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FRAUNHOFER INSTITUTE FOR MOLECULAR BIOLOGY AND APPLIED ECOLOGY IME

How can you possibly
improve on a dandelion?

ANNUAL REPORT 2015

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By reinvention:

Rubber from Dandelions
An alternative source for natural caoutchouc

Recycling of industrial exhaust gases
Gaining fuel and chemicals

Endocrine disruption in fish
New testing concept with molecular markers

ANNUAL REPORT
2015

With regard to our reporting requirements, we have compiled information on publications, patents, dissertations, master's/diploma and bachelor's theses as well as on our networks and cooperations in science and industry in a separate annex to this annual report. You can also download the 'FACTS 2015' of the Fraunhofer IME from our website:

http://www.ime.fraunhofer.de/en/publikationen/jahresberichte.html

Please note that we do not use academic titles in the body text of our articles.

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Legend

MB Department ..... Molecular Biology Division

AE Department ..... Applied Ecology Division

Molecular Biology

We focus on complex applied research projects in order to develop novel technologies for the diagnosis and treatment of human and animal diseases as well as the protection of crop plants and food sources. Our research and development portfolio also encompasses biopolymers, biomaterials and industrial biotechology-related product candidates and platforms. It is our mission to move innovative product candidates and technology solutions closer towards the market, to develop enabling technologies and platforms, and to provide scientific services to partners from academic institutions, NGOs, governments and industry.

Applied Ecology

We analyze substance-related risks to the environment as well as human exposure to substances in the environment. Our role is to act as scientific mediator between industry and regulatory bodies. Besides setting up experimental and model-based methods for exposure and effect analysis we also develop concepts for a sustainable agricultural production of substances.

Welcome

The mission of the Fraunhofer IME is "…to expand scientific frontiers and create innovative solutions for a healthy and sustainable tomorrow…" We are striving towards this goal, with enthusiasm and focus, at the two divisions of our institute – Molecular Biology and Applied Ecology – at our six sites in Germany, one in the US and one in Chile. In the year 2015, this goal remained firmly in our sights, and together with our international partners in industry and academia we again achieved exciting and promising results in several areas of the applied life sciences. Some of these achievements are highlighted in this Annual Report, which has been redesigned with an appealing new structure and layout.

For the Fraunhofer IME, 2015 was an outstanding year, including a record-breaking operating budget of around 33.9 million euro, of which an astounding 97.1% was from third party revenues. Business contracts accounted for around 47% of our turnover, which is also an extraordinary achievement.

Our research scientists won awards for excellent results in 2015. For example, one Joseph von Fraunhofer Prize 2015 went to a team of researchers from Continental Tires Germany GmbH, Fraunhofer IME and the University of Münster, developing natural rubber from dandelions as a sustainable raw material for the rubber processing industry (see page 26). This project is an excellent embodiment of the ideals of the Fraunhofer-Gesellschaft and our working approach, our aim being to perform top-level scientific research, to think in terms of ecological and economic sustainability, and to develop original solutions to key challenges. In collaboration with industrial partners, these solutions bring specific products onto the market that strengthen Germany's standing as a research and business location as well as benefiting society.

We meet our public mandate through active participation as experts on panels such as the Federal Government *Pharma-Dialog* think-tank and the health forum *Forum Gesundheit*. High-level recognition of our work was also clearly demonstrated prior to the G7 Summit Meeting 2015 when Chancellor Angela Merkel discussed with scientists from Sanofi and Fraunhofer IME the current status of their collaborative antibiotics research program, which was launched in 2014 at the Sanofi/Fraunhofer Natural Product Center of Excellence in Frankfurt.

For the Applied Ecology Division in Schmallenberg, 2015 was dominated by preparations for major building works scheduled to begin in 2017. Several minor construction projects have been undertaken to ensure that normal operations can continue during reconstruction (see page 68). Even amid this disruption, our industrial revenue and operating budget continued to increase. By developing research activities combining different core competencies, and by integrating perspectives from diverse fields of operation, we can enhance the value of our scientific and regulatory services. The contribution of our research scientists to the drawing up of guidelines and guidance documents is valued on a national and international level (see pages 62/63). In setting up the new business field 'Sustainable Agricultural Production of Substances', we have linked our competencies in analytics, soil science, active substance research and testing, as well as secondary raw materials and feedstuffs, with the knowhow of external partners in plant cultivation and geographical information systems.

Looking back over an eventful and successful year, we would like to thank all those who contributed to our success through their drive and active support. We are particularly grateful to our business and collaboration partners for their close and dependable cooperation, and to our staff for their incredible commitment. We wish all concerned an equally successful 2016.

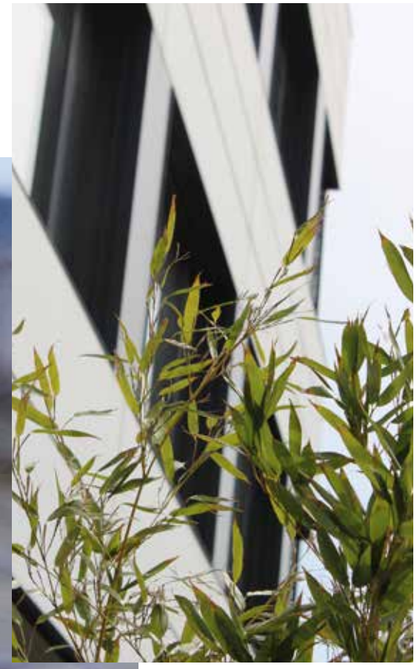
Aachen and Schmallenberg, March 2016

Prof. Dr. Rainer Fischer

Prof. Dr. Christoph Schäfers

The Institute

Fraunhofer IME profile



The Fraunhofer IME is an applied life sciences research institute focusing on two main areas: Molecular Biology and Applied Ecology. We offer services along the entire value chain of product development and assessment to our clients. An interdisciplinary organization allows us to integrate our expertise in relevant scientific disciplines covering both areas, in cooperation with external institutions and partners if required, providing a basis for the successful completion of complex projects. Our laboratories, with state-of-the-art equipment including GMP facilities and complex facilities for environmental simulations, allow a wide spectrum of research and development services. Our work is closely linked with basic research within our university departments and we benefit from large international networks.

