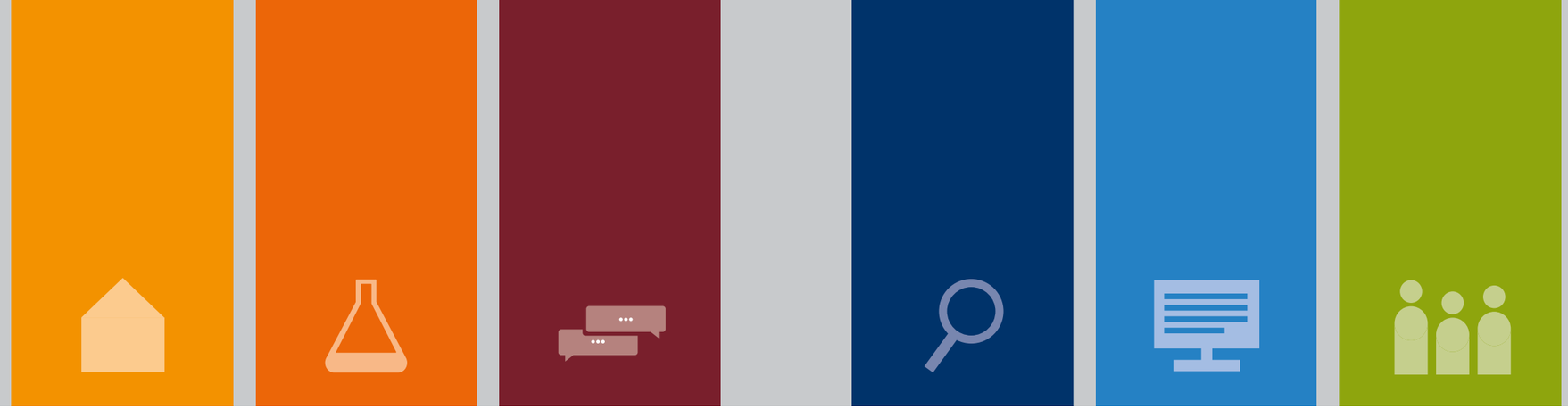
Fraunhofer

IME

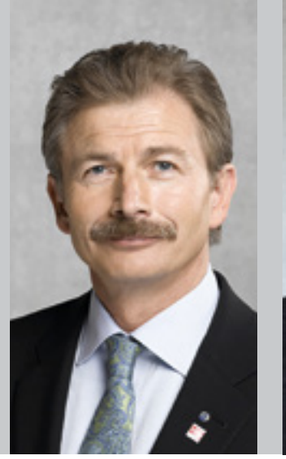
FRAUNHOFER INSTITUTE FOR MOLECULAR BIOLOGY AND APPLIED ECOLOGY IME

ANNUAL REPORT 2018

YOUNG SCIENTISTS FOR CURRENT AND FUTURE RESEARCH



WELCOME



In 2018, we continued working towards an ambitious goal: to extend scientific boundaries and develop innovative solutions for a healthy and sustainable future. This was the focus of all three of our institute divisions - Molecular Biotechnology, Applied Ecology and Bioresources, and Translational Medicine - at six locations in Germany. Our success in this area is underscored by the ongoing high level of support for our applied research from public funding agencies and companies.

Our colleagues of the Translational Medicine Division in Frankfurt, for example, continued to develop the strategic positioning and profile of the Fraunhofer-Gesellschaft in health research, and succeeded in many competitive funding applications. One of the highlights was the success in the proof-of-concept initiative for the clinical development of the second proprietary drug candidate TMP-002 for the treatment of chemotherapy-induced neuropathic pain. As part of the approved MED²ICIN lighthouse project, our locations in Frankfurt and Hamburg, in cooperation with other Fraunhofer Institutes, are positioning themselves within the growing market of artificial intelligence and machine learning for the development of a digital patient model, ultimately aiming to sustainably reduce health expenditure in Germany. The Fraunhofer Cluster of Excellence CIMD was established as a virtual institute that combines the interdisciplinary competence of the participating institutes in order to develop innovative therapies for immune-mediated diseases. Furthermore, in cooperation with industrial partners, multicenter interventional clinical trials with medicinal products in which Fraunhofer acts as sponsor were initiated in various indication areas. We also focused on further medical education activities, such as the certified Excellence Workshop "Psoriasis-Arthritis and Axial Spondarthritis", and workshops in the field of nanoformulation.

For the Molecular Biotechnology Division in Münster, the success story "Rubber from dandelion" continues. In June, the University of Münster awarded the transfer prize 2017/2018 for the "TARAXAGUMT" project to Prof. Dr. Dirk Prüfer and his team in cooperation with Continental Reifen Deutschland GmbH, and at the end of the year Continental inaugurated the "Taraxagum Lab Anklam". In cooperation with WWU Münster, the plant breeding company ESKUSA, Continental Reifen GmbH Germany and the Julius Kühn Institute, Dirk Prüfer and his team domesticated the Russian dandelion, converting it from a wild species to a crop plant within a few years. In Aachen, we advanced a novel cell-free expression platform which outperforms all current commercial systems based on eukaryotic cells, and is now marketed by a start-up company. We also focused on promoting our young researchers, encouraging them to take on important roles in a variety of projects, e.g. the establishment of a new rapid assay to detect cholera toxins, and an alternative strategy for the purification of monoclonal antibodies.

For the Applied Ecology and Bioresources division, 2018 was a year of large-scale construction in Schmallenberg and Gießen. Despite the extensive construction, the turnover and staff numbers in Schmallenberg continued to grow in 2018, with high levels of funding from industry sources. We expanded our research and development in the area of international guidelines. Under the leadership of the Fraunhofer IME, we began to validate new OECD guidelines for chronic fish toxicity (Zebrafish Extended One Generation Reproduction Test) and for an alternative test method for bioaccumulation (Hyalella Bioconcentration Test), and also conducted ring tests for the "transpiration stream concentration factor", and we continued to adapt OECD guidelines for the testing of nanomaterials. Our colleagues in Gießen further expanded their leading role in the field of insect biotechnology by acquiring industrial projects in the globally prospering field of insect farming for the production of proteins. They also established a German strain collection for biological plant protection, specifically identifying new insect pathogens and developing them for applications in the biological control of insect pests and vector insects. At Justus-Liebig University Gießen, the world's first Master's course in "Insect Biotechnology and Bioresources" was established. Prof. Dr. Marc Schetelig, who leads a Fraunhofer Attract group at Fraunhofer IME Gießen, was appointed professor of insect biotechnology in crop protection at Justus-Liebig University.

This year we are focusing on our junior researchers in the report section. With a view to the future, the promotion of young scientists is a high priority for us at Fraunhofer IME. Our young scientists make a substantial contribution to knowledge and innovation in our institute. The following articles illustrate the strength of our scientific and methodological expertise in a broad spectrum of life sciences research. Let us arouse your curiosity and inspire you by showcasing the work of our junior researchers in the three institute divisions.
Finally, we wish to thank all those who, through their continued commitment and support, have contributed to our success in 2018. We are most grateful to our business and research partners for their excellent and dependable cooperation, and to our staff for their dedication.
We wish everyone involved an equally successful year in 2019.

Frankfurt am Main, Schmallenberg and Aachen, March 2019

Prof. Dr. Dr. Gerd Geißlinger Prof. Dr. Christoph Schäfers Prof. Dr. Stefan Schillberg

THE INSTITUTE

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The institute at Schmallenberg was integrated into the Fraunhofer-Gesellschaft in 1959. Visualization of the new building.

FRAUNHOFER IME PROFILE

Since the beginning of 2017, Fraunhofer IME has comprised the three divisions of Molecular Biotechnology, Applied Ecology and Bioresources, and Translational Medicine. On July 1, 2018, the Executive Board of the Fraunhofer-Gesellschaft appointed Prof. Dr. Dr. Gerd Geißlinger as the Executive Director of Fraunhofer IME. He had been Acting Executive Director since January 2017. Prof. Dr. Schillberg and Prof. Dr. Schäfers will remain as acting members of the institute management.

Fraunhofer IME is a strong partner for contract research in the areas of pharmaceuticals, medicine, chemicals, the bioeconomy and agriculture, as well as environmental and consumer protection. Our research and development portfolio focuses on industry, small and medium enterprises and on the public sector. In 2018, Fraunhofer IME collaborated with more than 100 national and international industrial clients and several international industrial associations, for whom confidential projects were conducted.

Our interdisciplinary organization allows us to integrate expertise in relevant scientific disciplines covering all three areas, in cooperation with external institutions and partners if required, providing a basis for the successful completion of complex projects. Our work is closely linked with basic research and we benefit from large international networks. Our laboratories, with state-of-the-art equipment including GMP facilities and complex facilities for environmental simulations, allow a wide spectrum of research and development services.

At the end of 2018, the institute employed 534 personnel working at the Aachen, Münster, Schmallenberg, Gießen, Frankfurt and Hamburg locations. We have close ties with the Department of Biology and Biotechnology of Plants at the University of Münster, the Institute for Clinical Pharmacology at Goethe University, Frankfurt, the Department of Applied Entomology at the Justus-Liebig University Gießen, and the world's first Institute for Insect Biotechnology, founded in Gießen in 2016. We cooperate with many international research partners and remain in close contact with universities and other research organizations. Our aim is to recognize trends and developments as they emerge, and to develop and implement novel research strategies and technologies.

Molecular Biotechnology

Molecular Biotechnology is the basis of a modern bioeconomy and contributes sustainably to the knowledge-based production and industrial use of renewable raw materials. On behalf of our customers, the Molecular Biotechnology Division develops tailored plants, animal cells and microbes for applications such as the production of food and renewable raw materials, the manufacture of technical and pharmaceutical proteins, and the handling of anthropogenic pollutants including greenhouse gases, which we can exploit to produce valuable substances. In recent years, we have established ourselves successfully in the research landscape and on the market due to our synergistic activities in the fields of green and white biotechnology. We offer our partners in academia, industry and the regulatory authorities a comprehensive research and service portfolio.

Applied Ecology and Bioresources

We develop experimental and model-based methods for the assessment of risks to ecosystems posed by potentially hazardous substances, as well as for the analysis of consumer exposure to such substances within the environment. We often act as scientific mediators between commercial producers and the regulatory authorities. Another focal point of our work is the identification of active substances from bioresources such as plants, microbes and insects, plus the development of concepts for the sustainable agricultural production of active substances from plants. We also develop biological and biotechnological methods for the control of pest and vector insects and utilize insects to generate protein from organic waste.

Translational Medicine

Translational Medicine contributes steadily and substantially to the development of new approaches for the diagnosis and treatment of diseases that are inadequately understood or controlled. The field of translational medicine spans the value chain, from target identification through active agent screening and translational preclinical validation to clinical trials. One research focus is the repositioning of known active agents within the disease areas of pain, rheumatoid arthritis, sepsis, multiple sclerosis and inflammation. We offer a specialized spectrum of disease models as well as highly sensitive analysis, bioinformatics and biomarker platforms. Our clinical trials follow quality-by-design standards to reduce attrition rates and generate as much scientifically relevant information as possible.

Symbol used in the annual report

MB Division
Molecular Biotechnology

AE BR Division
Applied Ecology and Bioresources

TM Division
Translational Medicine

FRAUNHOFER IME WITHIN THE FRAUNHOFER-GESELLSCHAFT

The Fraunhofer-Gesellschaft is the leading organization for applied research in Europe, conducting research at 72 institutes and research units at locations throughout Germany. The Fraunhofer-Gesellschaft employs about 26,600 personnel working with an annual research budget of 2.6 billion euros, more than 2.2 billion euros of which is generated through contract research. Around 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. International collaborations with excellent research partners and innovative companies around the world ensure direct access to regions with the greatest importance for current and future scientific progress and economic development.

Fraunhofer institutes working in related subject areas cooperate as larger groups to promote collaboration in related disciplines and offer customers a unique source of coordinated joint services. Currently, there are eight such groups, representing different areas of the research and development market. They contribute to the corporate policy and implementation of the Fraunhofer-Gesellschaft's functional and financing model. Fraunhofer IME is part of the Fraunhofer Group for Life Sciences, a scientific and technological organization of highly qualified experts from the key areas of modern life sciences with the business fields Medical Translational Research and Biomedical Technology, Regenerative Medicine, Healthy Foods, The New Potential of Biotechnology, and Process, Chemical, and Pesticide Safety.

The Fraunhofer Group for Life Sciences includes six Fraunhofer Institutes as well as one Fraunhofer research institution. Since February 2017, Prof. Horst-Christian Langowski (Fraunhofer Institute for Process Engineering and Packaging IVV) has been the Chairman with Prof. Krug (Fraunhofer Institute for Toxicology and Experimental Medicine ITEM) serving as deputy.

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

Institutes or institute departments with complementary expertise cooperate in Fraunhofer Alliances to facilitate customer access to the services and research capability of the Fraunhofer-Gesellschaft. They provide expert advice on complex issues and coordinate the development of appropriate solutions. Fraunhofer IME is involved in two alliances:

Big Data: http://www.bigdata.fraunhofer.de/en.html
Food Chain Management: https://www.fcm.fraunhofer.de/en.html

The Fraunhofer-Gesellschaft strives to promote and implement sustainable development, and the Fraunhofer Sustainability Network actively supports this goal. At the forefront of this approach is a stronger linking of both the research topics and the personnel who have a close connection with sustainability. In this manner, Fraunhofer aims to make its research more efficient while taking account of the growing complexity of research in the context of sustainable development.

https://www.fraunhofer.de/en/about-fraunhofer/corporate-responsibility.html

ADVISORY BOARD

Advisory Board members advise the Fraunhofer-Gesellschaft as well as the individual institutes and promote their connection to partners from industry, science and the public sector.

In 2018, the following representatives from government, industry and academia were members of the Fraunhofer IME Advisory Board:

Dr. Harald Seulberger (Chairman)
BASF SE, Limburgerhof

Dr. Carl Bulich
German Plant Breeders' Association, Bonn

Dr. Friedrich Dechet
Industrial Association Agrar, Frankfurt am Main

Prof. Dr. Adolf Eisenträger
German Federal Environment Agency, Dessau-Roßlau

Dr. Gerhard Görlitz
Bayer CropScience AG, Monheim

Prof. Dr. Heyo Kroemer
Georg-August-Universität Göttingen

Prof. Dr. Roland Kubiak
RLP AgroScience GmbH, Neustadt a. d. Weinstraße

Ministerialrätin Andrea Noske
Federal Ministry of Education and Research, Berlin

Dr. Dr. Christian Patermann
Formerly Director Directorate General for Research and Innovation of the European Commission, Bonn

Prof. Dr. Joachim Schiemann
Federal Research Centre for Cultivated Plants Julius Kühn-Institut, Braunschweig

Dr. Karin Schlesier
German Federal Institute for Risk Assessment, Berlin

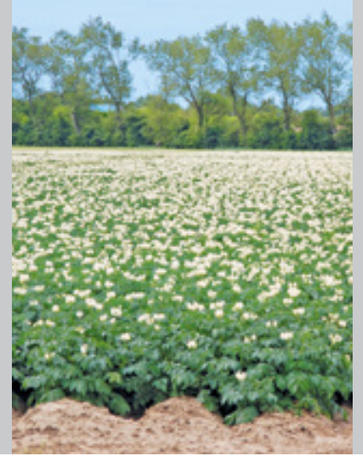
Prof. Dr.-Ing. Ernst Schmachtenberg
Rector of RWTH Aachen University

Prof. Dr. Angelika Vollmar
Ludwig-Maximilians-Universität München

Dr. Hans-Ulrich Wiese
Formerly member of the Executive Board of Fraunhofer (permanent guest)

The annual meeting of the Advisory Board was held on May the 3rd, 2018, at the Fraunhofer IME in Aachen. The Executive Board of the Fraunhofer-Gesellschaft was represented by Prof. Dr. Alexander Kurz.

BUSINESS FIELDS MOLECULAR BIOTECHNOLOGY



Bioproduction and Industrial Biotechnology

The business field Bioproduction and Industrial Biotechnology focuses on the identification, sustainable production, processing and optimization of high-value natural compounds, including chemical building blocks, bio based fuels, fine chemicals, biomaterials and proteins for industrial applications and consumer products. This can be produced using a diverse array of organisms, from microorganisms and plant cells through to animal cells.
Here the value chain is covered: from target discovery and screening, the development and optimization of production strains and the transfer of laboratory-scale processes to scale up and pilot-scale manufacturing for future industrial production and downstream processes, including the evaluation of economic feasibility.
Fraunhofer IME provides comprehensive expertise in the development of innovative biotechnology platforms and optimized processes. The departments and project groups involved cover a range of different product types, from bulk chemicals and fuels such as isopropanol, isoprene and hexanol, through to plant-based metabolites and polymers such as rubber, inulin, cellulose and industrial starches, and high-value fine chemicals, proteins and industrial enzymes.

Agroscience for Food and Feed

The business field Agroscience for Food and Feed covers the agricultural value chain "from farm to fork" and focuses on the development and improvement of plant traits, crops and enabling technologies to increase the biomass of crops, the quality and yield of agricultural products, the ability of plants to grow in diverse environments, and to withstand pests and diseases. These traits are developed using both genetic modification (GM) and non-GM approaches, and key technologies such as genome editing and TILLING.
The departments and project groups involved in this business field focus on precision breeding techniques and the development and testing of GM crops. Based on this wide-ranging expertise, Fraunhofer IME acts as a preferred partner for academic laboratories, SMEs and major agribusiness companies.

Production of Recombinant Proteins

Fraunhofer IME offers expertise in all aspects of the design, production, purification and characterization of recombinant proteins, including process development and scale-up from a laboratory process to the manufacture of kilograms of clinical material under GMP conditions. Different systems are available for the production of specific protein products, involving microorganisms, plant cells, animal cells and whole plants as well as cell-free expression systems. There has been a recent increase in the demand for recombinant proteins produced at the kilogram scale for the pharmaceutical, agriculture and cosmetic sectors, and for technological applications. In addition, the institute has its own new protein candidates in the pipeline, particularly technical enzymes, foodstuff proteins, diagnostic reagents and therapeutic proteins.

Molecular Biotechnology: Research, Development and Services

www.ime.fraunhofer.de/en/MB/RDS

MB

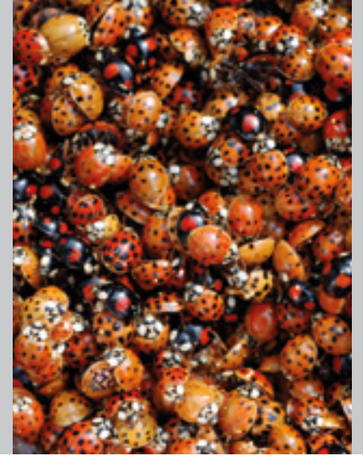
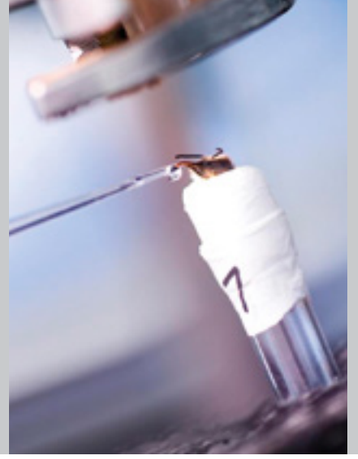
Prof. Dr. Stefan Schillberg
stefan.schillberg@ime.fraunhofer.de

MB

Prof. Dr. Dirk Prüfer
dirk.pruefer@ime.fraunhofer.de

BUSINESS FIELDS APPLIED ECOLOGY AND BIORESOURCES



Environmental Risk Assessment of Substances

We use our expertise in environmental analysis, experimental environmental chemistry and ecotoxicology, and modeling the bioaccumulation and effects of substances, to assess the risks such substances pose to the environment. We liaise with the regulatory authorities to formulate critical questions and draw up test guidelines to address these risks. On behalf of our partners in industry, we perform and evaluate complex experimental and model-based studies to the highest scientific standards. We use the analysis and classification of molecular mechanisms as screening tools to assess the environmental impact of candidate products. We manage the national Environmental Specimen Bank and perform environmental monitoring projects to identify potential environmental pollutants and check prospective assessments.

Food Safety and Quality

The safety and quality of food depend on the production method and on the primary and further processing of agricultural raw materials. We focus on the qualitative properties of raw materials and foods, and the damage caused by harmful substances. For example, we take existing methods used to analyze the metabolism of plant protection products in crops and farm animals and adapt them to study the metabolism of veterinary pharmaceuticals and feed supplements, and we develop cell-based alternatives to animal testing. We track breakdown and conversion products by radioactive labeling throughout the food production cycle. As part of the Fraunhofer Food Chain Management Alliance, we are developing rapid analytical techniques to monitor the food chain. Aroma research combined with geographical information systems has highlighted links between cultivation conditions and the quality of raw foodstuffs.

Sustainable Agricultural Production of Substances

We use local factors such as soil quality, microclimate and infrastructure to assess the potential of agricultural areas for specific uses. We consider both structural and material determinants in such evaluations, combining species range maps from nature protection agencies with probabilistic risk assessments for plant protection products and veterinary pharmaceuticals based on geographical information systems (see our business field “Environmental Risk Assessment of Substances”). We compare the economic potential of different value chains in order to achieve a sustainable bioeconomy. Ecological and social considerations can be reinforced through differentiated and targeted subsidies. Our main goal is to achieve the agricultural production of useful active substances.

Bioresources for the Bioeconomy

We use groups of organisms with great biodiversity as bioresources, including insects, bacteria and fungi. We combine innovative technologies and established platforms to isolate and characterize natural substances, and to evaluate their potential for use in medicine, plant protection and industrial biotechnology. In this way, novel molecules are identified to develop as antibiotics or ingredients for the food and feed industry, such as flavoring agents, preservatives and enzymes, leading to novel applications and value chains. The Sanofi-Fraunhofer Natural Product Research Center, which houses the world’s largest industrial collection of microbial strains, is available for projects with other industrial partners in pre-competitive areas of research.

Insect Biotechnology

The development and application of insect biotechnology allows us to use insects, insect-derived molecules, cells or organs, and insect-associated microbes as products or systems for diverse applications in medicine, industrial biotechnology, and the food and feed industry. We also exploit insect cells as protein expression systems and insect antennae as biosensors for drugs and explosives. Furthermore, we develop insect models for toxicology studies and use biotechnology to control pest and vector insects, for example RNA interference and the sterile insect technique. We also use insects for the conversion of organic waste into proteins and fats for the food and feed industry.

Applied Ecology and Bioresources: Research, Development and Services

www.ime.fraunhofer.de/en/AEBR/RDS

Dr. Dieter Hennecke
dieter.hennecke@ime.fraunhofer.de

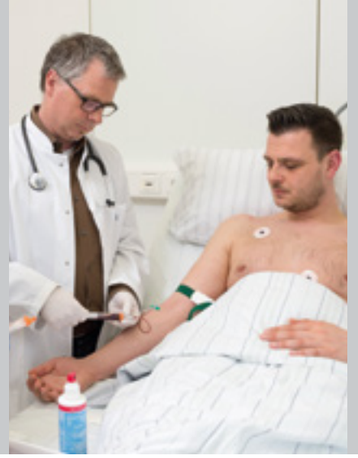
Prof. Dr. Mark Bücking
mark.buecking@ime.fraunhofer.de

Prof. Dr. Christoph Schäfers
christoph.schaefers@ime.fraunhofer.de

Prof. Dr. Andreas Vilcinskas
andreas.vilcinskas@ime.fraunhofer.de

Prof. Dr.-Ing. Peter Czermak
peter.czermak@ime.fraunhofer.de

BUSINESS FIELDS TRANSLATIONAL MEDICINE



Screening and Bioinformatics

The business field Screening and Bioinformatics uses automated procedures to identify new leads for defined therapeutic targets. The three-dimensional structure of lead molecules holds the key to understanding their function and the development of new active compounds. Our customer service includes the development, validation and implementation of biological screening assays for known and new targets. We have access to libraries comprising more than 500,000 compounds. Furthermore, using bioinformatics techniques, we can identify new active chemicals in virtual libraries. Our range of services is completed by the medicinal-chemical approaches needed for substance optimization and preclinical testing using in vitro and in vivo models.

TM

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

Translational Compound Validation

The business field Translational Compound Validation aims to develop differentiated translational disease models, measurement techniques, technologies and imaging procedures for early assessment of the efficacy and safety of active compounds. In addition to cell-based and cell-free systems, we also conduct experiments on rodents. Our range of models is far wider than the standard spectrum offered by commercial suppliers and thus allows detailed, mechanism-based research. The following platforms are available to our customers: preclinical disease models, epigenetics and optogenetics, biomedical analysis, protein engineering, predictive clinico-pharmacological models, data bionics, pharmaceutical technology and human pain models.

TM

Prof. Dr. Michael J. Parnham
michael.parnham@ime.fraunhofer.de

Medical Data Space

In terms of translational medicine, Fraunhofer IME Hamburg facility played the leading role in the establishment of the Fraunhofer “Medical Data Space”. Modeled on the basic functionalities offered by the “Industrial Data Space”, the Medical Data Space offers decentralized data management for medical bioinformatics – a service concept allowing autonomous and secure data storage as well as data exchange between networked databases. Fraunhofer IME Branch Lab ScreeningPort in Hamburg has applied this expertise in bioinformatics and has set up the Data Scientist for a number of projects, including the joint development of Fraunhofer IME products and services and, on a European scale, in collaboration with the Innovative Medicines Initiative. In this manner, the Hamburg laboratories contribute significantly to the digitization of pharmaceutical research.

TM

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

Clinical Research

Clinical research is the decisive step in the development of new discoveries in the life sciences for use in humans. We offer our customers the essential elements needed for successful clinical trials, including the definition of appropriate scientific hypotheses and the patient groups and subgroups to be treated, combined with an individual, adaptive study design, employing the latest statistical and biomedical analysis. The new Quality by Design approach implemented at our Frankfurt location addresses the complex challenges posed by clinical trials in an attempt to reduce exclusion rates. The combination of excellent study design and expertise in specific indications is a unique characteristic of this group.

TM

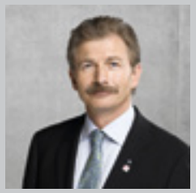
Dr. Frank Behrens
frank.behrens@ime.fraunhofer.de

Translational Medicine: Research, Development and Services

www.ime.fraunhofer.de/en/TM/RDS

INSTITUTE MANAGEMENT AND LOCATIONS

31.12.2018



Executive Director
Prof. Dr. Dr. Gerd Geißlinger
Phone +49 69 6301-7619
gerd.geisslinger@ime.fraunhofer.de

Members of the Institute Management acting
Prof. Dr. Christoph Schäfers and
Prof. Dr. Stefan Schillberg

Head of Administration
Dietmar Douven
Phone +49 241 6085-11030
dietmar.douven@ime.fraunhofer.de

MOLECULAR BIOTECHNOLOGY DIVISION

Head: Prof. Dr. Stefan Schillberg

Aachen

Molecular Biotechnology
Prof. Dr. Stefan Schillberg
Phone +49 241 6085-11050
stefan.schillberg@ime.fraunhofer.de

Industrial Biotechnology
Dr. Stefan Jennewein
Phone +49 241 6085-12120
stefan.jennewein@ime.fraunhofer.de

Integrated Production Platforms
Dr. Dr.-Ing. Johannes Buyel
Phone + 49 241 6085-13162
johannes.buyel@ime.fraunhofer.de

Integrated Production Platforms
Dr. Jürgen Drossard
Phone + 49 241 6085-13060
juergen.drossard@ime.fraunhofer.de

Münster

Functional and Applied Genomics
Prof. Dr. Dirk Prüfer
Phone +49 251 8322-302
dirk.pruefer@ime.fraunhofer.de

Plant Biotechnology
Dr. Stefan Rasche
Phone +49 241 6085-12321
stefan.rasche@ime.fraunhofer.de

Plant Biotechnology
Holger Spiegel
Phone +49 241 6085-12461
holger.spiegel@ime.fraunhofer.de

APPLIED ECOLOGY AND BIORESOURCES DIVISION

Head: Prof. Dr. Christoph Schäfers

Schmallenberg

Applied Ecology
Prof. Dr. Christoph Schäfers
Phone +49 2972 302-270
christoph.schaefers@ime.fraunhofer.de

Ecotoxicology
Dr. Elke Eilebrecht
Phone +49 2972 302-144
elke.eilebrecht@ime.fraunhofer.de

Ecotoxicology
Matthias Teigeler
Phone +49 2972 302-163
matthias.teigeler@ime.fraunhofer.de

Environmental and Food Analysis
Prof. Dr. Mark Bücking
Phone +49 2972 032-304
mark.buecking@ime.fraunhofer.de

Ecological Chemistry
Dr. Dieter Hennecke
Phone + 49 2972 302-209
dieter.hennecke@ime.fraunhofer.de

Gießen

Bioresources
Prof. Dr. Andreas Vilcinskas
Phone +49 641 9939-500
andreas.vilcinskas@ime.fraunhofer.de

Bioaccumulation and Animal Metabolism
Prof. Dr. Christian Schlechtriem
Phone +49 2972 302-186
christian.schlechtriem@ime.fraunhofer.de

Environmental Specimen Bank and Elemental Analysis
Dr. Heinz Rüdel
Phone +49 2972 302-301
heinz.ruedel@ime.fraunhofer.de

Quality Assurance
Dr. Cornelia Bernhardt
Phone + 49 972 032-137
cornelia.bernhardt@ime.fraunhofer.de

TRANSLATIONAL MEDICINE DIVISION

Head: Prof. Dr. Dr. Gerd Geißlinger

Frankfurt am Main

Biomedical Analytics and Imaging
Prof. Dr. Dr. Gerd Geißlinger
Phone +49 69 6301-7619
gerd.geisslinger@ime.fraunhofer.de

Drug Research and Formulation
Prof. Dr. Dieter Steinhilber
Phone +49 69 798-29324
dieter.steinhilber@ime.fraunhofer.de

Translational Drug Validation
Prof. Dr. Michael J. Parnham
Phone + 49 69 8700-25071
michael.parnham@ime.fraunhofer.de

Clinical Research
Dr. Frank Behrens
Phone + 49 69 6301-7302
frank.behrens@ime.fraunhofer.de

Hamburg

Digital Health Research
Prof. Dr. Carsten Claussen
Phone +49 40 303764-277
carsten.claussen@ime.fraunhofer.de

Drug Discovery
Dr. Philip Gribbon
Phone +49 40 303764-271
philip.gribbon@ime.fraunhofer.de

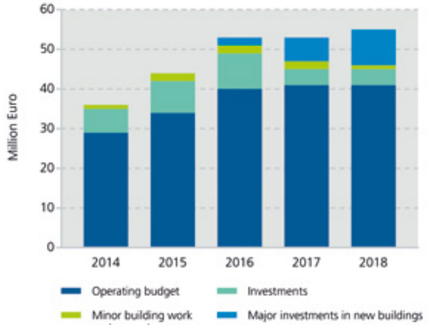
Assay Platforms
Dr. Ole Pless
Phone + 49 241 6085-13162
ole.pless@ime.fraunhofer.de

INSTITUTE DATA

Budget

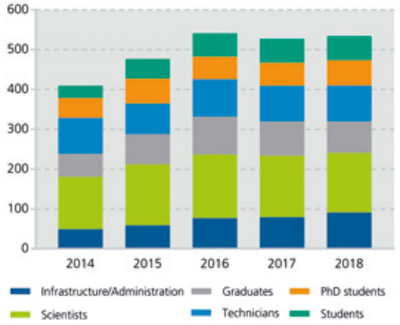
In 2018, the Fraunhofer IME operating budget increased by two percent compared to 2017, reaching 41.1 million euros. A further 3.5 million euros was invested in equipment. Once again, there was a marked increase in Fraunhofer IME building activity (10.6 million euros), the main projects being construction work on the new institute facilities in Gießen and Schmallenberg.
The budget included 71.1 percent from external revenues, equivalent to 81.3 percent when the largely state-funded locations in Gießen and Frankfurt are taken into account.
Industry revenues increased once again, reaching 14.9 million euros. This represents 47.8 percent of total revenues or 36.1 percent when Gießen and Frankfurt are included.
Fraunhofer IME has thus achieved an excellent outcome for the year 2018 in terms of key performance figures for the Fraunhofer-Gesellschaft.

