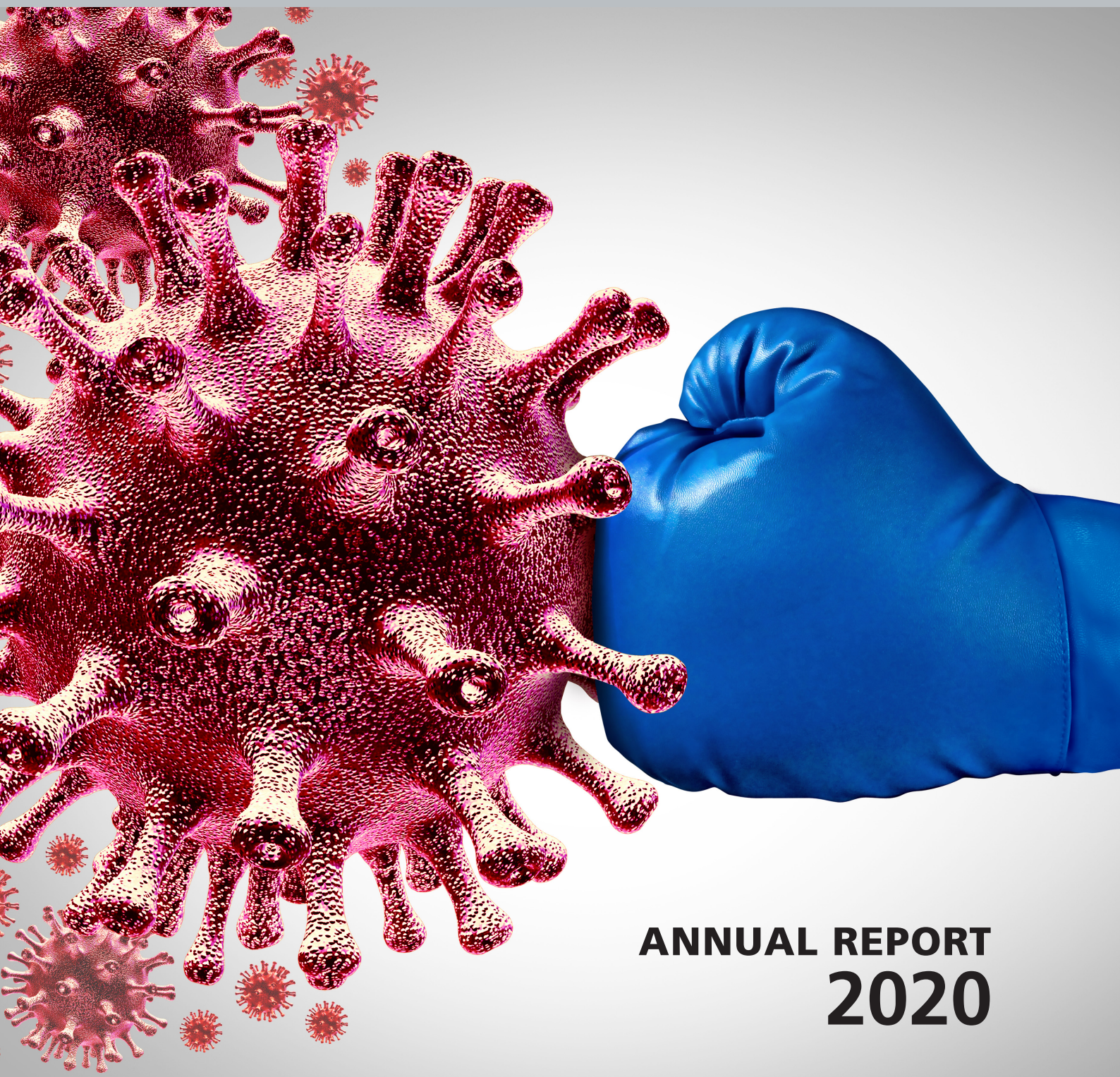
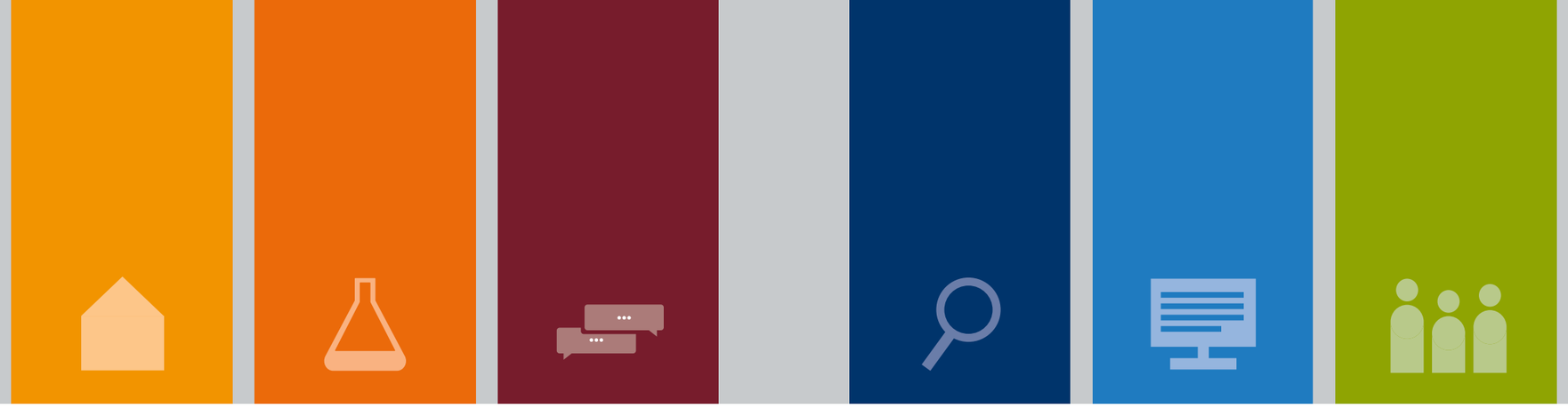
Fraunhofer
IME

FRAUNHOFER INSTITUTE FOR MOLECULAR BIOLOGY AND APPLIED ECOLOGY IME



ANNUAL REPORT 2020

FRAUNHOFER VS CORONA



FRAUNHOFER VS CORONA

The year 2020 was overshadowed by the COVID-19 pandemic. The novel SARS-CoV-2 virus quickly turned into a global challenge, bringing health systems worldwide to their limits, while the economy is struggling with the effects of the pandemic. One reason for that is the lack of effective drugs or, at that time, vaccines as well as efficient assays for a rapid and sensitive detection of the virus.

The institute's division "Translational Medicine", with its locations in Frankfurt am Main and Hamburg, was involved in fighting the COVID-19 crisis on a number of different levels. Both Prof. Dr. Gerd Geisslinger, executive director of Fraunhofer IME, and PD Dr. Frank Behrens, head of department Clinical Research of Fraunhofer IME, were called into the crisis committee of the Fraunhofer-Gesellschaft to contribute their medical expertise. As part of the Fraunhofer vs. Corona campaign, various temporary research projects for characterizing and fighting COVID-19 were initiated in both locations. The activities comprise the whole value chain of drug development, from the search for active ingredients to the clinical development as well as clinical practice and the support from authorities of the public health offices in dealing with the COVID-19 situation. The ScreeningPort Hamburg contributed its "Drug Repurposing" expertise to the search for therapeutic approaches and formed the crucial interface between biologists and computer scientists within the EU-funded consortium Exscalate4CoV (E4C). Furthermore, Frankfurt and Hamburg evaluates new therapeutic approaches in clinical studies along with partners from the pharmaceutical industry.

The division "Molecular Biotechnology", with its locations in Aachen and Münster, puts its focus on the development of novel methods for the rapid, sensitive detection of COVID-19 or virus-specific antibodies in human sera. For example, the previous minimum detection time of a SARS-CoV-2 test method could be reduced from four hours to 40 minutes - and by eliminating complex and costly analytical equipment, mobile on-site testing is now possible. Unlike other rapid detections, this is achieved using the so-called Loop-Mediated Isothermal Amplification (LAMP) method, which detects the genetic information of the virus. Other procedures developed at IME allow for the detection of SARS-CoV-2-specific antibodies in human serums – the indication of an overcome COVID-19 infection. The viral antigens required for the establishment of such tests can safely and recombinantly be produced at the institute in sufficient quantities.

The systemic relevance of the topic chemical safety could be shown in Schmallenberg: despite construction- as well as pandemic-related reorganizations of work processes and despite the economic struggles of clients, there were record-breaking achievements in in terms of both budget and yield. Thus, the European top position in research and development for the regulatory environmental risk evaluation of substances could be consolidated.

In Gießen, both the pandemic and the delayed completion of the new building caused considerable financial straits and scheduling problems. However, the aid of the state of Hesse as well as the commitment of the local management and the Fraunhofer headquarters allowed for the further development of the LOEWE center to continue in accordance with the Fraunhofer requirements.

At the turn of 2020/2021, Fraunhofer IME will split into two independet institutes: The locations of the division Translational Medicine in Frankfurt am Main and Hamburg, together with the new location in Göttingen, form the Fraunhofer Institute for Translational Medicine and Pharmacology ITMP. Fraunhofer ITMP will also become the core institute of the Fraunhofer Group for Health, which is currently being established, as well as of the Fraunhofer lead market Health Management.

Fraunhofer IME's competencies in plant and insect biotechnology (Molecular Biotechnology) as well as regulatory substance evaluation (Applied Ecology) at the locations in North-Rhine Westphalia and Gießen put a joint focus on agricultural and food production. Fraunhofer IME will be a member of the Fraunhofer Group for Ressource Technologies and Bioeconomy, which is currently in its foundation phase, and is a founding member of the lead market Chemical Industry, headed by the Fraunhofer ICT. Within the lead market Food Ecology, Fraunhofer IME holds the deputy chairmanship (Molecular Biotechnology) and place of the central office (Applied Ecology).

Frankfurt am Main, Schmallenberg and Aachen in June 2021

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

THE INSTITUTE

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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 are acting members of the institute management.

Fraunhofer IME is a strong partner for contract research in the areas of pharmaceuticals, medicine, chemicals, 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 2020, 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 process complex projects across departments and where appropriate, also focuses on cooperation with external institutes and partners. We work closely with basic research and are internationally networked. Our laboratories with state-of-the-art equipment and complex environmental simulation facilities allow us to offer a wide range of research and services as well as studies according to good laboratory practice (GLP).

At the end of 2020, the institute employed 527 people working at the locations in Aachen, Münster, Schmallenberg, Gießen, Frankfurt am Main and Hamburg. We have close ties with the Department of Biology and Biotechnology of Plants at the University of Münster, the Institute for Clinical Pharmacology at the Goethe University Frankfurt, Frankfurt am Main, 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

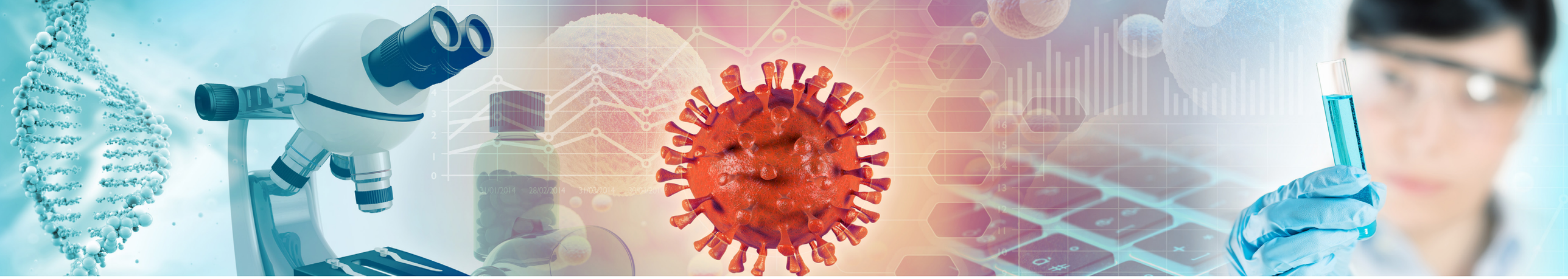
Translational Medicine contributes steadily and substantially to the development of new approaches for the diagnosis and treatment of diseases that are inadequately understood or controlled. The field of translational medicine spans the value chain, from target identification through active agent screening 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.

Symbols used in the annual report

MB Division
Molecular Biotechnology

AE BR Division
Applied Ecology and Bioresources

TM Division
Traslational Medicine



FRAUNHOFER IME WITHIN THE FRAUNHOFER-GESELLSCHAFT

The Fraunhofer-Gesellschaft is the world's leading applied research organization. With its focus on developing key technologies that are vital for the future and enabling the commercial exploitation of this work by business and industry, Fraunhofer plays a central role in the innovation process. As a pioneer and catalyst for groundbreaking developments and scientific excellence, Fraunhofer helps shape society now and in the future.

The Fraunhofer-Gesellschaft currently operates 75 institutes and research institutions throughout Germany. The majority of the organization's 29,000 employees are qualified scientists and engineers, who work with an annual research budget of 2.8 billion euros. Of this sum, 2.4 billion euros is generated through contract research.

The Fraunhofer Institutes are organized in eight thematically oriented alliances. Their goals are the technical coordination within the Fraunhofer-Gesellschaft, the bundling of core competencies and a joint appearance on the market. Fraunhofer IME is a member of the Life Sciences Network, a scientific-technological community of highly qualified experts from key areas of modern life sciences from six Fraunhofer Institutes and one Fraunhofer Research Institution.
www.lifesciences.fraunhofer.de/en.html

Institutes or departments of institutes with different competencies cooperate in Fraunhofer alliances to jointly develop and market a business segment. The Fraunhofer Alliances make it easier for customers to access the results and services of the Fraunhofer-Gesellschaft. Fraunhofer IME is involved in two alliances:
Fraunhofer Big Data and Artificial Intelligence Alliance: www.bigdata.fraunhofer.de/en.html
Food Chain Management: www.fcm.fraunhofer.de/en.html

Fraunhofer Clusters of Excellence promote the cooperative development and processing of system-relevant topics through an inter-institute research structure in a "virtual institute". Fraunhofer IME is one of the three core institutes of the Fraunhofer Cluster of Excellence for Immune-Mediated Diseases CIMD.
www.cimd.fraunhofer.de/en.html

High Performance Centers organize the collaboration between university and non-university research with industry. Universities, higher education institutions, Fraunhofer Institutes and further non-university research institutions work together at one location on specific topics in order to quickly transfer innovations to application. Fraunhofer IME in Aachen is involved in the "Networked, adaptive production" High Performance Center.
www.vernetzte-adaptive-produktion.de/en.html

Fraunhofer lighthouse projects put the focus on strategic objectives with a view to developing practical solutions from which economies such as Germany's can benefit. The projects aim to turn original scientific ideas into marketable products as quickly as possible. Fraunhofer IME is contributing its expertise to the lead project MED²ICIN.
https://websites.fraunhofer.de/med2icin/

The Fraunhofer Sustainability Network is an initiative of 20 Fraunhofer Institutes aiming to raise awareness within the Fraunhofer Gesellschaft for the integration of sustainability issues.
www.fraunhofer.de/en/about-fraunhofer/corporate-responsibility/governance/sustainability/fraunhofer-sustainability-network.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.
Members of the Fraunhofer IME Advisory Board:

Dr. Harald Seulberger (Chairman)
BASF SE, Limburgerhof

Dr. Friedrich Dechet
Industrial Association Agrar, Frankfurt am Main

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

Stefan Lütke Entrup
Gemeinschaft zur Förderung von Pflanzeninnovation e. V., Bonn

Prof. Dr. Heyo Kroemer (Deputy Chairman)
University of Göttingen, Göttingen

Prof. Dr. Joybrato Mukherjee
President of the University of Gießen, Gießen (guest)

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. Ulrich Rüdiger
Rector of RWTH Aachen University, Aachen (guest)

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

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

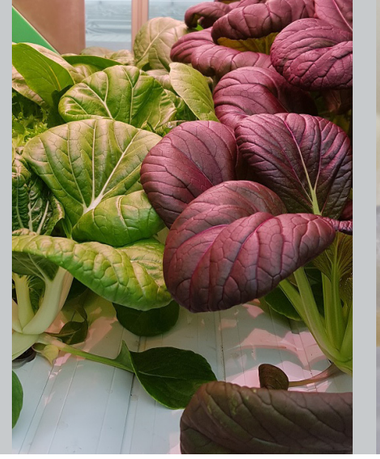
Prof. Dr. Johannes Wessels
Rector of the University of Münster, Münster (guest)

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

Prof. Dr. Birgitta Wolff
President of the Goethe University Frankfurt, Frankfurt am Main (guest)

The annual meeting of the Advisory Board was held virtually on November 6, 2020. The Executive Board of the Fraunhofer-Gesellschaft was represented by Dr. Hans-Otto Feldhütter, Director Strategic Projects / FFB.

BUSINESS FIELDS MOLECULAR BIOTECHNOLOGY



Molecular Biotechnology: Research, Development and Services

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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.

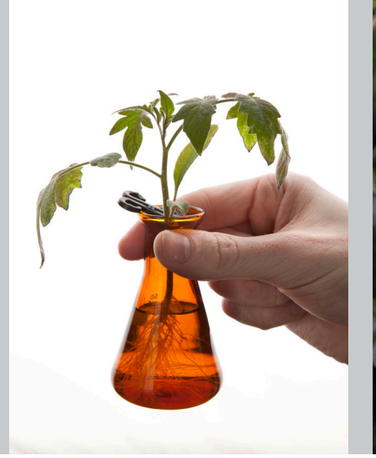
Agroscience for Food and Feed

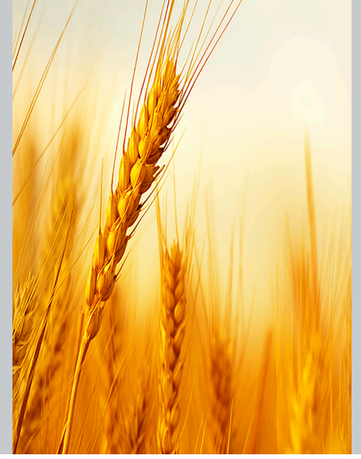
The business field Agroscience for Food and Feed covers the agricultural value chain "from farm to fork" and focuses on the development and improvement of plant traits, crops and enabling technologies to increase the biomass of crops, the quality and yield of agricultural products, the ability of plants 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.

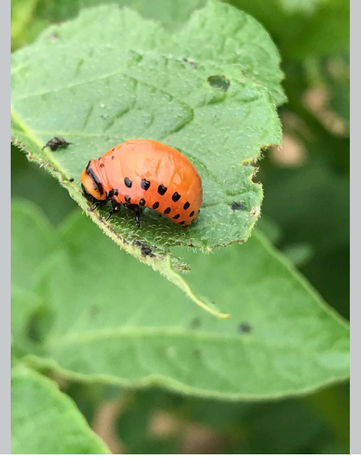
Production of Recombinant Proteins

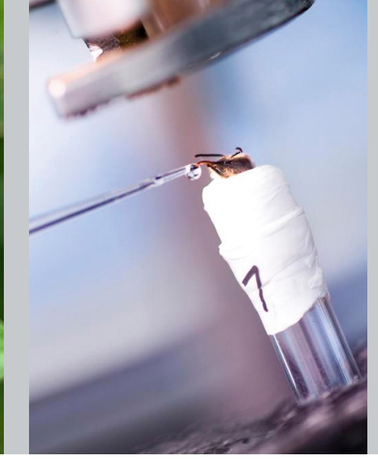
Fraunhofer IME offers expertise in all aspects of the design, production, purification and characterization of recombinant proteins, including process development and scale-up from a laboratory process to the manufacture of kilograms of clinical material under GMP conditions. Different systems are available 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.