Therefore, Fraunhofer IME is a strong partner for contract research in the areas of pharma, medicine, chemistry, agriculture, as well as environmental and consumer protection. Our reseach and development portfolio is focussed on industry, small and medium enterprises and on the public sector.
In 2015, the Fraunhofer IME cllaborated with around 100 national and international industrial clients and several international industrial associations for whom confidential projects were carried out.

At the end of 2015, the institute employed 477 personnel working at the Schmallenberg, Aachen, Münster, Gießen, Frankfurt/Main and Hamburg locations. We have close ties with the Institute of Molecular Biotechnology at the RWTH Aachen University, the Department of Biology and Biotechnology of Plants at the University Münster, the Department of Applied Entomology at the University Gießen and the Institute for Clinical Pharmacology at the Goethe University Frankfurt/Main, in terms of personnel and areas of work. An additional 200 employees at the Fraunhofer Center for Molecular Biotechnology (CMB) in Newark, Delaware, and the Fraunhofer Center for Systems Biotechnology (CSB) in Santiago de Chile provide Fraunhofer IME with a direct presence on the North and South American markets.

Closely linked to basic research, with a large international network: Fraunhofer IME is a strong partner for industry and academia

We cooperate with many international research partners and remain 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.
Within the Fraunhofer-Gesellschaft we have close cooperations with other institutes of the Fraunhofer Group for Life Sciences, the Fraunhofer Alliances Food Chain Management and Big Data, with the Fraunhofer Sustainability Network as well as other Fraunhofer institutes.

IME within the Fraunhofer-Gesellschaft

The Fraunhofer-Gesellschaft is the leading organization for applied research in Europe. Its research activities are conducted by 67 institutes and research units at locations throughout Germany. The Fraunhofer-Gesellschaft employs a staff of 24,000, who work with an annual research budget of more than 2.1 billion euro. Of this sum, more than 1.8 billion euro is generated through contract research. More than 70% of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. International collaborations with excellent research partners and innovative companies around the world ensure direct access to regions of the greatest importance to current and future scientific progress and economic development.

Cooperating within the Fraunhofer Group for Life Sciences – advancing key areas together

Fraunhofer institutes working in related subject areas cooperate in research groups in order to promote collaboration in related disciplines and offer customers a unique source of coordinated joint services.Currently, there are seven research groups, representing the different subject areas on the R & D market. IME is organized in the Fraunhofer Group for Life Sciences, a scientific and technological organization of highly qualified experts from the key areas of modern life sciences: personalized diagnostics and biopharmaceuticals, regenerative medicine for healthy aging, chemical safety and environmental quality, food safety and consumer protection, new sources and processes for biobased chemicals.

The Fraunhofer Group for Life Sciences includes six Fraunhofer Institutes as well as one Fraunhofer Research Institution. IME's Senior

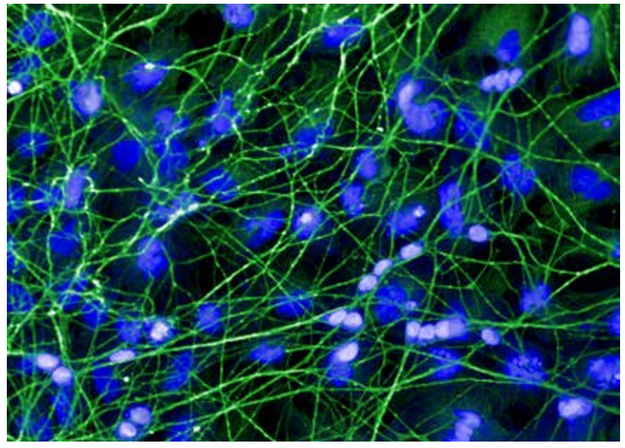
Executive Director Rainer Fischer assumed the Chairman's position on 1 October 2015, and was fully instated as the Chairman on 1 January 2016.
http://www.lifesciences.fraunhofer.de/en.html

The Fraunhofer alliances facilitate customer access to the services and research capability of the Fraunhofer-Gesellschaft. Institutes or institute departments with complementary competencies cooperate in alliances. They provide expert advice on complex issues and coordinate the development of appropriate solutions. In 2015, Fraunhofer IME was involved in two alliances:
Big Data:
http://www.bigdata.fraunhofer.de/en.html
Food Chain Management:
http://www.fcm.fraunhofer.de/en.html

The Fraunhofer-Gesellschaft strives to promote and implement sustainable development, and the Fraunhofer Sustainability Network actively

Engaged in alliances and Fraunhofer's Sustainability Network – uniting complementary competencies and promoting sutainable development

supports this goal. At the forefront of this approach is a stronger linking of both the research topics and the people engaged in research who have a close connection to sustainability. This way, Fraunhofer aims to enhance the efficiency of research even further while taking account of the growing complexity of research in the context of sustainable development.
https://www.fraunhofer.de/en/about-fraunhofer/profile/sustainability/fraunhofer-sustainability-network. html



Advisory Board

The board members advise the Fraunhofer-Gesellschaft as well as the individual institute and promote the connection of the Fraunhofer IME to partners from industry, science and the public sector. In 2015, the following representatives from government, industry and academia were members of the Advisory Board:

Dr. Harald Seulberger (Chairman)
BASF SE, Limburgerhof

Dr. Carl Bulich
German Plant Breeders' Association, Bonn

Dr. Friedrich Dechet
Industrial Association Agrar, Frankfurt

Dr. Gerhard Görlitz
Bayer CropScience AG, Monheim

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

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

Prof. Dr. Karl-Heinz Maurer
AB-Enzymes, Darmstadt

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

Dr. Thomas Reichelt
Federal Ministry of Defense, Bonn

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

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

Dr. Klaus Günter Steinhäuser
Formely German Federal Environment Agency, Dessau

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

The annual meeting of the Advisory Board was held on 23 April 2015, at the location of the IME Project Group Translational Medicine and Pharmacology in Frankfurt. The Executive Board of the Fraunhofer-Gesellschaft was represented by Dr. Hans-Otto Feldhütter.