Total budget of Fraunhofer IME



External financing of Fraunhofer IME

Employees of Fraunhofer IME

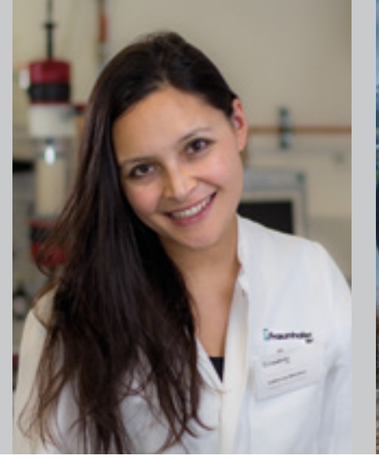


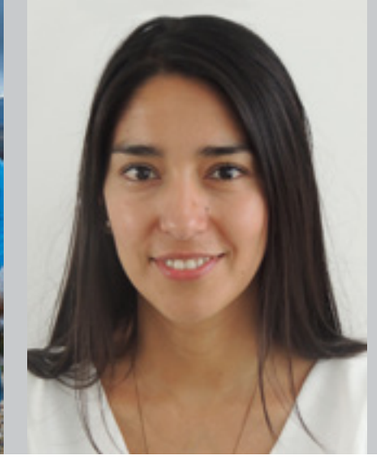
Personnel

At the end of 2018, 534 personnel were employed at the Fraunhofer IME locations in Aachen, Münster, Schmallenberg, Gießen, Frankfurt am Main and Hamburg. This is an increase of 1.3 percent on last year's figures.

In 2018, 53.2 percent of Fraunhofer IME personnel were female.

YOUNG SCIENTISTS FOR CURRENT AND FUTURE RESEARCH





The nurturing of young scientists is a high priority for us at the Fraunhofer IME with a view to the future. Well-qualified young scientists are needed to sustain our competitive research and innovation potential. Young scientists make a significant contribution to knowledge and innovation at our institute. As an internationally active institute, we offer attractive projects for young scientists from all over the world, who in turn enrich all aspects of our research and development activities. As well as promoting young scientists, who are directly embedded in our everyday research activities, Fraunhofer IME employees are strongly involved in teaching duties at our partner universities.

The Fraunhofer IME currently focuses on promoting the activities of two key groups of young researchers: Master's and doctoral students.

Fraunhofer IME Master Class

The Fraunhofer IME Master Class started in January 2018. To promote the Master's students, the Fraunhofer IME supports early involvement in application-oriented research projects, participation in external and internal workshops such as Drug Discovery, Translational Medicine, and Design of Experiments. In addition, we offer insights into everyday professional life in the Fraunhofer IME Career Insights network. As part of the network, Master's students exchange ideas with our researchers, project managers, and group and department heads. They are committed to providing young researchers with advice and support for the next stages of career planning. We also enable selected, excellent young researchers to actively participate in scientific congresses.

www.ime.fraunhofer.de/en/MasterClass

PhD with Fraunhofer IME

Doctoral training is a key strategy for the promotion of young scientists. We strive to achieve the highest quality of doctoral training and thus strengthen the competitiveness of our young scientists. By linking doctoral topics with publicly or privately funded research projects, doctoral students at Fraunhofer IME can look at scientific questions from an application-oriented perspective.
Some students undertaking the experimental part of their doctoral research at the Fraunhofer IME are involved in the structured doctoral programs of the partner universities, e.g. the graduate school Translational Research Innovation Pharma - TRIP in Frankfurt am Main.
In Aachen, the PhD coordinator, workers' council and institute management developed their own program. Its modules regulate the interaction between doctoral students and the supervision team to the mutual benefit of both parties. Important core elements include professional quality, scientific independence, and transparent mentoring. The PhD outline during this qualification phase is the common thread. The PhD students develop their outline before the experimental work begins, and it is revisited at regular intervals together with the supervisory team. The students unanimously consider this structural element as hard work, but very useful. The cross-departmental exchange of knowledge and ideas takes place at the annual PhD conference: During the discussions, doctoral students receive valuable tips and suggestions for their research.

www.ime.fraunhofer.de/en/PhD

The nurturing of young scientists is an important task for the Fraunhofer-Gesellschaft. In addition to a wide range of continuing education programs, there are also specific concepts to promote the development of young scientists.

Young Research Class

Space for creative ideas, co-designing Fraunhofer-Gesellschaft strategic research topics, and building networks across institute boundaries - these are central elements of the Young Research Class. This two-year career program combines the development of original research ideas with networking across hierarchies, disciplines and institutes. Scientists who have recently completed or will soon complete their PhD are eligible to participate.

The key theme in 2018 was biological transformation. Catherine Müschen, a doctoral student in Aachen, is enthusiastic because she gained one of the much sought-after places. In an interdisciplinary team of four, she developed the project idea "In silico-driven bioprocesses", which she presented to the President of the Fraunhofer-Gesellschaft, Prof. Dr.-Ing. Reimund Neugebauer, and the Think Tank, in autumn 2018. In the meantime, the project has been approved and experimental work at the Fraunhofer Institutes for Building Physics IBP, for Integrated Circuits IIS, for Industrial Mathematics ITWM and Fraunhofer IME is about to begin. For Catherine Müschen, the Young Research Class is a wonderful opportunity to apply for projects and carry them out independently. In her own words: "The networking and exchange of experience in the Young Research Class allows me to look beyond the horizon of biotechnology and also provides insights into selected Fraunhofer institutes."

Fraunhofer Attract

The Fraunhofer Attract grant offers outstanding external scientists an opportunity to develop their ideas towards real applications within an optimally-equipped Fraunhofer institute operating close to the market.
For a period of five years, the scientists have a maximum budget of 2.5 million euros to establish and lead a group.

In 2018, four Attract groups were active at the Fraunhofer IME. In Gießen, Prof. Dr. Marc Schetelig initiated the project "*Drosophila suzukii* – environmentally friendly pest control for the Spotted Wing Drosophila". In Aachen, Dr. Dr.-Ing. Johannes Buyel and his team are working on the project "FAST-PEP - an innovative and integrated approach to rational bioprocess development". Dr. Philip Känel in Münster developed the project "Longaevitas - PEBPs as a link in cross-species ageing research". Finally the Eco'n'OMICs project was established by our latest Attract candidate Dr. Sebastian Eilebrecht, and started in mid-2018 in Schmallenberg (p. 49).

TALENTA

The Fraunhofer-Gesellschaft is committed to attracting more women to applied research. The comprehensive TALENTA program for female scientists was developed for women at various career levels.
TALENTA start is a program for university graduates, who receive helpful orientation advice at the beginning of their applied research careers and further assistance to strengthen their interdisciplinary skills.
TALENTA speed up is tailored for Fraunhofer internal and external scientists with professional experience who would like to take on responsibility in a management or specialist position. They receive tailor-made offers to further qualify themselves and thus accelerate their careers.

In Schmallenberg, Dr. Cecilia Diaz participates in the TALENTA speed up program. "TALENTA enabled me to establish a new field of research with my working group after completing my doctoral thesis," she says. "The available leadership training supported me in this task, and participation in conferences helped me to form a network with other experts. The financial resources associated with TALENTA gave me the freedom to initiate scientific developments in this new field with the necessary creativity."

OUR RESEARCH

Crystal structure reveals insights into a plant mechanoprotein

Volatile chemicals: New test setup provides reliable biodegradation data

A new model system to study urinary tract infections

The eye as the window to the nervous system

Detecting microbial toxins in food using nanoprobes

Stem cell laboratory: Operation around the clock

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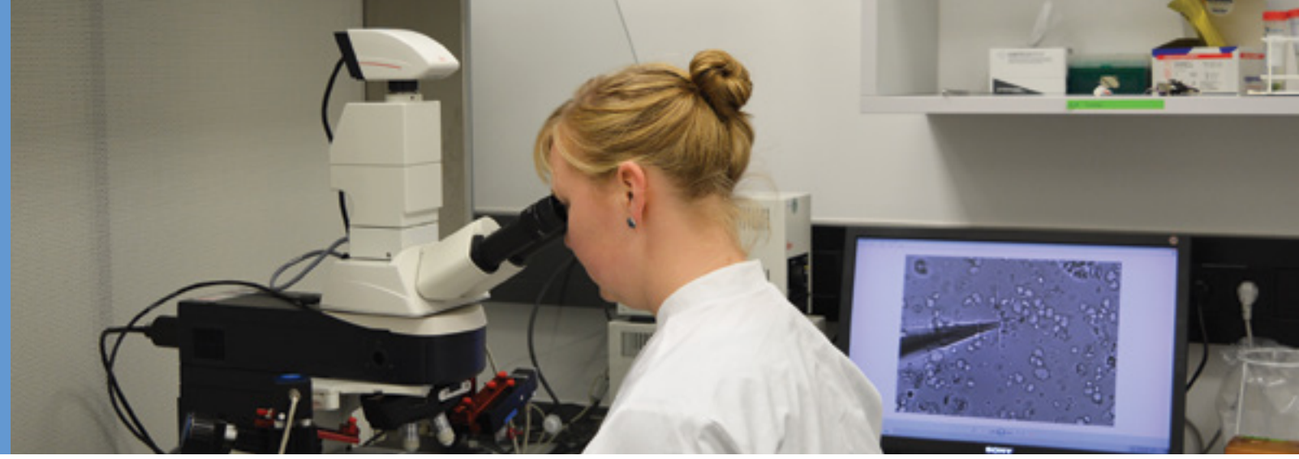
Our junior researchers work on projects from different areas of the life sciences – here are some examples.

CRYSTAL STRUCTURE REVEALS INSIGHTS INTO A PLANT MECHANOPROTEIN



Forisome's size and compactness make them visible even at low magnification in a light microscope.

Forisomes are gigantic protein complexes, comprising millions of monomers, which undergo reversible conformational changes between an elongated spindle and a thickened plug. By unlocking molecular mechanisms underlying this process, we have recently generated initial data on the crystal structure of forisome proteins.

Forisomes - multitalented complexes for biotechnology

In some plant species, forisomes help to close wounds in the tubular phloem tissue that transports sugars. Damaged phloem is plugged in milliseconds, thus preventing the loss of the nutrient-rich sap. The initially long, thin spindle thickens and shortens to a plug, accompanied by a six-fold increase in volume, thereby filling the diameter of the sieve tubes. This reversible process is triggered by calcium ions and requires no additional energy source, such as adenosine triphosphate. In vitro experiments have shown that forisomes can undergo more than 5000 shape change cycles. They generate a mechanical force of 0.1 N and are therefore unique plant mechanoproteins.

In vitro, we can also trigger forisomes to change shape by shifting the pH to a non-physiological value, allowing forisomes to be controlled by electro-titration. An American-German team subsequently demonstrated the use of forisomes as valves in microfluidic channels.

Interestingly, forisomes can also be produced and genetically modified in non-plant systems such as the yeast *Saccharomyces cerevisiae*. This allowed us to develop enzyme-coated forisomes, known as forizymes.

Forisomes already offer a wide range of biotechnological applications, and their potential is far from exhausted.

Protein structure as the key to understanding function

Forisomes possess a combination of fascinating properties. The range of applications could be extended greatly if characteristics such as size, shape change or force generation could be adjusted precisely. But to make this work, we need a deeper understanding of the underlying molecular mechanisms.

Physical experiments and microscopy demonstrated that forisomes consist of longitudinally arranged fibers, which in turn consist of bundles of fine fibrils. This implies a highly ordered and multi-layered complex based on chemical interactions between the individual building blocks, the protein monomers. Which interactions are involved, how the precise arrangement of the monomers is controlled and how the shape of the complex changes is still not understood. Thus far, we know that the increase in the concentration of calcium ions in the protein body leads to the influx of water and thus to the formation of the plug due to swelling. However, forisomes do not possess any of the known calcium-binding sites, so we can only speculate about how calcium triggers the swelling process.

We are convinced that these essential questions can be answered by the detailed elucidation of the structure of the protein monomers. This will explain how, and via which substructures, the monomers interact with each other, allowing us to build models of the forisomes complex formation. In addition, the crystal structure may explain how calcium influences the shape change, allowing us to formulate hypotheses to control the size or shape change in an application-adapted manner.

Protein interactions and the formation of proteinaceous super-complexes are of interest not only with respect to forisomes, but also in many other fields of biology and biotechnology. Given that forisomes are unique in size as protein complexes, and that there is no information about the diversity of protein interactions in similar complex systems, the structural elucidation of forisomes would provide general insights into molecular interactions and would support the development of new proteins for specific applications.

Structure elucidation requires scientific cooperation

The structure of proteins can be solved using the tools of structural biology, but this is a discipline requiring dedicated experts to generate useful data. Fortunately, our proposal was accepted and we will be supported by the EU-funded consortium iNEXT, which aims to give scientists from all over Europe access to state-of-the-art structural biology techniques and the specialists at various research institutions.

Solving the structure of forisome proteins first requires the production of a protein crystal. For this purpose, large quantities of the protein monomer must be generated, and this has required many years of optimization. In current experimental approaches, we are attempting to produce a crystal using various buffer substances and incubation conditions, similar to the cultivation of salt crystals. The crystal is then exposed to X-rays, which causes it to disintegrate but reveal its structure in a radiation pattern.

There are several critical steps on the way to solving the crystal structure of a protein. The cooperation with the iNEXT partners of the Netherlands Cancer Institute (Amsterdam) and the EMBL (Hamburg and Grenoble) enabled us to generate the first protein crystals for X-ray analysis.

These are the first important results on the way to the complete decoding of the underlying mechanisms that make forisomes unique.

MB

Judith Rose, PhD student
judith.rose@ime.fraunhofer.de

VOLATILE CHEMICALS: NEW TEST SETUP PROVIDES RELIABLE BIODEGRADATION DATA

Standard flow-through setup for biodegradation testing.

Standard biodegradation tests are used to obtain degradation half-life data of chemicals required for various regulatory purposes. However, existing standard biodegradation tests are not applicable for testing volatile chemicals. Therefore, an alternative test setup along with data handling measures has been developed at Fraunhofer IME.

Various organic chemicals resulting from human activities and use find their way into different environmental compartments such as soil, water bodies or sediment. To assess accumulation over time it is necessary to know, if, and how fast these chemicals are degraded. Chemicals that do not degrade within a certain time span are called "persistent". These chemicals might become a problem as they may cause adverse effects to organisms over long-term exposure. Particularly, persistent volatile chemicals have a tendency to be transported over long distances, ending up far away from their point of release. This can result in the contamination of pristine environments such as the Arctic and the Himalayas. In order to restrict and control the use of persistent chemicals, criteria were introduced based on degradation half-life cut-off values in different environmental compartments.

Common approach: Standard biodegradation testing

Normally, biodegradation data required for regulatory purposes are obtained using laboratory biodegradation tests following standard OECD guidelines. A tiered testing strategy is applied, starting with simple tests followed by more complex testing if the triggers are exceeded in the simple tests. At the highest tier simulation tests are performed that try to mimic environmental conditions in a standard laboratory setup. Respective guidelines are: OECD 307 (Aerobic and Anaerobic Transformation in Soil), OECD 308 (Aerobic and Anaerobic Transformation in Aquatic Sediment Systems), and OECD 309 (Aerobic Mineralization in Surface Water – Simulation Biodegradation Test).

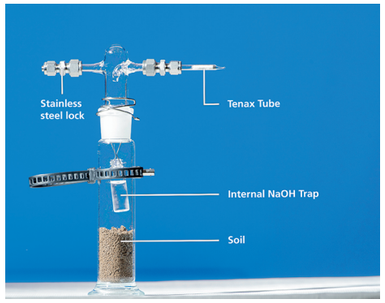
Testing biodegradation of volatile chemicals: A technical challenge

The above-mentioned test guidelines were originally developed and are extensively used in the framework of pesticide regulation. In these guidelines it is explicitly mentioned that they are unsuitable for testing highly volatile chemicals. As the guidelines are now adopted by further regulations such as REACH (EU regulation for industrial chemicals) that cover also highly volatile chemicals, alternative tests are urgently needed.

The major issues while testing volatile chemicals is the loss of the test chemical, which can be falsely interpreted as degradation. The standard guidelines recommend a closed flask test setup for testing slightly volatile chemicals. However, specific guidance on maintaining and measuring aerobic conditions during the test is not given, though the assay might run for up to 120 days (OECD 307). Additionally, the current models for generating degradation kinetics do not consider the influence of volatilization. Neglecting volatilization, however, might lead to overestimation of the degradation kinetics, finally resulting in false persistency assessment.

Biodegradation of volatile chemicals in soil: Improved test setup provides reliable data

We performed a series of preliminary tests for soil degradation studies (OECD 307) to develop an improved closed flask test setup. It comprised of a plastic-free test design with an internal trap for capturing mineralized and volatilized product and was combined with regular oxygen monitoring by using an optical oxygen measurement without the need to open the test flask. Using this test setup, we performed a full-scale OECD 307 test applying two ^{14}C-labelled volatile chemicals across four different types of soil.



Improved closed setup for testing volatile chemicals in soil (Shrestha et al. 2018).

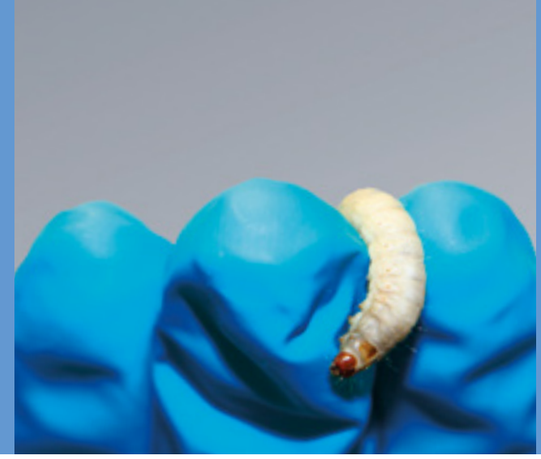
Our preliminary test series also revealed the significance of headspace volume. If a major drop in the O_2 saturation below 15% occurred, samples were re-oxygenated to achieve initial conditions of 20%. This demonstrates that measurement and maintenance of aerobic condition in a closed test setup is possible and even necessary when using organic co-solvent for application without evaporation. Furthermore, a complete mass balance could be attained even for highly volatile test chemicals. With the advantage of using ^{14}C-labelled chemicals, we could clearly distinguish between different competing processes such as volatilization, sorption and degradation which led to a better understanding of the underlying processes.

Prasit Shrestha: "Volatilization of chemicals was highly influenced by sorption to the organic carbon in the different soils. The volatilized fraction of both tested chemicals was not bioavailable for degradation in our test setup. Based on these results, Dr. Michael Klein, our modelling expert, developed an extended model considering volatilization as an additional sink in our system. The data estimated by the model were cross-compared with the observed data showing a very good fit."

With the use of the improved test setup together with the application of the extended model, it is possible to separate volatilization kinetics from the degradation kinetics. This is an important step in the field of persistency assessment of volatile chemicals. So far, we have applied the improved test setup in the context of soil degradation. Currently we are trying to apply similar test setup principles to the other OECD simulation tests (OECD 308: water/sediment, OECD 309: surface water, and additionally to the OECD 314B: Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater – Biodegradation in Activated Sludge Test).

Prasit Shrestha, PhD student
prasit.shrestha@ime.fraunhofer.de

A NEW MODEL SYSTEM TO STUDY URINARY TRACT INFECTIONS



Injection of uropathogenic E. coli into Galleria larvae.

With an annual total of 150 million affected people, urinary tract infections are a major public health challenge. The main causes are uropathogenic *Escherichia coli* with multi-resistant properties. The larvae of the greater wax moth *Galleria mellonella* are an ideal model system for studying the mode of action of urinary tract infections.

Urinary tract infections are the second most common type of infectious disease, accounting for 25% of all infections. The health burden for the German health system associated with urinary tract infections exceeds 1.5 billion euros per year. The serious consequences often include recurrent urinary tract infections, sepsis, premature births and complications due to the frequent use of antibiotics. The increasing abundance of antibiotic-resistant bacteria causing urinary tract infections will limit the effectiveness of our current antibiotic arsenal in the years to come.
A recent study shows that multi-resistant bacteria cause an average of 33,000 deaths per year in the EU. *E. coli*, the main cause of urinary tract infections, are gram-negative bacteria belonging to Enterobacteriaceae. According to the World Health Organization, these are among the 12 bacterial groups for which new antibiotics are most urgently needed. The continuing emergence of such bacterial strains emphasizes the need for a better understanding of these infections and the development of new therapeutic strategies. An example of a novel approach is the use of antimicrobial peptides from insects.

Galleria larvae as an alternative animal model

For the investigation of the mechanisms of this infection a suitable animal model is needed. Of interest is the effect of a urinary tract infection on the innate immune system, as this question is difficult to examine in the traditional mouse model. One reason is the close communication between the innate and adaptive immune system in mammals.

Insects do not possess an adaptive immune system, thus allowing a direct tracking of the innate immune response. The innate immune system of insects and mammals has many similarities in its mode of action. The study of pathogens in *Galleria* larvae can therefore lead to new insights which can be transferred to the functioning of the mammalian system.

The greatest advantage of this new model system is the housing temperature of 37 °C, which corresponds to the optimum ambient temperature of the pathogen and the human body temperature. Further advantages are the small size, the low cost compared to the mouse and rat models and their ethical acceptability.

Small excursion: Uropathogenic *E. coli*

E. coli is an essential component of the human intestinal flora without harming the host. However, there are also pathogenic strains that are among the most common causes of human infectious diseases and can cause different clinical symptoms. We distinguish uropathogenic *E. coli* strains from "normal" *E. coli* strains on the basis of pathogen-associated genes. These genes contain virulence factors such as hemolysin or fimbriae for adhesion to the bladder mucosa. These enable *E. coli* to colonize the "sterile" urogenital tract, preventing host defense and damaging host tissue. In addition, they can form biofilms which complicate treatment measures.

Theory in practice: Manipulation of the innate immune system by *E. coli*

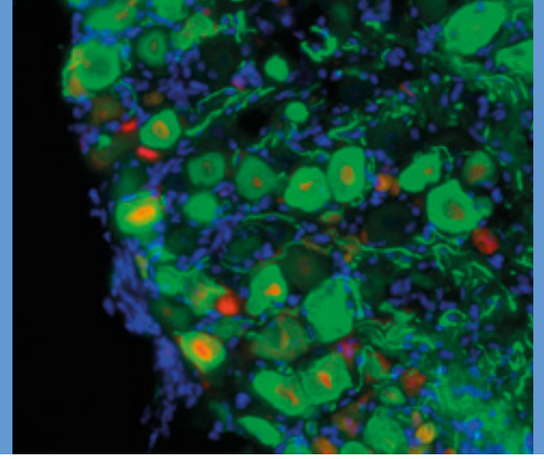
The specific genes of the innate immune system are encoded in the DNA and are exposed to various environmental influences, such as infections. In the case of a urinary tract infection, the genes for the innate immune response are activated. The activation/inactivation of the gene is controlled, among others, by epigenetic mechanisms, such as DNA methylation and histone acetylation. The release of toxins by pathogens can specifically influence these signaling pathways and block the innate immune response.

In order to determine whether altered epigenetic mechanisms cause the different behavior of pathogenic and "normal" bacteria, we infected Galleria larvae with different *E. coli* strains. In addition to viability of the infected wax moths, we studied the genes of the innate immune system and the results were bioinformatically analyzed. The characterization of infected larvae shows strain-specific variations in the class and expression level of genes encoding for antimicrobial peptides, cytokines and enzymes for DNA methylation and histone acetylation. Our results provide evidence for the differentiated epigenetic regulation of the innate immune system by different *E. coli* strains in Galleria larvae. Our findings are relevant for a better understanding of the different behavior of these bacterial strains in the human urogenital tract (Heitmueller et al., 2017).

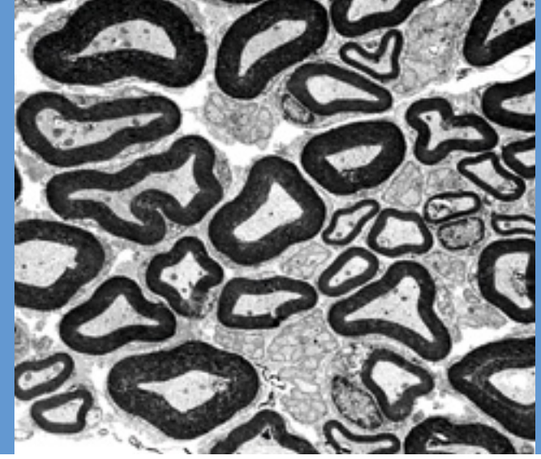
We further investigated the antimicrobial peptides for their efficacy and demonstrated a targeted antibacterial effect for some of these peptides. For example, one class of these molecules forms pores in the bacterial cell wall and is able to bind bacterial DNA. To date, a large number of insect-derived antimicrobial peptides with different properties have been found. The biotechnological potential of these molecules is being investigated in many fields to develop new pharmacological substances for the healthcare sector.

Miriam Kalsy, PhD student
miriam.kalsy@ime.fraunhofer.de

THE EYE AS A WINDOW TO THE NERVOUS SYSTEM



Immunofluorescence staining of a murine spinal ganglion stained with markers for different cells.



Electron microscopic image of a cross-section of nerve fibers with myelin (dark).

The development of neuropathies and neuropathic pain is accompanied by a regression of nerve fibers. Interestingly, this effect is already visible in the cornea of patients before the first symptoms appear. Therefore, corneal and lacrimal examinations may be used as early markers for nerve damage.

Neuropathies on the rise

Neuropathies and the related neuropathic pain are among the most common neurological diseases, and continue to increase with demographic change. Patients suffer in particular from numbness, unpleasant tingling, burning, and even cramp-like pain. Studies have shown a significant reduction in the quality of life of neuropathic patients. In addition, neuropathies usually remain chronic and complicate patients' lives for decades.
In most patients, the symptoms start at the fingertips and toes and are accompanied by a regression of the nerve fibres in these areas. If the entire foot is affected, this leads to walking disorders with an increased risk of falling.

Clinical observations show that the diseases can occur as a result of diabetes mellitus, after chemotherapy, dialysis, heavy alcohol consumption, various medications, infections, autoimmune diseases and mental shocks. However, these different triggers of the disease cannot be causal alone, since only some of the patients, for instance less than 50% of diabetics, develop polyneuropathy. Therefore, additional factors such as genetic predispositions, altered immune responses, and circulatory disorders seem to further increase the incidence of chronic neuropathies.

For the treatment of patients with neuropathies and associated neuropathic pain, there are currently few therapeutic options. In addition, the effectiveness of these therapies is significantly lower when the regression of nerve fibers in patients is already well advanced.
Therefore, there is a lack of prognostic markers which indicate the development and the severity of neuropathy at an early stage. This is a prerequisite for an early start to therapy to alleviate the course of the disease.

A view of the cornea of the eye

At present, two standard procedures are used to determine nerve fiber damage: measurement of nerve conduction velocity and nerve fiber examination by punch biopsy of the skin. Both methods have advantages and disadvantages. The measurement of the nerve conduction velocity provides only indirect information on the degree of regression of nerve fibers. Punch biopsies of the skin have the disadvantage that they are painful, which is in particular very unpleasant for pain patients. In addition, the location of the punch biopsy is chosen arbitrarily and may therefore, not be representative of the condition of the peripheral nerve fibers in the entire body.

An alternative to the classical methods is the examination of nerve fibers of the cornea. The cornea is very well suited to this purpose as it is the most innervated area in the peripheral nervous system and thus, provides a representative picture of the peripheral nervous system. With the help of new methods, such as the confocal corneal microscopy, parameters such as nerve fiber density, nerve fiber length and nerve fiber branching density can be measured directly in patients. Interestingly, this allows measurement of early changes in the nerve fiber composition of the cornea of patients even before the first symptoms of neuropathy occur in these patients.

The tear fluid in focus

Blood plasma is often used for the identification of biomarkers in various diseases. However, nerve damage in neuropathies is usually locally restricted, therefore no systemic changes of markers in blood plasma can be measured. An alternative for the measurement of biomarkers from plasma could be tear fluid. The cornea is not supplied with blood, but is surrounded by a film of tear fluid. Hence it is likely that the mediators responsible for nerve damage are present in the tear fluid and can accumulate in the pathophysiological process of neuropathy.

At Fraunhofer IME the working group lead by the junior researcher Dr. Marco Sisignano investigates the fine structure of the nerve fibers in different animal models for neuropathy. The work is carried out in close cooperation with the renowned glaucoma researcher and specialist for the physiology of the eye, Prof. Dr. Elke Lütjen-Drecoll of the Friedrich-Alexander-Universität Erlangen-Nürnberg. The analytical methods comprise molecular biological, histological, immunological and analytical measurements, as well as high-resolution electron microscopy. In addition, the potential migration of immune cells into the peripheral nervous system in the course of neuropathy and multi epitope ligand cartography (MELK) will be examined to detect early changes in neuronal plasticity in the course of neuropathy.

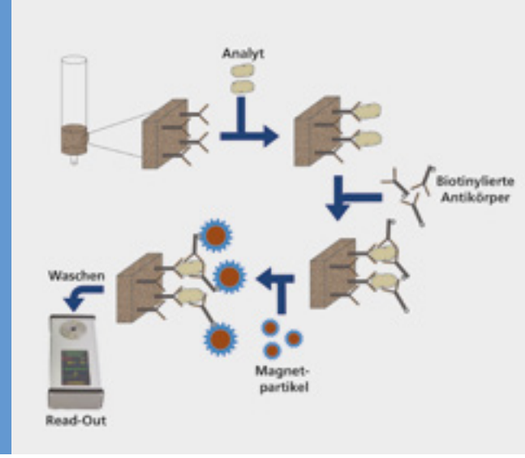
In addition, the tear fluid of patients with neuropathies of different origin will be sampled and analyzed. Similar to the Schirmer's test, a strip of paper is placed under the eyelid for five minutes. After the paper strip is soaked with tear fluid, lipids or proteins can be extracted from the tear fluid and measured by mass spectrometry. The aim is to obtain profiles of peptides, proteins and lipids for the respective patient groups in order to derive possible biomarkers for the incidence and severity of neuropathy.

TM

Dr. Marco Sisignano, Postdoc
marco.sisignano@ime.fraunhofer.de

In cooperation with Prof. Dr. Elke Lütjen-Drecoll.

DETECTING MICROBIAL TOXINS IN FOOD USING NANOPROBES



The process of magnetic immunodetection.

Microbial toxins pose an immense risk to health and should not be present in food. However, the detection of microbial toxins using established analytical methods is time-consuming and complex. There are few sensitive tests available. Fraunhofer IME is developing innovative rapid test solutions based on magnetic nanoprobes.

Detection of microbial toxins

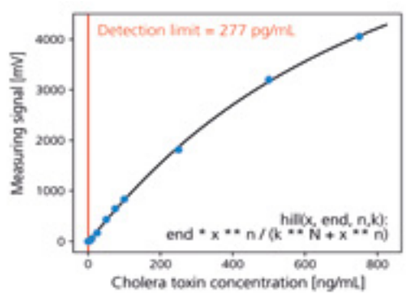
Germany has very high quality standards for drinking water but microbial contamination can never be completely ruled out. Microbial contamination is currently detected exclusively using cultivation-based methods, but microbial toxins cannot be identified in this manner, and are often overlooked. This leads to the costly recall of food products contaminated with microbial toxins.

Methods such as the enzyme-linked immunosorbent assay (ELISA) can be used to detect microbial toxins, but are time-consuming and costly. Fresh food is processed in very tight time windows, so if analytical results only become available after a few days, many foods are already processed and on their way to the customer. Expensive recalls are then unavoidable.