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 4C$_2$4C

We develop across divisions concepts for the sustainable agricultural production of substances for a diversified bioeconomy: **C**onnecting niches to **C**hains of bioeconomic value added for **C**ircular flow in a **C**limax economy. To achieve this, amongst other things, we use Fraunhofer technologies of the lead project **C**ognitive Agriculture to meet socio-economic and ecological requirements (**C**ommunity claims) with new **C**rops and changed livestock husbandry (**C**attle/livestock). We take into account differentiated soil and microclimate properties, the use and optimization of plants for the production of valuable and active substances (Aachen and Münster), and waste and insects for obtaining protein (Gießen). Regulatory requirements arising from digital agriculture in the application of plant protection products, veterinary medicines and fertilizers, are also taken into account (Schmallenberg).

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. With the world's largest industrial strain collection of microorgasnisms, taken over from Stanofi, we are also open to projects with other industrial partners from non-competing fields of application.

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

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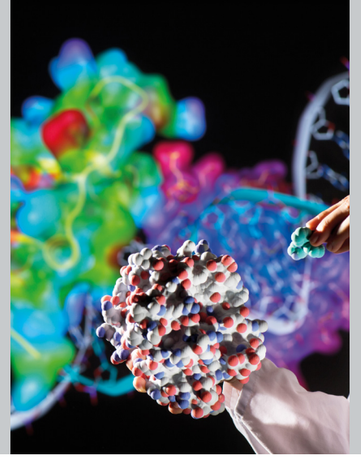
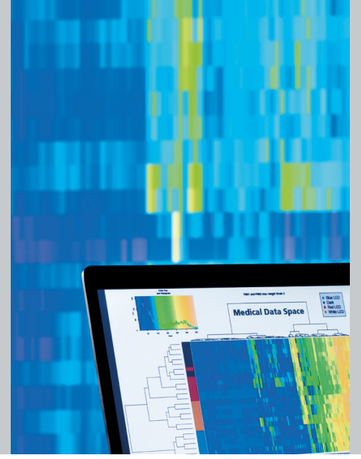
BUSINESS FIELDS TRANSLATIONAL MEDICINE





Assay Platforms and Drug Discovery

Our expertise is in modern drug discovery, enabled by our high quality screening collections totalling over 350,000 lead-like compounds, state of the art automated infrastructure and well-established in-house in silico screening platforms. This allows our partners to realise their projects from target validation through to preclinical studies. We have established an extensive portfolio of target, phenotypic and biophysical based assays, as well as in vitro disease models based on induced pluripotent stem cells. This allows us to investigate target "druggability" and enables mechanism of action studies. The "Fraunhofer IME Repurposing Collection" of over 5500 small molecules, also offers an alternative path to quick clinical application. As a screening partner site in the EU-OPENSCREEN infrastructure, we provide access to synthetic chemistry, chemical proteomics and structural biology platforms.

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.

Digital Health Research

We contribute to the digitalization of the pharmaceutical research by establishing the Fraunhofer "Medical Data Space", a decentralized data management system for the autonomous and secure storage and exchange of medical data between networked databases. For several pan-European projects we provide our expertise in bioinformatics by implementing a Data Scientist to ensure the highest standards in FAIR data management for drug discovery data analysis workflows, which integrate project, public and proprietary data. We further develop algorithms and AI tools for the statistical analysis of patient and virtual patient cohorts in the areas of diabetes, ageing research and - in collaboration with Germany-based cancer registries - in oncology.

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 am Main 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.

Translational Medicine: Research, Development and Services

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INSTITUTE MANAGEMENT AND LOCATIONS

31.12.2020

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INSTITUTE DATA

Budget

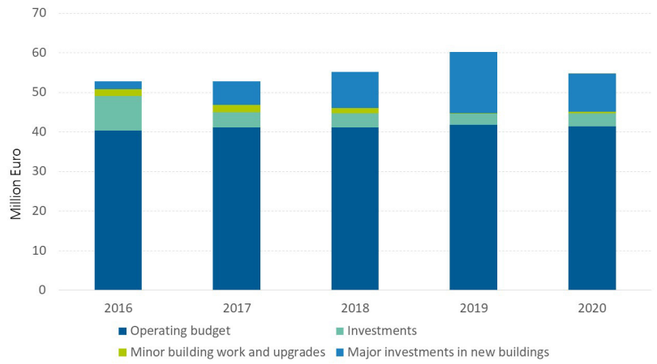
In 2020, the Fraunhofer IME had an operating budget of 41.4 million euros. In addition, about 3.3 million euros were invested in equipment. Fraunhofer IME recorded an expense of 10.1 million euros for construction activities, primarily the new institute buildings in Gießen and Schmallenberg.

74.3 percent of the budget was financed by external income, or 76.8 percent if the location in Frankfurt am Main, which is mainly financed by the federal state, is included.

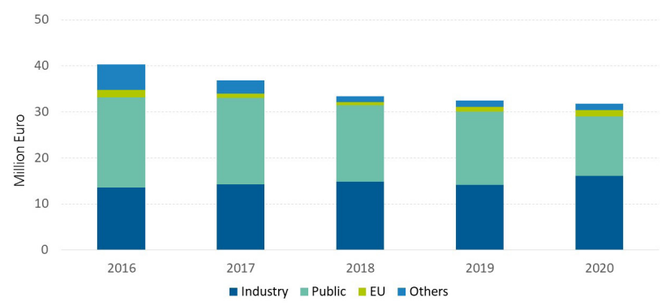
Economic earnings of 16.1 million euros remain at a constantly high level. This corresponds to an economic revenue share (Rho Wi) of 43.7 percent and 39 percent respectively.

Thus, in 2020 Fraunhofer IME once again achieved excellent results in the key figures of the Fraunhofer-Gesellschaft.

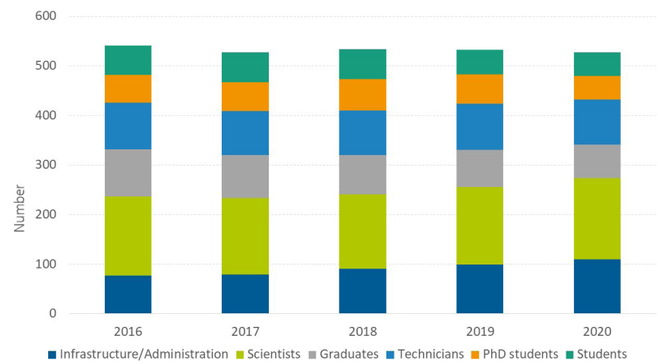
Total budget of Fraunhofer IME



External financing of Fraunhofer IME



Employees of Fraunhofer IME



Personnel

At the end of 2020, 527 personnel were employed at the Fraunhofer IME locations in Aachen, Münster, Schmallenberg, Gießen, Frankfurt am Main and Hamburg. 52.8 percent of Fraunhofer IME personnel were female.

OUR RESEARCH

Development of a test system to evaluate the bioaccumulation of nanomaterials

Plants as production system for Corona diagnostics

It's in our blood - Circulating proteins for precision medicine

Spider venom as a source for novel bioresources

Using bacteria to produce proteins for dietetic food therapy

Fraunhofer IME and UKE continue drug development targeting multiple sclerosis

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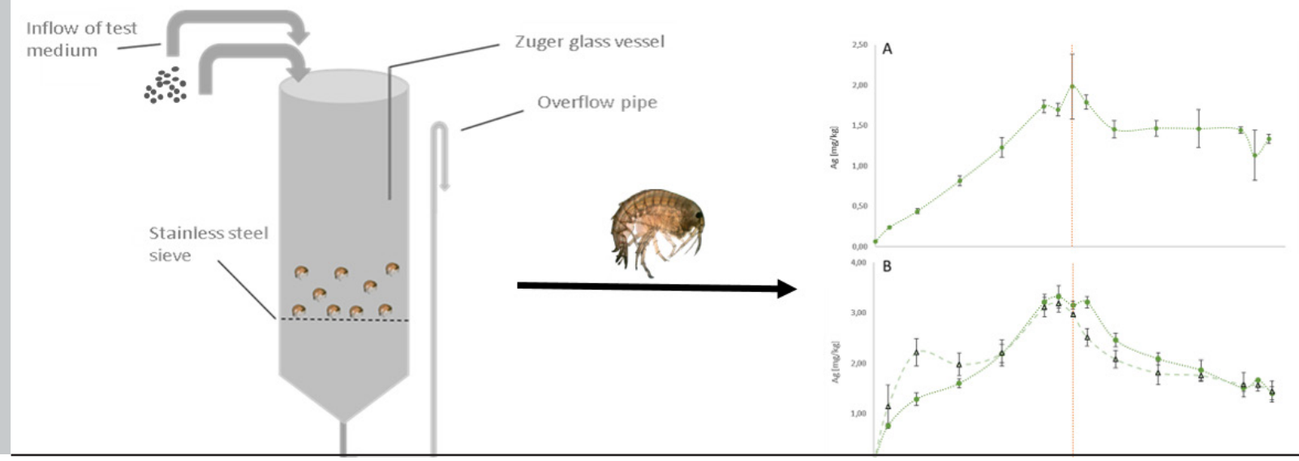
DEVELOPMENT OF A TEST SYSTEM TO EVALUATE THE BIOACCUMULATION OF NANOMATERIALS



Overview of the flow-through system to test nanomaterials.

The high production volume of technical nanomaterials (NMs) inevitably leads to environmental pollution. Therefore, a scientific assessment of the tiny particles that can potentially bioaccumulate in organisms and accumulate along the food chain is necessary. Consequently, scientists at Fraunhofer IME are working on the development of a test system that enables the assessment of the bioaccumulation potential of NMs.

Nanomaterials (NMs) are used in numerous fields of production and can be found in various consumer goods such as textiles, medicine, cosmetics, printer toners, car tires and even food, due to their broad spectrum of activity. For example, inert metals and metal oxides such as gold and titanium dioxide can be used as highly efficient catalysts in the form of NMs. Silver nanoparticles (AgNPs) are mainly used for their antimicrobial properties. However, NMs can be released into the environment during manufacture, use and disposal and thus pose a potential environmental risk.

NMs pose a potential environmental risk

Due to the high production volume of NMs, they are subject to an environmental assessment in accordance with the requirements of the "European Chemicals Registration REACH". As part of the regulatory assessment, the bioconcentration factor (BCF) is the standard criterion to identify bioaccumulative substances. The BCF value is usually determined in the context of fish flow tests in accordance with OECD test guideline 305. The test was developed for water-soluble and primarily lipophilic test substances. However, most NMs tend to deposit in water bodies and usually are not completely dissolved. For this reason, the aqueous concentrations of NMs cannot usually be kept at a constant level during flow-through tests, or only at considerable expense. The experimental conditions required to determine the bioaccumulation potential of NMs are therefore difficult to maintain. Given the tendency of NMs to deposit in water bodies, benthic organisms could be a suitable alternative to fish for bioaccumulation studies So far, however, there is a lack of standardized testing procedures to quantify the bioaccumulation potential of nanomaterials, especially for invertebrate benthic organisms, says Professor Dr. Christian Schlechtriem, who heads the Department for Bioaccumulation and Animal Metabolism at Fraunhofer IME in Schmallenberg.

A promising approach for bioaccumulation tests of NMs could be the bioaccumulation test "HYBIT" developed for testing soluble organic substances with the freshwater amphipod *Hyalella azteca*. The small crustacean is an established test organism for ecotoxicological studies and, due to its short life cycle and its sensitivity to environmental chemicals and metals, it is ideal for bioaccumulation tests. *H. azteca* can be easily grown in the laboratory and has a high reproductive rate and rapid growth.

The new test system enables the determination of the bioaccumulation potential of NMs

The flow-through test system with *H. azteca* allows bioaccumulation studies with NMs following dietary and aqueous exposure. Laboratory bioaccumulation studies with gold, titanium dioxide and silver nanoparticles as well as dissolved silver (AgNO3) carried out in Schmallenberg showed the bioaccumulation potential of the various nanomaterials and their exposure routes. Following constant exposure for several days, the animals were examined for their metal content in the whole body using inductively coupled mass spectroscopy (ICP-MS). Further analyses by single-particle ICP-MS were carried out to confirm the presence of NMs. However, it remained unclear whether the particles ingested by the small crustaceans were present in the tissue or only in the intestinal contents without any further tissue transfer.

In order to clarify the main route of exposure and the localization of silver nanoparticles (AgNPs), the freshwater crustaceans were again exposed for several days via water and food. ICP-MS and methods of correlative microscopy were used to determine the total silver content in the animals and the potential accumulation of nanoparticles in the tissue. Sebastian Kühr carried out the studies as part of his dissertation at Fraunhofer IME in cooperation with Fraunhofer IMWS. He describes that correlative microscopy could not detect any transfer of AgNPs from the intestine into animal tissue. The silver concentrations measured in the small crustaceans thus provided clear indications that the uptake of ions is the main uptake path for the bioaccumulation of Ag from AgNPs in *H. azteca,* as was confirmed in comparison with dissolved silver (AgNO3).

The results from the bioaccumulation studies with small crustaceans can be incorporated into a tiered evaluation system

Taking into account the potential release of ions from NMs, the flow-through test system with *H. azteca* enables the calculation of BCF values and biomagnification factors (BMF) that are suitable for assessing the bioaccumulation of NMs in the context of regulatory substance assessment. The results from the bioconcentration and biomagnification tests with H. azteca can be used in a tiered evaluation system that enables the tested nanomaterials to be defined as "bioaccumulating" or "non-bioaccumulating". If the flow-through test with *H. azteca* does not provide any evidence of bioaccumulation of an NM, further investigation in the fish test might be omitted. In this way, the amphipod test could help reduce the use of vertebrates in the context of regulatory substance assessment.

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PLANTS AS PRODUCTION SYSTEM FOR COVID DIAGNOSTICS

Plant production systems for the development of Covid testing procedures.

The Covid19 pandemic is a global challenge for societies and their healthcare systems. The spread of the SARS-COV-2 virus must be kept at bay until a sufficient amount of people can be successfully vaccinated against the disease. Besides protective measures such as face masks and social distancing, diagnostic detection procedures play an important part. The institute branch Molecular Biotechnology of Fraunhofer IME employs plant production systems for the development of such procedures.

The aim of such tests is, on the one hand, the reliable verification of a SARS-CoV-2 infection via the detection of viral components (genome or envelope proteins) in swab samples, and, on the other hand, the determination of the immune status through virus-specific antibodies. While the first approach allows to identify and isolate infected individuals, the second approach indicates whether a patient had already been infected before, or whether a sufficient amount of antibodies has been produced through vaccination. The detection of SARS-CoV-2-specific antibodies in the patient' blood requires virus surface proteins. Cultivating the virus in human cells can only be done under sterile circumstances, and is both costly as well as risky. Therefore, the required virus surface proteins for such detection procedures must be produced in suitable cell hosts by means of biotechnological procedures. Apart from established systems based on animal cell cultures, plants also qualify as possible production systems.

Transient plant production system as robust and flexible alternative for established systems

One particularly suitable detection reagent for SARS-CoV-2-specific antibody responses is the spike protein (S1), which is found in multitude on the virus particle surface. The S1 is a complex protein that is not suited for production in cheap bacterial production systems. Except for the animal cell cultures primarily used in the production of complex proteins, plants are also suited for their production. Besides protein production in stable transgene plant lines, transient transformation offers significant advantages in hard-to-plan pandemic events, especially with a view to speed and flexibility. While the cultivation of stable transgene plant lines takes at least 6 to 9 months – and usually much longer – the production of a recombinant protein by means of transient transformation can be carried out within 8 to 12 weeks.

This technology employs a method called the vacuum filtration procedure, where the genetic blueprint of the desired protein is inserted in previously cultivated, unmodified wild-type plants by means of a special bacterium (*Agrobacterium tumefaciens*). Subsequently, synthesis occurs within a couple of days, and the desired protein can then be isolated and purified from the plant material. The cultivation of wild-type plants can be carried out reliably and cost-efficiently in conventional green houses or in modern vertical farming systems. The agrobacteria required for the process can be cultivated in traditional bioreactors. Afterwards they are ready for instant use or they can be frozen. This is way the transient system is a much promising alternative to conventional production platforms based on animal cell cultures, especially when a sudden demand amidst, such as a pandemic, arises, where there is a shortage of available bio production systems.

Process development for plant-based production of SARS-CoV-2 spike protein S1

SARS-CoV-2 S1-based recombinant proteins are not only potential candidates for a vaccine, but also interesting with a view to diagnostic reagents. The project CDP (Corona Diagnostic Proteins) focused on the development of a production process for a S1-based protein, which is suitable for being applied in quick tests for the detection of SARS-CoV-2-specific immune responses. It fuses the immunologically relevant domain of the S1 protein with the constant domain of rabbit antibodies. The fusion with the antibody domain stabilizes the S1 molecule and at the same time facilitates protein purification.

Within the project, genetic information of the protein was first transferred to agrobacteria, which were then grown in a 40l bioreactor. Afterwards, the bacteria were then used for the vacuum filtration of up to 400 *Nicotiana benthamiana* plants. The plants were cultivated at the vertical farming unit (VFU) at Fraunhofer IME, which was specially constructed for such purposes in close collaboration with Fraunhofer ILT. The unit allows for the automated sowing, cultivation and harvest of 400 to 600 plants per week and is further equipped with an additional module for automated vacuum filtration and plant incubation.

The plants are automatically harvested 5 days after vacuum filtration, delivering the plant material for the following, non-automated steps of extraction and purification. Compared to other production systems, the purification of proteins in plants is a particular challenge for both extraction technology as well as fiber separation. The project could successfully establish an efficient workflow and purify several 100 mg of S1 protein in a pilot process.

Fast and flexible production of essential reagents in plants

The CDP project was able to demonstrate that the automated transient plant platform at Fraunhofer IME is able to establish a robust process to produce diagnostic reagents – in this case for the detection of Covid-specific antibodies – in a short period of time. The production of reagents, sufficient for hundred thousands of tests, is possible within only a few months.

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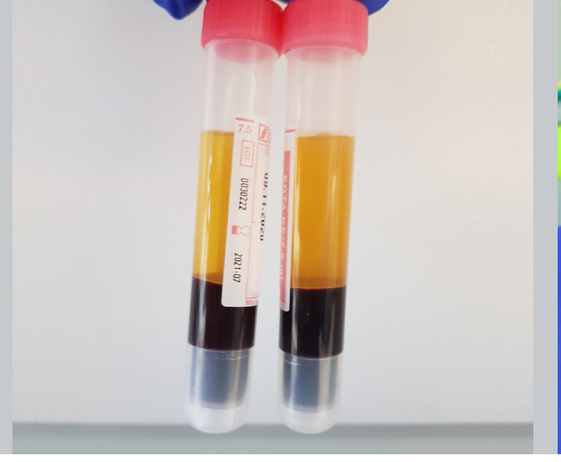
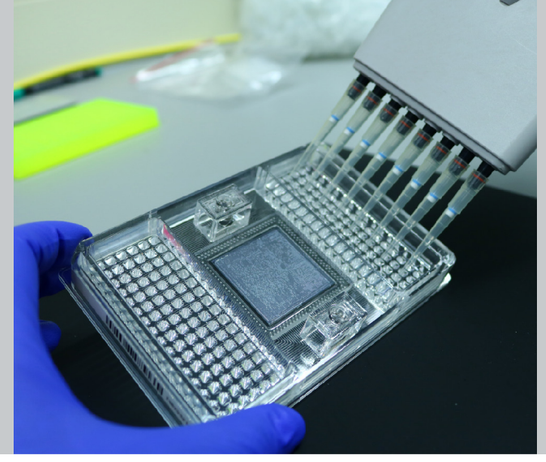
IT’S IN OUR BLOOD – CIRCULATING PROTEINS FOR PRECISION MEDICINE



Blood samples after centrifugation: Solid components of the blood (dark red) settle at the bottom of the tube. The blood plasma (yellow) with the liquid components remains as the supernatant.