Molecular Biology – strategic business fields

The Molecular Biology Division focuses its scientific activities on three strategic business fields that facilitate customer access to our extensive research and development portfolio: ‘Drugs and Biopharmaceuticals’, ‘Agroscience for Food and Feed’, ‘Bioproduction and Industrial Biotechnology’. These overarching business fields are based on interaction between the scientific departments and project groups by means of their corresponding technological core competences and platform technologies. IME’s Molecular Biology Division is divided into eight departments or project groups, (please see p. 19). Cooperation between these entities allows us to carry out interdisciplinary projects, to offer a wide spectrum of research and development services and to enable synergies.

With its three trans-departmental strategic business fields, the Molecular Biology Division is in the position to orient topics and projects along the value chain. This approach provides opportunities to develop and enhance projects with our partners in industry, bringing together existing and emerging IME knowhow.

A consistent Intellectual Property strategy in this context allows us to create additional value, ultimately supporting the growth of the division by generating licensing revenues. Within our business fields we also strive to contribute to translational research and the establishment of spin-off companies.

Molecular Biology
Research, Development and Services

http://www.ime.fraunhofer.de/content/dam/ime/en/documents/MB/Research-Development-Services_FINAL.pdf

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Prof. Dr. Stefan Schillberg
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Drugs and Biopharmaceuticals

The business field Drugs and Biopharmaceuticals focuses on the diagnosis, prevention and treatment of human disease. Projects within this business field encompass the discovery, development, production and early-phase clinical testing of small-molecule drugs and biologicals, like antibodies and vaccines, for infectious diseases, cancer, autoimmune and inflammatory diseases, sepsis and pain.
In order to strengthen IME’s position as a preferred partner for academic laboratories, SMEs and major pharmaceutical companies, the departments and project groups involved in this business field have aligned their scientific and technological competences along the pharmaceutical value chain. This approach includes bioresources, target discovery, assay development and screening, hit-to-lead development, strain and process development, GMP production, preclinical and clinical testing.

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 of new plant traits, crops and enabling technologies to improve 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 like genome editing or TILLING. The departments and project groups involved in this business field focus on precision breeding techniques, the discovery and efficacy evaluation of plant protection products 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 agrobusiness companies.

Bioproduction and Industrial Biotechnology

This business field focuses on the identification, sustainable production, processing and optimization of high-value natural compounds, including chemical building blocks, biobased fuels, fine chemicals, biomaterials and proteins for industrial applications and consumer products. These can be produced using a diverse array of organisms, from microbes and animal cells through to plant cells. Here again the value chain is covered: from discovery and screening, the development and optimization of production strains and the transfer of laboratory-scale processes to scale up and pilot-scale manufacturing. 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 low-margin bulk chemicals and fuels like isopropanol, isoprene and hexanol, through to plant-based polymers like rubber, inulin, cellulose and industrial starches, and high-value fine chemicals, proteins and industrial enzymes.

Applied Ecology – strategic business fields

Environmental Risk Assessment of Chemicals

Reliable statements about the environmental compatibility of chemical and biological agents, nanomaterials and products require the assessment of exposure levels and potential hazards. Our investigations encompass standard tests required e.g. for notification and labeling as well as complex studies addressing highly differentiated concerns. In addition to experimental investigations and computer simulations, we work on the improvement of strategies and methods in the context of environmental risk assessments. The legislative framework comprises the EU-wide regulations on hazard and risk assessment for industrial chemicals (REACH), biocides, and human and veterinary medicinal products, as well as corresponding regulations in the USA and Japan.

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Retrospective Evaluation of Substance Concentrations and Media Quality

For clients from regulatory bodies and industry we investigate trends of substance concentrations in environmental media (trend monitoring) or whether environmental quality standards are exceeded (surveillance monitoring). On behalf of the Federal Environment Agency (UBA) we maintain the German Federal Environmental Specimen Bank which is a central component of the ecological environmental observation program. By order of the authorities, we use results from our own monitoring studies and data from the literature to identify critical substance properties such as bioaccumulation, biomagnification and long-range transport. Furthermore we develop and implement monitoring programs for industry partners and offer to apply these in monitoring studies.

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Applied Ecology
Research, Development and Services

http://www.ime.fraunhofer.de/content/dam/ime/de/documents/AE/Research%20and%20Development_Applied%20Ecology.pdf

Environmental Risk Assessment of Agrochemicals

We investigate and assess the environmental risk of plant protection products according to national and international legislation covering their registration (especially EC 1107/2009). While also applying standardized test procedures we focus on the development and application of targeted higher-tier studies such as fish life cycle tests and mesocosm studies, including chemical analysis. Our experimental work is supported and augmented by statistics, and exposure and effect modeling. In the scope of national and international projects and committees, we contribute to the improvement of methods and strategies aiming to quantify the environmental risks of plant protection products and to minimize uncertainties.