At Fraunhofer IME, the Innovative Detection Technologies working group led by Dr. Florian Schröper is developing innovative test methods for the rapid an inexpensive detection of microbial toxins in food with high sensitivity. Specially coated nanoprobes are used, which magnetically label toxin molecules and simultaneously enable magnetic purification and concentration. The simple detection method uses a mobile device that reliably determines the quantity of toxins labeled by the nanoprobes.

Magnetic immunodetection

To enrich and subsequently detect the analyte using magnetic immunodetection, special detection columns are used. The matrix contains specific antibodies that capture toxins from the sample passing through the column. In a second step, nanoprobes functionalized with antibodies are applied, and they are concentrated in the detection column only if the toxin is bound. The toxin concentration can be determined in the pg/mL range by calibration using the quantity of magnetic particles remaining in the column. The nanoprobes are detected using a mobile measuring device developed by the Institute of Complex Systems (ICS-8), Forschungszentrum Jülich, as part of the AquaNANO project funded by the BMBF. The magnetic particles are detected using frequency mixing technology. Within the AquaNANO project, magnetic immunodetection was used, among other things, to detect the cholera toxin in drinking water.



Calibration series for the rapid detection of cholera toxin.

The exotoxin produced by the bacterium *Vibrio cholerae* causes vomiting and severe, sometimes bloody, diarrhea in humans. The rapid test developed at Fraunhofer IME detects the toxin with high sensitivity and allows quantification by calibration.

Advantages compared to conventional techniques

There are significant advantages over other immunoassays, such as the ELISA or lateral flow test. The sequential filtration principle minimizes unspecific binding, and the porous matrix increases the binding surface area by a factor of 40 compared to an ELISA, thus achieving much lower detection limits in shorter incubation times. The duration of magnetic immunodetection is only about 30 minutes, whereas a conventional sandwich ELISA often requires overnight incubation. Although rapid lateral flow tests are also very simple and fast, they are much less sensitive than magnetic immunodetection. ELISA results can be unreliable if the analytes are stained or turbid. Magnetic immunodetection is not affected by these issues.

A further advantage results from the simplicity of the assay. In contrast to most other analytical methods, magnetic immunodetection does not require the use of an elaborately equipped analytical laboratory. Instead, rapid on-site identification is possible.

Mycotoxins are difficult to detect, and are often found in raw materials such as cereals, nuts or fruits, which are processed into more complex products. But dairy products can also be contaminated. As part of the MykoNANO project funded by the state of NRW and the EU, nanoprobe-based magnetic immunodetection is now being adapted to detect mycotoxins in food. For this purpose, a separate approach will be established to magnetically separate the toxins from complex food samples before a second immunomagnetic detection step.

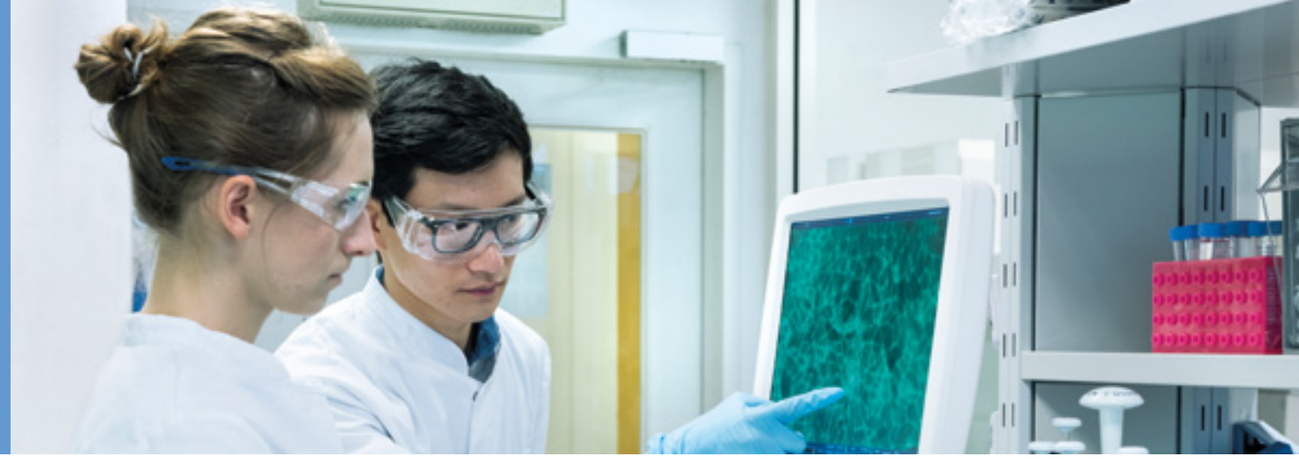
Conclusion

Fraunhofer IME has established a new rapid analysis method for the very sensitive detection of cholera toxin. For the future, as part of the MykoNANO project, we are developing a method for the rapid and reliable separation and magnetic detection of mycotoxins in food.

MB

Julia Toedter, Master student
julia.toedter@ime.fraunhofer.de

STEM CELL LABORATORY: OPERATION AROUND THE CLOCK



View in the stem cell laboratory at the ScreeningPort.

Stem cells are fascinating all-round biological tools. They can divide indefinitely and differentiate into the different body cells. These properties allow the production of difficult-to-access cell types in the laboratory. At Fraunhofer IME in Hamburg, human stem cells are combined with long-term screening expertise to find new drugs.

Working with stem cells always involves teamwork. The demanding cells require daily processing, therefore weekend work is required as well. As part of the Hamburg stem cell team, Dennis Lam, who has a Master's degree in Biology from Georg-August-University Göttingen came to Fraunhofer IME ScreeningPort a year ago and has established important new ways of quality control and functional tests for stem cells. Undine Haferkamp, on the other hand, a doctoral student at the University of Lübeck, is working on her doctoral thesis investigating the link between neurodegenerative diseases and alterations at the blood-brain barrier.

The enormous diversity of stem cells

Both Dennis and Undine are fascinated by the opportunities in their laboratory and they explain why this is the case. When discussing "stem cells" many people think of bone marrow donations or cells from embryos.

In 2006, it was demonstrated for the first time that cells from adult donors can be reprogrammed into stem cells, which in turn can differentiate into all tissues of the adult body. For the generation of these so-called induced pluripotent stem cells (iPS cells), skin biopsies a few millimeters in size are sufficient as starting material. In contrast to embryonic stem cells, the use of iPS cells is ethically acceptable. The potential applications of the Nobel prize-winning method to generate iPS cells are manifold and range from disease models, drug research to regenerative therapies.

Stem cells offer numerous advantages ...

In translational medicine, cellular systems are often used to model certain aspects of diseases. The closer the cells in the laboratory resemble those in the human body, the better the model is to a living organism for research purposes.
In principle, iPS cells can be made from primary cells that are extracted directly from human tissue. This source is restricted on the one hand by the number of donors and on the other hand by the low cell division capacity. Therefore, a long-established method is the utilization of immortalized cells. These cells are generated in tumors or by targeted genetic manipulation of primary cells. However, immortalized cell lines are genetically different from normal body cells.

... but also challenges

In contrast to immortalized cell lines, the cultivation of iPS cells is much more complex. While many established immortalized cell lines are relatively flexible in their handling, iPS cells require significant maintenance. Another challenge is the spontaneous differentiation into unwanted cell types. The undefined composition of conventional media and inter-batch variation can favor such random differentiation in iPS cells. Standardized and defined media make iPS cell culture considerably more expensive, therefore strict quality control is required.The ScreeningPort in Hamburg are part of the European Bank for induced Stem Cells (EBiSC) consortium which has developed an extensive quality assurance system for the characterization of iPS cells. This is based on parameters such as morphology, protein expression and differentiation potential of cells. These characteristics can be used to decide which cell lines are best suited for specific applications. Together with clinical partners, we can offer highly relevant cell lines for pharmaceutical research, as is currently being done in a project with Evotec AG.

Stem cell-based models for drug research

Most potential drugs show a lack of efficacy and toxicity in clinical trials. Since these clinical trials are complex, costly and potentially dangerous, it is essential that only the most promising drugs are progressed to his stage.
The use of iPS cells is well suited for this purpose, as they are able to represent human physiology very well and are available in large quantities. In combination with the screening technologies at the ScreeningPort in Hamburg, iPS cells are being used, among other things, for the validation of potential drugs to treat multiple sclerosis. Efficacy tests on neurons differentiated from iPS cells are expected to improve the selection of drug candidates for later clinical trials.

In a BMBF-funded project which includes Fraunhofer IME, a stem cell-based blood-brain barrier model is being developed and validated. This is an important research project as drugs which are supposed to act in the brain must be able to cross this barrier. This test platform being developed enables the early elimination of unsuitable drugs prior to clinical trials.
The use of iPS cells also allows the reduction of animal experiments being performed and an improved representation of diseases and their pathophysiology at the cellular level.

TM

Dennis Lam
dennis.lam@ime.fraunhofer.de

TM

Undine Haferkamp, PhD student
undine.haferkamp@ime.fraunhofer.de

IN DIALOG

An Interview with Dr. Frank Behrens

Background

Dr. Frank Behrens initially studied biology at the Johannes Gutenberg University in Mainz, later he moved to the Johann Wolfgang Goethe University in Frankfurt am Main to study human medicine. He then received his PhD and completed his training as a specialist in internal medicine and rheumatology. In 2003, as part of a scholarship, he moved to the Pharma-zentrum Frankfurt (immunopharmacology) to carry out a research project on regulatory T-cells, before later returning to rheumatology. He has been involved in clinical research and drug development since 2001 and established the Clinical Research Unit of Rheumatology of the Goethe University Hospital, which he is heading since 2007. Since 2012, he leads the Clinical Research Department of the Translational Medicine Division of Fraunhofer IME in Frankfurt am Main.

»3«
Clinical research

From vision to cure: Clinical research as an essential step from knowledge to true innovation.

CLINICAL RESEARCH: A KEY FACTOR FROM KNOWLEDGE TO INNOVATION

In order to meet the challenges of immune-mediated inflammatory diseases in translational research, Dr. Frank Behrens and his team are carrying out innovative clinical research projects for the early detection, diagnosis and treatment of such diseases. Fraunhofer is currently developing its own drug candidate, an innovative "first-in-class" drug for the treatment of rheumatoid arthritis. As a typical example of proof-of-concept and beyond, a completely new indication field in the field of pain has been found for an already approved drug, which is now also being tested in its clinical application. In developing innovative designs, Mr. Behrens uses both his expertise as a consultant in internal medicine and rheumatology and his experience as a responsible investigator in many hundreds of studies. Together with his team, he develops innovative study designs to improve patient care in a sustainable way.

The interdisciplinary team of the Department of Clinical Research in Frankfurt am Main.

Dr. Behrens, your department is involved in clinical research. What kind of projects are you working on there?

Clinical research describes what we consider the essential step of translation in biomedical research. The knowledge gained from basic research can only become a real innovation if it is applied to humans, e.g. by improving the early detection and diagnosis of diseases, for stratified individualized therapy or for improved therapy monitoring for the benefit of the patient.

That sounds like a big challenge.
How can I imagine this in concrete terms?

In basic research, molecules are discovered that are responsible for the outbreak of a disease or its chronicity. Laboratory assays are then used to find out whether these molecules can be influenced by active substances in order to influence the development and course of the disease. If this is the case, it is usually tested in the animal model whether the interaction between the active substance and the disease-associated molecule leads to a positive effect in the disease model. Until then, it is a scientifically high gain in knowledge, but not yet an innovation, since statistically > 90 percent of all active substances after this phase do not succeed in finding their way into the treatment of patients. Reasons for this may be insufficient safety, but often also a lack of proof of efficacy in humans.

How then is a successful step into the human being achieved?

Essentially, it works like any experimental set-up, but the method used to test a hypothesis, e.g. the efficacy of a drug, is the instrument of clinical testing in humans or clinical trials. The major challenge here is to choose an innovative study design in order to develop a proof of concept that is as intelligent as possible, tailor-made for the respective product and adapted to the respective target disease, while at the same time fulfilling all regulatory and legal framework conditions that a human study entails.

This sounds very complex and is normally only possible for large pharmaceutical companies.

In fact, such a clinical research project is only possible in a highly qualified interdisciplinary team. However, pharmaceutical companies often no longer have this infrastructure in-house. Our great strength at Fraunhofer IME on the Niederrad campus of the University Hospital Frankfurt is the close integration of scientific expertise with medical knowledge and experience regarding various diseases in the indications immunology and inflammation and patient care as well as many years of experience in the implementation of regulatory requirements for clinical studies.

What types of clinical trials do you conduct?

Clinical trials are often thought of as classic Phase III trials to obtain marketing authorization for a drug. This is not our focus, as these studies are more likely to fulfil regulatory requirements than to answer innovative scientific questions.
On the one hand, we focus on proof-of-concept studies in which new diagnostic methods or drugs are used for the first time to demonstrate their usefulness to patients.

Patient-oriented clinical research is at the forefront of our work.

This is where our strengths come into play: An intelligent study endpoint must be found, adapted to the corresponding mode of action or the relevant diagnostic method and the most suitable study population from the often heterogeneous patient populations identified in order to find an optimal study design for cost-effective and rapid development. In addition, we also carry out post-registration studies in order to sharpen the profile of different substances by better describing the most profitable patient population even after market approval, in order to make the highest patient benefit possible.

Why do you find Fraunhofer TMP to be the ideal environment for these tasks?

The great strength of the institute here in Frankfurt lies in the close integration of basic science, preclinical development and translation into human application. While the classical development of drugs and diagnostics takes exactly the order described here, our team gains knowledge and innovation in reverse order: Each clinical research project is flanked by a scientific accompanying program in order to associate clinical improvements at best with molecular biological changes. These findings then help us again as surrogate markers for the early recognition of the mechanism of action in proof-of-concept studies.

Do you also involve external partners in your projects?

The great advantage of Fraunhofer is the application-oriented research, which always includes product development as a goal. Fraunhofer thus pursues the same goals as, for example, biotech or pharmaceutical companies with which close cooperations arise. On the one hand, biotech companies turn to us to generate proof-of-concept for new products that are later licensed out to Big Pharma. On the other hand, we seek contact with the industry in order to bring our own development data, which we have further developed from basic research, into approval with partners.

Combining molecular biological investigations and clinical research to improve knowledge.

So why did you decide to move from direct patient care to clinical research?

This was not a real change. In addition to my work in the TMP department, I am still working in direct patient care at the University Hospital. In my opinion, this is also a crucial advantage over other organizations that carry out clinical research. The proximity to patient care enables us to identify and address questions and problems from clinical routine care in research projects. Ideas for study projects usually emerge from questions that arise during patient care or are discussed with colleagues. In addition, we carry out some of our planned studies ourselves in our university clinical trial unit and often see directly how our own projects affect the patient. This very close contact with patient care enables us to better understand clinical trial procedures and to adapt and optimize them in subsequent projects so that the needs of the patient are always at the center of our research projects. The implementation then takes place together with my colleagues in an interdisciplinary team consisting of physicians, statisticians, study coordinators, project managers and experts in data management.

Finally: What do you enjoy most about your work?

The networking of life sciences, biostatistics, machine learning and artificial intelligence with a direct influence on patient care is a great challenge that motivates and drives me again and again.

TM

Dr. Frank Behrens
frank.behrens@ime.fraunhofer.de

IN FOCUS

Fraunhofer Attract Group Eco'n'OMICs

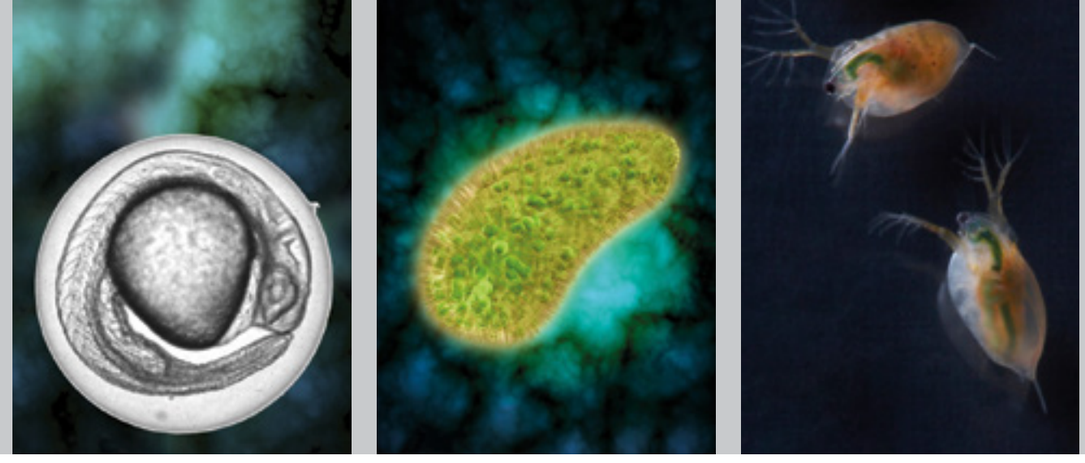
Molecular fingerprints:
Predicting environmental risk
Dr. Sebstian Eilebrecht, Prof. Dr. Carsten Claussen

»4«

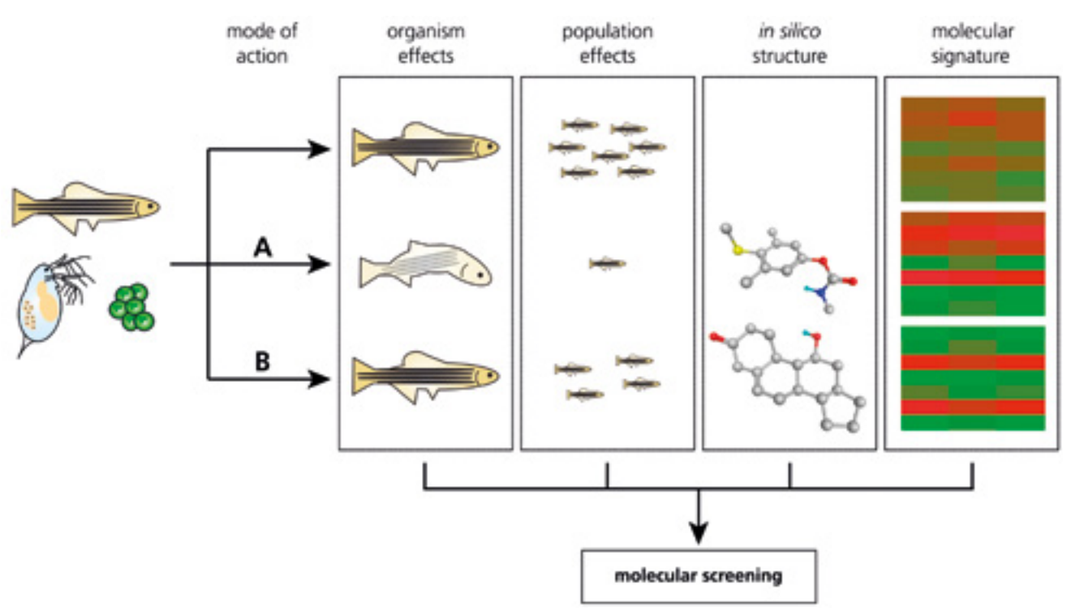
Molecules in focus

The junior research group investigates molecular fingerprints of harmful substances in the environment in order to enable the development of environmentally safe active substances.

MOLECULAR FINGERPRINTS: PREDICTING ENVIRONMENTAL RISK



Pesticides, biocides or pharmaceuticals can produce undesirable side effects in the environment. In July 2018, the Fraunhofer Attract group Eco'n'OMICs* commenced its work at Fraunhofer IME location in Schmallenberg. In the junior research team, we are working together with colleagues of the affiliate lab ScreeningPort in Hamburg on the analysis of molecular fingerprints of such active compounds in environmental organisms. Our goal is the application of molecular data for environmental risk prediction in the early development phase of active compounds.



The environmental impact screening database links the molecular fingerprint of a substance with its mode of action, the compound structure and the adverse effects on the organism and the population.

The molecular fingerprints of compounds are recorded in aquatic model organisms such as zebrafish embryos, algae or water fleas.

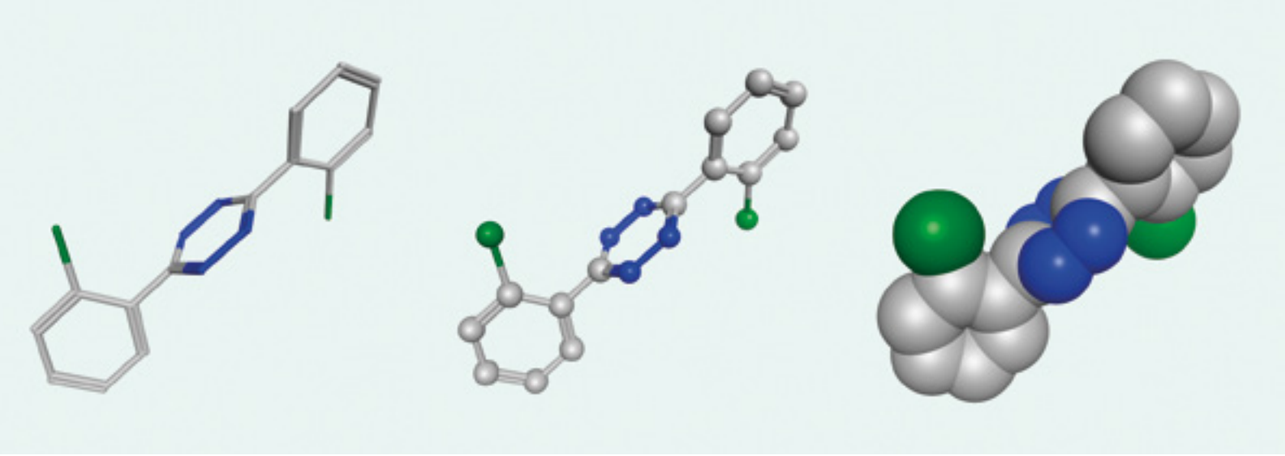
Pesticides are used for pest control but may also cause adverse side effects on non-target organisms. This may threaten communities, which could result in unacceptable changes of the ecosystem. Therefore, EU legislation requires manufacturers to provide data for environmental risk assessment of a new active compound for registration. The tests to collect this data are conducted by industry in the final stage of compound development. They are time and cost consuming and require a substantial number of animals. If a compound fails registration due to proven adverse environmental effects, the manufacturer loses development costs in the three-digit million dollar range.

As part of the Eco'n'OMICs project, we are working in a team with a PostDoc, two PhD students and a technician to investigate at the molecular level the negative effects of compounds on environmental organisms. Dr. Sebastian Eilebrecht, head of the junior research team: "The findings will be used to predict the environmental risk of industry development compounds in the early development phase and thus contribute to the sustainable development of environmentally friendly active compounds."

Harmful to the environment? Molecular changes as an early alert signal

Harmful substances first cause molecular disturbances in environmental organisms that trigger a specific response in cell metabolism. Such metabolic changes can eventually be reflected in a damaged organism and in an impaired population. For example, pesticides with specific modes of action can cause molecular changes in fish. At the organism level, these can be liver-toxic, neurotoxic or a reduced reproductive capacity and therefore may affect the fish population. On the other hand, safe active compounds do not cause significant changes in the environment, either at the molecular level or at the organism level. A certain adverse environmental effect is therefore always preceded by a specific change at the molecular and cellular level that can be used for prediction.
Most of the regulatory approved environmental risk assessments consider changes at the level of the organism or population. They allow little or no conclusion on the original modes of action and are not suitable for screening development compounds due to their duration and quantities of substance required. However, being able to distinguish between a hazardous and non-hazardous impact at an early stage of compound development is of high importance for industry with regard to compound registration.
Novel molecular biological and bioinformatic methods allow for a global and sensitive detection of even the smallest changes in cell metabolism.

**OMICS: generic term for molecular biological methods ending in "-omics" such as: "genomics", "transcriptomics", "proteomics", "metabolomics".*



The structure of active compounds can be computer simulated and allows predictions of the mode of action.

The analysis of the sample quality is of utmost importance for the sensitive OMICs analyses.

For several years, these so-called OMICs analyses have been applied successfully in drug discovery and in the assessment of pharmacological side effects in humans. However, OMICs are still in their infancy when it comes to analyzing environmental side effects. The development opens up new avenues for the detection of early metabolic changes as molecular fingerprints in environmental organisms differentiate different modes of action of environmentally adverse compounds.
Eilebrecht: "In the Fraunhofer Attract group Eco'n'OMICs, we use OMICs methods to identify molecular fingerprints of substances with known modes of action in aquatic model organisms such as fish larvae, water fleas or algae. Together with the mode of action and the known effects on the organism and population, the metabolic patterns form the basis for a comprehensive database". Finally, the database will be used to develop a molecular screening approach for predicting the specific environmental effects of development compounds in their early development phase.

3D-Active Agent Structures: computational environmental risk prediction

Compounds with an adverse effect on the environment usually exert these effects in the environmental organism via their structure, which is determined by their physical and chemical properties. An active compound whose structure resembles the environmental organism's own messenger can bind to its cellular receptor and thus prevent docking. The active compound would thus "switch off" the body`s own messenger. Such a mode of action would result in a change in cell metabolism detectable via OMICs before population effects occur.

Another way of predicting the environmental side effect of an active compound is to use information about its structure to derive a specific mode of action. The structure of the active compound can be computer simulated and compared with known compound structures whose modes of action have already been identified. Such a linking of the molecular structure with the corresponding harmful activity can be derived by structure activity relationship (SAR). SARs are used more and more for computer-based detection of environmental toxins.

Early environmental risk screening: number of animal testing could be significantly reduced

The cooperation with the working group "Structure-based Drug Design" at the Hamburg location provides the research group with many years of experience in computer-aided modelling of compound structures for the identification of new active pharmaceutical ingredients.

In the future, we will apply this expertise from the field of development compound research to predict the structures of environmentally harmful substances and link them to their molecular fingerprints in environmental organisms.
In close cooperation between the two sites, a bioinformatic tool is to be developed that can predict a specific environmental effect for any development compound based on its modelled structure. The availability of such a structure-based prediction will allow industry to focus on environmentally safe development compounds. It will also enable further, more targeted, testing of the environmental impact of these substances. Such prioritization of tests could significantly reduce the number of animal tests for the environmental risk assessment of new active compounds.

With further expansion of molecular research and the establishment of OMICs methods at the Schmallenberg location, we are opening up new, forward-looking applications for mass spectrometry, already established for a long time. In particular, we are extending our existing expertise on the environmental impact of compounds at the organism and population level to the molecular level. The gained knowledge on early molecular changes caused by an active compound resulting in an adverse environmental effect in non-target organisms allows an early high throughput prediction of the environmental side effects of development compounds. In combination with structure-based environmental risk prediction, this approach will enable industry to develop environmentally friendly compounds in a sustainable way.

AE BR

Dr. Sebastian Eilebrecht
sebastian.eilebrecht@ime.fraunhofer.de

TM

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

SELECTED PUBLICATIONS

Unfinished business: The demand for Taxol is growing

A new strategy to fight gram-negative bacteria

Early preventing of pain during its development

Natural viruses as biological pest control agents

An alternative strategy for the purification of monoclonal antibodies

Voltammetric platform for rapid detection of foodborne bacteria

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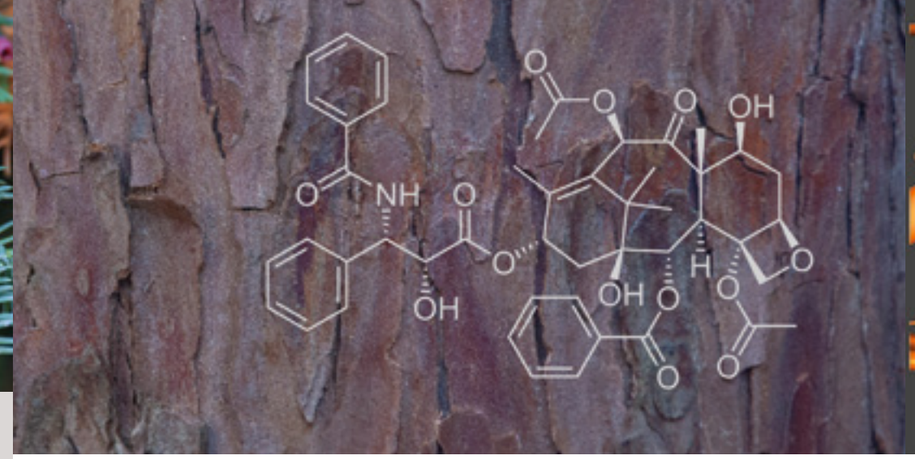
In 2018, Fraunhofer IME researchers published about 150 articles in peer-reviewed journals, most of them with the participation of our young scientists.



Christopher McElroy
PhD student
Industrial Biotechnology

Needles and bark from yew trees are the traditional taxol sources.

UNFINISHED BUSINESS: THE DEMAND FOR TAXOL IS GROWING

"WE NEED AN EFFICIENT, HETEROLOGOUS TAXOL PRODUCTION, FOR THIS TO BE ACHIEVED THE BIOSYNTHESIS PATHWAY MUST BE ELUCIDATED."

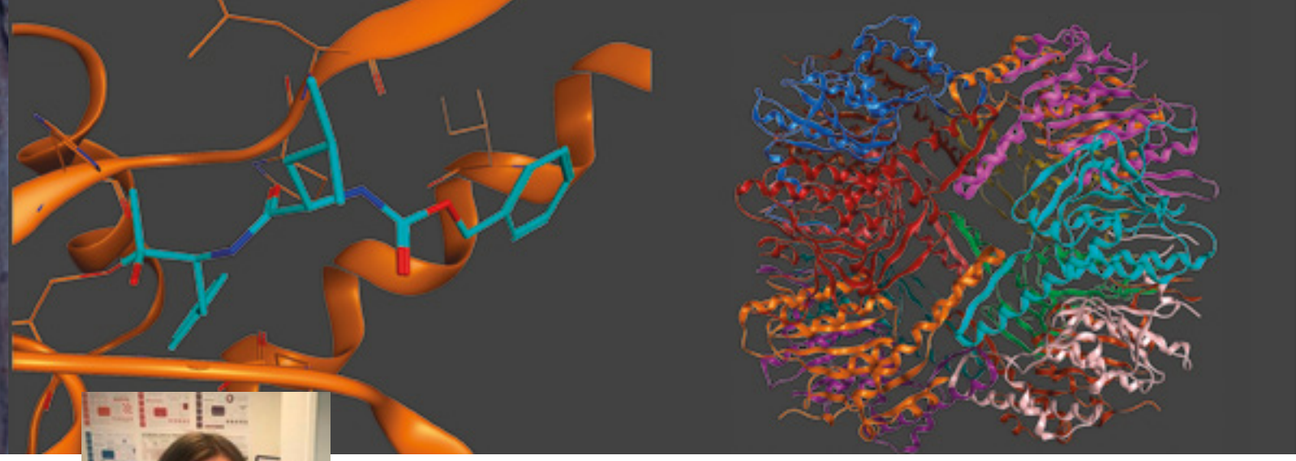
Taxol® (Paclitaxel) is one of the most well-known and lucrative plant derived natural products, responsible for a multi-billion dollar market share of modern anti-cancer pharmaceuticals. Taxol is now the registered trademark name for paclitaxel. Together with other taxane analogues it is used within anti-cancer drugs like Taxotere® or Abraxane®.

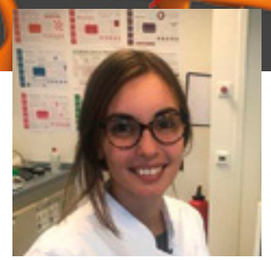
Since its initial isolation in 1971, this compound has become an invaluable tool in combatting a wide array of medical indications, particularly cancer. Herein this book chapter, we describe in detail the developmental process from initial investigation to application, the currently known steps of the biosynthesis pathway, discuss recent developments in Taxol research and suggest innovative avenues of investigation. Thereturn of yew tree plantations indicates that demand is not currently being met for this complex diterpenoid. Unfortunately, such plantations can be environmentally costly due to the exceedingly low yields attained from adult yew trees (1 g of Taxol from ~12 kg of tree bark).