The Proximity Extension Assay is conducted.

We know this procedure from a visit to the doctor’s: blood is collected to make a haemogram. With the help of the laboratory’s blood analysis, the doctor might better assess the patient's health status or diagnose a disease state. But in the blood - the liquid tissue – there is way more to find! Thousands of different protein molecules circulate through the body in tiny amounts. To detect them and to use that information to develop novel diagnostic, prognostic and individual therapeutic approaches is a goal of Fraunhofer IME.

At the doctor’s, blood is routinely taken for laboratory tests. In a blood test, very different components can be considered. The number and composition of the white blood cells might, for example, reveal a latent infection. The amount of glucose molecules bound to a specific protein of the red blood cells tells the doctor about the patient’s long-term blood sugar level, also known as the »HbA1c« value, which plays an important role in the fine adjustment of diabetes therapy. And this list of examples is by far not complete! In addition to standard checks for iron concentration or cholesterol levels, blood can also be tested for the presence of so-called antibodies. Our body generates these antibodies, which specifically bind to certain pathogens and thus help to fight them. Their existence in the blood indicates, whether a person has already been in contact with a particular pathogen, such as hepatitis viruses, the human immunodeficiency virus (HIV) or, as in the present public spotlight, the SARS-CoV-2.

Blood - the universal liquid tissue sample

With a few exceptions, our entire body is circulated by blood. The blood transports vital nutrients and oxygen to the cells, whereas degradation products and carbon dioxide are removed. But many other things produced in the body are distributed by the bloodstream throughout the whole body. A large set of messenger substances, which are transported through the blood, are available to the cells for their communication. Wouldn't it be interesting to find out which messages circulate through the whole body?

Blood is a “liquid tissue sample”, so to speak, that carries information from the whole body, and thus also from the most remote and difficult-to-reach areas such as inner organs. An entire research field deals with the development of liquid biopsy applications. The approach to obtain relevant information from just a few milliliters of blood, which helps to detect and predict disease states, is very attractive. And wouldn’t it also be desirable to know the success rate before starting a stressful therapy and, in risk of failure, choose an alternative therapy in advance? Or even better: using the messenger profiles in the blood, the appropriate therapy could be arranged individually for each patient. This precision medicine approach, as it is called, is still at the beginning of the development process, but first successes were already achieved in cancer therapy.

Tracking the protein molecules in the blood

The messenger substances circulating in the bloodstream belong to different molecule classes, such as nucleic acids, lipids or proteins. And each class of molecules requires its own special type of analytical method. We are now using a method to detect proteins in the liquid component of the blood, the blood plasma. These proteins, of which there are thousands of variants available, are generated by the cells and are released into the bloodstream in a targeted or untargeted manner. The concentration of the protein variants may differ enormously (sometimes more than one billion-fold). But particularly the protein variants with a messenger character are often low abundant in the blood plasma. Therefore, the challenge is to identify and reliably detect them.

The method: Proximity Extension Assay

Two technologies based on Nobel Prize-winning discoveries (1. the application of antibodies for detection purposes and 2. the polymerase chain reaction (PCR)) are combined in what is known as the Proximity Extension Assay (PEA). Here, two different antibodies are used, which bind the protein of interest to their specific recognition sites. Additionally, each antibody comes with a terminally bound nucleic acid single strand. When the two antibodies bind to the same protein molecule, the nucleic acid single strands, due to their proximity, form a nucleic acid double strand. The double strand – and only this one – serves as a template in the following PCR. In this reaction the template double strand is exponentially multiplied enabling a simple color-based detection which represents the protein of interest. The double antibody detection makes the method specific, because only the protein of interest is detected and bound by both antibodies at the same time. The subsequent exponential PCR makes the method sensitive, because even rare protein molecules are discovered and quantified by the strong amplification of the representative nucleic acid double strand. The PEA method is so sensitive that a blood drop with a volume of one thousandth of a milliliter is sufficient to examine more than 90 protein variants simultaneously.

It is assumed that for most complex diseases, for which marker molecules in the blood are investigated, it is necessary to consider several molecules together at the same time in order to obtain relevant information for precise diagnosis or therapy. Thus, it will be important to search broadly for different marker molecules to characterize and distinguish different complex diseases as clearly as possible.

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SPIDER VENOM AS A SOURCE FOR NOVEL BIORESOURCES

The venom of the native wasp spider Argiope bruennichi has recently been analysed.

Spider venom research has previously been focused on tropical species.

With over 49 000 species, of which most produce complex venom cocktails, spiders represent the most successful group among venomous animals. It has been estimated, that a total of 10 million biomolecules can be isolated from spider venoms, but less than one percent of this diversity has been discovered so far. That said, studies on this small selection already identified promising drug candidates for the treatment of ischemic stroke or epilepsy as well as molecules with potential as bioinsecticides.

Spider venom is a largely untapped bioresource with great potential

Spiders produce their complex venoms mostly to capture their prey, in particular insects. Their venoms have been fine-tuned throughout their 380 million years of evolution. As a result, spiders evolved an unprecedented degree of molecular diversity and pharmaceutical efficiency in their venoms. The venom of a single species may comprise up to three thousand different components which acquired a plethora of physico-chemical properties granting the mentioned efficiency. The majority of spider toxins belong to the class of knottins, a group of small peptides displaying a unique architecture with disulfide bridges forming a knot-like structure. This structure is referred to as inhibitor-cystein-knot (ICK) and provides knottins with increased stability against chemical, enzymatic or thermal degradation and leads to long biological half-lifes. Simultaneously, their small size corresponds to a fast distribution inside the organism. Toxins in spider venom are primarily neurotoxic. They bind with astonishing specificity to their ion-channel targets and mediate them via substantial inhibitory or excitatory action. Facing, that spider venoms evolved primarily to subdue insects, their abilities can be exploited for innovative application possibilities. On one hand agricultural applications as bioinsecticides are possible. On the other hand, ion-channels mediated by spider venom are often involved in human diseases which renders spider venom toxins as promising candidates for the development of novel therapeutics. Past studies identified spider venom toxins that were able to alleviate neuronal damage after stroke as well as epilepsy or chronic pain.

Novel biomolecules from the venom of wasp spiders

Regardless of this seemingly great potential, spider venoms remain largely unexplored. Previous research focused almost exclusively on large or dangerous tropical species, whereas the small and harmless native representatives have not received much attention so far. As a result of this bias, only 0,3 percent of spider species have been studied for their venoms and of the estimated 10 million spider venom components, less than one percent has been identified to date. Harnessing these neglected spider venom systems for translational research is the goal of our working group "Animal Venomics" in the department of Bioresources within the Fraunhofer Institute for Molecular Biology and Applied Ecology IME in Gießen. In coherence with this vision, the wasp spider *Argiope bruennichi* has recently been studied for its venom in context of the "LOEWE Centre for Translational Biodiversity Genomics".

Our work revealed, that wasp spider venom contains some typical knottin components, albeit these constitute only a minor fraction of the venom. It likewise contains several enzymes, such as serineproteases, metalloproteases or chitinases plus other proteins such as thyroglobulins in low concentration. Beyond these, the work identified a series of novel components with undetermined biological activity and function. First, it contains peptides that were also identified in the venom of a related species, the Asian cross spider *Araneus ventricosus*. Such "Aranetoxins" have so far exclusively been detected in the venoms of these two orb weaver spiders and seemingly represent lineage specific toxins for this group. Another assemblage of interesting compounds from wasp spider venom comprises three different classes with structural similarity to insect neuropeptides. Some of these classes have been recovered as spider venom components for the first time. Neuropeptides bind naturally to designated receptors and induce specific neuronal responses in insects. It is possible, that such neuropeptide-like toxins hijack the natural function of these and artificially modulate the involved receptors which may lead to neurotoxic symptoms. If this is verified by our ongoing functional investigation, such peptides may give rise to a new generation of bioinsecticides in the future.

Tracing venoms of neglected spiders

Apart of the wasp spider, native fauna harbors hundreds of other species which evolved unique venom cocktails along their evolutionary trajectory. Disentangling the neglected diversity within these venoms will certainly recover more promising biomolecules and may provide the basis for future pharmaceuticals and agricultural products. In particular the investigation of German species, such as the purse-web spider *Atypus affinis*, the common cross spider *Araneus diadematus* and the infamous yellow-sac spider *Cheiracanthium punctorium* has recently been started in our group and will provide further insights into the fascinating world of spider venoms.

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USING BACTERIA TO PRODUCE PROTEINS FOR DIETETIC FOOD THERAPY

Phenylalanine-free protein.

New dietary alternatives for PKU patients thanks to “Phe-frei3”.

Phenylketonuria (PKU) is a genetically inherited metabolic disorder, where patients have low levels of the enzyme that degenerates the amino acid phenylalanine, which is found in all animal and some plant-based proteins. People affected with it therefore have to follow a strict low-protein diet to avoid negative health effects such as irreversible brain damage. A phenylalanine-free protein derived from bacteria is now set to open up new diet approaches for PKU patients and boost their life quality.

Being diagnosed with PKU means one thing for those affected: a strict, low-protein diet – for a lifetime. A difficult task to undertake because the amino acid phenylalanine is found in all meat products as well as in a number of plant-based foods such as legumes, rice or wheat. Therefore, vegetables and fruits constitute the daily meal plan, which in the long run is very monotonous and takes away life quality. However, necessity enforces discipline: high concentrations of phenylalanine in the bloodstream, which the system cannot degenerate on its own due to the underlying metabolic disorder, will eventually lead to irreversible brain damage if not treated properly and timely. To counteract a deficiency of amino acids due to their low-protein diet, PKU patients are given special amino acid mixtures. These mixtures, however, are by no means a pleasant experience in terms of flavour since the amino acids have a very bitter taste. There are also a number of other disadvantages such as low solubility.

A designer protein free of phenylalanine

As part of the research project “Phe-frei3”, the Aachen-based division Molecular Biology of Fraunhofer IME has developed a phenylalanine-free protein to compensate the deficits of the synthetic production and to open up new dietary possibilities for PKU patients. The biotechnologically produced protein is called GSP105 and contains a number of essential amino acids, except for phenylalanine, and is supposed to optimise the nutritional management of the patients and therefore boost life quality. Instead of the already known amino acid mixtures with their unpleasant taste, the project opted to find a protein in nature that meets the requirements for a phenylalanine-free diet at the best possible rate. When it comes to producing proteins for the food industry, microbial cell factories like yeast or bacteria are commonly used. By means of an algorithm that took the aforementioned requirements into account, more than 830 000 proteins in animal, plant and microbial organisms were analysed, all of which are already used for human food production, such as lactic acid bacteria for the production of yogurt. One protein derived from the hay bacterium *Bascillus subtilis* proved to be best suited – yet, it still contained one phenylalanine and lacked the essential amino acid tryptophan. The employment of molecular biological methods ultimately allowed to substitute phenylalanine with tryptophan.

Neutral flavour and perfectly digestible

“Phe-frei3” uses the bacterium *Pseudomonas fluorescens*, which can derive proteins with particular efficiency. The new protein is characterised by its neutral flavour, thus counteracting one of the biggest flaws of the aforementioned amino acid mixtures. Furthermore, it is easily soluble, chemically stable and resistant to high temperatures. It is therefore perfectly suited for being processed into food for PKU patients, for example pasta or burgers which would be a much desired alternative to the usual vegetables and fruits. Another important aspect is the good digestibility that was proven through exposure to digestive enzymes (proteases).

First tests on mice with PKU-like symptoms showed that the protein GSP105 is both nutritional and well-tolerated. It was also shown that following the consumption of GSP105, the phenylalanine content in the blood of the mice was lowered by 80 percent as compared to the trial group that received regular feeding. Now the project requires further investigations in order to make the protein accessible to human PKU patients and, hopefully, provide them with new dietary alternatives and taste experiences.

Exploiting biological diversity

The biotechnological production of proteins offers various application scenarios – not only in the medical and pharmaceutical sector, but also in cosmetic and cleaning products, in environmental protection as well as part of various refining processes for food ingredients. It is an important focus of the acitivities within our Molecular Biology division that, along with “Phe-frei3”, is also researched in the project “NXPRESS”. Here, the exploitation of the microbial biodiversity is the centre of attention, and the development of new, productive microbial expression platforms, which will allow the cost-efficient biotechnological production of difficult-to-express proteins. The spectrum comprises well-established mammal and insect cells, various microorganisms such as different types of yeast, *E.coli* or bacillus, right to more exotic platforms such as plants and plant cells or cell-free systems. As of yet, most microbial platforms ignore the enormous biodiversity of such microorganisms that could be used to establish efficient screening and production processes for such proteins.

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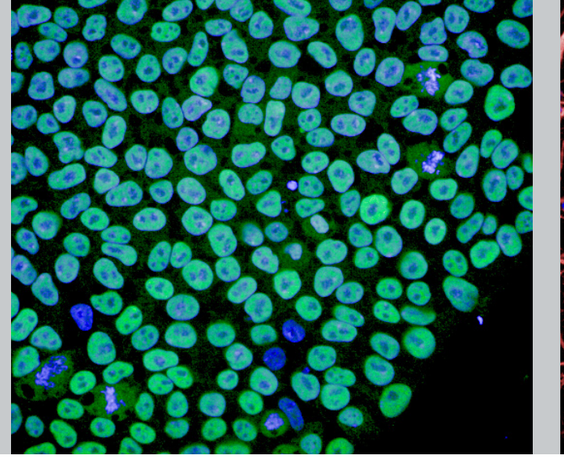
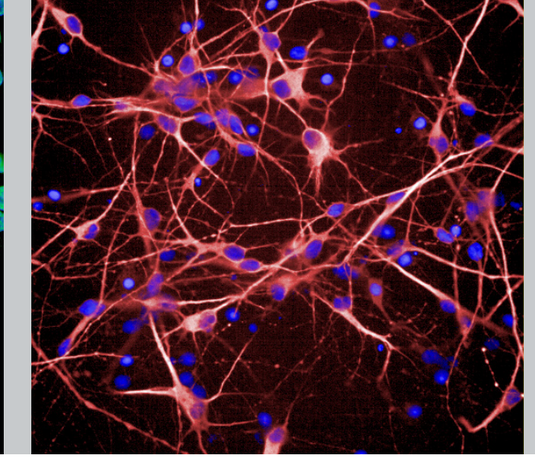
FRAUNHOFER IME AND UKE CONTINUE DRUG DEVELOPMENT TARGETING MULTIPLE SCLEROSIS



Human-induced pluripotent stem cells. Green staining: OCT3/4, a pluripotency factor. Blue staining: Cell nuclei.



Human nerve cells derived from iPS cells. Red staining: MAP2, a neuronal protein. Blue staining: Cell nuclei.

Based on the results of a long-standing cooperation with the University Medical Center Hamburg-Eppendorf (UKE), the aim is to pave the way for novel therapies against multiple sclerosis (MS). The goal is to not only treat the underlying inflammation in MS symptomatically, but also to prevent the resulting degeneration of nerve cells that is responsible for the progressive disability in MS. The Federal Ministry of Education and Research (BMBF) is providing 1.2 million euro for this purpose.

What is Multiple Sclerosis?

Multiple sclerosis (MS) is the most common chronic inflammatory disease of the central nervous system, affecting about 2.5 million people worldwide. The destruction of myelin sheaths and nerve cells in the central nervous system leads to symptoms that can affect all brain and spinal cord functions, but mainly motor functions, i.e. movement and coordination, sensitivity, i.e. the sense of touch and the function of the eye, leading to impaired vision. Depending on which nerve tract is damaged, different functions are compromised. In principle, any function controlled by the central nervous system can be affected. This can result in a disability which, depending on the course and progression of the disease, is hardly noticeable or has significantly life-limiting effects. Pain can also be caused by the disease. "Common MS therapies are exclusively directed against the inflammatory reaction with only a limited effect on the progressive disability", says Prof. Dr. Manuel Friese, Head of the Institute of Neuroimmunology and Multiple Sclerosis (INIMS) at the UKE.

Therapeutics preventing nerve cell death

The ion channel Transient Receptor Potential Melastatin 4 (TRPM4) is involved in the degeneration of nerve cells. Ion channels are pore-forming transmembrane proteins that allow charged particles to pass through cell membranes and thus control important cell functions. Activation of TRPM4 leads to the opening of the channel and an influx of single positively charged particles into the cell. This influx affects the calcium balance in the cell and, depending on the tissue or cell type, regulates various functions that are not yet understood in detail, such as the activity of nerve cells and heart muscle cells or the secretion of insulin. The role of TRPM4 in multiple sclerosis and its aberrant regulation was first described by the research group of Prof. Dr. Friese. Mediated by chronic inflammation in the brain of MS patients, the channel shows increased activity in nerve cells and thus contributes to cell degeneration. If the channel is blocked, however, the extent of cellular damage can be reduced. To date, however, only unspecific molecules or molecules that are unsuitable as drugs are available for this purpose. In a previous project, we therefore screened over 250,000 molecules for their ability to block TRPM4 and identified a series of five chemically distinct drug candidates that have the potential to be developed into clinical candidates. The aim of the project, now funded by the BMBF, is to learn more about TRPM4 as a possible target structure and existing drug candidates in order to reduce the irreversible damage to nerve cells, which is responsible for the increasing motor impairment in MS, by blocking TRPM4.

Human stem cells for the validation of new therapeutics

To facilitate subsequent clinical studies, the institutions are investigating the molecular properties of TRPM4 in interaction with the drug candidates in various preclinical models. These include models based on human nerve cells derived from stem cells. In particular, human induced pluripotent stem cells (hiPS cells) are used, which are stem cells produced in the lab from normal skin cells by a genetic trick. These are comparable to embryonic stem cells, which have the ability to multiply indefinitely and to form any cell type of the body. However, unlike these, they are ethically unproblematic, as no embryonic tissue needs to be destroyed for their generation. Based on the knowledge from developmental biology of the nervous system, detailed protocols have been developed during the last few years to reliably produce neurons from these hiPS cells in the cell culture dish. Since human nerve tissue is very limited and difficult to access, test systems based on hiPS cells are an important tool to verify findings from animal models in human cells. With this approach, we now want to understand whether the protective effect of the identified TRPM4 inhibitors can be confirmed in human iPS neurons and thus molecular disease mechanisms can be transferred 1:1 from mouse models to human cells. We hope to validate TRPM4 as a suitable target structure for the newly developed drug candidates. According to the coordinator of the project, Dr. Philip Gribbon from Fraunhofer IME, this could make them the first MS therapeutics available on the market that prevent the degeneration of nerve cells. In the long term, we want to build a path from the academic idea to the market access of a new therapeutic agent and thus build a bridge between basic research and clinical application - in line with the basic Fraunhofer idea.