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Evaluation of Food Safety and Consumer Risk Assessment

In this business area, investigations focus on the uptake and metabolism of chemicals in crops and farm animals. A wide range of crops representing different climatic regions is available for single or rotational crop studies. Further to the classic livestock studies with poultry or ruminants according to OECD 503, we also offer metabolism and feeding studies in fish. For the detection and identification of unknown metabolites via radiolabeling (^{14}C), high-resolution LC-MS/MS and LC-SPE/NMR according to GLP and ^{14}C food processing (‘radio kitchen’) are available. Instrumental biochemical and chemical special analytics to investigate food and feed as well as the services of the Fraunhofer Food Chain Management Alliance complement the service profile.

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Sustainable Agricultural Production of Substances

The aim of this new business area is to achieve a higher added value from natural resources while also protecting them. To achieve this goal we evaluate the potential use of active substances from renewable raw materials, especially from niche plants and residues, with respect to pesticidal and pharmacological effectiveness. At the same time, the resource efficiency of agricultural production is determined by considering the positive effects of crop rotation and increased agrobiodiversity. Evaluating the economic competitiveness of the approach includes knowledge on the efficacy of single substances versus extracts, the variability of the yield depending on plant varieties, soil and climatic conditions, pathogen infection and postharvest treatment.

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Institute data

Budget

In 2015, the Fraunhofer IME operating budget was 33.9 million euro, an increase of 4.8 million euro over 2014 representing a growth rate from operations of 16.5%. This growth reflected increased activity at all the IME locations: Schmallenberg, Aachen, Münster, Gießen, Frankfurt and Hamburg. The total external revenue (operating budget plus capital budget) increased by 6.5 million euro (23.1%) to 34.3 million euro and the overall budget increased by 17.3% to 41.9 million euro. Third party revenue (total rho) amounted to 97.1% and industry revenue to 47.1%, confirming the healthy business profile of the institute. New and replacement investments amounted to 8.1 million euro.

Personnel

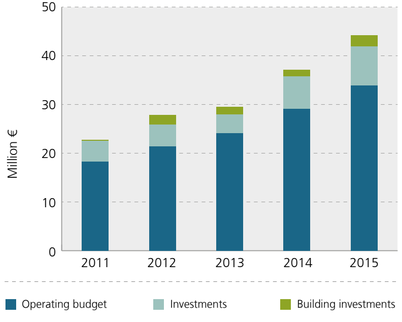
At the end of 2015, the Fraunhofer IME employed 477 personnel at its sites in Aachen, Schmallenberg, Gießen, Münster, Frankfurt and Hamburg, representing a 16.3% increase over 2014 (49.5% of these employees were female).

Fraunhofer CMB and CSB

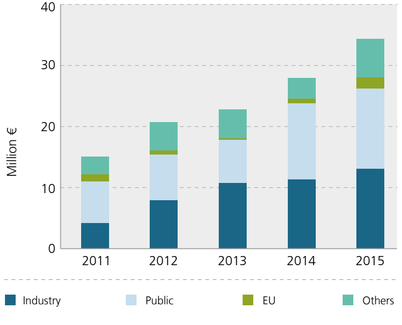
The operational budget of the Fraunhofer USA Center for Molecular Biotechnology in Newark, Delaware, was 13.5 million euro in 2015, nearly 13.7% of which resulted from industry contracts. At the end of 2015, the CMB employed 72 personnel.
The overall budget of the Fraunhofer Chile Research Center for Systems Biotechnology was 2.7 million euro in 2015, its fifth full year of operation. At the end of 2015, the CSB employed 98 personnel.

The cumulative operating budget of the Fraunhofer IME, CMB and CSB amounted to 49.8 million euro. With 58.1 million euro, the overall total budget rose to a new peak.

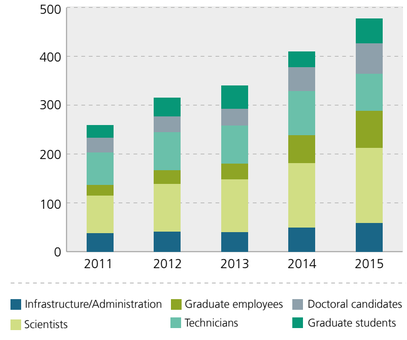
Total budget of the Fraunhofer IME, Germany



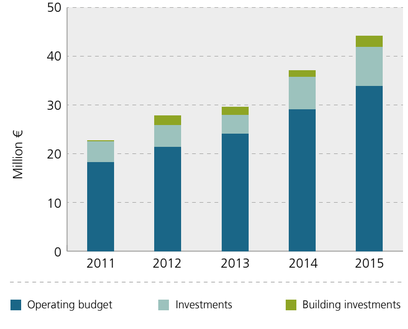
External financing of the Fraunhofer IME, Germany