Alternative methods, such as Taxus plant cell suspensions represent the state of the art until a heterologous production host is developed. Unfortunately, for this to be plausible at least five biosynthetic steps must first be elucidated before such a heterologous taxane production platform is foreseeable. Astonishingly, only recently substantial progress has been made in this area, with the regulatory network already suggesting complex orchestration of this secondary metabolite. Therefore, we aimed to induce greater effort within the scientific community to concentrate efforts on deciphering the remaining uncharacterized enzymatic steps so that within the next decade a microbial production platform can finally become a reality, not only to meet the ever-growing demand but also to reduce the environmental cost of harvesting this green gold.

MB Molecular Biotechnology

McElroy, C., Jennewein, S.
Taxol® biosynthesis and production: from forests to fermenters (2018) In Biotechnology of Natural Products (pp. 145-185). Springer, Cham. DOI: 10.1007/978-3-319-67903-7_7





Dr. Elisa Sassetti
PhD student until 11.2018
Drug Discovery

ClpP crystal structure showing a bound inhibitor in detail.

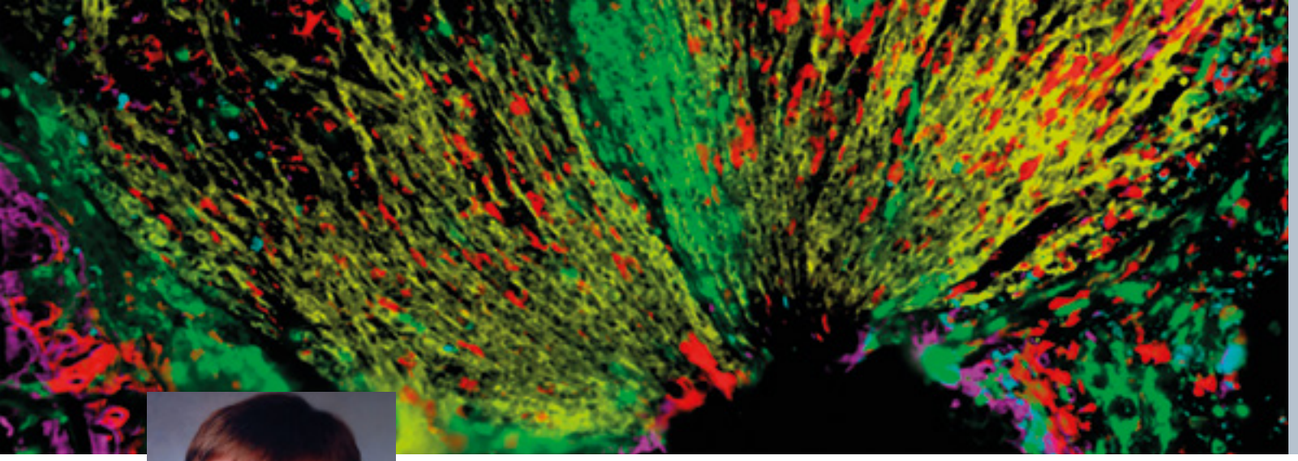
A NEW STRATEGY TO FIGHT GRAM-NEGATIVE BACTERIA

"THE DEVELOPMENT OF ANTIBIOTIC RESISTANCE IS A THREAT TO HUMAN HEALTH."

Caseinolytic protease proteolytic subunit (ClpP) is a serine protease, which is highly conserved among bacteria. ClpP plays central roles in many bacterial cellular processes, in particular functions linked to protein turnover and homeostasis, degradation of potentially cytotoxic proteins, such as misfolded or damaged ones. In some bacteria, ClpP is also involved in virulence, cell-wall metabolism, cell division, biofilm formation and stress response. Thus, ClpP represents a potential target for antivirulence therapies. In addition, the weakening of bacterial fitness by inhibiting ClpP could make bacteria more amenable for antibiotic therapies.
The aim of this study was to identify molecules that inhibit ClpP in Escherichia coli. To achieve this, we combined several in silico and experimental approaches. In total, nearly 3,000 compounds from various small molecule libraries of approved and clinical drugs, as well as other bioactive compounds and proprietary substances, were tested for ClpP inhibition using a high-throughput biochemical screening assay.
Identified inhibitors were further improved in several rounds of optimization by synthetic medicinal chemistry and experimental testing. Furthermore, we characterized the most potent compounds in terms of their binding properties by surface plasmon resonance studies, their possible binding modes by molecular docking, their enzyme selectivity and their cytotoxicity in different human cell lines. In addition, the antibacterial effects of these compounds against several *E. coli* strains were examined either alone or in the presence of chemically induced nitric oxide stress. With the strategy described, we were able to identify several compounds that inhibit ClpP at very low concentrations. Some compounds showed ClpP-mediated growth retardation under stress conditions. These compounds are promising starting point for the development of potent ClpP inhibitors.
This work was carried out within Marie Skłodowska-Curie ETN "INTEGRATE" in collaboration with research groups from Tübingen, Antwerp and Helsinki.

TM ScreeningPort

Moreno-Cinos, C., **Sassetti, E.**, Salado, I.G., Witt, G., Benramdane, S., Reinhardt, L., Durante Cruz, C., Joossens, J., Van der Veken, P., Brotz-Oesterhelt, H., Tammela, P., Winterhalter, M., Gribbon, P., Windshügel, B., Augustyns, K.
α-Amino diphenyl phosphonates as novel inhibitors of Escherichia coli ClpP protease (2019) Journal Medicinal Chemistry, 62(2), 774-797. DOI: 10.1021/acs.jmedchem.8b01466



Prof. Dr. Klaus Scholich
Group manager
Biomedical Analytics and Imaging

Immune cells repair an injured sciatic nerve.

EARLY PREVENTING OF PAIN DURING ITS DEVELOPMENT

"EARLY TREATMENT CAN PREVENT THE DEVELOPMENT OF HARD-TO-TREAT FORMS OF PAIN."

Neuropathic pain caused by nerve damage is one of the most common neurological diseases worldwide. There are currently few treatment options available for patients with neuropathies and the associated neuropathic pain. The effectiveness of these therapies is even more limited in cases where the regression of nerve fibers is already well advanced. Therefore, we need additional treatment options to prevent the development of neuropathic pain as early as possible. A very common form of neuropathic pain is trauma-induced nerve damage that can occur in accidents or after surgery.

We have shown in several studies that different lipids, released as signal molecules during injuries, control inflammatory reactions to the injured nerves. If the synthesis of these lipids is prevented early and permanently by non-steroidal anti-inflammatory drugs such as diclofenac or ibuprofen, neuropathic pain can be significantly reduced. In our work published in the renowned Journal of Biological Chemistry, we were able to identify the receptor that recognizes specific lipids involved in the development of neuropathic pain and, by eliminating this receptor, reduce significantly trauma-induced neuropathic pain. The downstream mechanisms that further amplify neuropathic pain via the inflammatory reaction were also elucidated. Here, it turned out that the signal molecule CCL2, which is responsible for the recruitment of immune cells to the site of injury, makes a crucial contribution to the development of neuropathic pain.

TM Translational Medicine

Treutlein, E.-M., Kern, K., Weigert, A., Tarighi, N., Schuh, C.-D., Nüsing, R.M., Schreiber, Y., Ferreirós, N., Brüne, B., Geißlinger, G., Pierre, S., **Scholich, K.**
The prostaglandin E2 receptor EP3 controls CC-chemokine ligand 2–mediated neuropathic pain induced by mechanical nerve damage (2018) Journal of Biological Chemistry, 293 (25), 9685-9695. DOI: 10.1074/jbc.RA118.002492

Tessa Carrau
PhD student
Branch for Bioresources

The spotted wing drosophila, a pest insect introduced to Europe from Asia.

NATURAL VIRUSES AS BIOLOGICAL PEST CONTROL AGENTS

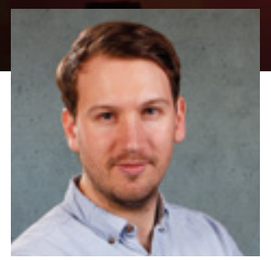
"INSECT VIRUSES ARE HOST-SPECIFIC. WE CAN DEVELOP BIOLOGICALLY SAFE CROP PROTECTION FROM NATURAL VIRUSES OF PESTS."

Sustainable management of natural resources is of major importance for the conservation of biodiversity. While insects cause billions of dollars of damages in agriculture, conventional control with chemical insecticides has had a strong negative impact on insect diversity. The ban on chemical insecticides leads to a gap in measures due to the lack of reliable and biologically safe alternatives.

This applies in particular to invasive insect pests such as the spotted wing fly *Drosophila suzukii*. As the name implies, this species originates from Asia and has rapidly developed into a serious threat to fruit growing worldwide. It has also spread to Germany, where an immense increase in the population led to the total economic collapse of several farms in 2014, including Hessen. One field of insect biotechnology in which we are engaged is the exploitation of associated insect microorganisms for crop protection purposes.
In biological crop protection, insect viruses have great potential because they usually infest only one species and are harmless to all other non-target organisms. The aim of our project was to isolate natural viruses from the spotted wing drosophila and evaluate their potential as biological pesticides. As anticipated, we were able to isolate some candidates that showed a promising effect on the spotted wing drosophila. The study we initiated now enables the development of tailor-made crop protection against individual pest species based on natural insect viruses.

AE BR Bioresources

Carrau T., Hiebert N., Vilcinskas A., Lee K.-Z.
Identification and characterization of natural viruses associated with the invasive insect pest *Drosophila suzukii* (2018) Journal of Invertebrate Pathology,154, 74-78. Doi: 10.1016/j.jip.2018.04.001



Matthias Knödler
Master student until 10.2018
Integrated Production Platforms

Fluorescent columns after affinity ligand coupling.

AN ALTERNATIVE STRATEGY FOR THE PURIFICATION OF MONOCLONAL ANTIBODIES

"THE DEMAND FOR THERAPEUTIC ANTIBODIES IS INCREASING. OUR GOAL IS TO IMPROVE THE COST EFFICIENCY OF THE PURIFICATION PROCESS."

Monoclonal antibodies dominate the biopharmaceuticals market. They are applied in the treatment of various diseases such as cancer and can be used for targeted immune therapies due to their specific binding. However, high production costs resulting from expression in mammalian cell cultures and purification by Protein A affinity chromatography limit the applicability of therapeutic antibodies on an even larger scale. Therefore, a more cost-effective production of such biopharmaceuticals is desirable.
As part of our research work, we tested an alternative antibody purification strategy to reduce production costs. First, we developed a new affinity ligand based on the fluorescent protein DsRed. DsRed served as a carrier for the linear epitope of an HIV-neutralizing antibody. The ligand was produced in transgenic tobacco plants and coupled in a purified form to a sepharose matrix. The resulting affinity resin was successfully used to recover the target antibody 2F5 from a crude protein mixture. We used a statistical design of experiments approach to identify conditions maximizing the amount of coupled ligand thereby increasing the number of binding sites for the antibody on the resin.
In a following step we showed that the affinity ligand was able to selectively bind the antibodies from a clarified tobacco plant extract.
By optimizing the buffer composition for product elution we achieved a purity of over 97 percent and yields of over 95 percent. In addition, we improved the reusability of the matrix through more gentle conditions during elution. Our method is not yet fully refined but a cost analysis showed that a further improvement of the binding capacity by a factor of four would make our method competitive to protein A and could thus replace or supplement established systems for the purification of antibodies. Especially for the purification of bi-specific antibodies or of antibody formats without Fc-part there are several advantages of our new resin compared to Protein A.

MB Molecular Biotechnology

Rühl, C., **Knödler, M.**, Opdensteinen, P., Buyel, J.F.
A linear epitope coupled to DsRed provides an affinity ligand for the capture of monoclonal antibodies (2018) Journal of Chromatography A, 1571, 55-64.
DOI: 10.1016/j.chroma.2018.08.014

Grigori Badalyan
PhD student
Ecotoxicology/Environmental and Food Analysis

The sensor platform consists of different components.

VOLTAMMETRIC PLATFORM FOR RAPID DETECTION OF FOODBORNE BACTERIA

"OUR NEW GENERATION OF VOLTAMMETRIC SENSORS CAN BE USED FOR IN PLACE, REAL TIME MONITORING OF FOODBORNE BACTERIA."

Contamination of food products is one of the main issues for the food industry. Rapid detection and quantification of bacteria during production will significantly decrease the cross contamination of ready to eat food products. The main objective of the doctoral thesis funded by the German Academic Exchange Service (DAAD) was to develop sensor platforms for rapid, real-time monitoring of bacteria in the food processing environment. By using specific substrates for each target group of microorganisms, it is possible to detect generated optical, electrochemical and fluoro-voltammetric signals.
In our study, we designed an electrochemical platform for rapid detection and quantification of coliform bacteria on food contact surfaces. We used screen-printed carbon electrodes, as they are chemically inert, have low background current, a readily renewable surface, a wide potential window and are relatively inexpensive. Graphene nanomaterial was applied as an enhancer of voltammetric signals. Polyacrylamide gel in combination with agar-agar increased the adhesive properties of the sensor.
With this platform, we could detect well-shaped, sharp voltammetric curves produced by the novel electrochemical substrate 6-Chloro-3-indoxyl-β-D-galactopyranoside. The curves were formed due to activity of the enzyme β-d-Galactosidase which is intrinsic in coliform bacteria.
The developed platform was able to detect bacterial cell concentrations ranging from 40 CFU/mL to 4x106 CFU/mL (CFU: Colony Forming Units) during three hours of incubation. However, electrochemical signals were already detectable after 30 minutes. With a shortened assay period compared to standard methods requiring 12 to 48 hours, a limit of detection of 10 CFU/mL and a coefficient of variation of 0.4% the newly developed platform represents a rapid, sensitive, reproducible as well as specific methodology for coliform bacteria. Our platform can be the basis for a novel generation of low cost electrochemical sensors that require no sample preparation. It can be used directly during food processing for detection of different bacterial groups even by unqualified personnel.

AE BR Applied Ecology

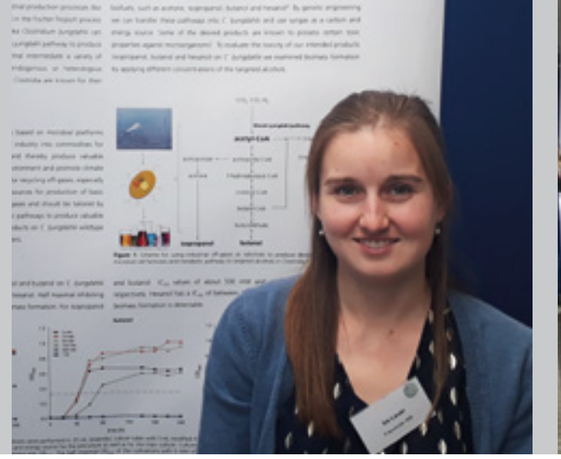
Badalyan, G., Díaz, C., Bücking, M., Lipski, A.
Novel sensor platform for rapid detection and quantification of coliforms on food contact surfaces (2018) Journal of Microbiological Methods 153 74–83.
Doi: 10.1016/j.mimet.2018.09.009

PEOPLE AND EVENTS

Brief reports:
Employees, meetings, successes and new perspectives at Fraunhofer IME

»6«

Our employees are also very active in sports. In April some of them started at the campus run in Aachen.



EU-Project BIOCON-CO_2 launched

Carbon dioxide (CO_2) is a naturally occurring greenhouse gas in the earth's atmosphere, but anthropogenic influences such as the combustion of fossil fuels have increased its abundance. The recycling of CO_2 is one of several potential technological strategies to reduce harmful CO_2 emissions, making CO_2 a valuable raw material. Research into CO_2 recycling solutions is still in its infancy and some technical problems remain, including industrial-scale implementation. A biotechnological approach for CO_2 recycling is fermentation with microorganisms, where CO_2 is converted into more desirable products using hydrogen as an energy source.

The BIOCON-CO_2 project is funded by the EU's Horizon 2020 research program and aims to exploit CO_2 from industrial exhaust gases for the synthesis of valuable platform chemicals. The consortium started work in January 2018 and brings together the knowhow of 18 partners from academia and industry. Fraunhofer IME participates in several work packages and will, among other approaches, use metabolically engineered microorganisms to produce different alcohols.

In September, the young scientist Ira Lauer, who is working on her doctoral thesis at Fraunhofer IME in Aachen, presented early results from the project "Syngas fermentation: Toxicity analysis of potential products on Clostridium ljungdahlii" at the international conference "Clostridium XV" in Freising, Germany. MB

Jump! Award ceremony "Jugend forscht" in Hamburg

Guided by their leaps of thought, 88 students posed exciting research questions for the "Jugend forscht" regional competition and presented their results at Fraunhofer IME in Hamburg. A total of 44 projects from the fields of work environment, biology, chemistry, geo- and spatial sciences, physics and technology were presented to the expert jurors. The young Hamburg researchers in the fifth to thirteenth grade first presented their projects to the public, before they went from the exhibition rooms to the award ceremony in the Volksparkstadion. Two young research teams from the "Schüler experimentieren" competition and four teams from the "Jugend forscht" competition qualified for the Hamburg state competition this year, two of which were admitted to the national competition. In line with the Fraunhofer IME ScreeningPort as the hosting institution, the specialist areas biology and chemistry were particularly strongly represented, with 13 and 16 projects respectively. Again, innovation, creativity and curiosity paid off: The victorious young researchers for example, asked themselves, what snails prefer to eat, which stain can be effectively removed with a vegetable washing paste, which geological, chemical and biological aspects make up the marine habitat of an east Irish bay, whether snail slime has an antibacterial effect, how a sustainable plastic is produced from milk and whether tropical life can be proven through the analysis of fossils in Ireland. The competition is organized and supported by the hosting organizations. For the Hamburg Volkspark regional competition, those are the Fraunhofer IME ScreeningPort and the HSV. Dr. Mira Grättinger from Fraunhofer IME has been organizing the competition with her team of students for the sixth year in a row. TM

Prize for the best State Examination Thesis

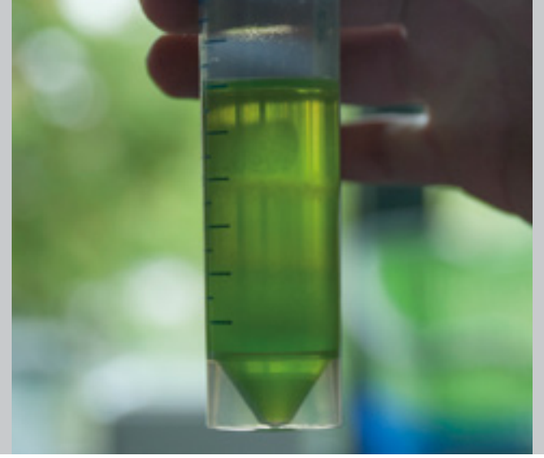
The Chamber of Industry and Commerce (IHK) Siegen annually awards students of the University of Siegen with the prize for two outstanding practice-oriented scientific theses. Among the prize winners in 2017 were Stefanie Schneider and Sebastian Kühr, who obtained the award for their state examination thesis performed jointly at Fraunhofer IME Schmallenberg. On March 15, 2018, the prize endowed with 15,000 Euro was presented to the winners at the awards ceremony of the IHK Siegen. In their thesis "Experimental investigations on the effect of silver nanomaterials in sewage effluent on the freshwater amphipod *Hyalella azteca*" Schneider and Kühr developed an innovative test system for the regulatory risk assessment of silver nanomaterials.

Thanks to their special properties, nanomaterials are found in many consumer products, medicines and personal care products and may be released into waste water in significant amounts. During waste water treatment some of the particles pass through the waste water treatment plant reaching the environment through the sewage effluent. In their study, Schneider and Kühr used a model sewage treatment plant filled with synthetic waste water spiked with silver nanoparticles to investigate potential effects of nanoparticles in sewage effluent on aquatic organisms. They found that the original toxicity of silver nanoparticles, which are used in particular due to their antibacterial properties, can no longer be detected in the sewage effluent. The test system developed by Schneider and Kühr allows the risk assessment of nanomaterials in aquatic systems under environmental conditions. By using invertebrates, i.e. lower animals, the test system can be applied without having to use vertebrates, such as fish. AE BR

Faster from laboratory to patient

In the development of new drugs and medical technology, there is a gap between the discovery of new potential active substances and products and the industrial development of drugs and medical products. Combining medical knowledge with engineering know-how facilitates the development of novel medical devices. However, one of the biggest obstacles on the stony path to new drugs and medical devices remains translation - the further development of new, potentially therapeutic agents and processes into suitable drugs and medical devices by industry.

The Fraunhofer-Gesellschaft and the Helmholtz Association, together with German university medical centres, have now launched the Proof of Concept Initiative. This promotes the translation of innovative, promising research projects to the clinic. The Fraunhofer-Gesellschaft and the Helmholtz Association will each provide up to twelve million euros over the next three years for the Proof-of-Concept Initiative. At the beginning of February, a high-ranking jury of experts from science, industry and regulatory authorities selected the most promising research projects for funding. The PrevTel project is one of the four projects selected from the Fraunhofer IME. Within the scope of the planned study, the efficacy of TMP-002, the company's second development candidate, will be investigated in a clinical study on chemotherapy-induced neuropathic pain in cooperation with the German Consortium for Translational Cancer Research (Helmholtz) and the Institute for Clinical Pharmacology (University Hospital of the Goethe University). TM



Start signal for the research centre “Translational Biodiversity Genomic“

At the beginning of March, Minister of State Boris Rhein handed over the funding certificate to the executive committee of the Research Centre “Translational Biodiversity Genomics“ and thus gave the official go-ahead. Researchers from the Goethe University in Frankfurt am Main, the Fraunhofer Institute for Molecular Biology and Applied Ecology IME in Frankfurt am Main and Gießen and the Justus Liebig University in Gießen are participating in the joint venture, which is led by the Senckenberg Nature Research Society. The participating partners complement each other very well because they bring together basic and applied research.

The genomes of organisms form the basis for biological diversity. The aim of the research centre is to make this genomic diversity visible by deciphering genomes and thus deciphering the blueprints of various organisms. The organisms studied also include exotic organisms such as hairybacks, arrowworms, egg fungi, isopods, snails and lichens, which have so far received little attention in genome research. The results of genome research are used, for example, to generate new active substances. For this purpose, natural substances from bacteria, lichens and fungi as well as from poisonous animals are examined with innovative in vitro test systems with regard to their suitability as new therapy options. Promising substances will be further developed and their effects will be analyzed in more detail in proof-of-concept studies. This approach is intended to identify natural substances with pharmacological potential. TM

Girls'Day/Boys'Day for the future researchers at Fraunhofer IME

The Fraunhofer IME locations in Aachen and Schmallenberg once again opened their doors this year for Girls’Day (Aachen) and for Girls’Day and Boys’Day (Schmallenberg). Interested girls and boys from the 6th to the 8th grades were offered a variety of insights into the day-to-day work of scientists. In Aachen, for instance, they learned how genetic material is extracted from plants and how plants can produce drugs.

Under the guidance of the young scientist Ann-Katrin Beuel, the girls were also able to be scientists themselves. Ann-Katrin Beuel was in charge of Girls’Day at Fraunhofer IME for the third time: “I really enjoy giving the pupils the opportunity to get a first glimpse into our work environment, and telling them about my fascination for the combination of biology and technology. It is also important to me to enable them to take their first steps in the laboratory. Some of the girls will carry out a biological experiment for the first time today.“ Dressed in lab coats and protective goggles, the young researchers isolated DNA from tobacco leaves.

Anna-Lena Willenbrink, also a supervisor of Girls’Day in Aachen, describes her experiences: “The girls were particularly interested in our greenhouses and the growing conditions of the plants, and were most impressed by the huge tobacco plants and the effects of different colored LEDs on the plants.“ MB

Topping-out ceremony in Gießen

The building shell is finished - the planned Fraunhofer Institute for Bioresources in Gießen is taking shape. The topping-out ceremony for the new research building of the Fraunhofer-Gesellschaft was celebrated on May 8, 2018 in the presence of the Hessian Prime Minister Volker Bouffier and the board member of the Fraunhofer-Gesellschaft, Andreas Meuer. The 30 million euro building at the corner of Leihgesterner Weg/ Ohlebergsweg is financed equally by the state of Hesse and the federal government. It is scheduled for completion in mid 2019. The topping-out ceremony in Gießen in 2018 was a highlight for Fraunhofer IME. Research in this new institute building will focus on new active substances for medicine, plant protection and industry from insects, bacteria and fungi as well as alternative protein sources.

With the new building, a new center for the development of bioresources for the bioeconomy is being built in Gießen. Bioresources, in which new biomolecules for medicine, plant protection and industry as well as alternative protein sources are sought, include insects, bacteria, fungi and animal toxins. The LOEWE Centre for Insect Biotechnology and Bioresources forms the basis for the planned Fraunhofer Institute - which would be the first of its kind in the Central Hesse region. It has developed very successfully in cooperation with the Justus Liebig University Gießen, the Technical University Mittelhessen and Fraunhofer IME. The state of Hesse has been supporting the LOEWE Centre for Insect Biotechnology and Bioresources, which emerged from a LOEWE focus on insect biotechnology, since 2014. AEBR

LOEWE Centre extended: Minister of State Boris Rhein presents certificates

In May 2018, the Minister of Science for Hessen, Boris Rhein, handed over on the west end campus of Goethe University in Frankfurt the official certificate for the second funding period of the LOEWE Centre for “Translational Medicine and Pharmacology“. The state of Hessen has thus been supporting the Centre since January 2018 with a sum of around 19.4 million euros lasting until the end of 2020 and, in addition, has approved the funding of a new building to the sum of 21.2 million euros. The partners are Goethe University Frankfurt am Main, the Translational Medicine and Pharmacology department of the Fraunhofer Institute for Molecular Biology and Applied Ecology IME and the Pharmacology department of the Max Planck Institute for Heart and Lung Research in Bad Nauheim.

Prof. Dr. Dr. Gerd Geißlinger, spokesman for the LOEWE Centre, states: “This is an important step for the further sustainable development of Frankfurt as a research location, from which both universities and non-university research institutions as well as companies in Hessen will benefit. We are very grateful to the Hessen state government for the LOEWE program. For us, the funding is an important milestone on the path to the establishment of the first Fraunhofer Institute in Frankfurt.“ From 2021, it is planned to transfer the centre to the Fraunhofer financing model. The business areas of the centre traverse the pharmaceutical value chain: from drug discovery and formulation to translational drug validation, biomedical analysis, predictive clinical models and clinical research. The main indications are pain, multiple sclerosis, sepsis and rheumatological/dermatological inflammatory diseases. TM

Plants for the pharma industry 4.0

Fraunhofer IME presented a living exhibit and it`s digital twin at the joint Fraunhofer booth "Future Factory" at the Hanover Trade Fair 2018. For most, the use of plants to produce protein-based pharmaceuticals was new territory.

Fraunhofer IME is one of the pioneers in Germany and worldwide in research on "Plant-made Pharmaceuticals". Federal Minister for Education and Research Anja Karliczek visited the pavilion of the Fraunhofer-Gesellschaft on the very first day of the fair. The Minister had Fraunhofer President Prof. Dr.-Ing. Reimund Neugebauer explain the details of some Fraunhofer exhibits, including the "Big data analytics in life sciences" exhibit of Fraunhofer IME. The living exhibit displayed the cultivation of tobacco plants at the age of two, four and six weeks under LED lighting. Via a tablet computer, various versions of the so-called digital twin of the plants, a virtual image of the growth process, were visualized to the visitors.

The trade fair presentation demonstrated according to Dr. Dr.-Ing. Johannes Buyel, Head of Integrated Production Platforms at Fraunhofer IME, how the production of biopharmaceuticals in tobacco plants can be improved by digital monitoring. Since plant growth is determined by many factors, such as light or temperature, and at the same time influences the quality parameters important for medical products, such as stability and effectiveness, a good understanding of the process is required. The basis for this understanding is formed by data-derived models, which allow a model predictive control of the cultivation conditions for each batch. MB

Hesse Day 2018: From insect to (finished) product

Science to touch - under this motto numerous LOEWE projects offered the opportunity to get into conversation with the visitors of the Hesse Day in Korbach. At the "Hessen creates knowledge" stand, established top researchers presented their work together with young scientists.

The Bioresources division of the Fraunhofer IME in Gießen presented its work to an interested audience as part of the LOEWE Centre for Insect Biotechnology and Bioresources. Among other things, the researchers clarified the question: What does the Asian ladybug have to do with my health?

The Asian ladybug (*Harmonia axyridis*) is increasingly replacing the native species. The Fraunhofer scientists therefore asked themselves the question how he could do this so successfully. And how does he protect himself from unknown pathogens in his new habitat? In the haemolymph of the Asian ladybug, the "insect blood", a strong activity against bacteria was found that does not occur in native species. Now the researchers at the Fraunhofer IME are investigating whether new active substances against human diseases can be obtained from the beetle's haemolymph. And they are trying to find out whether such agents also work against bacteria that are resistant to antibiotics. AE BR

Cooperation agreement with Jacobs University Bremen

In June 2018, Jacobs University Bremen and Fraunhofer Institute for Molecular Biology and Applied Ecology IME signed a cooperation agreement. The agreement provides for strategic collaboration on research projects in the field of antibiotics development.

A further goal is to promote the exchange between students, researchers and teachers. Fraunhofer IME will give Bachelor students at Jacobs University the opportunity to actively participate in the institute's research projects, either as part of internship programs or by conducting research at the institute as part of their Bachelor theses.This active integration into existing research projects supports the scientific education of the students and helps them to successfully pursue careers in the pharmaceutical or biotechnology industry. Fraunhofer IME offers internships in a variety of experimental and IT disciplines within economically important areas of the natural sciences. The focus is on the discovery and further development of drugs. Doctoral students at Jacobs University who work at Fraunhofer IME in Hamburg are also included in corresponding doctoral programs.

As part of this collaboration, Fraunhofer IME will share its expertise in applied research and modern drug development with Jacobs University. Experienced Fraunhofer IME scientists offer courses, lectures and seminars at Jacobs University, in particular as an integral part of the Bachelor's program "Medicinal Chemistry and Chemical Biology".

Jacobs University and Fraunhofer IME also intend to exchange scientific personnel to share the expertise of both institutions. TM

Dirk Prüfer and team awarded transfer prize

On June 13th, the Westfälische Wilhelms-Universität Münster awarded the transfer prize 2017/2018 for the project "TARAXAGUM™ - Innovations with Russian Dandelion" to Prof. Dr. Dirk Prüfer and his team in cooperation with the Continental Reifen Deutschland GmbH, Hanover. Since 2002, WWU has awarded the Transfer Prize to projects that have emerged from cooperation between research and industry. The prize is endowed with a total of 20,000 euros and was divided this year between two winners.

In the "TARAXAGUM™" project, everything revolves around the Russian dandelion. Although it looks like the domestic dandelion, it has an enormous advantage: Its latex contains large amounts of rubber. When the scientists started the project a few years ago, they faced major challenges. The Russian dandelion was still a wild plant with a branched root system and an elevated but still too low concentration of natural rubber for the industrial use. Through smart breeding, the researchers succeeded in doubling the rubber content within a short period of time. The successful cooperation with the partners Julius Kühn Institute and the plant breeding expert ESKUSA resulted in plants with a significantly less branched root system. MB

BMBF Innovation Forum "Civil Security"

In June, the fourth BMBF Innovation Forum "Civil Security" took place in Berlin. Researchers from Fraunhofer IME, together with project partners from the Forschungszentrum Jülich (Institute for Complex Systems, Bioelectronics) and DITABIS AG, presented their results from the "AquaNANO" project in the exhibition on practical solutions.

The joint BMBF project "AquaNANO" is investigating a novel analytical method for the rapid on-site identification of biological drinking water contaminations. The project is coordinated by Fraunhofer IME. Associated partners are the German Federal Agency for Technical Relief (THW), the Institute for Water and Wastewater Analysis-IWA GmbH and Stadtwerke Aachen AG (STAWAG).