TM

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IN CONVERSATION

An interview with Simon Vogel & Andreas Reimann

»3«
Molecular Biotechnology

About

Simon Vogel began his professional career as a biological laboratory technician in the area of biotechnological process development of fermentations at BASF AG. Subsequently, he spent five years doing melanoma research at Heidelberg University, specializing in the area of flow-cytrometry. Back at BASF AG he worked in fungicide research for one year. In 2000, he transferred to RWTH Aachen University and five years later to the newly established Fraunhofer IME where he contributed to various publicly and industry-funded projects and was involved in 12 patents. As the main inventor of the OrbiPlant® technology, Mr Vogel has put the primary focus of his work on co-creating new agricultural systems for the past five years.

Andreas Reimann studied biology at RWTH Aachen University, graduating with an honours Diploma in 2000. Subsequently, he completed several years of basic research at the Pasteur Institute in Paris and worked in life science consulting. He then joined the Fraunhofer IME Aachen and, from 2008 to 2018, was in charge of the overall project management of the Fraunhofer Future Foundation's Malaria-Vaccine project, coordinating the six interdisciplinary research activities of the Fraunhofer IME, IPT and IIS project consortium. This also included the development of a novel, automated vertical farming pilot facility for the plant-based production of biopharmaceuticals at the IME Aachen. Since 2019, he has been increasingly expanding the IME business field development in the area of indoor/ vertical farming and is responsible for the licensing of the novel OrbiLoop® and OrbiPlant® vertical farming technologies. As of 2020, he is the deputy head of the newly established department structure "New Agricultural Systems" and is in charge of project acquisition and management.

ORBIPLANT®: LETTUCE GROWN VIA VERTICAL FARMING

Simon Vogel inspecting the lettuce.

The world's population keeps growing, while farmland is becoming scarce. This calls for new cultivation methods such as vertical farming, where lettuce and other edible plants are grown in a vertical direction with minimum space requirements. Fraunhofer IME has developed OrbiPlant®, a cost-efficient, automated vertical farming technology, which allows for the cultivation of vegetables in arid regions. Simon Vogel explains the vertical farming approach of OrbiPlant®, which he developed at Fraunhofer IME. Andreas Reimann, who is in charge of commercializing the patented OrbiPlant® technology, talks about its market potential.

Mister Vogel, how exactly does OrbiPlant® or vertical farming work?

You can think of OrbiPlant® as a closed construction with an integrated conveyor belt that runs in a series of wave-like up and down movements, and to which the lettuce heads are attached vertically. The roots protrude towards the inner side of these "waves", hanging in the air, while misting nozzles are automatically spraying them with water enriched with all necessary nutrients. The pH value is also adjusted automatically. In fact, the 1.2 metres long and 28 centimetres wide conveyor belt is a specially converted, motor-driven window blind. Every hour, it moves three centimetres. The blue LED lights provide optimal light exposure, which helps the lettuce to develop its beautiful reddish colour. Except for the actual planting and harvesting, everything is fully automated, which leads to very reasonable staff expenses.

How many lettuce heads and herbs can OrbiPlant® produce and how long does the process take?

The pilot system can produce around 200 plants per week.

How did you get this idea?

At the public swimming pool. I saw a covering that worked like a roller blind – and that was it. Since it's very often about saving expenses in agriculture, I wanted to focus on cost-efficient components that are already available on the market – which is not the case with conveyor belts of this length and width. So the idea of the window blind worked best for our pilot system and it has become a standard feature within the whole project.

How does OrbiPlant® differ from other approaches to organic production?

Our approach is better than organic production. After all, we cultivate our plants entirely pesticide-free, which even in organic cultivation is not feasible. We also only use a minimal amount of fertiliser, 40 percent less than usual. All resources are used in a cycle, so at the end we get nothing else but the lettuce head.

Automated vertical farming: The OrbiPlant® system at the Fraunhofer IME.

Left: Dr. Andreas Reimann presents the fresh lettuce heads.

Right: Simon Vogel planting the lettuce.

Left: The wave-like conveyor belt of the vertical farming plant.

Right: The OrbiLoop® demonstrator at the Fraunhofer IME foyer.

Are there any technical novelties?

Two: aeroponics and the orbitropal effect. In the well-known aeroponic system the plants are fixated on the surface with their roots up in the air, which allows for an ideal oxygen supply. A study has shown that plants grow particularly fast this way. The orbitropal effect stems from the changing gravitational position of the plant on the conveyor belt, which releases growth hormones. We have combined these two approaches into a new one, first as a demonstrator. After it proved successful, we got Fraunhofer IML on board and the colleagues there took care of the construction, electronics and the technical implementation. In 2018, OrbiPlant® started and it was a hit.

What sector is the OrbiPlant® vertical farming approach best suited for?

OrbiPlant® is particularly well suited for hot, dry regions where farmland is only moderately suited for growing vegetables as the water evaporates too quickly. And there is an even bigger heat accumulation in greenhouses, so expensive cooling systems are needed. OrbiPlant® can grow lettuce in dark, windowless spaces that can easily be kept cool. At the beginning of the initial OrbiPlant® project it was all about one question: how can you resource-efficiently practise agriculture in arid regions?

What about energy consumption?

As of yet, ObriPlant® uses artificial lighting – and thus energy. If the energy demand could be lowered, the system would be even more attractive. Together with the Fraunhofer IOSB, we have therefore developed a hybrid lighting concept that uses fiber optics structures, converging lenses and filters to selectively feeds only the required wavelengths of daylight into the system – unlike in greenhouses, however, the heat remains outside. Depending on daylight quality and availability, this selective daylight spectrum is dynamically supplemented with artificial light spectra. That way, the plant is constantly provided with optimal light, ideally without any additional costs for electricity.

So the correct lighting plays an important part in vertical farming?

In vertical farming, the whole trick is to work out the optimal lighting spectra. And what's even more fascinating is that I can determine the vitamin content, for instance, by adjusting the light recipe – and grow arugula that has more vitamin C than a kiwi. Or in combination with an altered composition of fertilisers, I could grow lettuce that is low in potassium for hospital patients with kidney diseases.

Mr Reimann, have you hit a market niche there?

It was evident rather quickly. The hype around this market niche is really big right now. OrbiPlant® certainly has the potential to become a game changer in the field of vertical farming. First licencing negotiations are well underway. There is also an agrarian company that is showing interest. But we also have a demonstrator in the foyer here at Fraunhofer IME in Aachen called OrbiLoop®. It's a somewhat downscaled version of OrbiPlant® that runs in one single loop. In the future, this version might be found in supermarkets and produce the lettuce right there, where people come to buy it. We are already in talks with bigger supermarket chains.

MB

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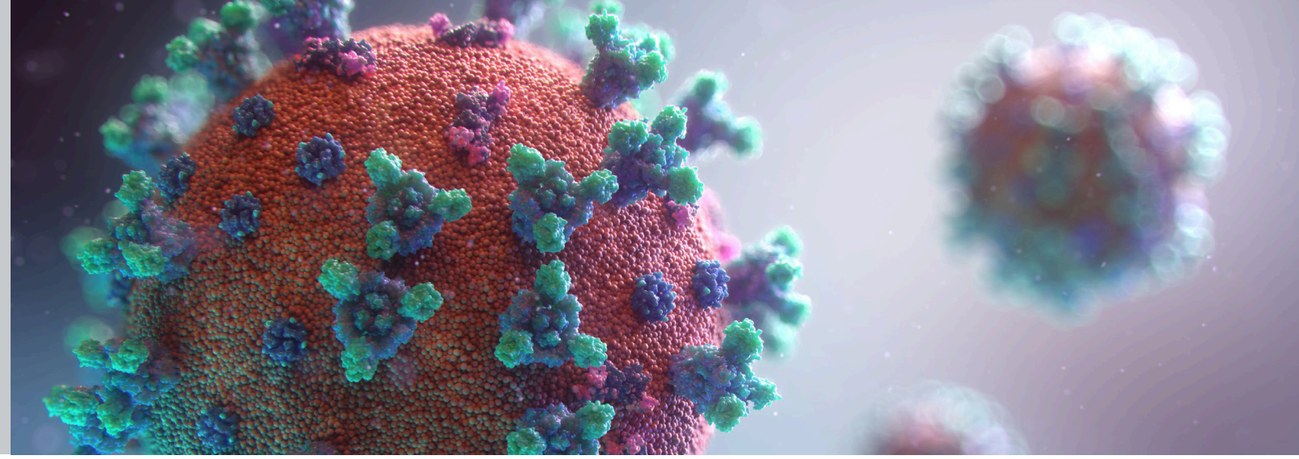
IN FOCUS

Fighting Covid-19 in 4D
Dr. Aimo Kannt

»4«

FIGHTING COVID-19 IN 4D



Visualization of the novel SARS-CoV-2 virus.

In the Division of Translational Medicine and Pharmacology TMP, located in Frankfurt and Hamburg, many research activities in 2020 were dominated by the global COVID-19 pandemic. In the four focus areas of Fraunhofer Health Research - Drugs, Devices, Data and Diagnostics - new projects to combat the pandemic and its consequences were launched at great speed. The spectrum of anti-corona activities, often pursued in close cooperation with other Fraunhofer institutes, ranges from the discovery of new active substances and hypotheses regarding their mechanisms of action to the investigation of long-term consequences of COVID-19 and the development of new diagnostic procedures and IT solutions.

For the development of innovative healthcare solutions, Fraunhofer Health Research takes an interdisciplinary approach that brings together the four major fields of Drugs, Devices, Data and Diagnostics, the "4D", and the different professions involved in them. This strategy of multidisciplinary and cross-institute cooperation, which has already been successfully implemented for some therapeutic areas such as immune-mediated diseases, was of particular importance in 2020 in the fight against the global COVID-19 pandemic and its effects on health and society. To this end, the Fraunhofer-Gesellschaft had very early on set up a fast and unbureaucratic program for the start-up financing of anti-corona projects in the medical and health care sector. The diverse anti-corona projects in which the TMP division of Fraunhofer IME is involved cover all 4D topic areas of Fraunhofer Health Research.

DATA: COVIMMUN, CorASiV and COPERIMOplus

What is the risk of developing a severe course of COVID-19 after a SARS-CoV-2 infection? What late complications or diseases are to be expected? These questions are addressed by the **COVIMMUN** project under the direction of Dr. Tilo Knape. For COVIMMUN, blood samples from corona patients with moderate and severe disease progression are examined for specific biomarker molecules linked to the activity of the immune system using "multi-omics" technologies at various points in time during the acute infection phase and subsequent long-term observation. With these analyses, we are investigating whether there are molecular patterns shortly after infection or in early stages of the disease, that indicate whether the patient is at particular risk of disease progression or complications, so that preventive or therapeutic measures can be initiated early and in a targeted manner, if necessary. In addition, we expect that these molecular patterns will tell us more about the mechanisms of COVID-19 development and thus open the way to innovative therapeutic approaches. The recognition of these molecular patterns by means of new analytical methods is carried out in close cooperation with the Fraunhofer institutes IAIS and IGD.

Health authorities are facing the major challenge of providing available data on the spread of COVID-19, linking them to other data sources and analyzing them for defining the next steps in dealing with COVID-19. **CorASiV** (Corona-Response by Analysis, Simulation and Visualization), under the leadership of the Fraunhofer Institute for Computer Graphics Research IGD, aims at supporting the health authorities in this area. Accompanied by the medical expertise of our TMP division, analysis methods and models are being developed with the aid of artificial intelligence in conjunction with visualization. They will be provided in a web-based system for analyzing corona data. In addition, we help public health authorities to automatically recognize new developments and to assess the benefits and risks of possible measures.

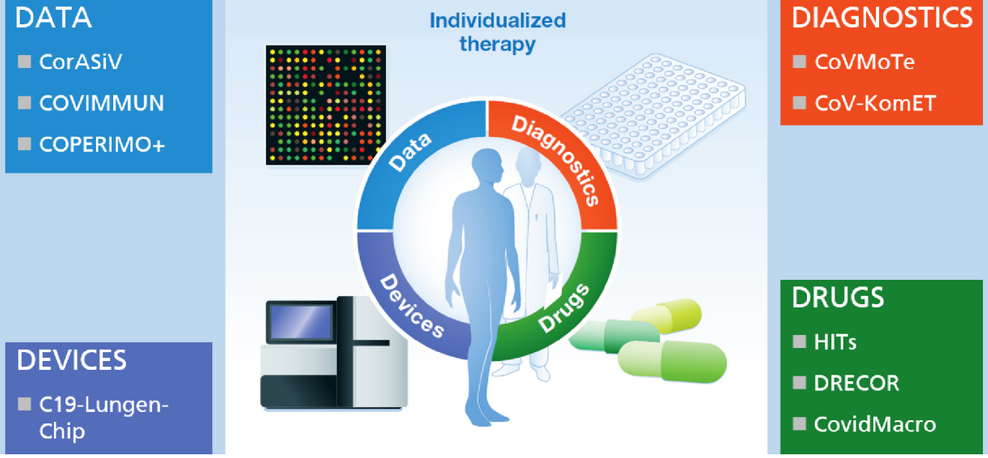
In the **COPERIMOplus** project, in which Fraunhofer IME is cooperating with five other institutes, particularly I&C institutes, a data-driven knowledge building system is being created to support individualized risk predictions. In addition to continuously updated literature information, own and external clinical studies or a self-test study will be included. The data are made "calculable" using the developed data model GECCOplus and corresponding analysis tools, and thus prepared in a way that is suitable for AI. With this systematic approach of analyzing a considerable amount of test and study data, a personalized risk assessment should become possible. This project is being intensively supported by the Legal Department of the Fraunhofer-Gesellschaft in order to ensure compliance with data protection and data rights.

DRUGS & DEVICES: DRECOR and CovidMacro

Can active ingredients already approved for other diseases be used to treat COVID-19? If so, this would be a much-needed shortcut to new corona drugs, because there is already extensive knowledge about the tolerability and side effects of these drugs that would not have to be assessed in long and very expensive clinical trials. The technical term for this approach is drug repurposing. At the ScreeningPort in Hamburg, we already tested a substance library of 5600 known active substances for the prevention of virus uptake or replication in human host cells using one of the first SARS-CoV-2 isolates obtained in Germany from a travel returnee from Wuhan province. Within a short period of time, different classes of substances were found which could be used for the treatment of COVID-19. With one of the identified compounds, a phase 1/2 clinical study with more than 450 COVID-19 patients could be started only 6 months after the laboratory work. The study is taking place in Italy (Rome, Milan), which has been severely affected by the pandemic, has been approved by the Italian AIFA and is coordinated by the cooperation partner Dompé Farmaceutici.

In the project **DRECOR** (Drug REpurposing for CORona), a collaboration between 7 different Fraunhofer institutes and the University of Jerusalem, we are now further developing these active ingredients for the treatment of earlier phases of COVID-19. To this end, they will be encapsulated in microparticles or liposomes so that they can be taken up directly into the respiratory tract and lungs. At the same time, a "smart" inhaler is being developed at the Fraunhofer institutes ITEM and EMFT, which exploits the respiratory movement to release the active ingredient. In addition, DRECOR is developing models and test systems for the identification and characterization of active ingredients that can also be used for other respiratory diseases. Last but not least, this project will enable us to establish a multidisciplinary network and efficient processes for follow-up projects in other indications or to improve our preparedness for future pandemics.

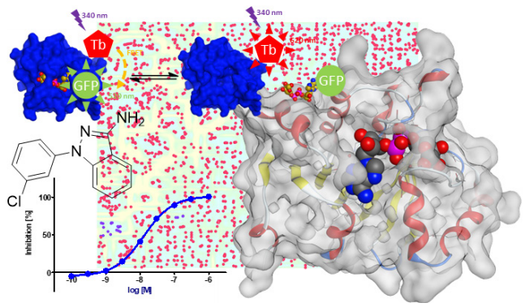
In a further project, **CovidMacro,** the team around project leader Prof. Dieter Steinhilber follows a different approach: here, the virus itself is the target of new potential drugs. Coronaviruses, but also other viruses such as the hepatitis C virus or the Chikungunya virus, produce a particular protein, nsP3. A part of nsP3, the macro domain, is essential for the replication and stabilization of the virus within the host cell. In



Developing new COVID19 test systems.

Selected anti-corona-projects with contributions from the TMP branch in the 4D-focus areas of Fraunhofer Health Research.

CovidMacro, a collaboration with the University of Frankfurt, we now develop active substances that bind to this macro domain and inhibit its activity. This novel therapeutic approach is possibly not only suited for COVID-19 but also for a number of other viral diseases.



CovidMacro – Protein ligand (blue) binding to the nsP3-macrodomain (grey).

DIAGNOSTICS: CovMoTe and CoV-2-KomET

"Testing, testing, testing" - a robust database and rapidly available results are among the most important prerequisites for developing an appropriate strategy to combat a pandemic. The current "gold standard" for SARS-CoV-2 infection diagnosis, the PCR method, is very reliable, but also labour- and time-intensive, so that the results are available after several hours at the earliest, but often only the following day. Prof. Dirk Prüfer's team at Fraunhofer IME in Aachen and Münster has therefore developed a new test system, based on the so-called LAMP method (Loop-mediated isothermal AMPlification). In contrast to PCR, no heating/cooling cycles are required. The amplification and detection of the viral RNA can therefore be accomplished much faster. In the projects **CoVMoTe** (CoronaVirus Mobile Test System) and **CoV-2-KomET** (CoV-2 Complementary Strategies for the Extension of Test Procedures) this test system is being clinically validated. At the same time, new procedures and measurement methods will be used to significantly increase the sample throughput and reduce the size of the system to such an extent that it fits into a suitcase, for example, and can be used directly at the point of sampling for the detection of a SARS CoV-2 infection. Another option is the integration of the test system into a mobile laboratory based on a box van. Both projects, CoVMoTe and CoV-2-KomET, build on each other and on a multidisciplinary network of 12 Fraunhofer institutes, which have combined their expertise and resources for this important program.

CovMoTe - Corona test vehicle developed in collaboration of Fraunhofer IBMT and Fraunhofer IME.