Employees of the Fraunhofer IME, Germany



Operational budget IME, CMB and CSB

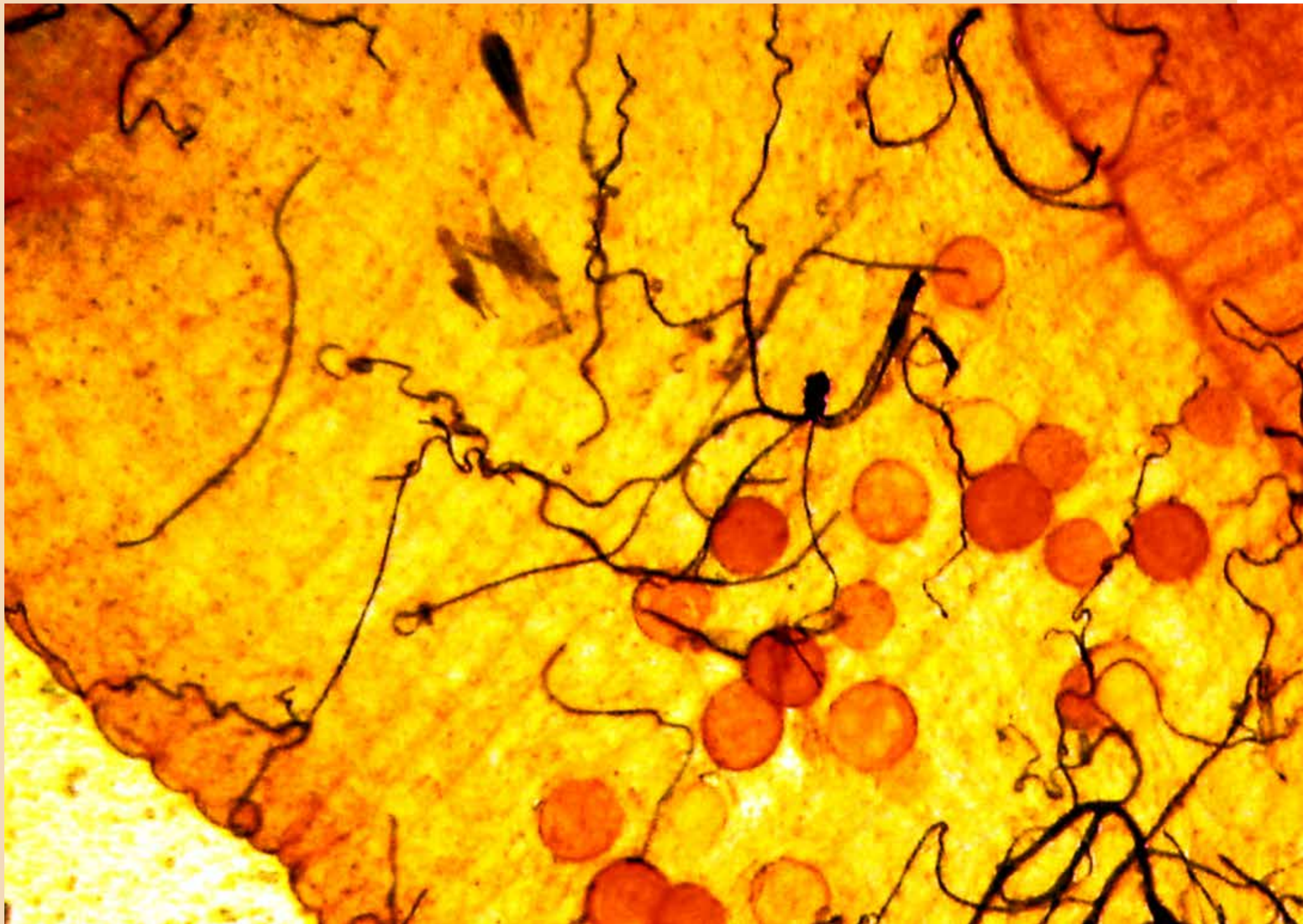


Reports on IME Research

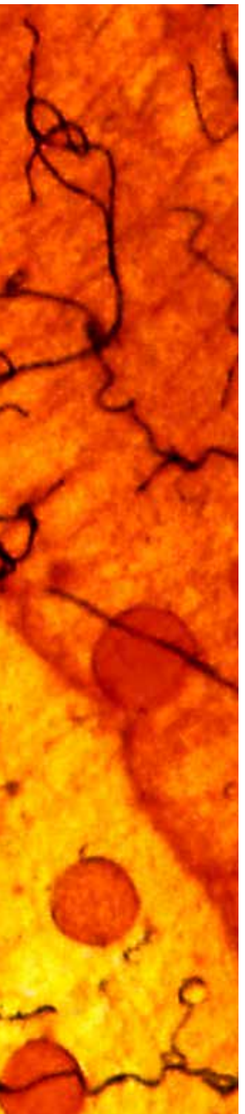
Rubber from dandelions

Recycling of industrial exhaust gases

Endocrine disruption – new testing concept with molecular markers



Rubber from dandelions



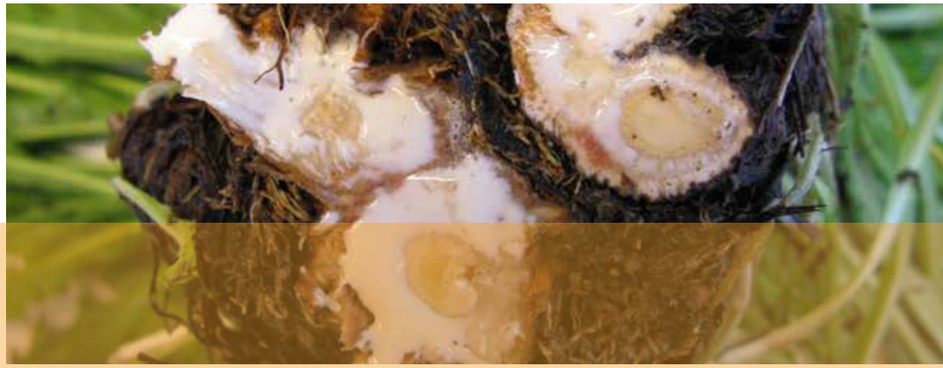
Can rubber be made from dandelions? Yes it can. The dandelion is an ecologically and economically attractive alternative to the tropical rubber tree. In a joint project with the tire manufacturer Continental, the Fraunhofer IME is tapping the potential of this robust plant with its golden-yellow flowers as a sustainable source of raw material for the rubber-processing industry.