Even if clean water is taken for granted in Germany, contamination can occur after floods, for example. These must be detected as quickly as possible. With the new analysis procedure, aid organizations responsible for drinking water supply in crisis situations should be given a tool to test reliably, mobile and quickly larger drinking water contingents for the presence of biological contaminations. Speed is required, already established test procedures take up to 24 hours too long. AquaNANO pursues an approach in which the results are already available after about one hour. Fully automatically, a drinking water sample is passed through special detection columns; bacterial pathogens and toxins contained in the water bind to magnetic nanoprobes, which are now comparatively easy to detect. This innovative detection method enables the reliable identification of harmful substances so that protective and countermeasures can be initiated quickly. MB

Interview on Hessischer Rundfunk: What we can learn from insects

In July, the Hessischer Rundfunk broadcasted the report insect biotechnology: "Learning from insects means learning to win" on hr-iNFO. In an interview with Professor Dr. Andreas Vilcinskas, manager of the Fraunhofer IME in Gießen, Stephan Hübner presented exciting facts from the field of insect biotechnology: Active ingredients from moth larvae destroy wound germs. The saliva of fly maggots contains substances that can be used effectively in disinfectant patches. What sounds like research science fiction is the result of a very young science: Insect biotechnology.
Germany's centre of insect biotechnology is located at the Justus Liebig University in Gießen. Prof. Vilcinskas is in charge of the research there. He defines insect biotechnology "as the development and application of biotechnological methods to transform insects and their molecules, cells, organs and microorganisms into products and services".
But what makes insects so interesting for Vilcinskas? With more than a million species described, they are by far the most species-rich group of organisms, he says - and thus also the most successful in terms of development history. "In my opinion, this diversity is also reflected on the biochemical level. I therefore see a huge library of natural substances in insects. And in this library we look for new molecules and try to develop them for the benefit of mankind." Insect biotechnology is currently regarded as a "market of the future on the verge of change". So it seems obvious that the coming years will hold many surprising discoveries in store, and some will certainly be made in Hesse.
There could therefore be some truth to the motto Andreas Vilcinskas gave to his work: "Learning from insects means learning to win". AE BR

Fraunhofer lighthouse project "Cost Intelligent Medicine" approved

Effective limitation of health expenditure, rather a more intelligent use of available resources, also requires technology-driven innovation and digitalization. As part of the "Cost Intelligent Medicine" initiative, Fraunhofer IME participates in the interdisciplinary Fraunhofer consortium consisting of the institutes IGD (speaker function), IAIS, IIS, IME, IMW, IOSB and MEVIS in order to advance the development of a digital patient model. The consortium has unique technological expertise in the fields of artificial intelligence and machine learning, knowledge extraction and modelling, data management and visualization, and the necessary medical expertise.

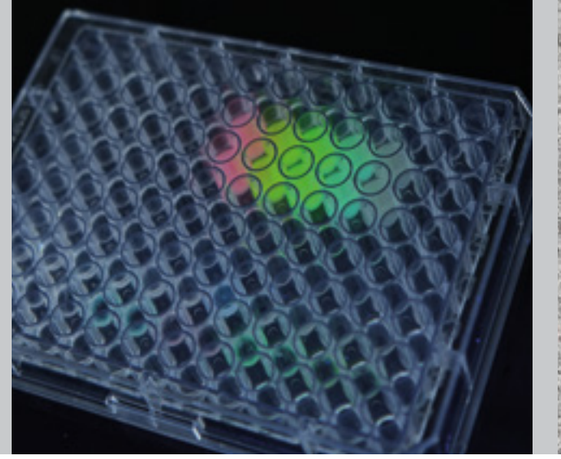
The aim of the lead project MED²ICIN - Medical Data Driving an Integrated cost-intelligent Model is to create a digital platform to link and analyze previously unstructured health and disease data of individuals in order to achieve an intelligent use of health expenditure through more effective prevention, diagnosis, therapy and care. The digital patient model to be developed will be prototypically implemented and evaluated using the example of (chronic) inflammatory bowel disease and (acute) oncological diseases.

With its lighthouse projects, the Fraunhofer-Gesellschaft is setting strategic priorities in order to develop concrete solutions that will benefit Germany as a business location. The topics are geared to the requirements of the economy. The goal is to quickly turn original scientific ideas into marketable products. TM

Cooperation agreement on childcare with the city of Schmallenberg

A better balance between work and family responsibilities and a sustainable equilibrium between company interests and employee interests - these goals have been continuously pursued at the Fraunhofer IME Schmallenberg location for more than two decades. Parents often face difficulties in finding day-care places, day-care mothers are fully occupied or care hours cannot be reconciled with working hours.

In July 2018, Fraunhofer IME entered into a cooperation agreement with the city of Schmallenberg to enable employees to provide care for their pre-school children close to the institute. The objective of this agreement is to secure two places in the newly founded Valentin-KiTa day care centre for children. The agreement is valid from the kindergarten year 2019/2020. Interested parents can contact the equal opportunity commissioner, who will forward the request to the KiTa. The child day care staff also discusses individual care options with interested parents. In return, Fraunhofer IME helps provide the basic equipment for day care for children with a one-time lump sum and a fixed annual rate. The money is used, for example, for child-friendly toys, sleeping facilities or other benefits in kind to make the rooms more attractive and child-friendly. AE BR



License Agreement with LenioBio

Life sciences startup LenioBio GmbH and Fraunhofer IME announced on August 1st the signing of an exclusive license agreement that allows LenioBio to utilize Fraunhofer's proprietary vector solution and technology for the cryopreservation of cell lysates.
Fraunhofer IME's optimized vector solution and cryopreservation technology have been specially developed for the broad range of cell-free biosynthesis applications targeted by LenioBio. With the license from Fraunhofer IME, LenioBio is now expanding its patent family for its innovative cell-free system. In the meantime, LenioBio has launched a cell-free expression kit under the brand name ALiCE™ which is intended for the development of novel proteins.

The development of ALiCE™ was a collaborative effort between Dow AgroSciences LLC and Fraunhofer IME under a long-standing strategic alliance, and the system has been used by where Fraunhofer IME contributed some of the unique materials that made the system best-in-class among all cell-free protein expression systems. Fraunhofer IME has applied this system for the expression of many different protein classes, including those that are known to be difficult to express, such as human growth factors and full-sized antibodies.

Professor Stefan Schillberg, Ph.D., stated, "Cell-free biosynthesis allows the rapid screening and production of even difficult-to-produce proteins. In addition, the high productivity of ALiCE™ opens new fields of applications for cell-free technology that we will develop further together with LenioBio." MB

Summer party of the Fraunhofer employees in Hamburg

At the invitation of Fraunhofer IME, the first summer party of all Fraunhofer employees in Hamburg took place on August 30, 2018. Since mid-2014, the Free and Hanseatic City of Hamburg has been the last federal state to join the Fraunhofer family and is now officially a so-called Fraunhofer home state. The fields of activity of the more than 300 employees in Hamburg are very diverse. In addition to the Branch Lab Screening-Port of the Fraunhofer IME, the Center for Marine Logistics CML, the Fraunhofer Center for Applied Nanotechnology CAN, the Fraunhofer Institution for Additive Production Technologies IAPT and the Fraunhofer MEVIS and IFAM facilities within the Center for Applied Aviation Research, are located in Hamburg. These application centers, formerly operating as GmbH or public private partnership, were integrated into the Fraunhofer-Gesellschaft in stages and thus fulfill another core element of Hamburg's innovation strategy, namely to establish Fraunhofer in Hamburg.

The aim of the summer party was to network the employees and to develop new perspectives through interdisciplinary exchange. The "Family Status" exhibition was chosen as the venue for this "Family Festival". In this exhibition of contemporary art, 17 artists approached this topic from very different perspectives. The aim of the exhibition was to bring together scientists and artists in order to provoke innovative ideas. This concept has already been successfully applied to the BMBF application "Im-Puls-Bio", in which researchers, including Fraunhofer IME, will work together with an artist collective on the challenges of the bioeconomy. TM

Colorful potatoes: Chilean-German project meeting

Beginning of August scientists of the Chilean-German project "MoMaPo" met at Fraunhofer IME in Aachen. The aim of the binational cooperation project is the identification of molecular markers for an increased anthocyanin content in potato tubers. The team combines the expertise of scientists from three institutions: The Universidad Austral de Chile based in Valdivia in the south of Chile, Fraunhofer Chile Research - Center for Systems Biotechnology CBS in Santiago de Chile and Fraunhofer IME in Münster and Aachen.
The researchers have access to the potato genebank of the Universidad Austral de Chile, which comprises about 500 landraces and varieties. A major part are the potatoes collected in the area of Chiloe Island, which are characterized by a particularly high diversity in the characteristic colored tubers. 290 of these plants were analyzed in the joint project with regard to potential molecular markers for an increased anthocyanin content and subsequently bioinformatically analyzed for association with the anthocyanin content determined. In the project meeting the researchers discussed the latest results and presented them on the following day to the interested audience at Fraunhofer IME.

The project is funded in Germany by the Federal Ministry of Education and Research (BMBF) and in Chile by the National Council for Scientific Research and Technology (CONICYT). As part of the project, young scientists also had the opportunity to do the experimental part of their final theses. Thus, during a two-month stay of a Chilean master student of the Universidad Austral de Chile at Fraunhofer IME in Aachen, experimental data were generated which, after careful evaluation, provide the basis for a master's thesis and a joint scientific publication. MB

Insecta 2018

Since 2015, the International Conference "Insecta" has provided an annual overview of the state of the art and perspectives of insect use. From 5 to 7 September 2018, representatives from science, industry and politics discussed the technological, ecological, political, legal and ethical aspects of insect products at the Justus Liebig University Gießen (JLU). With the participation of the Fraunhofer IME in Gießen, around 250 participants from 32 countries gave 60 lectures and 40 posters to highlight last year's main topics of the conference. These were the safety of insect products, production standards and non-food applications of insects, for example in pharmaceuticals or in the recycling of organic waste.

Insects could serve as an alternative source of protein to meet the protein needs of the world's growing population, which is not possible with conventional methods such as meat production. In addition, insects are used to produce high-quality proteins and fats from organic waste, for example for animal nutrition, in an ecologically sound way. There is therefore a considerable need to present and discuss new developments in the use of insects as feed and food as well as in the non-food sector.

Due to their biodiversity, insects also represent a gigantic, still largely unexplored library of natural substances. They can be used to produce new antibiotics or active substances for plant protection. AE BR

Dr. Philip Gribbon hands over the role as EU-OPENSCREEN coordinator

In a ceremony in Berlin on the 27th September 2018, Jean Eric Paquet, Director General of DG Research and Innovation presented the ERIC certificate on behalf of the European Commission to Georg Schütte, State Secretary at the Federal Ministry of Education and Research (BMBF) and Dr. Wolfgang Fecke, Director General of EU-OPENSCREEN. Dr Philip Gribbon from Fraunhofer IME ScreeningPort, who has been the Coordinator of EU-OPENSCREEN from 2014 to 2018 attended the meeting to represent the Fraunhofer-Gesellschaft and has been honoured to bring this pan European approach into a legal European Research Infrastructure Consortium (ERIC).
EU-OPENSCREEN integrates high-capacity screening platforms throughout Europe, which jointly use a rationally selected compound collection, comprising up to 140.000 commercial and proprietary compounds collected from European chemists. EU-OPENSCREEN offers to researchers from academic institutions, SME's and industrial organisations open access to its shared resources. EU-OPENSCREEN will collaboratively develop novel molecular tool compounds with external users from various disciplines of the life sciences.
The Fraunhofer IME is one of only 4 German EU-OPENSCREEN sites nominated by the BMBF and it was subsequently validated in April 2018 as one of 20 official EU-OPENSCREEN sites from across 7 European countries. In 2019, Fraunhofer IME will be part of the related EU-funded projects, EU-OPENSCREEN-DRIVE and the European Open Science Cloud – LIFE, which will improve the process of small molecule drug discovery and promote the widespread sharing and reuse of data across the scientific community. TM

Fraunhofer-Alumni-Summit in Aachen

The sun shined brightly on September 27, when the three Fraunhofer Institutes in Aachen (ILT, IPT and IME) opened their doors to the alumni of the Fraunhofer-Gesellschaft.
Almost 100 alumni had set out to visit the three institutes. For some it was an opportunity to come home to their former workplaces, and for others it was finally the opportunity to get to know the other institutes.

Fraunhofer IME, focusing on "Applied Life Sciences from Molecule to Ecosystem" was new territory for many alumni. Dr. Stefan Rasche, Ann-Katrin Beuel and Simon Vogel offered guided tours and used exhibits to explain the focus of current research and development in Aachen.
Simon Vogel presented a new concept for "nutrition in the future". Herbaceous plants such as lettuce and basil can be cultivated using indoor farms, not only horizontally but also orbitally.
Stefan Rasche and Ann-Katrin Beuel demonstrated the screening systems they use to determine the type of light plants and individual plant cells need for optimal product synthesis. MB

Kerstin Derz – new covenor of the ISO Working group "Human Exposure"

With regard to the environmental fate of pollutants, bioavailability becomes an increasingly greater focus of attention. Especially the bioavailability of a substance for soil-living micro-organisms is an important criterium for a chemical to be degraded or to accumulate, and thus will be potentially harmful for the environment. The bioavailability of a substance in soil can also be of importance for humans, for example when decisions have to be made on whether a contaminated site can be released for certain uses. In the context of various research projects Dr. Kerstin Derz, Deputy Head of the Department Ecological Chemistry, has developed methodologies regarding both aspects of bioavailability, which finally had an influence on legislation on the assessment of soils and contaminated sites.
Her interest in getting a deeper insight into questions of bioavailability motivated Kerstin Derz to become a member of the national DIN-Working Group of the standardization committee NA 119-01-02-02-01 AK "Bioavailability" which is dealing with the standardization of methods to determine bioavailabilty. Her committment on an international level led her to participate in the ISO Working Group ISO/TC 190/SC 7/WG4 "Human Exposure". At a meeting of the Group in Brno, Czech Republic, in September 2018 she was elected to take over the position of a convenor, which means that she will be leading this group as of 2019 for an initial period of two years. Further to developing ISO-standards the working group focuses on methods to determine bioavailability and on risk assessment methodologies. One of the standards currently under revision is the ISO 15800:2003 "Soil quality – Characterization of soil with respect to human exposure", which will ultimately become the ISO/DIS 15800. AE BR

Workshop Nanomedicine

On October 20, 2018, the LOEWE Center for Translational Medicine and Pharmacology hosted an interdisciplinary workshop on the characterization of fine particles in medicine and biology with the participation of Fraunhofer IME, Goethe University, House of Pharma e.V. and Malvern Panalytical.

The top-class event with more than 80 participants from academic research and the pharmaceutical industry discussed the importance of innovative measurement methods in pharmaceutical product development. After a brief introduction to the world of particle characterization, the latest research results from various areas of medical application were presented. Especially in this still relatively young field of application of nanotechnology, the creation of uniform standards plays an outstanding role in addition to the accuracy of the measurement method, as Dr. Matthias G. Wacker emphasized in his lecture. The measurement method determines the perception of the developer and thus becomes an indispensable tool in drug research.

The great importance of this topic was also underlined by the strong participation of innovation-friendly start-ups and biotech companies, which helped to shape the day through critical questions and lively discussions. The event was also supported by equipment manufacturers such as Malvern Panalytical, VWR International and Pharma Test Apparatebau AG. TM

ASPIRE Research Award 2018

The Clinical Research Department of the Translational Medicine and Pharmacology Division of the Fraunhofer IME received funding for a multinational, multicenter, randomized, controlled clinical trial through the highly competitive international ASPIRE Research Awards made by Pfizer (Europe, Israel, Turkey, Russia, Australia, New Zealand, Japan, South Korea).

In this study, the efficacy of non-steroidal anti-inflammatory drugs (NSAIDs) in patients with active rheumatoid arthritis, after new initiation of an innovative kinase inhibitor therapy, will be compared to TNF inhibition after failure of conventional basic therapies. In addition, pain characteristics will be measured by Quantitative Sensory Testing (QST). This clinical study serves to further our knowledge on the potential analgesic effects of kinase inhibition. This could represent a highly relevant patient benefit, since in rheumatic diseases, in addition to the systemic inflammation addressed by medication, severe pain in the musculoskeletal system is an omnipresent concern.

The development of the innovative study concept and the implementation of the project are carried out in close cooperation with the Department of Rheumatology of the University Hospital of the Goethe University and the University Medicine, Charité Berlin. The funding for this project amounts to 2 million euros. TM

Bioaccumulation: Two workshops on the optimization of test strategies

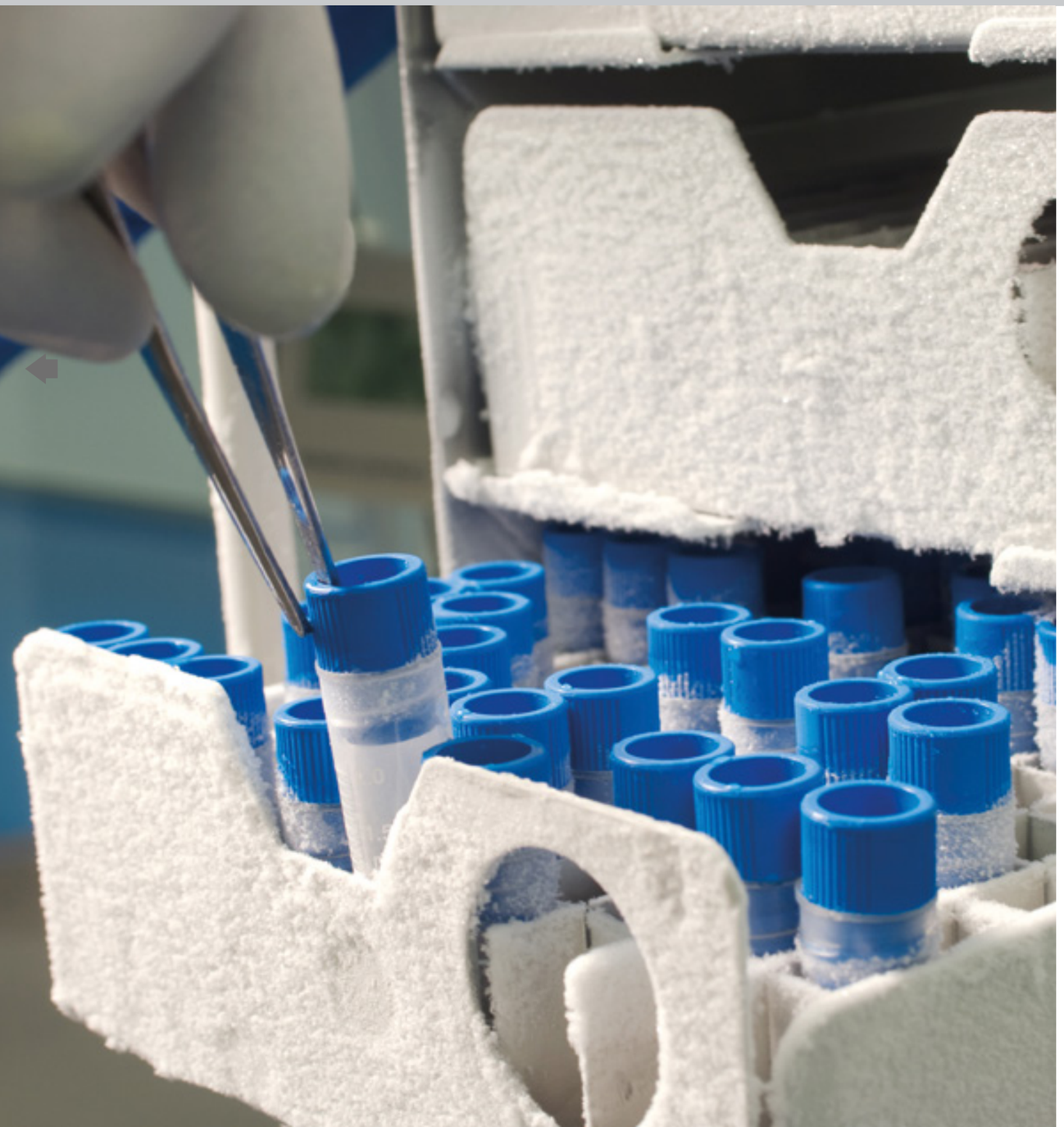
Do we need specific bioaccumulation tests to identify and evaluate bioaccumulative effects of nanomaterials in the environment? Are bivalvia representative test organisms for aquatic ecosystems? And does the testing of nanomaterials under laboratory conditions allow the evaluation of detrimental effects in the environment? These and further questions were addressed by Prof. Dr. Christian Schlechtriem and staff members in the last years as part of a research project funded by the German Environment Agency (UBA). Findings were presented at the workshop "Bioaccumulation of manufactured nanomaterials in freshwater bivalves", which took place in Dessau on October 23rd 2018.

In cooperation with the Helmholtz Centre for Environmental Research UFZ and the European Chemical Industry Council CEFIC, Professor Schlechtriem organized a workshop in Leipzig on February 21st 2018 about the application of toxicokinetic data for assessing bioaccumulation of pollutants. The featured strategies for the optimization of test systems were developed particularly against the backdrop of reducing animal experiments.

On both occasions, representatives of research and development as well as representatives of industry and regulation were involved. AE BR

The success story continues

An important milestone has been reached on the way to market readiness for dandelion rubber. On St. Nicholas Day, Continental Reifen GmbH Germany inaugurated the "Taraxagum Lab Anklam" research and test laboratory in Mecklenburg-Vorpommern. In the future, the cultivation and processing of the Russian dandelion as an alternative raw material to the tropical rubber tree will be investigated there. In the mid-term, about 20 employees from the fields of agricultural sciences, chemistry, production and process engineering will be employed there. According to Continental's own information, the company has invested 35 million euros in the new laboratory. The Ministry of Economics in Schwerin contributed around 11.6 million euros.
Continental Executive Board Member Nikolai Setzer emphasized "We see the Russian dandelion as an important alternative and supplement to conventional natural rubber from the tropics for meeting the worldwide increase in demand in an environmentally friendly and reliable way." Currently, farmers from the region are growing the Russian dandelion on an area of 30 hectares, which is to be increased to 20,000 hectares in the longer term.
Prof. Dr. Dirk Prüfer and his team laid the basis for the industrial use of the Russian dandelion. In cooperation with the Münster University, the plant breeding company ESKUSA, Continental Reifen GmbH Germany and the Julius Kühn Institute, they developed this dandelion species from a wild to a crop plant."
For many years now, we've been working on understanding the molecular basis of rubber synthesis in dandelions. This understanding of the biology involved has now brought industrial application within our grasp." emphasized Dirk Prüfer, Professor at WWU and head of department at Fraunhofer IME. MB



FACTS 2018

Publications

Patents

Bachelor's, Master's,
State Examination and Doctoral Theses

Networks in science and industry

PUBLICATIONS

MB Molecular Biotechnology

AEBR Applied Ecology and Bioresources

TM Translational Medicine

PUBLICATIONS

Molecular Biotechnology

A - C

Beinecke, F.A., Grundmann, L., Wiedmann, D.R., Schmidt, F.J., Caesar, A.S., Zimmermann, M., Lahme, M., Twyman, R.M., Prüfer, D., Noll, G.A.
The FT/FD-dependent initiation of flowering under long-day conditions in the day-neutral species *Nicotiana tabacum* originates from the facultative short-day ancestor *Nicotiana tomentosiformis* (2018) Plant Journal, 96 (2), 329-342. DOI: 10.1111/tpj.14033

Bröker, J.N., Laibach, N., Müller, B., Prüfer, D., Schulze Gronover, C.
***Taraxacum brevicorniculatum* rubber elongation factor TbREF associates with lipid droplets and affects lipid turn-over in yeast** (2018) Biotechnology Reports, 20, e00290. DOI: 10.1016/j.btre.2018.e00290

Bröker, J.N., Müller, B., van Deenen, N., Prüfer, D., Schulze Gronover, C.
Upregulating the mevalonate pathway and repressing sterol synthesis in *Saccharomyces cerevisiae* enhances the production of triterpenes (2018) Applied Microbiology and Biotechnology, 102 (16), 6923-6934. DOI: 10.1007/s00253-018-9154-7

Buyel, J.F.
Plants as sources of natural and recombinant anti-cancer agents (2018) Biotechnology Advances, 36 (2), 506-520. DOI: 10.1016/j.biotechadv.2018.02.002

Chouman, K., Korioth-Schmitz, B., Sack, M., Schmitz, J.E., Pham, A.T., Fischer, R., Barth, S., Klockenbring, T., Fendel, R.
Characterization of new anti-IL-6 antibodies revealed high potency candidates for intracellular cytokine detection and specific targeting of IL-6 receptor binding sites (2018) European Cytokine Network, 29 (2), 59-72. DOI: 10.1684/ecn.2018.0409

D - J

Gengenbach, B.B., Müschen, C.R., Buyel J.F.
Expression and purification of human phosphatase and actin regulator 1 (PHACTR1) in plant-based systems (2018) Protein Expression and Purification, 151, 46-55. DOI: 10.1016/j.pep.2018.06.003

Gresch, G., Schenke, L., Mladenov, R., Zwirner, S., Cremer, C., Niesen, J., Grieger, E., Brümmendorf, T., Jost, E., Fischer, R., Stockmeyer, B., Barth, S., Nachreiner, T., Stein, C.
Elimination of different leukaemia subtypes using novel CD89-specific human cytolytic fusion proteins (2018) British Journal of Haematology, 183 (2), 313-317. DOI: 10.1111/bjh.14971

Hausmann, R., Chudobová, I., Spiegel, H., Schillberg, S.
Proteomic analysis of CHO cell lines producing high and low quantities of a recombinant antibody before and after selection with methotrexate (2018) Journal of Biotechnology, 265, 65-69. DOI: 10.1016/j.jbiotec.2017.11.008

Holland, T., Buyel, J.F.
Bioreactor-based production of glycoproteins in plant cell suspension cultures (2018) Methods in Molecular Biology, 1674, 129-146. DOI: 10.1007/978-1-4939-7312-5_11

J - L

Jansing, J., Buyel, J.F.
The correlation between DsRed mRNA levels and transient DsRed protein expression in plants depends on leaf age and the 5' untranslated region (2018) Biotechnology Journal, 1800075. DOI: 10.1002/biot.201800075

Kern, K., Havenith, H., Delaroque, N., Rautenberger, P., Lehmann, J., Fischer, M., Spiegel, H., Schillberg, S., Ehrentreich-Foerster, E., Aurich, S., Treudler, R., Szardenings, M.
The immunome of soy bean allergy: Comprehensive identification and characterization of epitopes (2018) Clinical and Experimental Allergy, e13285. DOI: 10.1111/cea.13285

Laibach, N., Schmidl, S., Müller, B., Bergmann, M., Prüfer, D., Schulze Gronover, C.
Small rubber particle proteins from *Taraxacum brevicorniculatum* promote stress tolerance and influence the size and distribution of lipid droplets and artificial poly(cis-1,4-isoprene) bodies (2018) Plant Journal, 93 (6), 1045-1061. DOI: 10.1111/tpj.13829

Lim, S.S.Y., Chua, K.H., Nölke, G., Spiegel, H., Goh, W.L., Chow, S.C., Kee, B.P., Fischer, R., Schillberg, S., Othman, R.Y.
Plant-derived chimeric antibodies inhibit the invasion of human fibroblasts by *Toxoplasma gondii* (2018) PeerJ, 2018 (12), 5780. DOI: 10.7717/peerj.5780

M - R

Martínez, M.E., Poirrier, P., Prüfer, D., Schulze, C., Jorquera, L., Ferrer, P., Díaz, K., Chamy, R.
Kinetics and modeling of cell growth for potential anthocyanin induction in cultures of *Taraxacum officinale* G.H. Weber ex Wiggers (Dandelion) in vitro (2018) Electronic Journal of Biotechnology, 36, 15-23. DOI: 10.1016/j.ejbt.2018.08.006

McElroy, C., Jennewein, S.
Taxol® biosynthesis and production: from forests to fermenters. (2018) Biotechnology of Natural Products,145-185. Springer, Cham. DOI: 10.1007/978-3-319-67903-7

Menzel, S., Holland, T., Boes, A., Spiegel, H., Fischer, R., Buyel, J.F.
Downstream processing of a plant-derived malaria transmission-blocking vaccine candidate (2018) Protein Expression and Purification, 152, 122-130. DOI: 10.1016/j.pep.2018.07.012

Nölke, G., Barsoum, M., Houdelet, M., Arcalis, E., Kreuzaler, F., Fischer, R., Schillberg, S.
The integration of algal carbon concentration mechanism components into tobacco chloroplasts increases photosynthetic efficiency and biomass (2018). Biotechnology Journal, e1800170 DOI: 10.1002/biot.201800170

Nölke, G., Volke, D., Chudobová, I., Houdelet, M., Lusso, M., Frederick, J., Adams, A., Kudithipudi, C., Warek, U., Strickland, J.A., Xu, D., Schinkel, H., Schillberg, S.
Polyamines delay leaf maturation in low-alkaloid tobacco varieties (2018) Plant Direct, 2 (7), e00077. DOI: 10.1002/pld3.77

Rühl, C., Knödler, M., Opdensteinen, P., Buyel, J.F.
A linear epitope coupled to DsRed provides an affinity ligand for the capture of monoclonal antibodies (2018) Journal of Chromatography A, 1571, 55-64. DOI: 10.1016/j.chroma.2018.08.014

S - U

Santos, R.B., Chandrasekar, B., Mandal, M.K., Kaschani, F., Kaiser, M., Both, L., van der Hoorn, R.A.L., Schiermeyer, A., Abranches, R.
Low protease content in *medicago truncatula* cell cultures facilitates recombinant protein production (2018) Biotechnology Journal, 13 (7), 1800050. DOI: 10.1002/biot.201800050

Schubert, M., Spiegel, H., Schillberg, S., Nölke, G.
Aspergillus-specific antibodies – Targets and applications (2018) Biotechnology Advances, 36 (4), 1167-1184. DOI: 10.1016/j.biotechadv.2018.03.016

Spiegel, H., Stöger, E., Twyman, R.M., Buyel, J.F.
Current status and perspectives of the molecular farming landscape (2018) Molecular Pharming: Applications, Challenges and Emerging Areas, 1-23. DOI: 10.1002/9781118801512.ch1

V - Z

Tyutereva, E.V., Dobryakova, K.S., Schiermeyer, A., Shishova, M.F., Pawlowski, K., Demidchik, V., Reumann, S., Voitsekhovskaja, O.V.
The levels of peroxisomal catalase protein and activity modulate the onset of cell death in tobacco BY-2 cells via reactive oxygen species levels and autophagy (2018) Functional Plant Biology, 45(1-2), 247-258. DOI: 10.1071/FP16418

Wollschlaeger, C., Meinhold-Heerlein, I., Cong, X., Bräutigam, K., Di Fiore, S., Zeppernick, F., Klockenbring, T., Stickeler, E., Barth, S., Hussain, A.F.
Simultaneous and independent dual site-specific self-labeling of recombinant antibodies (2018) Bioconjugate Chemistry, 29 (11), 3586-3594. DOI: 10.1021/acs.bioconjchem.8b00545

PUBLICATIONS

Applied Ecology and Bioresources

A - C

Ahlborn, J., Calzolari, N., Spielmeyer, A., Avci, S.S., Zimmer, M., Rühl, M.
Enrichment of vitamin D2 in mycelium from submerged cultures of the agaric mushroom *Pleurotus sapidus* (2018) Journal of Food Science and Technology, 55 (9), 3833–3839. DOI: 10.1007/s13197-018-3290-z

Amorim, M.J.B., Lin, S., Schlich, K., Navas, J.M., Brunelli, A., Neubauer, N., Vilsmeier, K., Costa, A.L., Gondikas, A., Xia, T., Galbis, L., Badetti, E., Marcomini, A., Hristozov, D., Kammer, F., von der; Hund-Rinke, K., Scott-Fordsmand, J.J., Nel, A., Wohlleben, W.
Environmental impacts by fragments released from nano-enabled products: A multiassay, multimaterial exploration by the SUN approach (2018) Environmental Science and Technology, 52 (3), 1514-1524. DOI: 10.1021/acs.est.7b04122