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SELECTED PUBLICATIONS

»5«

Novel test method for antibiotic detection in milk

Improving target assessment for drug development

Rapid test for potato viruses

Artificial lighting influences the reproduction of flies

Automation of toxicological studies with stem cells

Molecular fin(ger)prints of thyroid disruption

Impact of sunlight on the degradation of organic chemicals in water

Jan Pietschmann
Research fellow
Plant Biotechnology

Raw milk often contains antibiotic residues

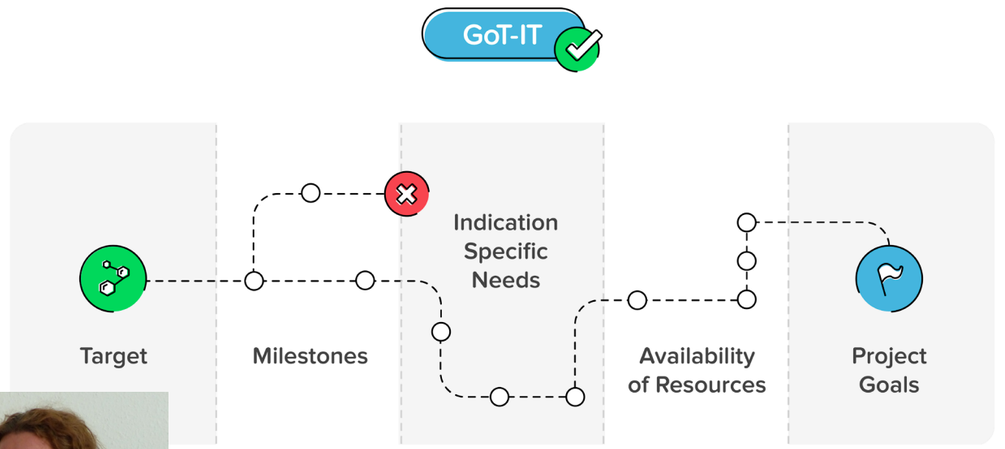
NOVEL TEST METHOD FOR ANTIBIOTIC DETECTION IN MILK

"OUR NOVEL NANOPARTICLE-BASED ASSAY APPROACH IS A SENSITIVE AND HIGHLY PRECISE METHOD TO DETECT ANTIBIOTICS"

Each year, more than 60 000 tons of different antibiotics are used worldwide to treat and prevent bacterial infections in veterinary medicine, predominantly within the livestock industry. Due to misuse, residues of pharmacologically active ingredients can be found in food like meat or dairy, but particularly raw milk. Continuous consumption of contaminated foods and longer exposure time to antibiotics can result in a serious threat to human health. Thus, the contamination of human foods must be minimized by means of suitable measures such as regular analyses, for example.the Fraunhofer IME is working on the development of an alternative, easily-to-handle and, most importantly, cost-efficient method that local dairy farmers can carry out by themselves. Magnectic immunodetection in a competitive assay format has brought us significantly closer to this aim. This novel, highly sensitive and mobile applicable test allows for a very precise quantitative detection of a very broad concentration range of the two most commonly used antibiotics penicillin and kanamycin in milk, thus facilitating the estimation of the required detoxification time. We were able to successfully demonstrate that the novel nanoparticle-based assay approach is a sensitive and highly precise method to detect antibiotics. The simple test system based on competitive magnetic immunodetection enables dairy farmers to carry out on-site milk assay examinations to detect a contamination with antibiotics and prevent the consumption of contaminated foods.

MB Molecular Biotechnology

Pietschmann, J., Dittmann, D., Spiegel, H., Krause, H.-J., Schröper, F.
A novel method for antibiotic detection in milk based on competitive magnetic immunodetection (2020) Foods, 9 (12), 1773. DOI: 10.3390/foods9121773



Dr. Martine Hofmann
Research fellow
Translational Drug Validation

The critical path according to the GOT-IT recommendations.

IMPROVING TARGET ASSESSMENT FOR DRUG DEVELOPMENT

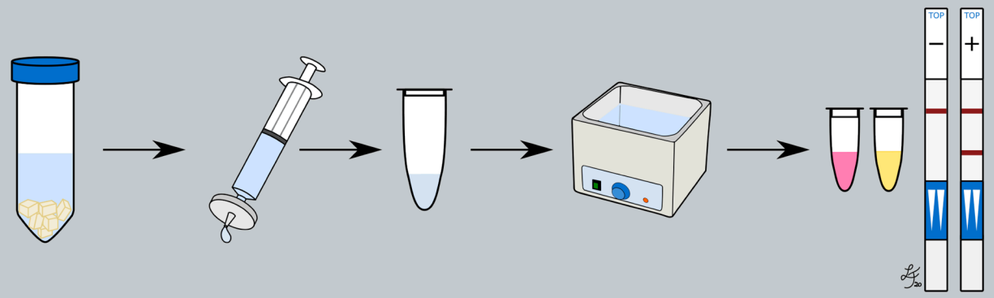
"GOT-IT ALLOWS FOR MORE EFFICIENT TRANSLATIONAL RESEARCH AT UNIVERSITIES AND PROMOTES THE TRANSITION TO INDUSTRY"

Academic research plays a key role in the identification of new targets for drug development. However, the development is mostly carried out by biopharmaceutical companies. To facilitate the transition from academic research to pharmaceutical development, we have developed guidelines for target assessment: the GOT-IT (**G**uidelines **o**n **T**arget Assessment for **I**nnovative **T**herapeutics) recommendations. These recommendations are the result of literature research and intensive discussions with partners from industry, funding agencies, academic research and contract research organizations. From the literature, we identified aspects of target assessment that have been investigated by research groups. We also found that quality characteristics are often only described to a limited extent in the literature. Based on these findings, we discussed important aspects of target evaluation with experts and developed recommendations. For a successful target evaluation and thus for a faster transition between basic research and drug development, scientists should consider the following aspects early in the target evaluation process: the link between the disease and the target, the innovative aspects, safety and toxicity, and technical feasibility. We have developed a tool that allows scientists to set up a "critical path" that is tailored to their project with the help of specific guiding questions.

The recommendations help to guide activities and support decision-making by considering not only which experiments have to be selected and prioritized, but also how they have to be designed and executed. We have also provided learning content for young scientists on our website www.got-it.app, as well as a link to an expert platform where scientists can exchange ideas and experiences.

TM Translational Medicine

Emmerich, C.E., Martinez Gamboa, L., **Hofmann, M.C.J.**, Bonin-Andresen, M., Arbach, O., Schendel, P., Gerlach, B., Hempel, K., Bespalov, A., Dirnagl, U., Parnham, M.J.
Improving target assessment in biomedical research: the GOT-IT recommendations (2020) Nat Rev Drug Discov. 2021 Jan, 20 (1): 64-81. DOI: 10.1038/s41573-020-0087-3. Epub 2020 Nov 16.



Lena J. Freund
Research fellow
Functional and Applied Genomics

Procedure for virus detection in potato tubers.

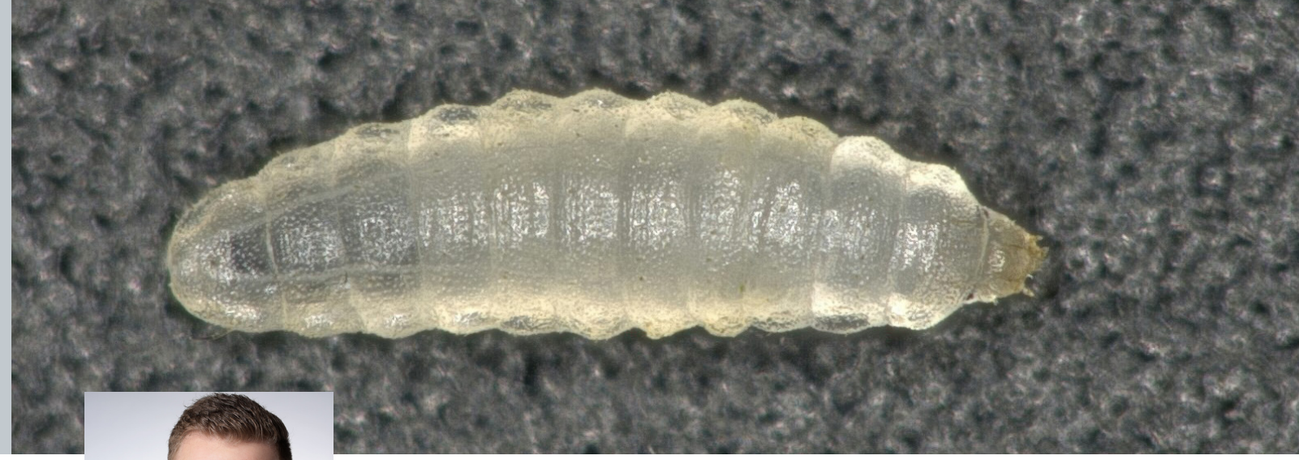
RAPID TEST FOR POTATO VIRUSES

"VIRUSES THREATEN THE POTATO HARVEST - INNOVATIONS FOR EASY DETECTION ARE URGENTLY NEEDED"

Potato is an important staple food crop in both developed and developing countries. However, potato plants are susceptible to several economically important viruses that affect tuber quality and reduce yields by up to 50 percent. One of the major threats is corky ringspot, which is a tuber necrosis caused by tobacco rattle virus (TRV) and transmitted by nematodes. Necrotic spots appear on the surface of the potato tubers. Inside the tuber necrotic lesions manifest as rust-like concentric patterns and/or mottling spots. The appearance of corky ringspot symptoms on tubers prior to commercialization results in about 45 percent of the affected tubers being downgraded in quality and value, while about 55 percent are declared unsaleable. The detection of potato viruses typically requires field samples to be sent to a well-equipped laboratory for nucleic acid extraction, followed by RT-PCR (reverse transcription polymerase chain reaction) and melt curve analysis. To improve current disease management practices, we have developed a simple diagnostic method for the reliable detection of TRV without prior RNA purification, involving minimalized sample handling (mini), subsequent improved colorimetric loop-mediated isothermal amplification (LAMP), and final verification by lateral-flow dipstick (LFD) analysis. Having optimized the mini-LAMP-LFD approach for the sensitive and specific detection of TRV, we confirmed the reliability and robustness of this approach by the simultaneous detection of TRV and other harmful viruses in duplex LAMP reactions. A major advantage of the method: It can be carried out outside specialized laboratories without the need for complex technical equipment such as PCR cyclers. Therefore, our new approach offers breeders, producers, and farmers an inexpensive and efficient new platform for disease management in potato breeding and cultivation

MB Molecular Biotechnology

Edgü, G., **Freund, L.J.**, Hartje, S., Tacke, E., Hofferbert, H.-R., Twyman, R.M., Noll, G.A., Muth, J., Prüfer, D.
Fast, precise, and reliable multiplex detection of potato viruses by loop-mediated isothermal amplification (2020) International Journal of Molecular Sciences, 21 (22), 8741: 1-19. DOI: 10.3390/ijms21228741



Patrick Klüber
PhD student
Food & Feed Improvement Agents

Image of a newly hatched larva of the black soldier fly.

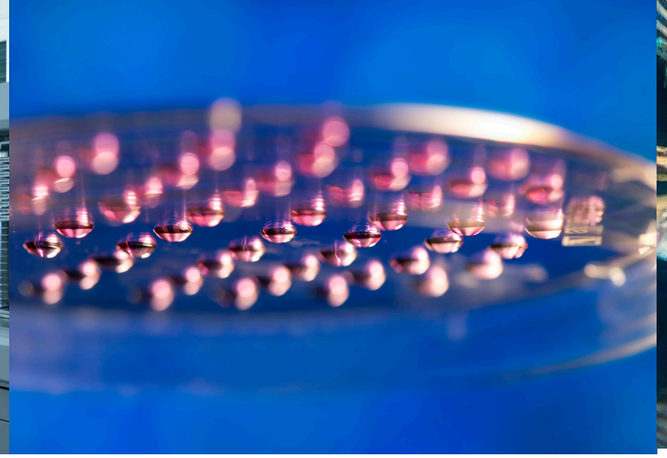
ARTIFICIAL LIGHTING INFLUENCES THE REPRODUCTION OF FLIES

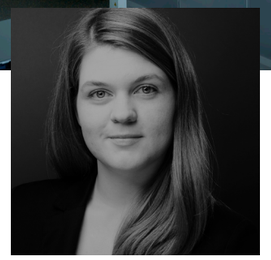
"OUR EXPERIMENTS SHOW THAT EXPOSING FLIES TO DIFFERENT LEDS AFFECTS THEIR OVIPOSITION BEHAVIOUR"

The larvae of the black soldier fly *Hermetia illucens* are increasingly coming into the focus of research and science. Due to their polyphagous diet, they have great potential for the bioconversion of various organic waste into high-quality insect protein and lipids. To this day, an effective reproduction and oviposition of adult flies is still a bottleneck in Hermetia breeding. In our investigations, we dealt with the question whether artificial LED lighting systems influence various reproductive parameters of the flies and if these could contribute to an optimisation in an industrial context. For this purpose, we constructed light chambers with LED panels to illuminate adult flies while excluding sunlight. We observed that under the wavelength spectrum of the three lamps examined both mating and laying of fertilized eggs took place. These findings are in agreement with previously published data of other LED construction types and enable year-round, consistent breeding success, which is particularly important in latitudes with seasonally fluctuating hours of sunshine. Due to their excellent energy efficiency, LEDs reduce the costs of cultivating flies. The period in which eggs were laid and the weight of the eggs per female did not differ between the colour temperature treatments. Interestingly, at warm white colour temperatures (3000 K), the flies occasionally showed a significantly shortened egg-laying period of two days in relation to the maximum period of up to 15 days. In particular, the day on which the majority of the eggs were laid correlated positively with the tested colour temperatures. We conclude that the use of warm white LEDs encourages adult flies to lay eggs earlier, which means that the next generation can be available for biotechnological applications more quickly. The shortening of the reproductive generation period could result in significant savings in terms of time and money in commercial breeding projects.

AE BR Bioresources

Klüber, P., Bakonyi, D., Zorn H., Rühl M.
Does light color temperature influence aspects of oviposition by the black soldier fly (Diptera: Stratiomyidae)? (2020) Journal of Economic Entomology 113, 2549-2552, DOI: 10.1093/jee/toaa182





Gesa Witt
Research fellow
Drug Discovery

Left: Laboratory automation platform for the embryonic stem cell test (EST).

Right: Embryoid bodies in a hanging drop.

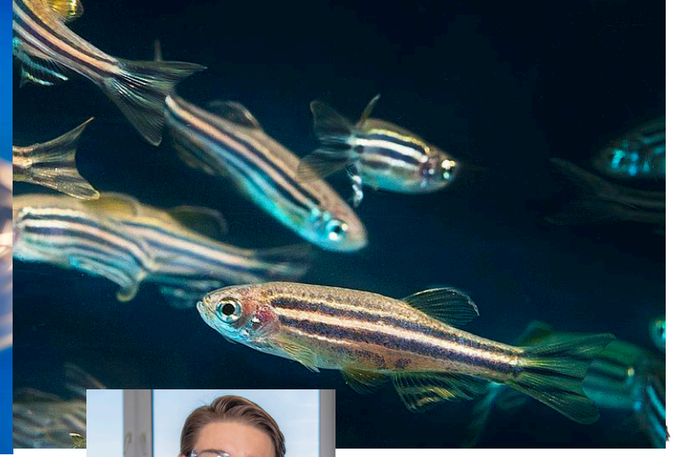
AUTOMATION OF TOXICOLOGICAL STUDIES WITH STEM CELLS

"FRAUNHOFER IME AND IBMT ESTABLISH AN AUTOMATION PLATFORM FOR STEM CELL-BASED TOXICITY TESTS WITHIN THE EU PROJECT DROPTECH"

The embryonic stem cell test (EST) is the only validated and accepted in vitro test procedure for the classification of chemicals according to their teratogenic potency, which is their influence on developmental biological processes in humans. However, a broad application of EST, especially for routine use in pharmaceutical development, has not yet been achieved. Several disadvantages currently still limit the high-throughput screening of potential drug candidates in this format: The long test duration, the use of heterogeneous measurement methods, the low throughput and the low compatibility with automation solutions. We were able to offer optimization solutions for some of the above mentioned bottlenecks in the EST workflow: The reduced time to perform the test, the introduction of a homogeneous assay format and a simpler analysis of marker proteins using flow cytometry as well as high-content imaging to assess the influence of small molecules on the differentiation capacity of embryonic stem cells. Most importantly, we were able to transfer essential process steps of the assay procedure in the 96-well format to a laboratory automation platform, thus enabling the standardized testing of several chemical compounds simultaneously. In addition, we performed extensive investigations to evaluate the predictive capacity of this optimized EST. For this purpose, we have tested a number of well characterized compounds covering the entire spectrum of possible chemically-inherent embryotoxic potencies and compared the result with the effects described in the literature. Using the automation platform we achieved an identical classification of the chemicals compared to manual testing. Due to the improvements introduced, the advanced EST provides a basis for a sensitive, efficient and screening-compatible platform for the prediction of in vivo developmental toxicity from in vitro data, paving the way for application and dissemination in an industrial environment.

TM Translational Medicine

Witt, G., Keminer, O., Leu J., Tandon, R., Meiser, I., Willing, A., Winschel, I., Abt, JC., Brändl, B., Sébastien, I., Friese, M.A., Müller, F.J., Neubauer, J.C., Claussen, C., Zimmermann, H., Gribbon, P., Pless, O. An automated and high-throughput-screening compatible pluripotent stem cell-based test platform for developmental and reproductive toxicity assessment of small molecule compounds. Cell Biol Toxicol. 2020 Jun 20. DOI: 10.1007/s10565-020-09538-0



Hannes Reinwald
PhD student
Attract Eco'n'OMICs

Left: Zebrafishes.

Right: Embryo of a zebrafish.

MOLECULAR FIN(GER)PRINTS OF THYROID DISRUPTION

"BIOMARKERS OF THYROID DISRUPTION IN ZEBRAFISH EMBRYOS IN THE LONG TERM CAN SAVE ANIMAL EXPERIMENTS FOR SUBSTANCE APPROVAL"

Substances with adverse effects on the endocrine system of environmental organisms, known as endocrine disruptors, usually do not receive marketing authorization from the regulatory authorities because of these harmful properties. Endocrine disruptors include substances with adverse effects on the thyroid hormone system (thyroid disruptors). Currently, thyroidal disruption is assessed as standard by studies on the African clawed frog. Since these studies are conducted in addition to chronic toxicity studies in fish as part of a regulatory approval process, regulatory decision-making requires a significant number of animal studies, which are also time and cost intensive. The research and development of new approaches using modern technologies is therefore a financial and ethical imperative. We have combined ecotoxicological studies with molecular systems biology to identify genome-wide fingerprints of thyroid disrupting model substances in the zebrafish embryo. These signatures of gene expression can be measured both at the level of protein-coding mRNA and at the level of proteins and precede the adverse physiological changes of thyroid disruption. They are the starting point for the detection of adverse effects on the thyroid hormone system in fish and their investigation could be perspectively integrated into regulatory required chronic fish tests. In addition, we could contribute to the elucidation of molecular mechanisms of thyroid disruption in fish by functional analysis of fingerprints. Our results make an important contribution to the development of adverse outcome pathways (AOPs) related to the thyroid hormone system. Established AOPs form the basis for the development of animal-free in vitro approaches for the identification of thyroid disruption. The methodology we have developed for molecular fingerprinting forms the basis for the creation of a database for ecotoxicity prediction within the Fraunhofer Attract project Eco'n'OMICs.

AE BR Applied Ecology

Reinwald, H., König, A., Ayobahan, S., Alvincz, J., Sipos, L., Göckener, B., Böhle, G., Shomroni, O., Hollert, H., Salinas, G., Schäfers, C., Eilebrecht, E., Eilebrecht, S. Toxicogenomic fin(ger)prints for thyroid disruption AOP refinement and biomarker identification in zebrafish embryos (2020) Science of the Total Environment, DOI: 10.1016/j.scitotenv.2020.143914.

Dr. Dieter Hennecke
Head of Department
Ecological Chemistry

Left: Working on the test system and complying with the necessary safety measures.

Right: Steel tubes for water sampling at different depths.

IMPACT OF SUNLIGHT ON THE DEGRADATION OF ORGANIC CHEMICALS IN WATER

"CAN THE APPLICATION OF STANDARD OECD TEST GUIDELINES LEAD TO ARTIFACTS IN THE PERSISTENCE ASSESSMENT OF CHEMICALS?"