We use rubber-based products every day. For mobility. To lie or sit on. For protection against germs or to glue things together. The list is long, and car tires, mattresses, gloves and glue are just the start. Around 40,000 articles used in day-to-day life contain rubber, an enormously versatile raw material – elastic, water-repellent and robust. And currently, no synthetic equivalent meets the quality of the natural product. Currently, natural rubber is extracted almost exclusively from the milky sap of the rubber tree. However, *Hevea brasiliensis* grows only in tropical latitudes. About 95% of the worldwide production comes from Southeastern Asia. A domestic source of raw rubber from land close to the production facility would be an extremely attractive commercial prospect and a sustainable alternative for manufacturers. It has been known since the middle of the 20th century that rubber can be extracted from dandelions. The Russian dandelion *(Taraxacum koksaghyz)* is well suited for this purpose due to the high rubber content in the roots. In recent years, Dirk Prüfer and Christian Schulze Gronover of the Fraunhofer IME and the Institute of Plant Biology and Biotechnology (IBBP) at the University of Münster have focused their work on the development of Russian dandelion as an alternative crop for rubber production.

Rubber from domestic farmland: Improved carbon footprint, greater independence from fluctuating market prices

"The dandelion is extremely resilient, grows under moderate climates and on marginal land that is barely suitable for the cultivation of food and feed crops. Transport costs from the tropics are eliminated, thus the carbon footprint of the raw material is improved considerably. And greater independence from fluctuating market prices presents a huge advantage for the industry," explains Dirk Prüfer. Moreover, dandelion cultivation on marginal soils in the mid-latitudes will help to protect tropical rainforests that would otherwise have to be clear-cut to make way for new rubber tree plantations to meet a rising worldwide demand. In addition, harmful fungi are endangering rubber production on tropical plantations.

In order to develop Russian dandelion as an alternative crop plant, IME and IBBP scientists have identified genes controlling rubber biosynthesis. With this knowledge they have managed to double the rubber yield from the Russian dandelion through conventional breeding, as the wild plant contains too little for production on an industrial scale.



The sought-after raw material for rubber is mainly contained in the roots. In a mill, the root tissue is crushed and the caoutchouc subsequently harvested.

Outstanding work: Dr. Christian Schulze Gronover, Prof. Dr. Dirk Prüfer (both IME and University of Münster) and Dr. Carla Recker of Continental received a Joseph von Fraunhofer Prize 2015 for their research on the Russian dandelion and its application as a source of natural rubber.

First, the research team developed a laboratory-scale extraction unit: a special mill, about the size of a washing machine. Inside the mill is a grinding unit that allows the precise extraction of high-quality rubber from the roots in large amounts. In the next step, the project partners succeeded in manufacturing prototype car tires. The tires made with dandelion rubber, registered under the trademark 'Taraxagum™', have already been confirmed to perform well in tests under summer and winter conditions. According to Carla Recker, Project Leader at Continental, "These tires display a property profile equivalent to conventional tires made with natural rubber." And the suppliers to the automotive industry already have another application in the pipeline: Sister company ContiTech presented the first prototype for vibration and mounting elements made from Taraxagum™ at the IAA (International Motor Show) 2015. And there are many other possible applications. "Manufacturers of a wide range of products have expressed interest," says Dirk Prüfer. Inquiries for the manufacture of mattresses and adhesives have come in already. Another attractive characteristic of dandelion rubber is that it does not trigger the allergy that is caused by natural rubber. That makes it an interesting alternative for rubber gloves, as used in the medical and domestic sectors.

How is rubber extracted from the plant? The research team has developed an economical and efficient process

So why not go ahead: sow dandelion seeds, harvest the roots, throw them in the grinder and get production rolling? It sounds simple but in reality the process is highly complex.

The next task is to optimize the whole process on an industrial scale. The next level of the extraction unit is under construction and should be completed in 2016. The Conti-IME team have set themselves the goal of obtaining one metric ton of dandelion rubber per hectare of cultivated land. But the plants themselves must be further optimized before large-scale cultivations can be initiated. Christian Schulze Gronover of IME says, "On the one hand, we aim to breed plants to further increase the rubber content. On the other hand, they must be improved for sowing, cultivation and harvesting. Additionally, appropriate guidelines for good agricultural practices have to be established." In other words, there is a fair amount of homework to do before dandelion rubber can be exploited on a commercial scale. But every day brings the Conti-IME team closer to this goal.

Dandelion rubber could have diverse applications – it is now being prepared for industrial production

For their research on the Russian dandelion and the development of the prototype car tires based on dandelion rubber, the researchers were awarded a Joseph von Fraunhofer prize 2015. The award was presented to Dr. Christian Schulze Gronover and Prof. Dirk Prüfer of IME and the Institute of Plant Biotechnology and Biology at the University of Münster, together with Dr. Carla Recker of Continental.

Industrial manufacture of products based on dandelion rubber should be possible within a few years. The German Government is supporting this endeavor through the Research Funding Strategy Bio-economy 2030.

MB Functional and Applied Genomics

Prof. Dr. Dirk Prüfer
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Recycling of industrial exhaust gases – gaining fuel and chemicals

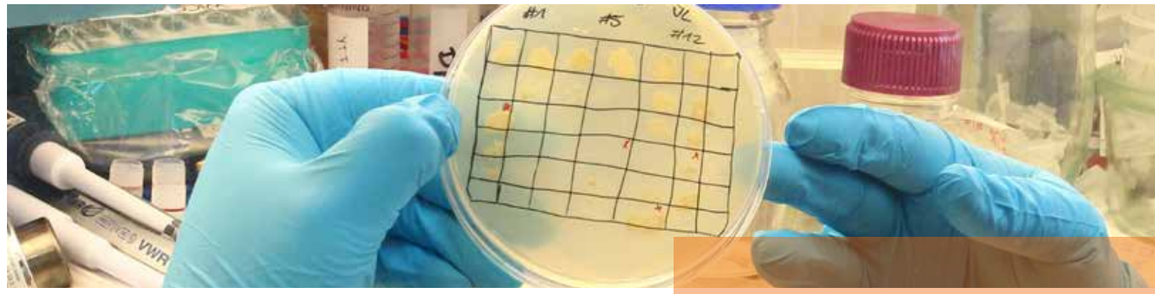
Dr. Stefan Jennewein of the Fraunhofer IME coordinates the project in which three Fraunhofer Institutes are involved.