Ankenbrand, M.J., Hohlfeld, S.C.Y., Weber, L., Förster, F., Keller, A.
Functional exploration of natural networks and ecological communities (2018) Methods in Ecology and Evolution, 9 (9), 2028-2033. DOI: 10.1111/2041-210X.13060

Aumann, R.A., Schetelig, M.F., Häcker, I.
Highly efficient genome editing by homology-directed repair using Cas9 protein in Ceratitis capitata (2018) Insect Biochemistry and Molecular Biology, 101, 85-93. DOI: 10.1016/j.ibmb.2018.08.004

Badalyan, G., Diaz, C., Bücking, M., Lipski, A.
Novel sensor platform for rapid detection and quantification of coliforms on food contact surfaces (2018) Journal of Microbiological Methods, 153, 74-83. DOI: 10.1016/j.mimet.2018.09.009

Baudach, A., Lee, K.-Z., Vogel, H., Vilcinskas, A.
Immunological larval polyphenism in the map butterfly *Araschnia levana* reveals the photoperiodic modulation of immunity (2018) Ecology and Evolution, 8 (10), 4891–4898. DOI: 10.1002/ece3.4047

Carrau, T., Hiebert, N., Vilcinskas, A., Lee, K.-Z.
Identification and characterization of natural viruses associated with the invasive insect pest *Drosophila suzukii* (2018) Journal of Invertebrate Pathology, 154, 74-78. DOI: 10.1016/j.jip.2018.04.001

Corman, A.-M., Schwemmer, P., Mercker, M., Asmus, H., Rüdel, H., Klein, R., Boner, M., Hofem, S., Koschorreck, J., Garthe, S.
Decreasing δ13C and δ15N values in four coastal species at different trophic levels indicate a fundamental food-web shift in the southern North and Baltic Seas between 1988 and 2016 (2018) Environmental Monitoring and Assessment, 190 (8), 461. DOI: 10.1007/s10661-018-6827-8

Couto, J., Tonk, M., Ferrolho, J., Antunes, S., Vilcinskas, A., La Fuente, de J., Domingos, A., Cabezas-Cruz, A.
Antiplasmodial activity of tick defensins in a mouse model of malaria (2018) Ticks and Tick-borne Diseases, 9 (4), 844–849. DOI: 10.1016/j.ttbdis.2018.03.011

D - F

Diaz, C., Badalyan, G., Bücking, M.
Molecular techniques for the detection and identification of yeasts in wine (2018) Molecular Techniques in Food Biology: Safety, Biotechnology, Authenticity and Traceability. Hoboken/NJ: Wiley, 323-340. DOI: 10.1002/9781119374633.ch14

Dreyer, A., Neugebauer, F., Rüdel, H., Klein, R., Lohmann, N., Rauert, C., Koschorreck, J.
Halogenated flame retardants in tree samples applied as bioindicators for atmospheric pollution (2018) Chemosphere, 208, 233-240. DOI: 10.1016/j.chemosphere.2018.05.033

EFSA Panel on Plant Protection Products and their Residues (PPR), Ockleford, C., Adriaanse, P., Berny, P., Brock, T., Duquesne, S., Grilli, S., Hernandez-Jerez, A.F., Hougaard Bennekou, S., Klein, M., Kuhl, T., Laskowski, R., Machera, K., Pelkonen, O., Pieper, S., Smith, H., Stemmer, M., Sundh, I., Tiktak, A., Topping, C.J., Wolterink, G., Cedergreen, N., Charles, S., Focks, A., Reed, M., Arena, M., Ippolito, A., Byers, H., Teodorovic, I.
Scientific opinion on the state of the art of toxicokinetic/toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms (2018) EFSA Journal, 16 (8), e05377. DOI: 10.2903/j.efsa.2018.5125

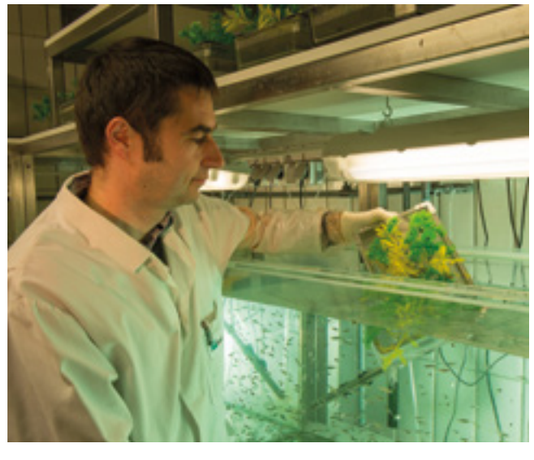
EFSA Panel on Plant Protection Products and their Residues (PPR), Ockleford, C., Adriaanse, P., Berny, P., Brock, T., Duquesne, S., Grilli, S., Hernandez-Jerez, A.F., Hougaard Bennekou, S., Klein, M., Kuhl, T., Laskowski, R., Machera, K., Pelkonen, O., Pieper, S., Stemmer, M., Sundh, I., Teodorovic, I., Tiktak, A., Topping, C.J., Wolterink, G., Craig, P., Jong, F., de, Manachini, B., Sousa, P., Swarowsky, K., Auteri, D., Arena, M., Smith, R.
Scientific opinion on the state of the science on pesticide risk assessment for amphibians and reptiles (2018) EFSA Journal, 16 (2), e05125. DOI: 10.2903/j.efsa.2018.5377

EFSA Panel on Plant Protection Products and their Residues (PPR), Ockleford, C., Hernandez-Jerez, A.F., Hougaard Bennekou, S., Klein, M., Adriaanse, T.P., Berny, P., Brock, T., Duquesne, S.G., Kuhl, T., Laskowski, R., Machera, K., Pelkonen, O., Pieper, S., Stemmer, M., Sundh, I., Teodorovic, I., Topping, C.J., Wolterink, G., Smith, R.H., Gimising, A.L., Kasteel, R., Boivin, A., van der Linden, T., Magrans, J.O., Egsmose, M., Tiktak, A.
Scientific opinion about the guidance of the Chemical Regulation Directorate (UK) on how aged sorption studies for pesticides should be conducted, analysed and used in regulatory assessments (2018) EFSA Journal, 16 (8), e05382. DOI: 10.2903/j.efsa.2018.5286

EFSA Panel on Plant Protection Products and their Residues (PPR), Ockleford, C., Adriaanse, P., Hougaard Bennekou, S., Berny, P., Brock, T., Duquesne, S., Grilli, S., Hernandez-Jerez, A.F., Klein, M., Kuhl, T., Laskowski, R., Machera, K., Pelkonen, O., Pieper, S., Smith, R., Stemmer, M., Sundh, I., Teodorovic, I., Tiktak, A., Topping, C.J., Gundert-Remy, U., Kersting, M., Waalkens-Berendsen, I., Chiusolo, A., Court, M.D., Dujardin, B., Kass, G.E., Mohimont, L., Nougadere, A., Reich, H., Wolterink, G.
Scientific opinion on pesticides in foods for infants and young children (2018) EFSA Journal, 16 (6), e05286. DOI: 10.2903/j.efsa.2018.5286

Eisenhardt, M., Schlupp, P., Höfer, F., Schmidts, T., Hoffmann, D., Czermak, P., Pöppel A.-K., Vilcinskas, A., Runkel, F.
The therapeutic potential of the insect metalloproteinase inhibitor against infections caused by *Pseudomonas aeruginosa* (2018) The Journal of Pharmacy and Pharmacology, 71 (3), 316-328. Online first. DOI: 10.1111/jphp.13034

Erdős, B., Grachten, M., Czermak, P., Kovács, Z.
Artificial neural network-assisted spectrophotometric method for monitoring fructo-oligosaccharides production (2018) Food and Bioprocess Technology, 11 (2), 305-313. DOI: 10.1007/s11947-017-2011-3



Finnegan, M.C., Emburey, S., Hommen, U., Baxter, Leilan R., Hoekstra, P., Hanson, M.L., Thompson, H., Hamer, M.
A freshwater mesocosm study into the effects of the neonicotinoid insecticide thiamethoxam at multiple trophic levels (2018) Environmental Pollution, 242, 1444-1457. DOI: 10.1016/j.envpol.2018.07.096

Fishilevich, E., Bowling, A., Frey, M.L.F., Wang, P.H., Lo, W., Rangasamy, M., Worden, S.E., Pence, H. E., Gandra, P., Whitlock, S.L., Schulenberg, G., Knorr, E., Tenbusch, L., Lutz, J.R., Novak, S., Hamm, R.L., Schnelle, K.D., Vilcinskas, A., Narva, K.E.
RNAi targeting of rootworm Troponin I transcripts confers root protection in maize (2018) Insect Biochemistry and Molecular Biology, 104, 20–29. DOI: 10.1016/j.ibmb.2018.09.006

Fliedner, A., Rüdel, H., Knopf, B., Lohmann, N., Paulus, M., Jud, M., Pirntke, U., Koschorreck, J.
Assessment of seafood contamination under the marine strategy framework directive: contributions of the German environmental specimen bank (2018) Environmental Science and Pollution Research International: ESPR, 25 (27), 26939-26956. DOI: 10.1007/s11356-018-2728-1

Fliedner, A., Rüdel, H., Lohmann, N., Buchmeier, G., Koschorreck, J.
Biota monitoring under the Water Framework Directive: On tissue choice and fish species selection (2018) Environmental Pollution, 235, 129-140. DOI: 10.1016/j.envpol.2017.12.052

G - I

Gegner, T., Carrau, T., Vilcinskas, A., Lee, K.-Z.
The infection of *Harmonia axyridis* by a parasitic nematode is mediated by entomopathogenic bacteria and triggers sex-specific host immune responses (2018a) Scientific Reports, 8 (1), 15938. DOI: 10.1038/s41598-018-34278-x

Gegner, T., Schmidtberg, H., Vogel, H., Vilcinskas, A.
Population-specific expression of antimicrobial peptides conferring pathogen resistance in the invasive ladybird *Harmonia axyridis* (2018b) Scientific Reports, 8 (1), 3600. DOI: 10.1038/s41598-018-21781-4

Goss, K.-U., Linden, L., Ulrich, N., Schlechtriem, C.
Revisiting elimination half live as an indicator for bioaccumulation in fish and terrestrial mammals (2018) Chemosphere, 210, 341-346. DOI: 10.1016/j.chemosphere.2018.07.017

Grein, T.A., Loewe, D., Dieken, H., Salzig, D., Weidner, T., Czermak, P.
High titer oncolytic measles virus production process by integration of dielectric spectroscopy as online monitoring system (2018) Biotechnology and Bioengineering, 115 (5), 1186-1194. DOI: 10.1002/bit.26538

PUBLICATIONS

Grigoryan, K., Badalyan, G., Nersisyan, L., Tavadyan, L., Sargsyan, M.
Inactivation kinetics of *Escherichia coli* and S*taphylococcus aureus* by a hydrogen peroxide based disinfectant (2018) Journal of Hygienic Engineering and Design, 23, 8-11.

Gupta, D.K., Rühl, M., Mishra, B., Kleofas, V., Hofrichter, M., Herzog, R., Pecyna, M.J., Sharma, R., Kellner, H., Hennicke, F., Thines, M.
The genome sequence of the commercially cultivated mushroom Agrocybe aegerita reveals a conserved repertoire of fruiting-related genes and a versatile suite of biopolymer-degrading enzymes (2018) BMC Genomics, 19 (1), 48. DOI: 10.1186/s12864-017-4430-y

Häcker, I., Schetelig, M.F.
Molecular tools to create new strains for mosquito sexing and vector control (2018) Parasites & Vectors 11 (Suppl 2), 645. DOI: 10.1186/s13071-018-3209-6

Harmsen, J., Hennecke, D., Hund-Rinke, K., Lahr, J., Deneer, J.
Advances in the development of procedures to establish the toxicity of non-extractable residues (NER) in soil LRI-ECO25 (2018) Wageningen University & Research. DOI: 10.18174/463765

Hennecke, D., Bauer, A., Herrchen, M., Wischerhoff, E., Gores, F.
Cationic polyacrylamide copolymers (PAMs): Environmental half life determination in sludge-treated soil (2018) Environmental Sciences Europe, 30, 16. DOI: 10.1186/s12302-018-0143-3

Hirsch, R., Wiesner, J., Marker, A., Pfeifer, Y., Bauer, A., Hammann, P.E., Vilcinskas, A.
Profiling antimicrobial peptides from the medical maggot *Lucilia sericata* as potential antibiotics for MDR Gram-negative bacteria (2018) The Journal of Antimicrobial Chemotherapy, 74 (1), 96–107. Online first. DOI: 10.1093/jac/dky386

Hoffmann, D., Ebrahimi, M., Gerlach, D., Salzig, D., Czermak, P.
Reassessment of inclusion body-based production as a versatile opportunity for difficult-to-express recombinant proteins (2018) Critical Reviews in Biotechnology, 38 (5), 729-744. DOI: 10.1080/07388551.2017.1398134

Hoffmann, D., Eckhardt, D., Gerlach, D., Vilcinskas, A., Czermak, P.
Downstream processing of Cry4AaCter-induced inclusion bodies containing insect-derived antimicrobial peptides produced in *Escherichia coli* (2018) Protein Expression and Purification, 155, 120–129. Online first. DOI: 10.1016/j.pep.2018.12.002

Hund-Rinke, K., Schlich, K., Kühnel, D., Hellack, B., Kaminski, H., Nickel, C.
Grouping concept for metal and metal oxide nanomaterials with regard to their ecotoxicological effects on algae, daphnids and fish embryos (2018) NanoImpact, 9, 52-60. DOI: 10.1016/j.impact.2017.10.003

J - L

Joachim, M., Schäfer, J.G., Gerlach, D., Czermak, P.
High cell density cultivation of Δgor/ΔtrxB E. coli in a chemically defined minimal medium with an enhanced iron concentration (2018) Process Biochemistry, 73, 1-5. DOI: 10.1016/j.procbio.2018.07.022

Jürjens, G., Schuler, S.M.M., Kurz, M., Petit, S., Couturier, C., Jeannot, F., Nguyen, F., Wende, R.C., Hammann, P.E., Wilson, D.N., Bacqué, E., Pöverlein, C., Bauer, A.
Total Synthesis and Structural Revision of the Antibiotic Tetrapeptide GE81112A (2018) Angewandte Chemie - International Edition, 57 (37),12157-12161. DOI: 10.1002/anie.201805901

Kampe, S., Kaegi, R., Schlich, K., Wasmuth, C., Hollert, H., Schlechtriem, C.
Silver nanoparticles in sewage sludge: Bioavailability of sulfidized silver to the terrestrial isopod Porcellio scaber (2018) Environmental Toxicology and Chemistry, 37 (6), 1606-1613. DOI: 10.1002/etc.4102

Kidd, K.A., Burkhard, L.P., Babut, M., Borgå, K., Muir, D.C.G., Perceval, O., Rüdel, H., Woodburn, K., Embry, M.R.
Practical advice for selecting or determining trophic magnification factors for application under the European Union water framework directive (2018) Integrated Environmental Assessment and Management, Online first. DOI: 10.1002/ieam.4102

Knorr, E., Fishilevich, E., Tenbusch, L., Frey, M.L. F., Rangasamy, M., Billion, A., Worden, S.E., Gandra, P., Arora, K., Lo, W., Schulenberg, G., Valverde-Garcia, P., Vilcinskas, A., Narva, K.E.
Gene silencing in *Tribolium castaneum* as a tool for the targeted identification of candidate RNAi targets in crop pests (2018) Scientific Reports, 8 (1), 2061. DOI: 10.1038/s41598-018-20416-y

Kögel-Knabner, I., Teutsch, G., Adrian, R., Blanckenburg, F., von, Flügge, U.-I., Kolle, O., Kleinn, C., Küsel, K., Lischeid, G., Löw, A., Schäfers, C., Schmid, H.P., Simmer, C., Vereecken, H., Walz, R.
Empfehlung zur Einrichtung eines nationalen Observatorien-Netzes für die terrestrische Ökosystemforschung: Abschlussbericht der Arbeitsgruppe "Infrastrukturen in der terrestrischen Forschung" der Allianz der Wissenschaftsorganisationen, Leipzig (2018). http://www.klima-umwelt.kit.edu/downloads/abschlussbericht-infrastrukturen-terrestrische-forschung.pdf

Kosak née Röhder, L.A., Brandt, T., Sigg, L., Behra, R.
Uptake and effects of cerium(III) and cerium oxide nanoparticles to *Chlamydomonas reinhardtii* (2018) Aquatic Toxicology, 197, 41-46. DOI: 10.1016/j.aquatox.2018.02.004

Kotthoff, M., Bücking, M.
Four chemical trends will shape the next decade's directions in perfluoroalkyl and polyfluoroalkyl substances research (2018) Frontiers in Chemistry, 6, 103. DOI: 10.3389/fchem.2018.00103

Kotthoff, M., Rüdel, H., Jürling, H., Severin, K., Hennecke, S., Friesen, A., Koschorreck, J.
First evidence of anticoagulant rodenticides in fish and suspended particulate matter: Spatial and temporal distribution in German freshwater aquatic systems (2018) Environmental Science and Pollution Research, 1-11. Online first. DOI: 10.1007/s11356-018-1385-8

Kühr, S., Schneider, S., Meisterjahn, B., Schlich, K., Hund-Rinke, K., Schlechtriem, C.
Silver nanoparticles in sewage treatment plant effluents: Chronic effects and accumulation of silver in the freshwater amphipod *Hyalella azteca* (2018) Environmental Sciences Europe, 30 (1), 7. DOI: 10.1186/s12302-018-0137-1

Laux, P., Tentschert, J., Riebeling, C., Braeuning, A., Creutzenberg, O., Epp, A., Fessard, V., Haas, K.-H., Haase, A., Hund-Rinke, K., Jakubowski, N., Kearns, P., Lampen, A., Rauscher, H., Schoonjans, R., Störmer, A., Thielmann, A., Mühle, U., Luch, A.
Nanomaterials: certain aspects of application, risk assessment and risk communication (2018) Archives of Toxicology, 92 (1), 121-141. DOI: 10.1007/s00204-017-2144-1

Leis, B., Held, C., Andreeßen, B., Liebl, W., Graubner, S., Schulte, L.-P., Schwarz, W.H., Zverlov, V.V.
Optimizing the composition of a synthetic cellulosome complex for the hydrolysis of softwood pulp: Identification of the enzymatic core functions and biochemical complex characterization (2018) Biotechnology for Biofuels, 11 (1), 220. DOI: 10.1186/s13068-018-1220-y

PUBLICATIONS

M - R

Mukherjee, K., Vilcinskas, A.
The entomopathogenic fungus *Metarhizium robertsii* communicates with the insect host *Galleria mellonella* during infection (2018) Virulence, 9 (1), 402–413. DOI: 10.1080/21505594.2017.1405190

Nichols, J., Fay, K., Bernhard, M.J., Bischof, I., Davis, J., Halder, M., Hu, J., Johanning, K., Laue, H., Nabb, D., Schlechtriem, C., Segner, H., Swintek, J., Weeks, J., Embry, M.
Reliability of in vitro methods used to measure intrinsic clearance of hydrophobic organic chemicals by fish: Results of an international ring trial (2018) Toxicological Sciences, 164 (2), 563–575. DOI: 10.1093/toxsci/kfy113

Pachernegg, S., Eilebrecht, S., Eilebrecht, E., Schöneborn, H., Neumann, S., Benecke, A.G., Hollmann, M.
The siRNA-mediated knockdown of GluN3A in 46C-derived neural stem cells affects mRNA expression levels of neural genes, including known iGluR interactors (2018) PLoS ONE, 13 (2), e0192242. DOI: 10.1371/journal.pone.0192242

Petry, F., Weidner, T., Czermak, P., Salzig, D.
Three-dimensional bioreactor technologies for the cocultivation of human mesenchymal stem/stromal cells and beta cells (2018) Stem Cells International 2018, 2547098. DOI: 10.1155/2018/2547098

Regnery, J., Friesen, A., Geduhn, A., Göckener, B., Kotthoff, M., Parrhysius, P., Petersohn, E., Reifferscheid, G., Schmolz, E., Schulz, R.S., Schwarzbauer, J., Brinke, M.
Rating the risks of anticoagulant rodenticides in the aquatic environment: A review (2018) Environmental Chemistry Letters, Online first. DOI: 10.1007/s10311-018-0788-6

Rühl, M., Lange, K., Kües, U.
Laccase production and pellet morphology of *Coprinopsis cinerea* transformants in liquid shake flask cultures (2018) Applied Microbiology and Biotechnology, 102 (18), 7849–7863. DOI: 10.1007/s00253-018-9227-7

S - U

Schetelig, M.F., Yan, Y., Zhao, Y., Handler, A.M.
Genomic targeting by recombinase-mediated cassette exchange in the spotted wing drosophila, *Drosophila suzukii* (2018) Insect Molecular Biology, 1-9. Online First. DOI: 10.1111/imb.12537

Schlechtriem, C., Kampe, S., Bruckert, H.-J., Bischof, I., Ebersbach, I., Kosfeld, V., Kotthoff, M., Schäfers, C., L'Haridon, J.
Bioconcentration studies with the freshwater amphipod *Hyalella azteca*: Are the results predictive of bioconcentration in fish? (2018) Environmental Science and Pollution Research International, Online first. DOI: 10.1007/s11356-018-3677-4

Schlich, K., Hoppe, M., Kraas, M., Schubert, J., Chanana, M., Hund-Rinke, K.
Long-term effects of three different silver sulfide nanomaterials, silver nitrate and bulk silver sulfide on soil microorganisms and plants (2018) Environmental Pollution, 242, 1850-1859. DOI: 10.1016/j.envpol.2018.07.082

Shukla, S.P., Plata, C., Reichelt, M., Steiger, S., Heckel, D.G., Kaltenpoth, M., Vilcinskas, A., Vogel, H.
Microbiome-assisted carrion preservation aids larval development in a burying beetle (2018a) Proceedings of the National Academy of Sciences of the United States of America, 115 (44), 11274–11279. DOI: 10.1073/pnas.1812808115

Shukla, S.P., Vogel, H., Heckel, D.G., Vilcinskas, A., Kaltenpoth, M.
Burying beetles regulate the microbiome of carcasses and use it to transmit a core microbiota to their offspring (2018b) Molecular Ecology, 27 (8), 1980–1991. DOI: 10.1111/mec.14269

Skaljac, M., Kirfel, P., Grotmann, J., Vilcinskas, A.
Fitness costs of infection with Serratia symbiotica are associated with greater susceptibility to insecticides in the pea aphid Acyrthosiphon pisum (2018) Pest Management Science, 74 (8), 1829-1836. DOI: 10.1002/ps.4881

V - Z

Vogel, H., Müller, A., Heckel, D.G., Gutzeit, H., Vilcinskas, A.
Nutritional immunology: Diversification and diet-dependent expression of antimicrobial peptides in the black soldier fly *Hermetia illucens* (2018) Developmental and Comparative Immunology, 78, 141-148. DOI: 10.1016/j.dci.2017.09.008

Zitzmann, J., Schreiber, C., Eichmann, J., Bilz, R.O., Salzig, D., Weidner, T., Czermak, P.
Single-cell cloning enables the selection of more productive *Drosophila melanogaster* S2 cells for recombinant protein expression (2018) Biotechnology Reports, 19, e00272. DOI: 10.1016/j.btre.2018.e00272

Zitzmann, J., Weidner, T., Eichner, G., Salzig, D., Czermak, P.
Dielectric spectroscopy and optical density measurement for the online monitoring and control of recombinant protein production in stably transformed *Drosophila melanogaster* S2 cells (2018) Sensors, 18 (3), 900. DOI: 10.3390/s18030900

Translational Medicine

A - C

Al-Hujaily, E.M., Khatlani, T., Alehaideb, Z., Ali, R., Almuzaini, B., Alrfaei, B.M., Iqbal, J., Islam, I., Malik, S., Marwani, B.A., Massadeh, S., Nehdi, A., Alsomaie, B., Debasi, B., Bushnak, I., Noibi, S., Hussain, S., Wajid, W.A., Armand, J.P., Gul, S., Oyarzabal, J., Rais, R., Bountra, C., Alaskar, A., Knawy, B.A., Boudjelal, M.
Therapeutics discovery: from bench to first in-human trials (2018) Biomedical Reports**,** 8, 275-282**.** DOI: 10.3892/br.2018.1052

Alten, R., Burkhardt, H., Feist, E., Krüger, K., Rech, J., Rubbert-Roth, A., Voll, R.E., Elbez, Y., Rauch, C.
Abatacept used in combination with non-methotrexate disease-modifying antirheumatic drugs: A descriptive analysis of data from interventional trials and the real-world setting (2018) Arthritis Research and Therapy, 20 (1), 1. DOI: 10.1186/s13075-017-1488-5

Ashtikar, M., Wacker, M.G.
Nanopharmaceuticals for wound healing – Lost in translation? (2018) Advanced Drug Delivery Reviews, 129, 194-218. DOI: 10.1016/j.addr.2018.03.005

Aygören-Pürsün, E., Bygum, A., Grivcheva-Panovska, V., Magerl, M., Graff, J., Steiner, U.C., Fain, O., Huissoon, A., Kinaciyan, T., Farkas, H., Lleonart, R., Longhurst, H.J., Rae, W., Triggiani, M., Aberer, W., Cancian, M., Zanichelli, A., Smith, W.B., Baeza, M.L., Du-Thanh, A., Gompels, M., Gonzalez-Quevedo, T., Greve, J., Guilarte, M., Katelaris, C., Dobo, S., Cornpropst, M., Clemons, D., Fang, L., Collis, P., Sheridan, W., Maurer, M., Cicardi, M.
Oral plasma kallikrein inhibitor for prophylaxis in hereditary angioedema (2018) New England Journal of Medicine, 379 (4), 352-362. DOI: 10.1056/NEJMoa1716995

Behrens, F., Koehm, M., Schwaneck, E.C., Schmalzing, M., Gnann, H., Greger, G., Tony, H.-P., Burkhardt, H.
Minimal disease activity is a stable measure of therapeutic response in psoriatic arthritis patients receiving treatment with adalimumab (2018) Rheumatology (Oxford, England), 57 (11), 1938-1946. DOI: 10.1093/rheumatology/key203

Behrens, F., Meier, L., Prinz, J.C., Jobst, J., Lippe, R., Löschmann, P.-A., Lorenz, H.-M.
Simultaneous response in several domains in patients with psoriatic disease treated with etanercept as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs (2018) Journal of Rheumatology, 45 (6), 802-810. DOI: 10.3899/jrheum.170932

Blum, L., Schiffmann, S., Parnham, M.J.
Immunomodulation by antibiotics (2018) Fighting Antimicrobial Resistance (IAPC Book). DOI: 10.5599/obp.15.11

Blum, L., Tafferner, N., Spring, I., Kurz, J., deBruin, N., Geißlinger, G., Parnham, M.J., Schiffmann, S.
Dietary phytol reduces clinical symptoms in experimental autoimmune encephalomyelitis (EAE) at least partially by modulating NOX2 expression (2018) Journal of Molecular Medicine, 96 (10), 1131-1144. DOI: 10.1007/s00109-018-1689-7

Böhm, B.B., Fehrl, Y., Janczi, T., Schneider, N., Burkhardt, H.
Cell adhesion-induced transient interaction of ADAM15 with poly(A) binding protein at the cell membrane colocalizes with mRNA translation (2018) PLoS ONE, 13 (9), e203847. DOI: 10.1371/journal.pone.0203847

Bosma, R., Witt, G., Vaas, L.A.I., Josimovic, I., Gribbon, P., Vischer, H.F., Gul, S., Leurs, R.
The target residence time of antihistamines determines their antagonism of the G protein-coupled histamine H1 receptor (2017) Front Pharmacol, 8:667. DOI: 10.3389/fphar.2017.00667

Brachtendorf, S., Wanger, R.A., Birod, K., Thomas, D., Trautmann, S., Wegner, M.-S., Fuhrmann, D.C., Brüne, B., Geißlinger, G., Grösch, S.
Chemosensitivity of human colon cancer cells is influenced by a p53-dependent enhancement of ceramide synthase 5 and induction of autophagy (2018) Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids, 1863 (10), 1214-1227. DOI: 10.1016/j.bbalip.2018.07.011

Brand, S., Roy, S., Schröder, P., Rathmer, B., Roos, J., Kapoor, S., Patil, S., Pommerenke, C., Maier, T., Janning, P., Eberth, S., Steinhilber, D., Schade, D., Schneider, G., Kumar, K., Ziegler, S., Waldmann, H.
Combined proteomic and in silico target identification reveal a role for 5-Lipoxygenase in developmental signaling pathways (2018) Cell Chemical Biology, 25 (9), 1095-1106.e23. DOI: 10.1016/j.chembiol.2018.05.016

Brandt, S.C., Ellinger, B., van Nguyen, T., Thi, Q.D., van Nguyen, G., Baschien, C., Yurkov, A., Hahnke, R.L., Schäfer, W., Gand, M.
A unique fungal strain collection from Vietnam characterized for high performance degraders of bioecological important biopolymers and lipids (2018) PLoS ONE, 13 (8). DOI: 10.1371/journal.pone.0202695

Büttner, D., Kramer, J.S., Klingler, F.-M., Wittmann, S.K., Hartmann, M.R., Kurz, C.G., Kohnhäuser, D., Weizel, L., Brüggerhoff, A., Frank, D., Steinhilber, D., Wichelhaus, T.A., Pogoryelov, D., Proschak, E.
Challenges in the development of a thiol-based broad-spectrum inhibitor for metallo-β-lactamases (2018) ACS Infectious Diseases, 4 (3), pp. 360-372. DOI: 10.1021/acsinfecdis.7b00129

PUBLICATIONS

Burk, O., Kuzikov, M., Kronenberger, T., Jeske, J., Keminer, O., Thasler, W.E., Schwab, M., Wrenger, C., Windshügel, B.
Identification of approved drugs as potent inhibitors of pregnane X receptor activation with differential receptor interaction profiles (2018) Archives of Toxicology, 92 (4), 1435-1451. DOI: 10.1007/s00204-018-2165-4

D – F

Dauth, S., Köhm, M., Rossmanith, T., Herrmann, E., Lehn, A., Burkhardt, H., Behrens, F.
Stellenwert der Kombination von Biologika mit Methotrexat in der Behandlung der Psoriasisarthritis - Fragen bleiben offen (2018) Zeitschrift für Rheumatologie. DOI: 10.1007/s00393-018-0533-3

de Bruin, N., Ferreirós, N., Schmidt, M., Hofmann, M., Angioni, C., Geißlinger, G., Parnham, M.J.
Mutual inversion of flurbiprofen enantiomers in various rat and mouse strains (2018) Chirality, 30 (5), 632-641. DOI: 10.1002/chir.22826

de Witte, W.E.A., Versfelt, J.W., Kuzikov, M., Rolland, S., Georgi, V., Gribbon, P., Gul, S., Huntjens, D., van der Graaf, P.H., Danhof, M., Fernández-Montalván, A., Witt, G., de Lange, E.C.M.
In vitro and in silico analysis of the effects of D2 receptor antagonist target binding kinetics on the cellular response to fluctuating dopamine concentrations (2018) Br J Pharmacol, 175 (21), 4121-4136. DOI: 10.1111/bph.14456

Eresch, J., Stumpf, M., Koch, A., Vutukuri, R., Ferreirós, N., Schreiber, Y., Schröder, K., Devraj, K., Popp, R., Hattenbach, L.-O., Pfeilschifter, J., Pfeilschifter, W.
Sphingosine kinase 2 modulates retinal neovascularization in the mouse model of oxygen-induced retinopathy (2018) Investigative Ophthalmology and Visual Science, 59 (2), 653-661. DOI: 10.1167/iovs.17-22544