In the European chemical regulation (REACH) degradability of an organic chemical is an important parameter for risk assessment. Determination of degradability is based on OECD standard test guidelines. They define standard laboratory conditions but photolysis is not addressed. Consequently, the hypothesis was that chemicals that are hydrolytically stable but sensitive to photolysis might be falsely assessed as persistent based on the standard test.
In the current project, we studied on behalf of BASF SE the influence of sunlight simulation on the degradation of a chemical known to be sensitive to photolysis. Beside the photolytic processes in the upper layer of a water body, we wanted in particular to investigate to which water depth photolysis might contribute to degradation since light intensity decreases with water depth. To reach this goal we scaled up the test system from around 300 ml standard laboratory size to a 900 liter container with a water depth of 140 cm. Using a tube system we could investigate different water depths without mixing the water layers. Two additional containers, maintained at similar conditions but without sunlight simulation, served as dark control. 14C radioactive labeled test substance ensured that we did not miss any relevant degradation pathway.
As a result, we observed the fastest degradation in the simulated sunlight setups in the upper water layer. Thus, the concentrations of the photolysis products were highest in the upper water layer, where the highest light intensity was measured. We measured mineralization of up to 22 percent over the entire system. Without simulated sunlight significantly lower degradation rates and no mineralization were observed. The study proves that for a substance sensitive to photolysis, exposure to simulated sunlight leads to a significantly faster degradation in surface water. Degradation tests according to standard OECD guidelines which do not take into account photolysis can thus lead to the overestimation of the persistency of chemicals in surface water.

Applied Ecology

Hennecke, D., Hassink, J., Klein, J., Kruse, M.
Impact of simulated sunlight on the degradation of pendimethalin in surface water in a scale-up experiment in accordance to OECD TG 309 (2020) Environmental Sciences Europe ESEU, 32 (127), 10. DOI: 10.1186/s12302-020-00402-w

PEOPLE AND EVENTS

Brief reports
Empolyees, meetings, successes and new perspectives at Fraunhofer IME

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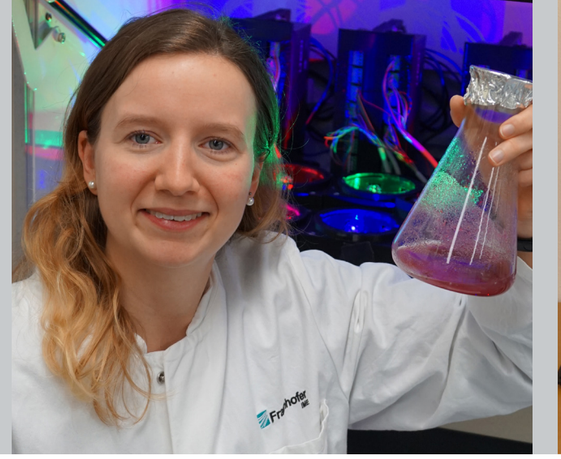
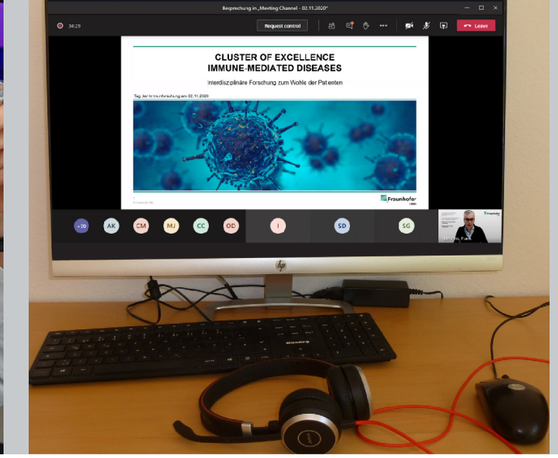


Ann-Katrin Beuel receives the "EPSO Young Plant Scientist Award"

In 2020, Ann-Katrin Beuel of the Fraunhofer IME in Aachen was given the “EPSO Young Plant Scientist Award”. She developed an intelligent, modular lighting system to optimize the production of secondary metabolites in plant cell cultures. Plants produce an almost infinite amount of secondary metabolites, which men have been using for thousands of years. We use plant-based secondary metabolites for drugs and nutraceutics or as industrial chemicals, for example. However, extracting the naturally occurring substances from the produced plants can be a major challenge. Thus the concentration of the naturally occurring substances can vary in terms of composition and quantity, depending on individual environmental conditions. For her research, Ann-Katrin Beuel relies on plant cell cultures, which are grown under standardized conditions. She combined plant biotechnology with 3D printing and LED. The LEDitGROW system is very flexible and enables to test 12 different lighting conditions in order to choose the optimal lighting for the production of high-quality metabolites in cell cultures. In parallel, several experiments are being carried out to lower both costs and work effort, an important step towards sustainable production of metabolites.

Since 2001, EPSO has been working on furthering plant science in Europe, increasing its influence and visibility and promoting both scientific advisors in politics as well as the education of plant scientists. The “EPSO Young Plant Scientist Award” was initiated by EPSO to further the progress of creative thinking and ideas within plant science. MB



Fraunhofer CIMD's second Day of Immune Research - Virtual edition

The second Day of Immune Research of the Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD took place on November 2, 2020. Due to the COVID-19 situation, the second Day of Immune Research, which had originally been scheduled for June 2020 in Frankfurt, had to be postponed and conducted virtually. 120 participants from 26 Fraunhofer institutes, universities and university hospitals as well as industry attended the online event.

The event was opened by Prof. Dr. Dr. Gerd Geisslinger, head of Fraunhofer IME and spokesman of Fraunhofer CIMD, with an overview of the goals, tasks and work of the cluster. In the first part of the event, Hanno Fischer, Head of Transfer Strategies at the Fraunhofer headquarters, took the floor. He gave an exciting insight into various Fraunhofer structures for research and transfer, including the lead market-oriented alliance Healthcare Sector. Further speakers in this first part of the event were Prof. Stefan Schreiber, Director of the Clinic for Internal Medicine I at the University Medical Center Schleswig-Holstein, Prof. Oliver Ambacher, Director of Fraunhofer IAF and Prof. Stefan Wrobel, Director of Fraunhofer IAIS.

After a short break, the program continued with presentations on selected Fraunhofer CIMD research projects, providing the participants with an insight into the research work of the cluster.

Despite the necessary changeover to an online format, the second virtual Day of Immune Research was a successful continuation of networking, collaboration and cooperation opportunities along the 4D within the entire Fraunhofer-Gesellschaft. Despite all this, we hope to welcome our participants in person again next year. TM

New research building for bioresources opened in Giessen

Almost exactly four years after the first groundbreaking ceremony and accompanied by a strict hygiene concept, the new building was officially handed over to the Branch for Bioresources of the Fraunhofer Institute for Molecular Biology and Applied Ecology IME on 21st October. Prof. Dr. Andreas Vilcinskas, head of the Bioresources Division of Fraunhofer IME, welcomed selected guests from politics and industry on this day. “The new building is a dream come true for the university city Gießen“, announced Gießen's Mayor Dietlind Grabe-Bolz.

Among the guests were also Federal Minister Prof. Dr. Helge Braun, who emphasized the medically relevant research at Fraunhofer IME in his welcoming speech, and Hesse's Minister President Volker Bouffier. The latter praised the exemplary cooperation between the universities in Gießen and Fraunhofer IME, “The new building of the Branch for Bioresources of the Fraunhofer Institute for Molecular Biology and Applied Ecology IME will now also create an important network for local researchers, which we need for a sustainable science”.

Due to their biodiversity, insects represent a gigantic, still largely unexplored natural substance library that is being developed in Giessen. The building, which cost around 33 million euros, is now a globally unique centre for the development of bioresources for use in medicine, plant protection and the food industry. The construction of the four-storey building with its glazed atrium was funded by the state of Hesse and the federal government. “With the new building, insect biotechnology gets a temple”, said Prof. Dr. Andreas Vilcinskas. gie einen Tempel«, so Prof. Dr. Andreas Vilcinskas. AE BR

In deep mourning: Farewell to Dr. Jürgen Drossard

2020 was a particularly sad year for the colleagues of the Fraunhofer IME in Aachen, as they had to bid their farewell to an esteemed colleague: Dr. Jürgen Drossard passed away far too early at the age of 61 due to illness.

Jürgen Drossard was a scientist and head of the department Integraded Production Platforms since 2004. He significantly contributed to the positive development of the Fraunhofer IME throughout the years. His helpfulness and loyalty were exemplary.

We are deeply grateful to Jürgen and we will kindly remember him as a very special person. MB

Fraunhofer ITMP becomes the 75th Fraunhofer Institute

On January 1, 2021 the Translational Medicine division of Fraunhofer IME is being transfered to an independent Fraunhofer institute: The Fraunhofer Institute for Translational Medicine and Pharmacology ITMP.
The Frankfurt am Main location was founded in 2012 with the help of LOEWE funding from the state of Hessen (Hessen State Offensive for Development of Scientific-Economic Excellence) as a project group for Translational Medicine and Pharmacology TMP of Fraunhofer IME. Since then, the institute branch TMP, with its expertise ranging from areas such as drug screening, pharmaceutical technology, highly differentiated and indication-specific pharmacological models through clinical research, has established international visibility in the area of immune diseases. The institute branch has become one of the driving forces in Fraunhofer health research, not least with the important concepts of the 4D strategy, cost intelligence in medicine, the proof-of-concept platform and the Fraunhofer Cluster of Excellence for Immune-Mediated Diseases CIMD.
In the course of the independence, the locations Hamburg "ScreeningPort" and Göttingen "Translational Neuroinflammation and Automated Microscopy" are associated with Fraunhofer ITMP. The new institute Fraunhofer ITMP can thus cover almost all aspects along the pharmaceutical value chain. The higher-order goal of further development is the strengthening of the German health economy through consistent translational-oriented research, development services tailored to suit market demand and effective transfer of innovations for the benefit of patients. TM

New high-security laboratories in Gießen are nearly completed

Infectious diseases are one of the leading causes of death worldwide. Newly emerging pathogens such as SARS-CoV-2 and the increasing development of resistance to previously effective therapies show the great need for the development of new anti-infective strategies.
Due to a lack of therapy, work with highly pathogenic pathogens, such as dengue or chikungunya viruses, is characterized by a high risk potential for both employees and the population. Working with such pathogens is therefore only permitted in special laboratories that meet the federal regulations. These high-security laboratories are characterized by the fact that they are completely sealed off from the outside world so that no pathogen accidentally escapes from the system.
Such laboratories are currently under construction in the new building of the branch for bioresources of the Fraunhofer Institute for Molecular Biology and Applied Ecology IME. Equipped with two state-of-the-art laboratories, the scientists will be able to work on highly pathogenic pathogens and their transmission routes as well as therapeutic options. For example, work with highly pathogenic influenza viruses by the BMBF junior research group led by Dr. Kornelia Hardes is planned.
The premises are also suitable for insect breeding and will be used for work with arboviruses and their vectors.
In the spring of 2021, the high-security laboratory should be ready for the test phase and trial operation. Once the work processes have been successfully established and the technical systems checked, the two laboratories should then be opened in autumn 2021. AE BR

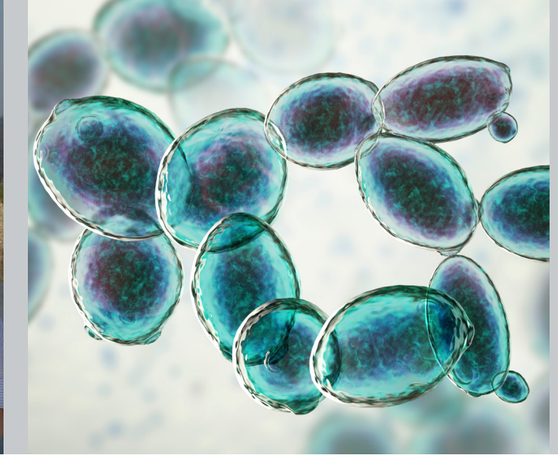
BioökonomieREVIER Rhineland: Innovation laboratory AZUR

The Federal Ministry of Education and Research (BMBF) is funding an initiative to support the structural change in the Rhenish mining area away from lignite towards a sustainable bioeconomy: The model region BioökonomieREVIER Rhineland. On 21 January, Parliamentary State Secretary to the Federal Minister of Education and Research Thomas Rachel handed over the funding certificates for the "Innovation Laboratories" project. These are 15 promising regional research approaches with excellent economic implementation potential. Situated at the interface between (agri-)business and science, the innovation labs are intended to facilitate the rapid transfer of new processes from science to industry. Participants in the interdisciplinary consortium are the Forschungszentrum Jülich, the Fraunhofer-Gesellschaft, RWTH Aachen University and FH Aachen University of Applied Sciences as well as companies from the region.

Prof. Dirk Prüfer and his team from Fraunhofer IME are applying their expertise to the innovation lab "AZUR: From cultivation to active ingredient - regional added value with medicinal plants using the example of arnica". Extracts from the yellow flowers of arnica have long been used successfully in medicine, for example for bruises, contusions or contusion. Cultivation is hardly focused and the flower yield and quality need to be improved. Together with researchers from the Forschungszentrum Jülich IGB2 Plant Sciences and Fraunhofer UMSICHT, the researchers led by Dirk Prüfer aim to test high-yielding arnica plants from breeding programs for outdoor cultivation and sensor-controlled cultivation in indoor systems, as well as to establish phenotyping systems as a basis for the development of an innovative harvesting process for the targeted collection of the flowers richest in active ingredients. MB

HIPPOCRATES – Better understanding of Psoriatic Arthritis

The Clinical Research department of the institutes' branch TMP, together with their partner institutes Fraunhofer IAIS and IGD as part of the Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD, has successfully reached the first step for the application to the "Innovative Medicines Initiative" program for psoriatic arthritis. In HIPPOCRATES, European experts on psoriatic arthritis (PsA) investigate characteristics of the disease with a focus on early diagnosis, the transition of psoriasis to psoriatic arthritis including risk factors for the development of PsA, as well as the identification of predictors of severe disease, which involve severe bone erosions and thus result in loss of function. Furthermore, aspects of individualized and stratified therapy will be investigated. The TMP branch of Fraunhofer IME leads and coordinates the work package on early diagnosis of PsA. Within the scope of the existing partnership "Healthcare Analytics in Translational Medicine" with Fraunhofer IAIS, several aspects of artificial intelligence-based analyses were successfully incorporated in the working plan. Hence, the Fraunhofer-Gesellschaft also holds the lead in the work package data integration and analysis. TM



Excellent research on endocrine disrupting chemicals

Elke Eilebrecht and Matthias Teigeler have headed the Ecotoxicology department at the site Applied Ecology in Schmallenberg since April 2017. The group, which has more than 30 employees, has made a significant contribution to the site's economic strength in recent years and initiated numerous research activities. One research focus is the investigation of potentially hormone-active chemicals. There is great pressure from the authorities to identify hormonal effects of substances on human health and the environment and to restrict and control the use of these substances. In this context, the elucidation of molecular pathways and the identification of indicative biomarkers are of importance.
The Fish Toxicology and Biomarkers Group, led by the leadership tandem, conducts quality-assured, regulatory-relevant long-term fish studies for large-scale industry in the fields of pesticides, industrial chemicals and pharmaceutical manufacturing, and is a European leader in this field. The Group's research portfolio includes the development of new guidelines. For example, a new OECD guideline developed in collaboration with the German Environment Agency is currently being validated to study the effect of endocrine disruptors on the life cycle of zebrafish.
The Fraunhofer team's expertise is in demand, and in November 2020, for example, a training event was held for expert colleagues from the European Chemicals Agency (ECHA) - virtually, of course, due to Covid-19.
Shared management responsibility allows tasks to be handled efficiently and the respective strengths to be used in the best possible way. The success proves Elke Eilebrecht and Matthias Teigeler right: The Fraunhofer Executive Board recognized the performance of the scientific and technical team with an excellence award. AE BR

Terpenoids in focus

Just in time for the Science Year 2020/21 Bioeconomy, the project "ASPIRANT" funded by the Federal Ministry of Education and Research (BMBF) was launched on 1 February 2020. The interdisciplinary research consortium has set itself the goal of opening up further terpenoids for science and industry. With over 40,000 compounds, they represent the largest class of natural substances and are of enormous economic importance. Their industrial use ranges from pharmaceuticals such as taxol to vitamins and ingredients of cosmetics or food to biofuels or natural rubber.

The team of the joint research project ASPIRANT, coordinated by Fraunhofer IME in Münster, combines scientific know-how from the fields of chemistry, biology, process engineering and pharmacy. Scientists from Fraunhofer IME, the Technical University of Munich and the SMEs VivaCell Biotechnology GmbH and Phytowelt GreenTechnologies GmbH are pooling their expertise and planning to jointly build the value chain to use novel triterpenoids for the development of innovative pharmaceutical products. The project leader of Fraunhofer IME Dr. Christian Schulze Gronover explicates: ”Initially, suitable terpenoids will be identified from plants, isolated and examined in detail for their efficacy in pharmaceutical tests. For positive terpenoid candidates, it is planned to carry out the biosynthesis in yeasts and modify it in a pharmaceutically beneficial way. Yeasts are unicellular fungi that have long been used in biotechnology as production organisms. For terpenoid production in "ASPIRANT", we are using the yeasts specially adapted by Fraunhofer IME, which will be further improved to enable an efficient, cost-effective and sustainable production method.” MB

Fraunhofer IME takes over chair of EU-OPENSCREEN Partner Site Forum

On September 1, 2020, Dr. Philip Gribbon was elected Chairman of the Partner Site Forum (PSF), which represents EU-OPENSCREEN sites across Europe. He takes over this position from Prof. Petr Bartunek of the Institute of Molecular Genetics AS CR (IMG) in Prague, who had chaired this group for the first two years of the operation of the Research Infrastructure. EU-OPENSCREEN is an EU and nationally funded ERIC that integrates high-capacity screening and chemistry sites throughout Europe. It offers researchers from academic institutions, SME’s and industrial organizations open access to its screening and chemistry resources. All partner sites contribute to the PSF, with its function being to support and advise the Director General of EU-OPENSCREEN in the overall strategy, annual work plan and budget aspctes of the ERIC. It further advocates the needs of the participating Partner Sites. Dr. Philip Gribbon from the Fraunhofer IME ScreeningPort, will get support from Prof. Krister Wennerberg from the DTU Technical University of Denmark, who has been elected as Vice Chairman.

On October 26, Dr. Philip Gribbon hosted the yearly PSF meeting – for the first time in an online format. Topics of discussion of the 24 partner sites from eight participating European countries have been the feedback to be given to Dr. Wolfgang Fecke, Director General on the current performance of EU-OPENSCREEN and the establishment of standards in the areas of screening, medicinal chemistry and data analysis. TM

New Department of Environmental Microbiology at Fraunhofer IME with connection to WWU Münster

Microorganisms such as bacteria and fungi have a variety of functions in the environment. Their metabolic capabilities are essential for the build-up and decomposition of biomass and is, therefore, indispensable for the maintenance of global cycles of matter. Humans make use of these abilities of microorganisms. To this end, the decomposition of biomass is the basis for the purification of waste water and contaminated soils. The build-up of biomass by microorganisms is an important part of the bio-economy, especially for the replacement of fossil by bio-based raw materials as well as for the production of complex substances such as vitamins and hormones. Microorganisms are also co-inhabitants of plants, animals and humans: These so-called microbiomes have important effects on the health of their hosts. All these aspects are to be dealt with in the newly founded Department of Environmental Microbiology at the IME-AE together with local staff. This department is headed by Bodo Philipp, who holds a professorship for Microbial Biotechnology & Ecology at the WWU Münster. After studying biology at the University of Osnabrück and the Research Center in Jülich, Bodo Philipp completed his PhD at the University of Konstanz. Followed by a stay at the University of Nottingham, he established his own research group in Konstanz and habilitated there. Since 2011 he is working at the WWU Münster. His research focuses on microbial metabolism and its use for sustainable production processes and environmental protection on the one hand, and on the use and prevention of microbial biofilms (antifouling strategies) on the other. AE BR

Bioeconomy and sustainable production systems

On the occasion of the Science Year 2020/21, the Fraunhofer Group for Life Sciences organized the virtual Bioeconomy Day "Bioeconomy and Sustainable Production Systems" on October 1, 2020. The symposium brought together Fraunhofer scientists and experts from politics and industry, provided information on current developments in the field of bioeconomy.
Prof. Dirk Prüfer from Fraunhofer IME in Münster gave the introductory talk to the panel. In his presentation, he talked about "Taraxagum - Innovations with Dandelion". The demand for natural rubber is high - it is an important component of car and bicycle tires. Up to now, rubber is extracted from tropical trees, and their cultivation causes ecological damage. Together with selected partners, the researchers address the entire value chain for sustainable rubber extraction from dandelions in Germany. The Fraunhofer IME is involved, for example, in the breeding of new, high-yielding dandelion lines suitable for cultivation, as well as the environmentally friendly extraction process of the raw material.
Dandelion rubber was also the inspiration for the development of the biomimetic synthetic rubber BISYKA. Together with the Fraunhofer Institutes IAP, IMWS, ISC and IWM, the researchers developed BISYKA based on the rubber from dandelions. With around 30 percent less abrasion, it is ideally suited for application as a truck tire.