‘Energy efficiency’ and ‘emissions neutrality’ were key words at the World Climate Conference 2015 in Paris. One contribution towards reduction of global greenhouse gas emissions and conservation of fossil fuel reserves could be a process developed by researchers from three Fraunhofer Institutes for the recycling of exhaust gases from industrial production facilities.

Could tankers one day sail the seas and planes fly from A to B on fuel derived from industrial exhaust gases? Or from gas collected from waste incineration at landfill sites? That is an interesting and exciting prospect. And the reality is not so far away. A research team drawn from three Fraunhofer Institutes has discovered a new recycling pathway for such gases. The researchers use genetically modified strains of bacteria to ferment the gases, forming acetone or short and medium-length alcohols such as butanol and hexanol. These are catalytically converted to a diesel-type intermediate, which is used to produce kerosine and speciality chemicals. The new process could help to reduce emissions and conserve crude oil resources. It could also present a new source of revenue for industry, as only a small portion of industrial exhaust gases is currently re-used for power or heat generation. The greater portion of these carbon sources has lain untapped until now. The technology was developed as part of an internal Fraunhofer innovative research project and through individual initiatives with industrial partners. The collaborating institutes are the Fraunhofer Institute for Environmental, Safety and Energy Technology UMSICHT, the Fraunhofer Institute for Chemical Technology ICT and the IME.

The researchers have modified bacteria to ferment exhaust gases as source material for fuel production

To recycle industrial exhaust gases, researchers have used bacteria of the Clostridium family, because these can synthesize industrially relevant chemicals or biofuels – or, put differently: their metabolism is able to convert CO_2 accordingly. For the bacteria, CO and CO_2 are a substrate, that is: food. However, the microbes cannot convert the exhaust gases into the end-product directly. Instead they ferment the gases into the source material needed for fuel production. A prerequisite for the project was to use the correct strain of *Clostridium bacteria* that would function efficiently as recycling agents. These then needed to be genetically modified to ensure that they formed the desired fermentation products, such as acetone or isopropanol. After all, these minute creatures were not intended by nature to aid fuel production. Now they can. “Advances in gene technology have made this possible,” explains project leader Stefan Jennewein of IME. “For instance, we can now integrate large gene clusters into the Clostridium genome. From syngas, a mixture of carbon monoxide, CO_2 and hydrogen, the metabolically engineered bacteria form the exact products that we need for fuel production through fermentation.” To get to this point, thousands of bacteria had to be screened: using mass spectrometry, the researchers analyzed whether, and if so in what quantities,

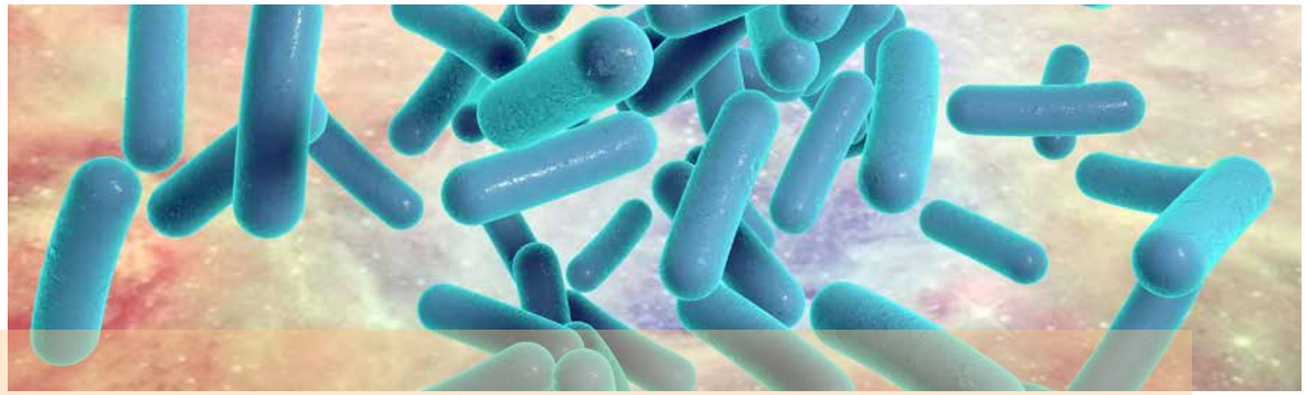


The researchers have investigated genetically modified Clostridium bacteria and identified those candidates that ferment the desired substrates.

the genetically modified bacteria would form the desired products. “It was like looking for a needle in a haystack,” recalls Stefan Jennewein. And the team succeeded.

Step by step: From fermentation product to marine diesel oil, DERV fuel and speciality chemicals

The three Fraunhofer Institutes have worked hand in hand to develop this new process. UMSICHT took the next step: catalytic transformation of the fermentation mixture to produce marine diesel oil. A further stage in the process produced a form of diesel, chemically identical to diesel-engine road vehicle (DERV) fuel available at gas stations.
In a subsequent step, the researchers obtain high-quality kerosine. Scientists at the ICT can then extract specialty chemicals that can replace products based on crude oil. Amines, for instance, used by the pharmaceutical industry to produce surfactants and dyes. “Just as it was with crude oil as the source material, we can now use our synthetically made products either for fuel or for speciality chemicals,” explains Jennewein. Bench-scale trials have so far been successful, and the process is already patented. Scaled-up industrial production will be the next step. Other potential areas of application are cement plants, wood or coal gasification power plants, steelworks and domestic or industrial waste incinerators.