Fiehn, C., Holle, J., Iking-Konert, C., Leipe, J., Weseloh, C., Frerix, M., Alten, R., Behrens, F., Baerwald, C., Braun, J., Burkhardt, H., Burmester, G., Detert, J., Gaubitz, M., Gause, A., Gromnica-Ihle, E., Kellner, H., Krause, A., Kuipers, J., Lorenz, H.-M., Müller-Ladner, U., Nothacker, M., Nüsslein, H., Rubbert-Roth, A., Schneider, M., Schulze-Koops, H., Seitz, S., Sitter, H., Specker, C., Tony, H.-P., Wassenberg, S., Wollenhaupt, J., Krüger, K.
S2e guideline: treatment of rheumatoid arthritis with disease-modifying drugs (2018) Zeitschrift für Rheumatologie, 77, 35-53. DOI: 10.1007/s00393-018-0481-y

G - I

Genovese, M.C., Combe, B., Kremer, J.M., Tsai, T.-F., Behrens, F., Adams, D.H., Lee, C., Kerr, L., Nash, P.
Safety and efficacy of ixekizumab in patients with PsA and previous inadequate response to TNF inhibitors: week 52 results from SPIRIT-P2 (2018) Rheumatology (Oxford, England), 57 (11), 2001-2011. DOI: 10.1093/rheumatology/key182

Giller, K., Drews, B., Berard, J., Kienberger, H., Schmicke, M., Frank, J., Spanier, B., Daniel, H., Geißlinger, G., Ulbrich, S.E.
Bovine embryo elongation is altered due to maternal fatty acid supplementation. (2018) Biology of Reproduction, 99 (3), 600-610. DOI: 10.1093/biolre/ioy08

Gossec, L., McGonagle, D., Korotaeva, T., Lubrano, E., De Miguel, E., Østergaard, M., Behrens, F.
Minimal disease activity as a treatment target in psoriatic arthritis: A review of the literature (2018) Journal of Rheumatology, 45 (1), 6-13. DOI: 10.3899/jrheum.170449

Häupl, T., Skapenko, A., Hoppe, B., Skriner, K., Burkhardt, H., Poddubnyy, D., Ohrndorf, S., Sewerin, P., Mansmann, U., Stuhlmüller, B., Schulze-Koops, H., Burmester, G.R.
Biomarkers and imaging for diagnosis and stratification of rheumatoid arthritis and spondylarthritis in the BMBF consortium ArthroMark (2018) Zeitschrift für Rheumatologie, 77, 16-23. DOI: 10.1007/s00393-018-0458-x

Hausen, J., Otte, J.C., Legradi, J., Yang, L., Strähle, U., Fenske, M., Hecker, M., Tang, S., Hammers-Wirtz, M., Hollert, H., Keiter, S.H., Ottermanns, R.
Fishing for contaminants: identification of three mechanism specific transcriptome signatures using *danio rerio embryos* (2018) Environmental Science and Pollution Research, 25 (5), 4023-4036. DOI: 10.1007/s11356-017-8977-6

Heitel, P., Gellrich, L., Heering, J., Goebel, T., Kahnt, A., Proschak, E., Schubert-Zsilavecz, M., Merk, D.
Urate transporter inhibitor lesinurad is a selective peroxisome proliferator-activated receptor gamma modulator (sPPARγM) in vitro (2018) Scientific Reports, 8 (1), 13554. DOI: 10.1038/s41598-018-31833-4

Hering, Y., Berthier, A., Duez, H., Lefebvre, P., Deprez, B., Gribbon, P., Wolf, M., Reinshagen, J., Halley, F., Hannemann, J., Böger, R., Staels, B., Gul, S.
Development and implementation of a cell-based assay to discover agonists of the nuclear receptor REV-ERBα (2018) Journal of Biological Methods, 5 (3), e94. DOI: 10.1038/s41598-018-31833-4

Hitzel, J., Lee, E., Zhang, Y., Bibli, S.I., Li, X., Zukunft, S., Pflüger, B., Hu, J., Schürmann, C., Vasconez, A.E., Oo, J.A., Kratzer, A., Kumar, S., Rezende, F., Josipovic, I., Thomas, D., Giral, H., Schreiber, Y., Geißlinger, G., Fork, C., Yang, X., Sigala, F., Romanoski, C.E., Kroll, J., Jo, H., Landmesser, U., Lusis, A.J., Namgaladze, D., Fleming, I., Leisegang, M.S., Zhu, J., Brandes, R.P.
Oxidized phospholipids regulate amino acid metabolism through MTHFD2 to facilitate nucleotide release in endothelial cells (2018) Nature Communications, 9 (1), 2292. DOI: 10.1038/s41467-018-04602-0

Hofmann, M.C.J., Schmidt, M., Arne, O., Geißlinger, G., Parnham, M.J., de Bruin, N.M.W.J.
Non-invasive bioluminescence imaging as a standardized assessment measure in mouse models of dermal inflammation (2018) Journal of Dermatological Science, 91 (2), 153-163. DOI: 10.1016/j.jdermsci.2018.04.013

J – L

Jung, F., Nothnagel, L., Gao, F., Thurn, M., Vogel, V., Wacker, M.G.
A comparison of two biorelevant in vitro drug release methods for nanotherapeutics based on advanced physiologically-based pharmacokinetic modelling (2018) European Journal of Pharmaceutics and Biopharmaceutics, 127, 462-470. DOI: 10.1016/j.ejpb.2018.03.010

Kern, K., Schäfer, S.M.G., Cohnen, J., Pierre, S., Osthues, T., Tarighi, N., Hohmann, S., Ferreiros, N., Brüne, B., Weigert, A., Geißlinger, G., Sisignano, M., Scholich, K.
The G2A receptor controls polarization of macrophage by determining their localization within the inflamed tissue (2018) Frontiers in Immunology, 9, 2261. DOI: 10.3389/fimmu.2018.02261

Kirchner, J., Brüne, B., Namgaladze, D.
AICAR inhibits NFκB DNA binding independently of AMPK to attenuate LPS-triggered inflammatory responses in human macrophages (2018) Scientific Reports, 8 (1), 7801. DOI: 10.1038/s41598-018-26102-3

Knecht, K.M., Buzovetsky, O., Schneider, C., Thomas, D., Srikanth, V., Kaderali, L., Tofoleanu, F., Reiss, K., Ferreirós, N., Geißlinger, G., Batista, V.S., Ji, X., Cinatl, J. Jr., Keppler, O.T., Xiong, Y.
The structural basis for cancer drug interactions with the catalytic and allosteric sites of SAMHD1 (2018) Proceedings of the National Academy of Sciences of the United States of America, 115 (43), E10022-E10031. DOI: 10.1073/pnas.1805593115

Kraft, C., Boya, P., Codogno, P., Elazar, Z., Eskelinen, E.-L., Farrés, J., Kirkin, V., Jungbluth, H., Martinez, A., Pless, O., Primard, C., Proikas-Cezanne, T., Simonsen, A., Reggiori, F.
Driving next-generation autophagy researchers towards translation (DRIVE), an international PhD training program on autophagy (2018) Autophagy. 13,1-5. Online first. DOI: 10.1080/15548627.2018.1515532

Kramer, J., Désor, V., Brunst, S., Wittmann, S.K., Lausen, J., Heering, J., Proschak, A., Proschak, E.
A coupled fluorescence-based assay for the detection of protein arginine N-methyltransferase 6 (PRMT6) enzymatic activity (2018) Analytical Biochemistry, 547, 7-13. DOI: 10.1016/j.ab.2018.01.023

Kringel, D., Geißlinger, G., Resch, E., Oertel, B.G., Thrun, M.C., Heinemann, S., Lötsch, J.
Machine-learned analysis of the association of next-generation sequencing-based human TRPV1 and TRPA1 genotypes with the sensitivity to heat stimuli and topically applied capsaicin (2018) Pain, 159 (7), 1366-1381. DOI: 10.1097/j.pain.0000000000001222

Kringel, D., Kaunisto, M.A., Lippmann, C., Kalso, E., Lötsch, J.
Development of an AmpliSeqTMPanel for next-generation sequencing of a set of genetic predictors of persisting pain (2018) Frontiers in Pharmacology, 9, 1008. DOI: 10.3389/fphar.2018.01008

Kringel, D., Lippmann, C., Parnham, M.J., Kalso, E., Ultsch, A., Lötsch, J.
A machine-learned analysis of human gene polymorphisms modulating persisting pain points to major roles of neuroimmune processes (2018) European Journal of Pain, 22 (10), 1735-1756. DOI: 10.1002/ejp.1270

Kronenberger, T., Windshügel, B., Wrenger, C., Honorio, K.M., Maltarollo, V.G.
On the relationship of anthranilic derivatives structure and the FXR (Farnesoid X receptor) agonist activity (2018) Journal of Biomolecular Structure and Dynamics, 36 (16): 4378-4391. DOI: 10.1080/07391102.2017.1417161

Kühn, B., Brat, C., Fettel, J., Hellmuth, N., Maucher, I.V., Bulut, U., Hock, K.J., Grimmer, J., Manolikakes, G., Rühl, M., Kühn, A., Zacharowski, K., Matrone, C., Urbschat, A., Roos, J., Steinhilber, D., Maier, T.J.
Anti-inflammatory nitro-fatty acids suppress tumor growth by triggering mitochondrial dysfunction and activation of the intrinsic apoptotic pathway in colorectal cancer cells (2018) Biochemical Pharmacology, 155, 48-60. DOI: 10.1016/j.bcp.2018.06.014

Kurz, J., Brunkhorst, R., Foerch, C., Blum, L., Henke, M., Gabriel, L., Ulshöfer, T., Ferreirós, N., Parnham, M.J., Geißlinger, G., Schiffmann, S.
The relevance of ceramides and their synthesizing enzymes for multiple sclerosis (2018) Clinical Science, 132 (17), 1963-1976. DOI: 10.1042/CS20180506

PUBLICATIONS

Linciano, P., Moraes, C.B., Alcantara, L.M., Franco, C.H., Pascoalino, B., Freitas-Junior, L.H., Macedo, S., Santarem, N., Cordeiro-da-Silva, A., Gul, S., Witt, G., Kuzikov, M., Ellinger, B., Ferrari, S., Luciani, R., Quotadamo, A., Costantino, L., Costi, M.P.
Aryl thiosemicarbazones for the treatment of trypanosomatidic infections (2018) European Journal of Medicinal Chemistry, 146, 423-434. DOI: 10.1016/j.ejmech.2018.01.043

Lippmann, C., Kringel, D., Ultsch, A., Lötsch, J.
Computational functional genomics-based approaches in analgesic drug discovery and repurposing (2018) Pharmacogenomics, 19 (9), 783-797. DOI: 10.2217/pgs-2018-0036

Lötsch, J., Geißlinger, G., Heinemann, S., Lerch, F., Oertel, B.G., Ultsch, A.
Quantitative sensory testing response patterns to capsaicin- and ultraviolet-B-induced local skin hypersensitization in healthy subjects: A machine-learned analysis (2018) Pain, 159 (1), 11-24. DOI: 10.1097/j.pain.0000000000001008

Lötsch, J., Kringel, D.
Use of computational functional genomics in drug discovery and repurposing for analgesic indications (2018) Clinical Pharmacology and Therapeutics, 103 (6), 975-978. DOI: 10.1002/cpt.960

Lötsch, J., Lerch, F., Djaldetti, R., Tegder, I., Ultsch, A.
Identification of disease-distinct complex biomarker patterns by means of unsupervised machine-learning using an interactive R toolbox (Umatrix) (2018) BMC Big Data Analytics, 3. DOI: 10.1186/s41044-018-0032-1

Lötsch, J., Schiffmann, S., Schmitz, K., Brunkhorst, R., Lerch, F., Ferreiros, N., Wicker, S., Tegeder, I., Geißlinger, G., Ultsch, A.
Machine-learning based lipid mediator serum concentration patterns allow identification of multiple sclerosis patients with high accuracy (2018) Scientific Reports, 8 (1), 14884. DOI: 10.1038/s41598-018-33077-8

Lötsch, J., Sipilä, R., Dimova, V., Kalso, E.
Machine-learned selection of psychological questionnaire items relevant to the development of persistent pain after breast cancer surgery (2018) British Journal of Anaesthesia, 121 (5), 1123-1132. DOI: 10.1016/j.bja.2018.06.007

Lötsch, J., Sipilä, R., Tasmuth, T., Kringel, D., Estlander, A.-M., Meretoja, T., Kalso, E., Ultsch, A.
Machine-learning-derived classifier predicts absence of persistent pain after breast cancer surgery with high accuracy (2018) Breast Cancer Research and Treatment, 171 (2), 399-411. DOI: 10.1007/s10549-018-4841-8

Lötsch, J., Ultsch, A.
Machine learning in pain research (2018) Pain, 159 (4), 623-630. DOI: 10.1097/j.pain.0000000000001118

Lötsch, J., Weyer-Menkhoff, I., Tegeder, I.
Current evidence of cannabinoid-based analgesia obtained in preclinical and human experimental settings (2018) European Journal of Pain, 22 (3), 471-484. DOI: 10.1002/ejp.1148

Lukin, A., Kramer, J., Hartmann, M., Weizel, L., Hernandez-Olmos, V., Falahati, K., Burghardt, I., Kalinchenkova, N., Bagnyukova, D., Zhurilo, N., Rautio, J., Forsberg, M., Ihalainen, J., Auriola, S., Leppänen, J., Konstantinov, I., Pogoryelov, D., Proschak, E., Dar'in, D., Krasavin, M.
Discovery of polar spirocyclic orally bioavailable urea inhibitors of soluble epoxide hydrolase (2018) Bioorganic Chemistry, 80, 655-667. DOI: 10.1016/j.bioorg.2018.07.014

M – O

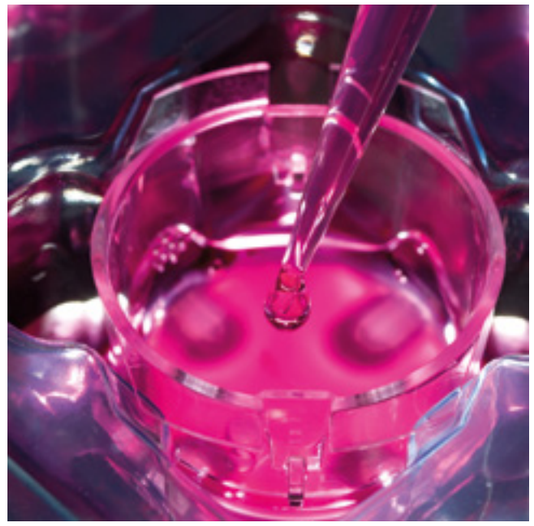
Maltarollo, V.G., Kronenberger, T., Windshügel, B., Wrenger, C., Trossini, G.H.G., Honorio, K.M.
Advances and Challenges in Drug Design of PPARδ Ligands (2018) Curr Drug Targets. 19 (2),144-154. DOI: 10.2174/1389450118666170414113159

Mertens, C., Mora, J., Ören, B., Grein, S., Winslow, S., Scholich, K., Weigert, A., Malmström, P., Forsare, C., Fernö, M., Schmid, T., Brüne, B., Jung, M.
Macrophage-derived lipocalin-2 transports iron in the tumor microenvironment (2018) OncoImmunology, 7 (3), e1408751. DOI: 10.1080/2162402X.2017.1408751

Moreno-Cinos, C., Sassetti, E., Salado, IG., Witt, G., Benramdane, S., Reinhardt, L., Durante Cruz, C., Joossens, J., Van der Veken, P., Brotz-Oesterhelt, H., Tammela, P., Winterhalter, M., Gribbon, P., Windshügel, B., Augustyns, K.
α-Amino diphenyl phosphonates as novel inhibitors of *Escherichia coli* ClpP protease (2018) Journal of Medicinal Chemistry, American Chemical Society. Online first. DOI: 10.1021/acs.jmedchem.8b01466

Nash, P., Behrens, F., Orbai, A.-M., Rathmann, S.S., Adams, D.H., Benichou, O., Deodhar, A.
Ixekizumab is efficacious when used alone or when added to conventional synthetic disease-modifying antirheumatic drugs (cDMARDs) in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor inhibitors (2018) RMD Open, 4 (2), e000692. DOI: 10.1136/rmdopen-2018-000692

Nothnagel, L., Wacker, M.G.
How to measure release from nanosized carriers? (2018) European Journal of Pharmaceutical Sciences, 120, 199-211. DOI: 10.1016/j.ejps.2018.05.004



P – R

Patas, K., Willing, A., Demiralay, C., Engler, J.B., Lupu, A., Ramien, C., Schäfer, T., Gach, C., Stumm, L., Chan, K., Vignali, M., Arck, P.C., Friese, M.A., Pless, O., Wiedemann, K., Agorastos, A., Gold, S.M.
T cell phenotype and T cell receptor repertoire in patients with major depressive disorder (2018) Frontiers in Immunology, 9 (291). DOI: 10.3389/fimmu.2018.00291

Piña, M., Colas, P., Cancio, I., Audic, A., Bosser, L., Canario, A., Gribbon, P., Johnston, I.A., Kervella, A.E., Kooistra, W.H.C.F., Merciecca, M., Magoulas, A., Nardello, I., Smith, D., Pade, N., Robinson, D., Schoen, A., Schultz, F., Kloareg, B.
The european marine biological research infrastructure cluster: an alliance of european research infrastructures to promote the blue bioeconomy (2018) Grand Challenges in Marine Biotechnology, Springer, 405-421. DOI: 10.1007/978-3-319-69075-9_10

Pleli, T., Mondorf, A., Ferreiros, N., Thomas, D., Dvorak, K., Biondi, R.M., Heringdorf, D.M.Z., Zeuzem, S., Geißlinger, G., Zimmermann, H., Waidmann, O., Piiper, A.
Activation of adenylyl cyclase causes stimulation of adenosine receptors (2018) Cellular Physiology and Biochemistry, 45 (6), 2516-2528. DOI: 10.1159/000488270

Proft, F., Schulze-Koops, H., Grunke, M., Schrezenmeier, E., Halleck, F., Henes, J., Unger, L., Schmidt, E., Fiehn, C., Jacobi, A., Iking-Konert, C., Kneitz, C., Schmidt, R.E., Bannert, B., Voll, R.E., Fischer-Betz, R., Kötter, I., Tony, H.P., Holle, J., Aringer, M., Erler, A., Behrens, F., Burmester, G.R., Dörner, T.
Safety and efficacy of off-label use of biologic therapies in patients with inflammatory rheumatic diseases refractory to standard of care therapy: Data from a nationwide German registry (GRAID2) (2018) Zeitschrift für Rheumatologie, 77 (1), 28-39. DOI: 10.1007/s00393-017-0330-4

Ringleb, J., Strack, E., Angioni, C., Geißlinger, G., Steinhilber, D., Weigert, A., Brüne, B.
Apoptotic cancer cells suppress 5-lipoxygenase in tumor-associated macrophages (2018) Journal of Immunology, 200 (2), 857-868. DOI: 10.4049/jimmunol.1700609

Roos, J., Peters, M., Maucher, I.V., Kühn, B., Fettel, J., Hellmuth, N., Brat, C., Sommer, B., Urbschat, A., Piesche, M., Vogel, A., Proschak, E., Blöcher, R., Buscató, E., Häfner, A.-K., Matrone, C., Werz, O., Heidler, J., Wittig, I., Angioni, C., Geißlinger, G., Parnham, M.J., Zacharowski, K., Steinhilber, D., Maier, T.J.
Drug-mediated intracellular donation of nitric oxide potently inhibits 5-lipoxygenase: A possible key to future antileukotriene therapy (2018) Antioxidants and Redox Signaling, 28 (14), 1265-1285. DOI: 10.1089/ars.2017.7155

S – U

Sala, A., Proschak, E., Steinhilber, D., Rovati, G.E.
Two-pronged approach to anti-inflammatory therapy through the modulation of the arachidonic acid cascade (2018) Biochemical Pharmacology, 158, 161-173. DOI: 10.1016/j.bcp.2018.10.007

Schierle, S., Flauaus, C., Heitel, P., Willems, S., Schmidt, J., Kaiser, A., Weizel, L., Goebel, T., Kahnt, A.S., Geißlinger, G., Steinhilber, D., Wurglics, M., Rovati, G.E., Schmidtko, A., Proschak, E., Merk, D.
Boosting anti-inflammatory potency of zafirlukast by designed polypharmacology (2018) Journal of Medicinal Chemistry, 61 (13), 5758-5764. DOI: 10.1021/acs.jmedchem.8b00458

Sehnert, B., Burkhardt, H., Finzel, S., Dübel, S., Voll, R.E.
The sneaking ligand approach for cell type-specific modulation of intracellular signalling pathways (2018) Clinical Immunology, 186, 14-20. DOI: 10.1016/j.clim.2017.08.018

PUBLICATIONS

Sekar, D., Govene, L., Del Río, M.-L., Sirait-Fischer, E., Fink, A.F., Brüne, B., Rodriguez-Barbosa, J.I., Weigert, A.
Downregulation of BTLA on NKT cells promotes tumor immune control in a mouse model of mammary carcinoma (2018) International Journal of Molecular Sciences, 19 (3), 752. DOI: 10.3390/ijms19030752

Shiratori, H., Feinweber, C., Luckhardt, S., Wallner, N., Geißlinger, G., Weigert, A., Parnham, M.J.
An in vitro test system for compounds that modulate human inflammatory macrophage polarization (2018) European Journal of Pharmacology, 833, 328-338. DOI: 10.1016/j.ejphar.2018.06.017

Snodgrass, R.G., Zezina, E., Namgaladze, D., Gupta, S., Angioni, C., Geißlinger, G., Lütjohann, D., Brüne, B.
A novel function for 15-Lipoxygenases in cholesterol homeostasis and CCL17 production in human macrophages.
(2018) Front Immunol 1906 (9), 1-16. DOI: 10.3389/fimu.2018.01906

Sonnack, L., Klawonn, T., Kriehuber, R., Hollert, H., Schäfers, C., Fenske, M.
Comparative analysis of the transcriptome responses of zebrafish embryos after exposure to low concentrations of cadmium, cobalt and copper (2018) Comparative Biochemistry and Physiology - Part D: Genomics and Proteomics, 25, 99-108. DOI: 10.1016/j.cbd.2017.12.001

Spry, C., Sewell, A.L., Hering, Y., Villa, M.V.J., Weber, J., Hobson, S.J., Harnor, S.J., Gul, S., Marquez, R., Saliba, K.J.
Structure-activity analysis of CJ-15,801 analogues that interact with Plasmodium falciparum pantothenate kinase and inhibit parasite proliferation (2018) European Journal of Medicinal Chemistry, 143, 1139-1147. DOI: 10.1016/j.ejmech.2017.08.050

Stoessel, D., Stellmann, J.-P., Willing, A., Behrens, B., Rosenkranz, S.C., Hodecker, S.C., Stürner, K.H., Reinhardt, S., Fleischer, S., Deuschle, C., Maetzler, W., Berg, D., Heesen, C., Walther, D., Schauer, N., Friese, M.A., Pless, O.
Metabolomic profiles for primary progressive multiple sclerosis stratification and disease course monitoring (2018) Frontiers in Human Neuroscience, 12, 226. DOI: 10.3389/fnhum.2018.00226

Stürner, K.H., Stellmann, J.-P., Dörr, J., Paul, F., Friede, T., Schammler, S., Reinhardt, S., Gellissen, S., Weissflog, G., Faizy, T.D., Werz, O., Fleischer, S., Vaas, L.A.I., Herrmann, F., Pless, O., Martin, R., Heesen, C.
A standardised frankincense extract reduces disease activity in relapsing-remitting multiple sclerosis (the SABA phase IIa trial) (2018) Journal of Neurology, Neurosurgery and Psychiatry, 89 (4), 330-338. DOI: 10.1136/jnnp-2017-317101

Tandon, R., Brändl, B., Baryshnikova, N., Landshammer, A., Steenpaß, L., Keminer, O., Pless, O., Müller, F.-J.
Generation of two human isogenic iPSC lines from fetal dermal fibroblasts (2018) Stem Cell Research, 33, 120-124. DOI: 10.1016/j.scr.2018.10.004

Thalman, C., Horta, G., Qiao, L., Endle, H., Tegeder, I., Cheng, H., Laube, G., Sigrudsson, T., Hauser, M.J., Tenzer, S., Distler, U., Aoki, J., Morris, A.J., Geißlinger, G., Röper, J., Kirischuk, S., Luhmann, H.J., Radyushkin, K., Nitsch, R., Vogt, J.
Synaptic phospholipids as a new target for cortical hyperexcitability and E/I balance in psychiatric disorders (2018) Molecular Psychiatry, 23 (8), 1699-1710. DOI: 10.1038/s41380-018-0053-1

Thalman, C., Horta, G., Qiao, L., Endle, H., Tegeder, I., Cheng, H., Laube, G., Sigrudsson, T., Hauser, M.J., Tenzer, S., Distler, U., Aoki, J., Morris, A.J., Geißlinger, G., Röper, J., Kirischuk, S., Luhmann, H.J., Radyushkin, K., Nitsch, R., Vogt, J.
Astrocytic ATX fuels synaptic phospholipid signaling involved in psychiatric disorders (2018) Molecular Psychiatry, 23 (8), 1685-1686. DOI: 10.1038/s41380-018-0238-7

Toewe, A., Balas, L., Durand, T., Geißlinger, G., Ferreirós, N.
Simultaneous determination of PUFA-derived pro-resolving metabolites and pathway markers using chiral chromatography and tandem mass spectrometry (2018) Analytica Chimica Acta, 1031, 185-194. DOI: 10.1016/j.aca.2018.05.020

Treutlein, E.-M., Kern, K., Weigert, A., Tarighi, N., Schuh, C.-D., Nüsing, R.M., Schreiber, Y., Ferreirós, N., Brüne, B., Geißlinger, G., Pierre, S., Scholich, K.
The prostaglandin E2 receptor EP3 controls CC-chemokine ligand 2–mediated neuropathic pain induced by mechanical nerve damage (2018) Journal of Biological Chemistry, 293 (25), 9685-9695. DOI: 10.1074/jbc.RA118.002492

Trillhaase, A., Haferkamp, U., Rangnau, A., Märtens, M., Schmidt, B., Trilck, M., Seibler, P., Aherrahrou, R., Erdmann, J., Aherrahrou, Z.
Differentiation of human iPSCs into VSMCs and generation of VSMC-derived calcifying vascular cells (2018) Stem Cell Research, 31, 62-70. DOI: 10.1016/j.scr.2018.07.008

Tunaru, S., Bonnavion, R., Brandenburger, I., Preussner, J., Thomas, D., Scholich, K., Offermanns, S.
20-HETE promotes glucose-stimulated insulin secretion in an autocrine manner through FFAR1 (2018) Nature Communications, 9 (1), 177. DOI: 10.1038/s41467-017-02539-4

Uliassi, E., Piazzi, L., Belluti, F., Mazzanti, A., Kaiser, M., Brun, R., Moraes, C.B., Freitas-Junior, L.H., Gul, S., Kuzikov, M., Ellinger, B., Borsari, C., Costi, M.P., Bolognesi, M.L.
Development of a Focused Library of Triazole-Linked Privileged-Structure-Based Conjugates Leading to the Discovery of Novel Phenotypic Hits against Protozoan Parasitic Infections (2018) ChemMedChem, 13 (7), 678-683. DOI: 10.1002/cmdc.201700786

V – Z

Van Vollenhoven, R.F., Keystone, E.C., Strand, V., Pacheco-Tena, C., Vencovský, J., Behrens, F., Racewicz, A., Zipp, D., Rharbaoui, F., Wolter, R., Knierim, L., Schmeidl, R., Zhou, X., Aigner, S., Dälken, B., Wartenberg-Demand, A.
Efficacy and safety of tregalizumab in patients with rheumatoid arthritis and an inadequate response to methotrexate: Results of a phase IIb, randomised, placebo-controlled trial (2018) Annals of the Rheumatic Diseases, 77 (4), 495-499. DOI: 10.1136/annrheumdis-2017-212478

Vögtle, F.-N., Brändl, B., Larson, A., Pendziwiat, M., Friederich, M.W., White, S.M., Basinger, A., Kücükköse, C., Muhle, H., Jähn, J.A., Keminer, O., Helbig, K.L., Delto, C.F., Myketin, L., Mossmann, D., Burger, N., Miyake, N., Burnett, A., van Baalen, A., Lovell, M.A., Matsumoto, N., Walsh, M., Yu, H.-C., Shinde, D.N., Stephani, U., Van Hove, J.L.K., Müller, F.-J., Helbig, I.
Mutations in PMPCB encoding the catalytic subunit of the mitochondrial presequence protease cause neurodegeneration in early childhood (2018) American Journal of Human Genetics, 102 (4), 557-573. DOI: 10.1016/j.ajhg.2018.02.014

Vollert, J., Magerl, W., Baron, R., Binder, A., Enax-Krumova, E.K., Geißlinger, G., Gierthmuhlen, J., Henrich, F., Hullemann, P., Klein, T., Lotsch, J., Maier, C., Oertel, B., Schuh-Hofer, S., Tolle, T.R., Treede, R.-D.
Pathophysiological mechanisms of neuropathic pain: Comparison of sensory phenotypes in patients and human surrogate pain models (2018) Pain, 159 (6), 1090-1102. DOI: 10.1097/j.pain.0000000000001190

Wacker, M.G., Janas, C., Ferreira, F.S., Vieira, F.P.
Manufacturing and Safety Guidelines for Manufactured Functionalized Nanomaterials in Pharmaceutics (2018) Biomedical Applications of Functionalized Nanomaterials: Concepts, Development and Clinical Translation, 623-651. DOI: 10.1016/B978-0-323-50878-0.00021-5

Wegner, M.-S., Gruber, L., Mattjus, P., Geißlinger, G., Grösch, S.
The UDP-glucose ceramide glycosyltransferase (UGCG) and the link to multidrug resistance protein 1 (MDR1) (2018) BMC Cancer, 18 (1), 153. DOI: 10.1186/s12885-018-4084-4

Wegner, M.-S., Schömel, N., Gruber, L., Örtel, S.B., Kjellberg, M.A., Mattjus, P., Kurz, J., Trautmann, S., Peng, B., Wegner, M., Kaulich, M., Ahrends, R., Geißlinger, G., Grösch, S.
UDP-glucose ceramide glucosyltransferase activates AKT, promoted proliferation, and doxorubicin resistance in breast cancer cells (2018) Cellular and Molecular Life Sciences, 75 (18), 3393-3410. DOI: 10.1007/s00018-018-2799-7

Weigert, A., von Knethen, A., Fuhrmann, D., Dehne, N., Brüne, B.
Redox-signals and macrophage biology (2018) Molecular Aspects of Medicine, 63, 70-87. DOI: 10.1016/j.mam.2018.01.003

Weyer-Menkhoff, I., Lötsch, J.
Human pharmacological approaches to TRP-ion-channel-based analgesic drug development (2018) Drug Discovery Today, 23 (12), 2003-2012. DOI: 10.1016/j.drudis.2018.06.020

Weyer-Menkhoff, I., Thrun, M.C., Lötsch, J.
Machine-learned analysis of quantitative sensory testing responses to noxious cold stimulation in healthy subjects (2018) European Journal of Pain, 22 (5), 862-874. DOI: 10.1002/ejp.1173

Winau, L., Hinojar Baydes, R., Braner, A., Drott, U., Burkhardt, H., Sangle, S., D'Cruz, D.P., Carr-White, G., Marber, M., Schnoes, K., Arendt, C., Klingel, K., Vogl, T.J., Zeiher, A.M., Nagel, E., Puntmann, V.O.
High-sensitive troponin is associated with subclinical imaging biosignature of inflammatory cardiovascular involvement in systemic lupus erythematosus (2018) Annals of the Rheumatic Diseases, 77 (11), 1590-1598. DOI: 10.1136/annrheumdis-2018-213661

Windshügel, B.
Structural Insights into Ligand-Binding Pocket Formation in Nurr1 by Molecular Dynamics Simulations (2018) Journal of Biomolecular Structure and Dynamics. DOI: 10.1080/07391102.2018.1559099