The many questions in the subsequent panel discussion showed that rubber from dandelions is an exciting topic. For example, the participants wanted to know how much the tires made of dandelion rubber cost. The price of the bicycle tires is in the range of the similar products. MB

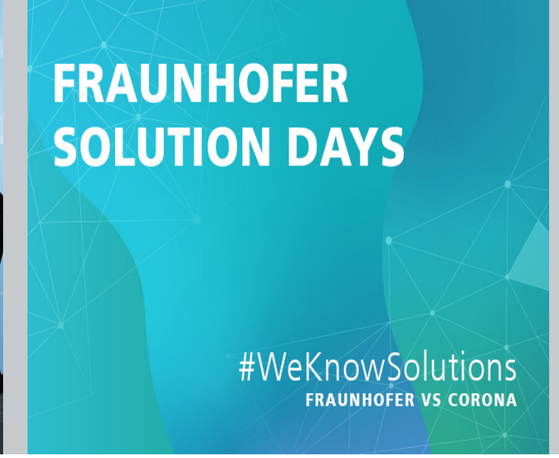
eDNA Workshop at the Fraunhofer IME in Schmallenberg

DNA-based methods offer multiple new possibilities for natural conservation and environmental management. In this way, threatened or invasive species can be identified or entire species communities determined using environmental DNA (eDNA). The rapid advances in method development also result in new opportunities for concrete use in practice. It is currently difficult for users and authorities to maintain an overview and to know which procedures are best suited for which issues in the field of nature conservation and environmental management and how can be implemented in practice.

At the eDNA-workshop 15 research experts and interested parties discussed the various eDNA-based strategies for biomonitoring and collaboration opportunities and new ideas that will help fill this gap. The meeting included the presentations of research conducted in the eDNA field for different applications, and ended with an extended discussion on perspectives and collaboration possibilities. AE BR

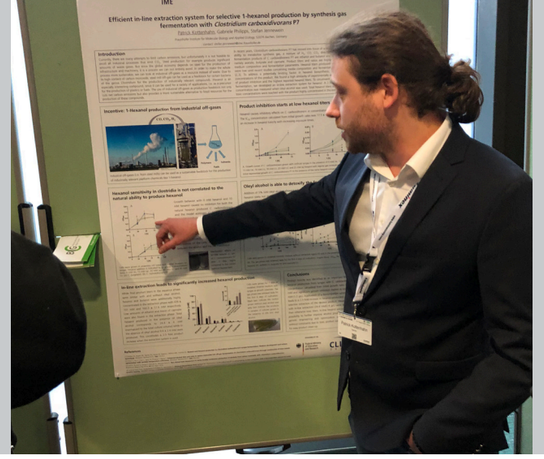
Federal Minister Julia Klöckner handed over funding certificates

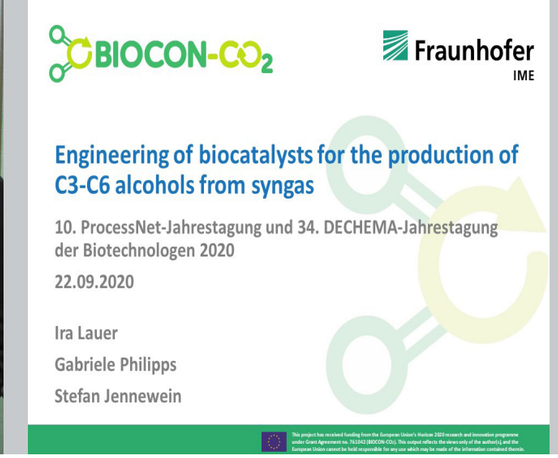
On 24 November 2020, Federal Minister of Agriculture Julia Klöckner presented the funding certificates to the "ADLATUS" project consortium in Berlin. The aim of the joint project is to strengthen existing defense levels of potatoes and to establish new mechanisms against several viruses and nematodes.
The advancing climate change, the discontinuation of important plant protection products as well as the risk of worldwide spread of pathogens pose major challenges for future potato production. Both, exposure to abiotic factors and infection with more than one pathogen can drastically affect the susceptibility of potato plants. The project "ADLATUS" focuses on the economically relevant pathogens: Root gall nematodes, potato virus Y, potato leafroll virus and tobacco rattle virus. They cannot be sufficiently controlled and already cause enormous losses in potato crops worldwide every year. In addition, various virus vectors are considered, without which viruses cannot be transmitted or can only spread to a limited extent in a potato cultivation. Due to the number of pathogens and vectors, the broadest possible host resistance will be required in the future to safeguard yields and prevent individual and/or mixed infections.
Partners in the collaborative project are Böhm-Nordkartoffel Agrarproduktion GmbH & Co. OHG, the Julius Kühn Institute Federal Research Centre for Cultivated Plants, the University of Münster and the Fraunhofer Institute for Molecular Biology and Applied Ecology IME. Fraunhofer IME in Aachen is involved in the project through its department "Functional and Applied Genomics" and will address several work packages. MB



Fraunhofer IME at Fraunhofer Solution Days 2020

At the virtual edition of the Fraunhofer Solution Days, which took place from October 26 to 29, 2020, scientists of the Fraunhofer-Gesellschaft presented innovative solutions for the challenges of tomorrow. The third day of the event focused on health management. Thus, the Fraunhofer Group for Life Sciences played an important role in the digital congress. Fraunhofer IME is also one of the participating institutes within the Group.
In this context, Prof. Carsten Claussen, Head of Fraunhofer IME ScreeningPort in Hamburg, held the introductory keynote speech “The contribution of Fraunhofer to health management – in 4D”. Furthermore, in his presentation “DRECOR: Drug Repurposing for Corona”, Dr. Aimo Kannt, Head of the department Drug Discovery at Fraunhofer IME’s Translational Medicine Division , gave an insight into Fraunhofer IME’s research activities to identify drugs for the treatment of COVID-19. TM





6th joint Annual Meeting of the DGHM & VAAM

From March 8 to 11, 2020, the 72nd annual meeting of the Association for General and Applied Microbiology (VAAM) took place, for the sixth time as a joint conference with the German Society for Hygiene and Microbiology (DGHM). Due to the imminent Covid-19 pandemic, the event was held with 1250 instead of the originally planned 1700 participants. Handling of the novel coronavirus was thus the subject of several presentations. Apart from the hygienic and distancing concept, which had improved compared to previous years, several foreign conference participants, who were unable to travel due to the rising numbers, held their presentations via video this year.

The Fraunhofer IME was represented by Patrick Kottenhan and Dr. Gabriele Philipps who contributed a poster titled "Efficient in-line extraction system for selective 1-hexanol production by synthesis gas fermentation with Clostridium carboxidivorans P7". Die presented research data was generated a spart of the BioCOnversion project. The objective is the utilization of carbonic process gases from steel manufacturing for the production of plastics, in order to reduce both CO2 emissions in the steel industry as well as the plastic industry's dependence on oil. The poster session generated much interest and stirring discussions with scientist colleagues from related subject areas. MB

From waste gas to useful chemicals: Presentation of current results

The 10th ProcessNet Annual Meeting and the 34th DECHEMA Annual Meeting of Biotechnologists took place from September 21 to 24, 2020. The conference, which is usually held in Aachen, was carried out virtually this year. Under the motto "Process for Future", participants were provided with a diverse programme that included presentations from areas such as (algae) biotechnology, bioprocess technology as well as energy and resource transition. In a 15-minute video presentation titled "Engineering of biocatalysts for the production of C3-C6 alcohols from syngas", Ira Lauer, PhD student at the Fraunhofer IME in Aachen, presented the current results of her research work within the EU project BIOCON-CO2. Around 120 listeners were informed about the possibility to use CO2 emissions, e.g. from steel mills, as a substrate for anaerobic acetogenic bacteria to produce high-quality alcohols. These can, among other things, be utilized as fuels, lubricants or plasticizers. With Metabolic Engineering, the targeted insertion of foreign genes to alter the cell metabolism, the formation of the desired alcohols could be achieved and further improved. Furthermore, potential bottlenecks could be identified, which can contribute to the further stem optimization. MB

FACTS 2020

Publications

Patents

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

Networks in science and industry

PUBLICATIONS

Molecular Biotechnology

Applied Ecology and Bioresources

Translational Medicine

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Molekulare Biotechnologie

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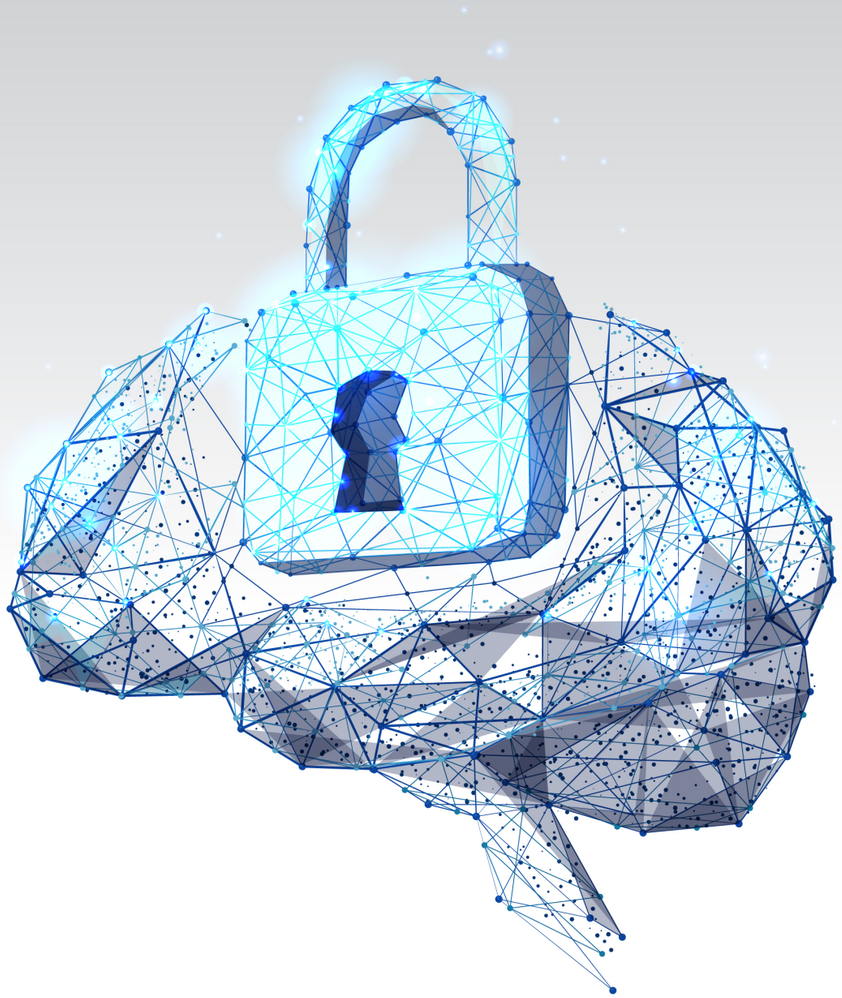

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PATENTS

Patent applications

Augustine, Sruthy Maria; Vadakan Cherian, Anoop; Selling, Kerstin; Raven, Nicole; Di Fiore, Stefano; Schillberg, Stefan; Commandeur, Ulrich
Cavitation bubble-induced shock waves for efficient DNA-free transformation of plants

Augustine, Sruthy Maria; Vadakan Cherian, Anoop; Selling, Kerstin; Raven, Nicole; Di Fiore, Stefano; Schillberg, Stefan; Commandeur, Ulrich
Method for efficient generation of DNA-free genome edited plants

Bornscheuer U, Balke K, Geißler T, Ley J, Backes M, Harms C, Hammer A, Fraatz MA, Zorn H (2020)
Verfahren zur biotechnologischen Herstellung von Aldehydgemischen

Edgü, Güven; Freund, Lena Julie; Muth, Jost; Prüfer, Dirk
Designer-Oligonukleotide für den hochspezifisch und schnellen Nachweis von SARS-CoV-2 mittels Reverse Transcription Loop-Mediated Isothermal Amplification (RT-LAMP)

Gribbon, Philip; Geißlinger, Gerd; Zaliani, Andrea; Claussen, Carsten
Compounds active against SARS-Cov-2 in cells

Gribbon, Philip; Geisslinger, Gerd; Zaliani, Andrea; Ellinger, Bernhard; Ciesek, Sandra; Cinatl, Jindrich; Bojkova, Denisa
Compounds as COVID-19 medicine

Gribbon, Philip; Zaliani, Andrea; Geißlinger, Gerd; Claussen, Carsten
Compouns that are able to inhibit the 3C-like protease (3CLP) of Covid-19, SARS-CoV-2
Gribbon, Philip; Geißlinger, Gerd; Zaliani, Andrea; Claussen, Carsten; Kuzikov, Maria
Small molecule inhibitors of the 3CL-Pro enzyme of SARS-CoV-2

Hernández Olmos, Víctor; Heering, Jan; Proschak, Eugen; Steinhilber, Dieter
Novel agonists of Leukotriene B4 Receptor 2

Müller, Boje; Prüfer, Dirk; Schulze Gronover, Christian; Behm, Frank; Janczak, Norbert; Venz, Carsten; Recker, Carla; Herzog, Katharina
Verfahren zur Gewinnung von Naturkautschuk, Kautschukzusammensetzung mit Naturkautschuk und deren Verwendung

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Fermentative production of pyrazines using microorganisms of the genus Pasteurellaceae
EP 3 680 339 A1

Putyrski, Mateusz; Ernst, Andreas; Wiechmann, Svenja; von Knethen, Andreas; Parnham, Michael John
Engineered PD-L1 variants with improved affinity towards PD-1 to prevent multiple organ failure in sepsis

Patents issued

Arora, Kanika; Frey, Meghan; Gandra, Premchand; Geng, Chaoxian; Knorr, Eileen; Narva, Kenneth E.; Rangasamy, Murugesan; Veeramani, Balaji; Vilcinskas, Andreas; Worden, Sarah E.
Nucampholin nucleic acid molecules to control insect pests
3037432

Barsoum, Mirna; Fischer, Rainer; Kreuzaler, Fritz; Nölke, Greta; Schillberg, Stefan
Genetically modified higher plants with increased photosynthesis and/or biomass production, methods and uses thereof
EP 3 227 316 A1

Barth, Stefan; Fischer, Rainer; Mladenov, Radoslav; Schenke, Lea Christin; Stein, Christoph; Stockmeyer, Bernhard
Anti-CD89 cytotoxic complex
US-2018-0050102-A1

Barth, Stefan; Kolberg, Katharina; Püttmann, Christiane; Schmies, Serverin
Monoclonal antibody for the detection of SNAP/CLIP tag
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Brüne, Bernhard; Dillmann, Christina; Geisslinger, Gerd; Mora, Javier; Parnham, Michael John; Weigert, Andreas
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US 2017/0218039 A1; 2017-528115 (JP)

Buntru, Matthias; Schillberg, Stefan; Vogel, Simon
Cell-free protein synthesis system
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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
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Engels, Benedikt; Jennewein, Stefan
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JP2017503504; CN 105849258 A

Fischer, Rainer; Müller, Lowis-Gerrit-Boje; Prüfer, Dirk
Artifizielle Forisomenkörper mit SEOF-Fusionsproteinen, pflanzliche oder Hefezellen mit Vektoren, die für diese Proteine codieren, sowie Vektoren, die für SEO-F-Fusionsproteine codieren
EP 2 662 447 A1

Fischer, Rainer; Müller, Lowis-Gerrit-Boje; Prüfer, Dirk
Nucleic acid sequences and peptides/proteins of the FT family providing flower-repressing properties in tobacco and transgenic plants transformed therewith
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Holmdahl, Rikard
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Novel peptides that bind to types of MHC class II and their use on diagnosis and treatment
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B7-H1 fusion polypeptides for treating and preventing organ failure
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Rademacher, Thomas
Method for the generation and cultivation of a plant cell pack
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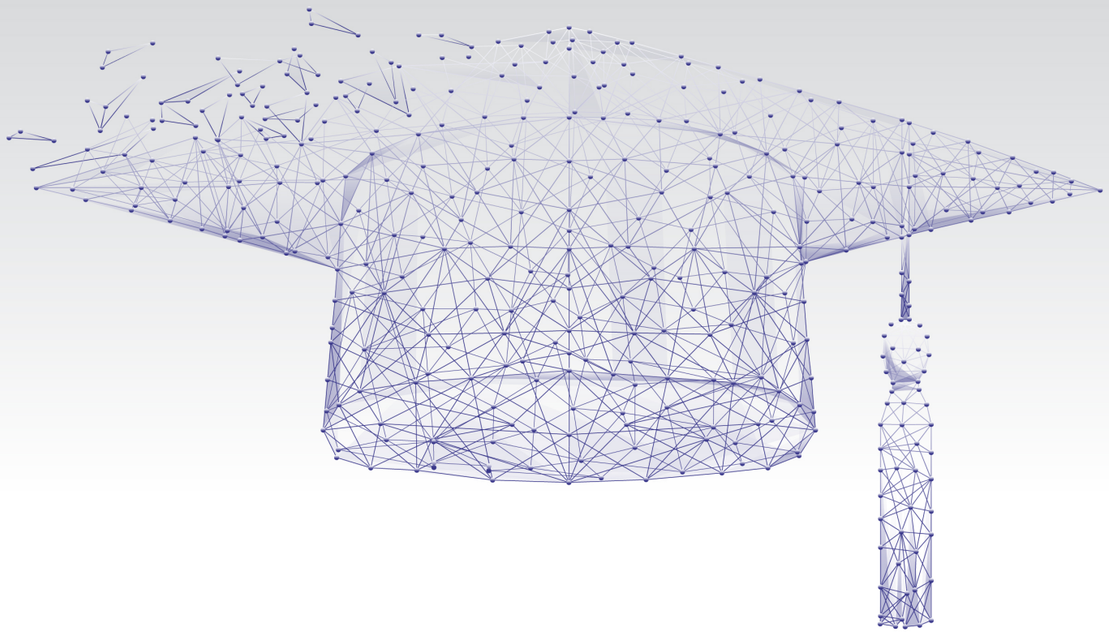
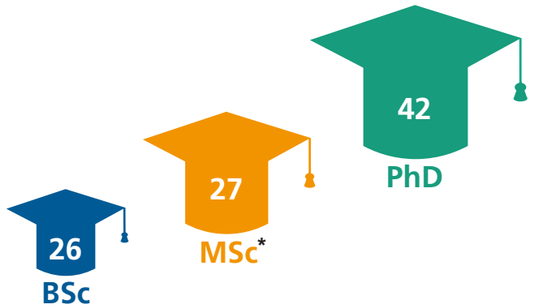


Bachelor’s, Master’s, State Examination and Doctoral Theses

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

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



Theses with the experimental part carried out at Fraunhofer IME (* including 1 state examination thesis).