Zezina, E., Snodgrass, R.G., Schreiber, Y., Zukunft, S., Schürmann, C., Heringdorf, D.M.Z., Geißlinger, G., Fleming, I., Brandes, R.P., Brüne, B., Namgaladze, D.
Mitochondrial fragmentation in human macrophages attenuates palmitate-induced inflammatory responses (2018) Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids, 1863 (4), 433-446. DOI: 10.1016/j.bbalip.2018.01.009

Zhong, J., Scholz, T., Yau, A.C.Y., Guerard, S., Hüffmeier, U., Burkhardt, H., Holmdahl, R.
Mannan-induced Nos2 in macrophages enhances IL-17-driven psoriatic arthritis by innate lymphocytes (2018) Science Advances, 4 (5), eaas9864. DOI: 10.1126/sciadv.aas9864

Zimmer, B., Angioni, C., Osthues, T., Toewe, A., Thomas, D., Pierre, S.C., Geißlinger, G., Scholich, K., Sisignano, M.
The oxidized linoleic acid metabolite 12,13-DiHOME mediates thermal hyperalgesia during inflammatory pain (2018) Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids, 1863 (7), 669-678. DOI: 10.1016/j.bbalip.2018.03.012

PATENTS

PATENTS

Patent applications

Baumann, Isabell; Jakobsson, Per-Johan; Saul, Meike Julia; Steinhilber, Dieter; Süß, Beatrix
MiRNA-574-5p as a biomarker for stratification of prostaglandin E-dependent tumors. PCT/EP2018/065318

Biel, Martin; Geißlinger, Gerd; Kallenborn-Gerhardt, Wiebke; Lu, Ruirui; Michalakis, Stylianos; Schmidtko, Achim
Means and methods for treating neuropathic pain.
PCT/EP2018/065915

Brüne, Bernhard; Ernst, Andreas; Mora, Javier; Parnham, Michael John; Putyrski, Mateusz; Weigert, Andreas
Inhibitors of IL-38 for use in treating and/or preventing cancer in a subject. PCT/EP2018/061706

Buntru, Matthias; Fischer, Rainer; Schillberg, Stefan; Vogel, Simon
Development of a novel BY-2-cell-free-protein expression system that does not require an artificial energy regeneration system. PCT/US18/17602; US 15/893,346

Buntru, Matthias; Schillberg, Stefan; Vogel, Simon
Cell-free protein synthesis system. PCT/EP2018/051822; AR P180100164

Buntru, Matthias; Schillberg, Stefan; Vogel, Simon
Promoter construct for cell-free protein synthesis.
PCT/EP2018/051831, AR P180100165

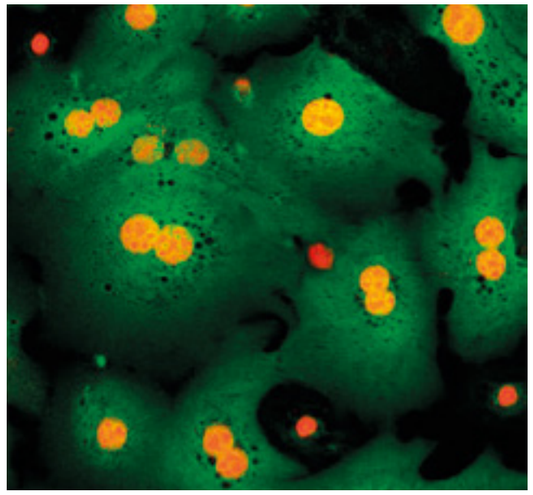
Buyel, Johannes Felix; Gengenbach, Benjamin
Method for automated transformation of a Plant Cell Pack.
PCT/EP2018/064477

Buyel, Johannes Felix; Kastilan, Robin; Müschen, Catherine Rose
Means and methods for protein quantification.
PCT/EP2018/071152

Friese, Manuel; Pleß, Ole; Schauer, Nicolas; Stoessel, Daniel
Novel biomarkers for diagnosis and progression of primary progressive multiple sclerosis (PPMS). US 15/911,945

Maculins, Timurs; Ernst, Andreas; Putyrski, Mateusz; Kuzikov, Maria; Parnham, Michael John
Method for detecting a modulator compound for chemical targeting of protein-protein interactions. EP 18191813.7

Rasche, Stefan; Schubert, Max; Beuel, Ann-Katrin; Spiegel, Holger
LEDitShake. DE 10 2018 110 329.8



Schiederig, Tim; Zaliani, Andrea; Gul, Sheraz; Chachulski, Laura; Claussen, Carsten
Method and devices for age determination. EP 18199156.3

Schillberg, Stefan; Vogel, Simon
Pflanzenanzuchtsystem basierend auf einem modularen, vertikal in Schleifen geführtem Förderband mit mechanisch angepasster Pflanzenabstandsanpassung. PCT/EP2018/064182

Schulze Gronover, Christian; Müller, Lowis-Gerrit-Boje; van Deenen, Nicole; Bröker, Jan Niklas
Methods for increasing the yield of oxidosqualene, triterpenes and/or triterpenoids and host cells therefore. EP 18166374.1

Schulze Gronover, Christian; Unland, Kristina
A method to obtain low triterpene/triterpenoid-containing natural rubber latex. EP 18205121.9

Vilcinskas, Andreas; Knorr, Eileen; Fischer, Rainer; Gandra, Premchand; Geng, Chaoxian; Frey, Meghan; Young, Catherine; Narva, Kenneth E.; Balachandran, Abhilash
Pre-mRNA processing factor 19 (PRP19) nucleic acid molecules to control insect pests. PCT/US2018/023225; US 15/927,672

Vilcinskas, Andreas; Knorr, Eileen; Narva, Kenneth E.; Gandra, Premchand; Geng, Chaoxian; Fishilevich, Elane; Young, Catherine; Balachandran, Abhilash; Rangasamy, Murugesan; Frey, Meghan
Sytaxin 7 nucleic molecules to control coleopteran and hemipteran pests. PCT/US2018/023264; US 15927656

Patents issued

Barth, Stefan; Tur, Mehmet Kemal; Hussain, Ahmad
Novel photoimmunoconjugates for use in photodynamic therapy.
US 9,872,904 B2

Barth, Stefan; Schiffer, Sonja
Novel immunoproteases.
US 9,944,706 B2

Barth, Stefan; Thepen, Theo; Hristodorov, Dimitrij; Mladenov, Radoslav
A microtubuli-modifying compound.
EP 2 912 057 B1 (DE, FR, GB, IT, NL)

Barth, Stefan; Tur, Mehmet Kemal; Fitting, Jenny
A new fusion protein to target and treat acute myeloid leukemia cells.
EP 3 016 983 (AT, CH, DE, FR, GB, IT, NL); US 2016/0152724 A1

Barth, Stefan; Wüllner, Ulrich; Neef, Inga
Immuno-RNA-constructs.
CA 2,633,776 C

Boes, Alexander; Spiegel, Holger; Edgü, Güven, Beiss, Veronique, Sack, Markus; Reimann, Andreas; Firscher, Rainer
Novel vaccines against apicomplexan pathoges.
EP 2 988 776 B1

Buyel, Johannes Felix
Gehäuse für einen Einwegbeutelfilter.
EP 2 687 279 A1 (DE, ES, FR, GB, IE, IT)

Christen, Urs; Lasch, Stanley; Parnham, Michael John
Combination therapy for the treatment of autoimmune diseases.
EP 3 129 483 A1 (AT, BE, CH, DE, ES, FR, GB, IE, IT, LU, NL, PL)

Geißlinger, Gerd; Tegeder, Irmgard
Novel treatment of multiple sclerosis (ms).
CA 2,816,911 C; KR 101877587 B1

Harig, Lena; Prüfer, Dirk; Fischer, Rainer
Nucleic acid sequences and peptides/proteins of the FT family providing flower-repressing properties in tobacco and transgenic plants transformed therewith.
JP 6381517 B2, RU 2644685 C2

Jennewein, Stefan; Engels, Benedikt
Melleolid-Biosynthesegencluster aus *Armillaria gallica* FU02472 und Beschreibung seiner möglichen Anwendung.
US 10,011,821 B2

Kirchhoff, Janina; Schillberg, Stefan; Schiermeyer, Andreas; Schinkel, Helga; Fischer, Rainer
Method for the generation of a monoclonal plant cell line.
CA 2,835,253 C

Knape, Tilo; von Knethen, Andreas; Parnham, Michael John; Schubert-Zsilavecz, Manfred; Wurglics Mario; Flesch, Daniel
Competitive PPAR-Gamma antagonists.
US 10,093,628 B2

Lötsch, Jörn; Ultsch, Alfred; Oertel, Bruno; Geißlinger, Gerd
Non-Invasive method for prediction of opioid-analgesia and opioid-blood-concentrations.
CN 105142517 A

Müller, Boje; Prüfer, Dirk; Fischer, Rainer
Artifizielle Forisomenkörper mit SEO-F-Fusionsproteinen, pflanzliche oder Hefezellen mit Vektoren, die für diese Proteine codieren, sowie Vektoren, die für SEO-F-Fusionsproteine codieren.
JP 6341909 B2

Ostafe, Raluca; Fischer, Rainer; Prodanovic, Radivoje
Novel glucose oxidase variants.
EP 2 989 201 B1 (AT, CH, DE, FR, GB, IE, IT, NL)
CN 105209611 A; JP 6322279 B2; RU 2652913 C2

Thepen, Theophilus; Hristodorov, Dimitrij; Mladenov, Radoslav; Barth, Stefan
Targeted modulation of macrophages.
EP 3 003 350 B1 (CH, DE, FR, GB, IT, NL)

Vilcinskas, Andreas; Pöppel, Anne-Kathrin; Wiesner, Jochen
Polypeptides against plant-pathogenic fungi.
EP 2 956 474 (AT, CH, DE, ES, FR, GB, IT, NL); JP 6396330 B2

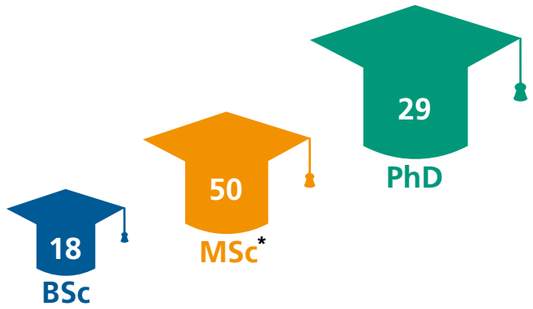
Vilcinskas, Andreas; Salzig, Mark; Fischer, Rainer
Insect metalloproteinase inhibitors.
EP 3 024 481 B1 (CH, DE, DK, FR, GB, NL)

Will, Torsten; Vilcinskas, Andreas; Fischer, Rainer
Novel pest control methods.
EP 3 004 148 B1 (BE, CH, DE, FR, GB)

Bachelor's, Master's, State Examination and Doctoral Theses

BACHELOR'S, MASTER'S, STATE EXAMINATION AND DOCTORAL THESES

Bachelor's, Master's, State Examination and Doctoral Theses



Theses at a glance (* inluding one state examination thesis).

Doctoral Theses

Abdel Malik, Randa
The function of the AMP-activated protein kinase in vascular remodeling.
Goethe-Universität Frankfurt am Main

Ball, Ann-Katrin
Charakterisierung und zelluläre Lokalisation der humanen 5-Lipoxigenase und deren Isoformen 5-LOΔ13, 5-LOΔ4 und 5-LOp12.
Goethe-Universität Frankfurt am Main

Bischof, Ina
Primary fish hepatocytes as in vitro test system to study the metabolism of xenobiotics in fish.
Universität Bern

Biswas, Tilottama
When facing multiple enemies : the impact of host development time and exposure to multiple parasites in shaping coevolutionary adaptations in host and parasites.
Justus-Liebig-Universität Gießen

Karinna Chouman
Characterization of interleukin-6 monoclonal antibodies for future applications.
RWTH Aachen University

Drabkin, Dmitri
Nutzung von Biokohlesubstraten zur Wiederaufforstung von Windwurfflächen und auf Weihnachtsbaumkulturen.
Freie Universität Berlin

Fei, Yang
Mechanistic understanding of enhanced human oral bioavailability of fenofibric acid from novel lipid carriers using semi-physiologically based pharmacokinetic model and various analytical approaches including biorelevant dissolution testing.
Goethe-Universität Frankfurt am Main

Fettel, Jasmin
Untersuchungen zur Regulation der Leukotrienbiosynthese durch Sphingosin-1-Phosphat.
Goethe-Universität Frankfurt am Main

Gresch, Gerrit
Generierung und Charakterisierung rekombinanter single chain Fv-Derivate für therapeutische und diagnostische Anwendungen an unterschiedlichen Leukämie Subtypen.
RWTH Aachen University

Gupta, Sahil
Functional and mechanistsic insights into cytokine induced macrophage polarization.
Goethe-Universität Frankfurt am Main

Hansmann, Simone
Simulation of oral absorption with physiologically based pharmacokinetic models with a focus on weakly basic active pharmaceutical ingredients.
Goethe-Universität Frankfurt am Main

Jansing, Julia
CRISPR/Cas9-mediated knockout of six plant-specific glycosyltransferase genes in *Nicotiana benthamiana* for the production of α-1,3-fucose- and β-1,2-xylose-free recombinant proteins.
RWTH Aachen University

Kern, Katharina
Regulation of macrophage polarization during acute inflammation by CD200R and G2A.
Goethe-Universität Frankfurt am Main

Klein, Judith
Analysis and optimization of ecotoxicological models under uncertainty.
Universität Duisburg-Essen

Koscher, Eva
Essays in corporate social responsibility and strategic management.
Goethe-Universität Frankfurt am Main

Kretschmer, Simon Benedikt Maximilian
Structure-activity relationships, series evolution and characterization of aminothiazole comprising 5-lipoxygenase inhibitors.
Goethe-Universität Frankfurt am Main

Kühn, Benjamin
Untersuchungen zur inhibitorischen Wirkung von Nitrofettsäuren auf das Wachtum kolorektaler Tumorzellen und Tumore.
Goethe-Universität Frankfurt am Main

Lehmann, Andreas
Qualitativ unzureichende Arzneimittel im internationalen Kontext - Gefahren und Gegenmaßnahmen.
Goethe-Universität Frankfurt am Main

Menzel, Stephan
Downstream processing of malaria vaccine candidates and modeling of chromatography.
RWTH Aachen University

Müller, Hagen
Development of an antimicrobial peptide production process platform in *Pichia pastoris*.
Justus-Liebig-Universität Gießen

Oppermann, Tobias
***Mannheimia haemolytica* - Bioprocess improvement of leukotoxin production using fed-batch process and a ceramic membrane based downstrean processing.**
Justus-Liebig-Universität Gießen

Pütter, Katharina Mareike
Isoprenoid pathway engineering in the rubber-producing genus *Taraxacum*.
Westfälische Wilhelms-Universität Münster

Ruff, Aaron
Optimierung des in vitro-Transfer Modells, um das Übersättigungs- und Präzipitationsverhalten von schwer löslichen, schwach basischen Arzneistoffen vorherzusagen.
Goethe-Universität Frankfurt am Main

Sassetti, Elisa
Identification and optimisation of bacterial caseinolytic protease inhibitors as potential novel antibiotics.
Jacobs University Bremen

Schmidt, Jurema
Entwicklung und Charakterisierung neuer Farnesoid X Rezeptor-Modulatoren.
Goethe-Universität Frankfurt am Main

Shiratori, Hiromi
Establishment of systemic in vitro screening system to identify modulatory compounds for human macrophage polarization.
Goethe-Universität Frankfurt am Main

Wiechmann, Svenja
Engeneering of intracellular affinity reagents targeting protein-protein interactions.
Goethe-Universität Frankfurt am Main

Zezina, Ekaterina
Mitochondrial dynamics in response to fatty acids in human macrophages.
Goethe-Universität Frankfurt am Main

NETWORKS IN SCIENCE AND INDUSTRY

NETWORKS IN SCIENCE AND INDUSTRY

Networks in Science and Industry

International activities and cooperations with industry

Fraunhofer IME 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 2018, Fraunhofer IME cooperated with around 100 national and international industrial clients and carried out confidential projects for several international industrial associations.

Cooperation with universities

Fraunhofer IME has close ties with the Institute of Plant Biology and Biotechnology at the University of Münster as well as with the Institute for Evolution and Biodiversity and the Institute for Molecular Microbiology and Biotechnology at the University of Münster. There is also close cooperation with the Institute for Insect Biotechnology at the Justus Liebig University in Gießen, the Institute for Clinical Pharmacology, the Institute for Pathobiochemistry, the Institute for Pharmaceutical Chemistry and the Institute for Pharmaceutical Technology, all at the Johann Wolfgang Goethe University in Frankfurt am Main. Fraunhofer IME also collaborates with the Aachen-Maastricht Institute for Biobased Materials (AMIBM) at the University of Maastricht, the Institute for Biology V (Environmental Research) at RWTH Aachen University, the Institute for Biology at the University of Siegen, the Center for Fish and Wildlife Medicine at the University of Bern and the School of Chemistry at Monash University in Melbourne.

Lecturing assignments

Prof. Dr. Mark Bücking holds lectures at the Faculty of Mathematics and Natural Sciences at the University of Wuppertal and is Associate Professor at the School of Chemistry at Monash University, Melbourne, Australia.

Prof. Dr. Harald Burkhart is Head of the Division of Rheumatology at the University Hospital Frankfurt and Professor of Internal Medicine/ Rheumatology at the Goethe University Frankfurt am Main.

Dr. Dr.-Ing. Johannes F. Buyel holds lectures in the master program "molecular and applied biotechnology" at the RWTH Aachen University.

Dr. Natasja de Bruin holds seminars at the Goethe University Hospital Frankfurt and participated in Fraunhofer IME Master Class Workshop "Translational Medicine".

Prof. Dr. Carsten Claussen is Honorary Professor for Information Systems at the Heinz-Nixdorf Institute of the University of Paderborn.

Prof. Dr. Jennifer Dressman is Professor of Pharmaceutical Technology in the Department of Biochemistry, Chemistry and Pharmacy at the Goethe University Frankfurt am Main.

Dr. Jürgen Drossard holds lectures in the master program "molecular and applied biotechnology" at the RWTH Aachen University.

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

Dr. Andreas Ernst holds seminars at the Goethe University Hospital Frankfurt and participated in Fraunhofer IME Master Class Workshop "Translational Medicine".

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

Dr. 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. Kerstin Hund-Rinke holds lectures in ecotoxicology at Hochschule Osnabrück (University of Applied Sciences).

Dr. Matthias Kotthoff held lectures in the degree program food chemistry at the Bergische Universität Wuppertal.

Prof. Dr. Michael Parnham is Professor of Pharmacology and Toxicology in the Faculty of Biochemistry, Chemistry and Pharmacy at Goethe University Frankfurt. He offers the module Pharmaceutical Research and Development of the Master of Pharma Business Administration (MPBA) of the Goethe Business School.

Dr. Ole Pless and **Prof. Dr. Carsten Claussen** hold lectures, seminars and internships at the Faculty of Medicine of the University Hamburg (UKE).

Dr. Ole Pless holds seminars at the Goethe University Hospital Frankfurt am Main.

Prof. Dr. Dirk Prüfer is Professor of Plant Biotechnology at the University of Münster.

Prof. Dr. Christoph Schäfers holds an Extraordinary Professorship for Eco (system) toxicology at the University of Münster.

Prof. Dr. Marc F. Schetelig is Professor for Insect Biotechnology in Plant Protection at the Justus-Liebig University Gießen.

Dr. Andreas Schiermeyer and **Holger Spiegel** provide lectures on Plant Biotechnology at the FH Aachen, University of Applied Sciences.

PD Dr. Susanne Schiffmann holds seminars at the Goethe University Hospital Frankfurt am Main.

Prof. Dr. Stefan Schillberg is Honorary Professor at the Justus-Liebig University Gießen.

Prof. Dr. Christian Schlechtriem is Honorary Professor for Ecotoxicology at the University Siegen and holds lectures and courses at the RWTH Aachen University.

Matthias Teigeler holds lectures on Ecotoxicology at the University for Applied Sciences Bingen and the Technical University Braunschweig and is a lecturer for the Module Ecotoxicology, Advanced animal welfare training in fish toxicology, of "Berliner Fortbildungen".

Prof. Dr. Andreas Vilcinskas is Professor for Applied Entomology and Director of the recently established Institute for Insect Biotechnology, both at the Justus-Liebig University Gießen.

Dr. Carmen Walter and **Dr. Miriam Wolters** hold seminars at the Goethe University Hospital Frankfurt am Main.

Dr. Matthias Wacker lectures in biochemistry, chemistry and pharmacy at the Goethe University Frankfurt am Main.

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Scientific Journals

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Editorial Board: Dr. Sheraz Gul

Drug Target Review, Russell Publishing Ltd.
Scientific Contributing Editor: Dr. Sheraz Gul

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Frontiers in Bioengineering and Biotechnology,
Frontiers Media S.A.;
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Editorial Board: Prof. Dr. Dieter Steinhilber

Handbuch der Bodenuntersuchung, Wiley-VCH
Beirat: Dr. Dieter Hennecke

Integrated Environmental Assessment and Management, Wiley
Editorial Board: Dr. Udo Hommen

Journal of Applied Ichthyology, Wiley-Blackwell
Editorial Board: Prof. Dr. Christian Schlechtriem

Journal of Oil Palm Research, Malaysian Palm Oil Board
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Journal of Pharmaceutical Sciences, Elsevier
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Plant Cell Reports, Springer
Editorial Board: Prof. Dr. Stefan Schillberg

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

Transgenic Research, Kluwer Academic Publishers
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EU Cost Action DNAqua-Net
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DFG, Fachkollegium, Medizin
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Dr. Kerstin Derz

- NA 119-01-02-04 UA Biologische Verfahren
Dr. Kerstin Hund-Rinke

- NA 119-01-02 AA Abfall und Bodenuntersuchung, UA 1 Probenahme
Karlheinz Weinfurtner

- NA 119-01-02-06 UA Bodenschutz, Entsorgung, Altlastensanierung, UA 2 Entsorgung
Karlheinz Weinfurtner

DIN SPEC 92001 Künstliche Intelligenz – Qualitätsanforderungen und Life Cycle Management für KI Module
Dr. Sebastian Eilebrecht

Dutch NeuroFederation
Dr. Natasja de Bruin

ECHA/EFSA, Endocrine Disrupting Guidance Consultation Group
Hearing expert:
Prof. Dr. Christoph Schäfers

ECNP, European College of Neuropsychopharmacology
Dr. Natasja de Bruin

EFSA, Scientific Panel on Plant Protection Products and their Residues
Dr. Michael Klein

EFSA PPR Panel, Working Group on TK-TD-Modelling
Dr. Michael Klein

EFSA PPR Working Group on how to consider aged sorption for pesticides in regulatory assessments
Dr. Michael Klein

EFSA Working Group Developing an EFSA scientific report for the FOCUS surface water repair action
Dr. Michael Klein

EFSA Working Group on the new guidance document about persistence in soil
Dr. Michael Klein

European Federation for Pharmaceutical Sciences
Vice president:
Prof. Dr. Dieter Steinhilber

FBU, Fachbeirat Bodenuntersuchungen
Dr. Dieter Hennecke

Fachbeirat zum Masterstudiengang "Boden, Gewässer, Altlasten" an der Hochschule/Universität Osnabrück
Dr. Kerstin Hund-Rinke

FENS Federation of European Neuroscience Societies
Dr. Natasja de Bruin

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Mitglied
Prof. Dr. Dirk Prüfer

FOCUS (Forum for international coordination of pesticide fate models and their use), Work group "Version Control"
Dr. Michael Klein

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

Forum "Gesundheitsforschung" des BMBF
Prof. Dr. Dr. Gerd Geißlinger

Food and Agricultural Organization of the United Nations
Scientific consultant and expert:
Prof. Dr. Marc F. Schetelig

FPI e.V., Food-Processing Initiative
Mitglied des Vorstands:
Prof. Dr. Mark Bücking

Fraunhofer Chile Research Board of Directors
Prof. Dr. Dirk Prüfer

Fraunhofer-Cluster of Excellence für immunmediierte Erkrankungen
Geschäftsführer:
Prof. Dr. Dr. Gerd Geißlinger

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

GDCh, Fachgruppe Umweltchemie und Ökotoxikologie:

- Arbeitskreis Boden
Leitung: Dr. Dieter Hennecke

- Arbeitskreis Chemikalienbewertung
Dr. Martin Müller

- Arbeitskreis Umweltmonitoring
Leitung: Dr. Heinz Rüdel

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Prof. Dr. Dr. Gerd Geißlinger

Hochschulforum der Hamburger Wirtschaft
Prof. Dr. Carsten Claussen

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International Society for Stem Cell Research (ISSCR)
Member of the international committee:
Dr. Ole Pless

ISO/TC 190 SC2, WG10 Soil quality – Elaborating general aspects of sampling
Karlheinz Weinfurtner

ISO/TC 190 SC7, WG6 Leaching tests
Dr. Dieter Hennecke

ISO/TC 190 SC7, WG4 Human exposure
Convenor: Dr. Kerstin Derz

ISPE, Community of Practice: Process analytical technologies, Active Pharmaceutical Ingredients
Dr. Jürgen Drossard

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

Kommission zur Bewertung wassergefährdender Stoffe (KBwS) des BMU
Prof. Dr. Christoph Schäfers

Lenkungskreis LOEWE-Zentrum TBG
Prof. Dr. Dr. Gerd Geißlinger

NORMAN – Network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances:

- Working Group "Prioritization of emerging substances"
Dr. Heinz Rüdel

- Working Group "Bioassays and biomarkers in water quality monitoring"
Dr. Elke Eilebrecht

OECD Expert Group on Fish Bioaccumulation
Prof. Dr. Christian Schlechtriem

OECD Fish Drafting Group
Matthias Teigeler,
Prof. Dr. Christoph Schäfers

OECD Validation Management Group on Ecotoxicity Testing (VMG-eco)
Invited national experts:
Matthias Teigeler,
Prof. Dr. Christoph Schäfers

OECD Working Party on Manufactured Nanomaterials (WPMN)
Dr. Kerstin Hund-Rinke

Research Data Alliance, GEDE - Group of European Data
Experts in RDA
Dr. Manfred Kohler

Senat der WWU Münster
Stellvertretendes Mitglied
Prof. Dr. Dirk Prüfer

SETAC Europe Interest Group: Mechanistic Effect Models
Steering Committee:
Dr. Udo Hommen

SETAC Global Interest Group: Bioaccumulation Science
Co-Chair:
Prof. Dr. Christian Schlechtriem

SETAC Global Plants Advisory Group
Steering Committee:
Dr. Udo Hommen

Society for Neuroscience
Dr. Natasja de Bruin

Society for Laboratory Automation and Screening
Chair of the Europe council:
Dr. Philip Gribbon

Society for Laboratory Automation and Screening
Europe Education Committee:
Dr. Sheraz Gul

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Kuratoriumsmitglied:
Prof. Dr. Carsten Claussen

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

Stiftungsrat der Freundlich-Stiftung
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Transcriptogen Ltd.
Scientific Co-Founder:
Dr. Sheraz Gul

UBA, Arbeitskreis Fortentwicklung von Prüfmethoden im Rahmen des Stoffrechts, AK Ökotoxikologie, Akkumulation und Abbau in der Umwelt
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VDI/VDE "Datenmanagement im Bereich Life Sciences" VDI 6320
Vice chairman:
Dr. Manfred Kohler

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

World Health Organization (WHO), Vector Control Advisory Group (VCAG)
Prof. Dr. Marc F. Schetelig

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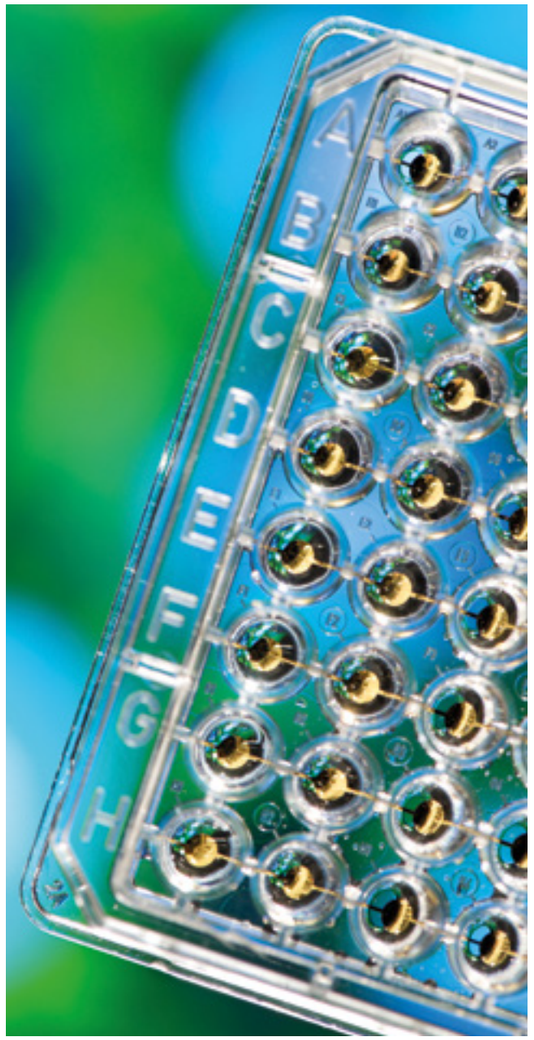

Organization of Scientific Meetings and Courses

2nd Excellence Course SPA Psoriasis Arthritis and Axial Spondarthritis
Berlin, August 30 to September 1, 2018, led by Dr. med. Frank Behrens in cooperation with House of Pharma and Healthcare

INSECTA 2018
Fourth International Conference on technical, economic, ecological, political and ethical issues relating to the use of insects, September 5 to 7, 2018 in Gießen, coordinated with the participation of Fraunhofer IME

Nano and micro formulations - bringing together science, authority and industry
Berlin, March 13 to 14, 2018, led by Dr. Matthias G. Wacker

Workshop: 3rd MuTaLig COST Action Training School, CA 15135
Hamburg, December 5 to 7, 2018, organized by the MuTaLig COST Action Committee and Fraunhofer IME (Dr. Sheraz Gul)

Workshop: Bioaccumulation of manufactured nanomaterials in freshwater bivalves
Dessau-Rosslau, October 23, 2018, organized by the Federal Environment Agency (UBA) in cooperation with Fraunhofer IME (Prof. Dr. Christian Schlechtriem)

Workshop: Data scientist specialized in data management
Sankt Augustin, June 11 to 14, 2018 and November 5 to 8, 2018, organized by the Fraunhofer Academy, in cooperation with Fraunhofer IME (Dr. Manfred Kohler) and Fraunhofer FIT

Workshop: Particle characterization in medicine and biology
Frankfurt am Main, September 20, 2018, in cooperation with the House of Pharma & Healthcare

Workshop: The use of toxicokinetic data to assess bioaccumulation
Leipzig, February 21, 2018, organized by the Helmholtz Centre for Environmental Research - UFZ, Fraunhofer IME and CEFIC LRI

SETAC Europe 1st Special Science Symposium "Extrapolation of Effects across Biological Levels: Challenges to Implement Scientific Approaches in Regulation"
Brussels, Belgium, October 23 to 24, 2018, Member of the Steering Committee: Dr. Udo Hommen

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Prof. Dr. Christoph Schäfers
Prof. Dr. Stefan Schillberg

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Fraunhofer IME

Fraunhofer IME

Molecular Biotechnology Division
Forckenbeckstr. 6
52074 Aachen
Phone +49 241 6085-0

Fraunhofer IME
Branch Lab for Plant Biopolymers
Schlossplatz 8
48143 Münster
Phone +49 251 8322-302

Fraunhofer IME
Applied Ecology and Bioresources Division
Auf dem Aberg 1
57392 Schmallenberg
Phone +49 2972 302-0

Fraunhofer IME
Branch for Bioresources
Winchesterstr. 2
35394 Gießen
Phone+49 641 9939-500

Fraunhofer IME
Translational Medicine Divison
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Phone +49 69 630-7619

Fraunhofer IME
Branch Lab ScreeningPort
Schnackenburgallee 114
22525 Hamburg
Phone +49 40 303764-0

www.ime.fraunhofer.de/en