Doctoral Theses

Amsel, Daniel
Elucidating the potential of microRNAs – towards a functional landscape of microRNAs in the model organisms *Tribolium castaneum* and *Galleria mellonella*
Justus Liebig University Giessen

Ayobahan, Uwa Steve
Etablierung eines Proteom-Ansatzes zur Untersuchung von endokrin wirksamen Substanzen im Vergleich zu lebertoxischen Substanzen bei der Fischspezies Zebrabärbling
RWTH Aachen University

Badalyan, Grigory
Sensor platform for rapid detection and quantification of indicator and pathogenic bacteria in food processing environment
University of Bonn

Berger, Benedict-Tilman
Structural Mechanisms of Binding Kinetics
Goethe University Frankfurt

Benninghaus, Vincent Alexander
Molecular analyses of laticifer function, a novel type of latex-specific lipid droplet protein ab a regulatory protein of the MEP pathway of *Taraxacum koksaghyz*
University of Münster

Blum, Leonard
Charakterisierung neuartiger immunmodulierender Wirkstoffkandidaten
Goethe University Frankfurt

Brandenburger, Isabell
The role of metabolite receptors in tumor progession
Goethe University Frankfurt

Brauß, Thilo
The role of HuR in the crosstalk between tumor cells and macrophages
Goethe University Frankfurt

Bußwinkel, Franziska
Molecular characterization of the *A. thaliana* and *N. tabacum* YPEL protein family with emphasis on its role in plant development
University of Münster

Cienciala, Sylcia
Therapeutische Immunmodulation der Rheumatoiden Arthritis mittels rekombinanter MHC-Klasse-II/Peptidkomplexe: Molekulare Mechanismen der Induktion regulatorischer T-Zellen
Goethe University Frankfurt

de los Reyes Jiménez, Marta
Helminth-derives products modulate the myeloid arachidonic acid metabolism and type 2 inflammation: chances for new therapeutics against airway inflammation
Goethe University Frankfurt

Els, Gregor
Indoxylsulfat als Diversitätsmarker - eine Diagnostikstudie (DIVA)
University of Göttingen

Elwakeel, Eiman
Role of mPGES-1-derived PGE2 in activation of breast cancer stromal fibroblasts
Goethe University Frankfurt

Fink, Annika
IL27Rα deficiency alters endothelial cell function and subverts tumor angiogenesis in mammary carcinoma
Goethe University Frankfurt

Hartmann, Magnus
Characterization of Mitochondrial Calcium Uniporter in Barth Syndrome Models
University of Cologne

Heep, John
Ant venom – an untapped source of bioactive peptides
Justus Liebig University Giessen

Hefke, Lena
Using fingerprints and machine learning tools for the prediction of novel dual active compounds for leukotriene A4 hydrolase and soluble epoxide hydrolase
Goethe University Frankfurt

Hiebert, Nils
Entwicklung neuer biologischer Bakterien-basierter Insektizide gegen den invasiven Schädling *Drosophila suzukii*
Justus Liebig University Giessen

Hiesinger, Kerstin
Design, Synthese und Charakterisierung dualer Inhibitoren der Arachidonsäure-Kaskade
Goethe University Frankfurt

Hilpert, Catharina
Die Mikrobiota der Harnblase bei gesunden Frauen - eine longitudinale Pilotstudie (MiHoP)
University of Cologne

Huth, Alexandra
Chlohexidine containing IV-catheder securement dressings for the prevention of central venous catheder-related bloodstream infections in neutropenic patients
University of Cologne

Jablonka, Laura
Entwicklung Physiologie-basierter Freisetzungs- und Pharmakokinetik-Modelle für liposomale Drug-Delivery-Systeme
Goethe University Frankfurt

Joachim, Mathias
Prozessintensivierung der rekombinanten Herstellung und neuartigen membranbasierten Aufreinigung eines Elastin-Like-Polypeptid gekoppelten antimikrobiellen Peptids
TH Mittelhessen University of Applied Sciences

Jung, Fabian
Entwicklung eines Physiologie-basierten pharmakokinetischen Modells für mikro- und nanopartikuläre Arzneiformen unter besonderer Berücksichtigung von Umweltaspekten
Goethe University Frankfurt

Kalsy, Miriam
Epigenetic regulation of the innate immunity during uropathogenic Escherichia coli infection in the surrogate insect model *Galleria mellonella*
Justus Liebig University Giessen

Kirchhoff, Kim Nadine
Integrative bioprospecting of toxic natural products – Evolution-guided toxinological exploitation of the stingray venom system
Justus Liebig University Giessen

Klumpp, Lukas Konstantin
Evaluierung von biorelevanten Medien
Goethe University Frankfurt

Lippmann, Catharina
Die funktionserhaltende, integrative Genselektion: eine Methode zur Reduktion von krankheitsbezogenen Gensätzen auf ihre Schlüsselkomponenten
Goethe University Frankfurt

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

Litou, Charalampia
Predicting the in vivo performance of bio-enabling formulations by combining biorelevant in vitro tools with physiologically based absorption modelling
Johann Wolfgang Goethe-Universität Frankfurt am Main

Lüddecke, Tim
How the integration of phylogenetics and venomics resolves persistent challenges in evolutionary systematics and toxinology – lessons from the spider kingdom
Justus-Liebig-Universität Gießen

Marner, Michael
Metabolomics-guided discovery and characterization of five new cyclic lipopeptides from freshwater *Isolate Pseudomonas* sp.
Justus-Liebig-Universität Gießen

Niephaus, Eva
Molecular characterization of cis-prenyltransferases and reticulons with regard to natural rubber biosynthesis and rubber particle formation in *Taraxacum koksaghyz*
Westfälische Wilhelms-Universität Münster

Maul, Bernd Patrick
The PGE2/cAMP signaling axis in macrophages during inflammation
Johann Wolfgang Goethe-Universität Frankfurt am Main

Pflüger-Müller, Beatrice
Inflammatorische Modulation des vaskulären Systems durch das Endocannabinoid Anandamid
Johann Wolfgang Goethe-Universität Frankfurt am Main

Prgomet, Stefan
Characterization of SPRTN, the first mammalian metalloprotease that repairs DNA-protein-crosslinks
Johann Wolfgang Goethe-Universität Frankfurt am Main

Rehwald, Claudia
Lipocalin-2 and ist sepcific receptor LCN-2R in clear cell renal cell carcinoma
Johann Wolfgang Goethe-Universität Frankfurt am Main

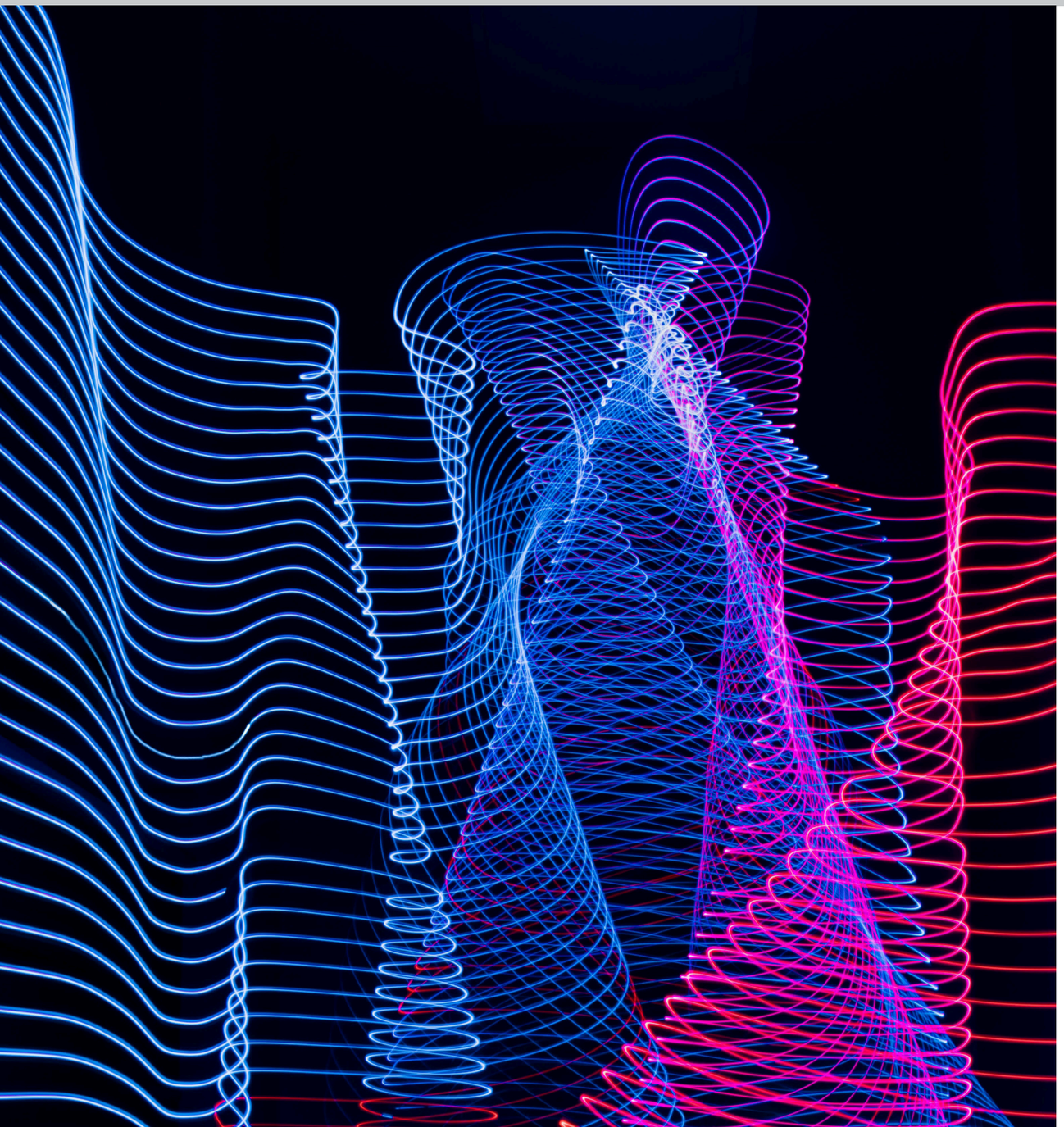
Röhm, Sandra
Synthesis and investigation of Novel p38 MAPK and DDR Kinase Inhibitors
Johann Wolfgang Goethe-Universität Frankfurt am Main

Schlag, Katharina
Studies on the human ALOX5 promoter: Analysis of promotor-interacting proteins by quantitative proteomics and evaluation of secondary DNA stuctures
Johann Wolfgang Goethe-Universität Frankfurt am Main

Schmidt, Florentin Joscha
Molecular characterization of the key regulators CONSTANS and FLOWERING LOCUS T with emphasis on photoperiodic flower induction in *Nicotiana tabacum*
Westfälische Wilhelms-Universität Münster

Scholz, Anica
Translational regulation in the inflammatory tumor micro-environment
Johann Wolfgang Goethe-Universität Frankfurt am Main

Schulz, Martin
Untersuchungen zur Genexpression von B7-H1 in Hepatozyten und Antigen-präsentierenden Zellen
Johann Wolfgang 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 2020, 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 and the Institute for Pharmaceutical Chemistry at the Justus Liebig University in Gießen, the Institute for Virology at the Philipps-University Marburg, the Senckenberg Biodiversity and Climate Research Center, Institute for Biochemistry II at the University Hospital Jena, as well as the Institute for Clinical Pharmacology, the Institute for Biochemistry I - Pathobiochemistry, the Institute for Pharmaceutical Chemistry and the Institute for Pharmaceutical Technology, and several clinics, 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. Fraunhofer IME collaborates with the Bernhard Nocht Institute of Tropical Medicine in Hamburg and hosts members of the anti-virus focused research group of Dr. Maria Rosenthal.

Lecturing assignments

PD Dr. Frank Behrens holds courses, seminars and lectures in Internal Medicine and Clinical Pharmacology at the University Hospital Frankfurt am Main.

Prof. Dr. Bernhard Brüne is Professor and Director of the Institute for Biochemistry I at the Department of Medicine at Goethe University Frankfurt am Main. He lectures within the framework of GRK AVE ("Resolution of Inflammation"), as well as in biochemistry for medical students.

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

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

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

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

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

Prof. Dr.-Ing. Peter Czermak is Professor of Bioprocess Engineering and Pharmazeutical Technology and Managing Director of the Institute of Bioprocess Engineering and Pharmazeutical Technology - IBPT at the Technical University of Central Hesse.

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

Dr. Elke Eilebrecht holds lectures in ecotoxicology at University Hamm-Lippstadt.

Dr. Bernhard Ellinger holds seminars and internships at the Faculty of Medicine of the University Hamburg (UKE) as well as a seminar in the master course "Molecular Life Science" at Hamburg University.

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).

PD Dr. Aimo Kannt gives lectures in experimental and clinical pharmacology and in translational medical research at the Medical Faculty Mannheim, University of Heidelberg.

Dr. Tilo Knape supervises practical courses in the Department of Medicine at Goethe University Frankfurt am Main.

Dr. Michael Klein holds lectures about modelling the environmental fate of chemicals at RWTH Aachen University.

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

Dr. Kwang-Zin Lee lectures at the Institute for Insect Biotechnology in the field of Applied Entomology at the Justus Liebig University of Giessen.

Dr. Martin Müller holds lectures on modelling the environmental fate of chemicals at RWTH Aachen University.

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

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

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

Prof. Dr. Till Schäberle is Professor of Natural Product Research with a focus on insect biotechnology at Justus Liebig University Giessen.

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

Prof. Dr. Christoph Schäfers holds an Extraordinary Professorship for Eco (system) toxicology at the University of Münster, giving courses and lectures for the Master studies of Biosciences and of Water Sciences (combined Master at FH Münster and the WWU).

Dr. Andreas Schiermeyer provides lectures on plant biotechnology at FH Aachen.

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

Prof. Dr. Stefan Schillberg is Honorary Professor at Justus Liebig University Giessen.

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

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

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

Holger Spiegel provides lectures on plant biotechnology at FH Aachen.

Prof. Dr. Dieter Steinhilber is Professor for Pharmaceutical Chemistry at Goethe University Frankfurt am Main.

Matthias Teigeler holds lectures on Ecotoxicology at the Universities for Applied Sciences Bingen and Hamm-Lippstadt 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. Maria Vehreschild holds lectures at the Goethe University Frankfurt am Main and leads a series of training courses for in-service training of doctors with recognition by the LÄK (Landesärztekammer). LÄK (Landesärztekammer).

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

Dr. Matthias Wacker is Associate Professor in the department of Pharmacy of the National University of Singapore and lectures in Pharmacy and Pharmaceutical Sciences.

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

Dr. Björn Windshügel holds lectures at Jacobs University Bremen.

Andrea Zaliani holds lectures at "Data Science in Hamburg webinar series" – organized by Helmholtz Graduate School for the Structure of Matter (DASHH) and University of Hamburg

Prof. Dr. Holger Zorn is Professor of Food Chemistry and Food Biotechnology and Managing Director of the Institute of Food Chemistry and Food Biotechnology at Justus Liebig University Giessen.

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Editorial Board: Prof. Dr. Jennifer Dressman

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Environmental Sciences Europe, Springer
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European Journal of Pharmaceutics and Biopharmaceutics
Editorial Board: Prof. Dr. Jennifer Dressman

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

European Pharmaceutical Review, Russell Publishing Ltd.
Editorial Board: Dr. Sheraz Gul

Frontiers in Bioengineering and Biotechnology, Frontiers Media S.A.;
Associate Editor: Dr. Dr.-Ing. Johannes F. Buyel

Frontiers in Pharmacology, Frontiers Media S.A.
Editorial in Chief: Prof. Dr. Dieter Steinhilber

Frontiers in Plant Biotechnology, Frontiers Media S.A.
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Handbuch der Bodenuntersuchung, Wiley-VCH
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Scientific Report, Springer Nature Limited
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- NA 119-01-02-02-01 AK Bioverfügbarkeit
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

- NA 119-01-03-05-03 AK Marine Biotests
Dr. Karsten Schlich

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

Dutch NeuroFederation
Dr. Natasja de Bruin

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

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

ECNP, European College of Neuropsychopharmacology & Preclinical Data Forum Network
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Prof. Dr. Holger Zorn

EFSA PPR Working Group on how to consider aged sorption for pesticides in regulatory assessments
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, Scientific Panel on Plant Protection Products and their Residues
Dr. Michael Klein

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

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Organization of Scientific Meetings and Courses

4. Exzellenz-Kurs SPA Psoriasis-Arthritis und axiale Spondyloarthritis
Virtual, Oktober23–24, 2020, led by PD Dr. Frank Behrens in cooperation with House of Pharma & Healthcare

Workshop: "Bioakkumulation: Umgang mit Tests nach neuen Richtlinien"
Dessau-Rosslau, February 27, 2020, organized by Umweltbundesamt (UBA) in cooperation with Fraunhofer IME, Prof. Dr.Christian Schlechtriem)

Day of Immune Research 2020
Virtual, November 2, 2020, organized by Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

ECHA-Workshop: "Training on Non-target organisam testing – especially fish" (digital event)
Helsinki, November 26, 2020, organized by Prof. Dr. Christoph Schäfers, Dr. Sebastian Eilebrecht and Matthias Teigeler

Fraunhofer CIMD 4D-Workshop "Data Science"
Virtual, September 1, 2020, organized by Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

Fraunhofer CIMD 4D-Workshop "Toxikologie in 4D"
Virtual, November 23, 2020, organized by Fraunhofer Cluster of Excellence Immune-Mediated Diseases CIMD

82. Annual Meeting of the German Association for Management Management Professors (VHB) e.V.
March 2020 at Goethe-University Frankfurt am Main
Prof. Dr. Lars Schweizer, Member of the organization committee

11th International Akademie Fresenius Conference Endocrine Disruptors
Presentation: "Population effects on fish - The current status of ZEOGRT validation" on November 24–25, 2020, Matthias Teigeler

Fresenius Tagung 20th International ECOTOX Conference, Aquatic and Terrestrial Ecotoxicology and Risk Management
Presentation: "The Minimum Detectable Difference in ecotoxicology – current practice, critiques and new developments", November 25–26, 2020, Dr. Udo Hommen

Regional Contest Hamburg Volkspark – Jugend forscht
Hamburg, February 12–13, 2020, Organisational representative Dr. Mira Grättinger

Strategic Entrepreneurship and Innovation Research Seminar - Goethe Universität Frankfurt & TU Darmstadt
Januar 2020 und Juni 2020, Initiator und Mitglied des Organisationskommitees:
Prof. Dr. Lars Schweizer

Workshop "MSc Toxicology – Screening Molecular Libraries Module"
NUI Galway, College of Medicine, Nursing & Health Sciences, Ireland, May 27–29, 2020, Dr. Sheraz Gul

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