Clostridium bacteria can synthesize industrially relevant chemicals or biofuels – via their metabolism, they can convert industrial exhaust gases accordingly.

Industrial exhaust gases as source materials – what works on a bench scale will now be opened up for industrial use

Project coordinator Jennewein: “We will not be able to substitute for the dwindling supply of crude oil through biomass alone. Biofuels recovered from waste residues or plant material cannot cover the demand. The particular attraction of the innovative fermentation approach is that it gives us access to high-volume carbon sources. A steelworks, for instance, produces two tonnes of CO_2 per tonne of steel. Those are gigantic amounts.” The question to be answered by researchers is: How can we obtain our fuel in the future? Syngas or industrial exhaust gases or waste incineration could play a key role providing future source materials. The recycling of industrial exhaust gases is a very attractive option for industry. Not only as a way of lowering emissions, but because emitters of CO_2 face spiralling costs.
In Jennewein’s view, if the production of fuel and specialty chemicals could really be revolutionized in this way, then the entire global market demand for Plexiglas could be covered by the acetone yielded as a by-product. And many further products such as adhesives could be manufactured from recycled source materials. This recycling approach would be particularly interesting for mineral oil companies. In Germany, however, there is no large mineral oil company that could push the project forward. Over the next few years the task will be to open up this recycling approach for industry, together with commercial partners. The next goal of the Fraunhofer researchers is to register the new fuels for certification. Their practical suitability will then be officially confirmed.

MB Industrial Biotechnology

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New testing concept: Molecular markers help to track endocrine disruption in fish

Environmental pollutants present a significant danger to living organisms in aquatic environments. So-called 'endocrine disruptors' can cause hormone imbalance and have a harmful effect on fish development and reproduction. To take measures to control these substances, they must first be accurately identified. Fast reacting molecular biomarkers offer promising perspectives here.

The identification of endocrine disruptors is usually both time-consuming and expensive and involves the use of large numbers of test animals. At the same time, the number of possible endocrine disruptors requiring registration is growing. There is therefore a drive to develop new concepts to meet these demands. One concept, entitled Adverse Outcome Pathways (AOP) sets out to discover what takes place between an initial molecular event and a subsequent negative effect on an individual or a whole population. Applying this concept to the field of ecotoxicology could be very promising. In short, harmful substances can trigger a chain of reactions at the molecular level that may have a negative influence on the development of a living organism. Molecular biomarkers are measurable parameters occurring with the organism that react rapidly to toxins and can provide information about the negative impact of a substance within this chain of events.

Elke Muth-Köhne of the Department Ecotoxicology sees great potential in the idea of integrating molecular markers into existing tests to detect endocrine disruptors. "In detail, it could work like this," she explains: "The initial event may be the interaction of an endocrine disruptor or other substance with one of the basic building blocks of a cell, such as DNA, RNA or proteins. These basic components constitute the molecular level of each and every living organism. The specific mode of action of a substance emerges at this level. This initial interaction triggers a cascade of events, which is transmitted from cells and organs to the whole organism or even to an entire population. "To be usefully implemented within the AOP concept, the measured events must be directly connected to each other and be measurable by available techniques. When these conditions are fulfilled, molecular measurement of a reaction can be used to identify endocrine disruptors and to determine their specific mode of action."

Applying the AOP concept in ecotoxicology: Integrating molecular markers into existing tests

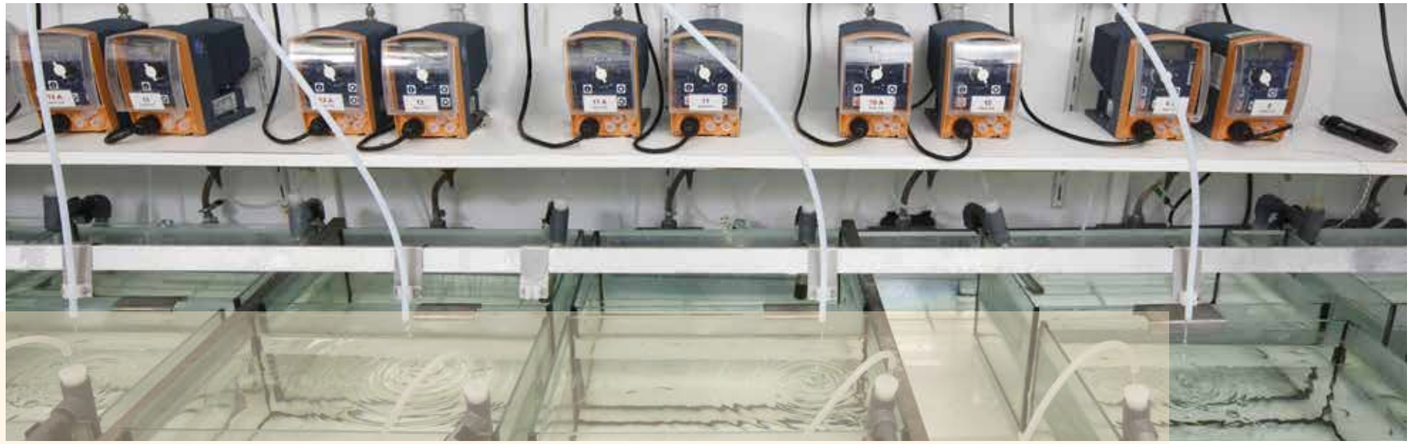
Fish are particularly sensitive to disturbances of the balance of sexual hormones. Existing test guidelines for the identification of endocrine disruptors do not currently cover investigations of molecular events and therefore no specific recommendations have yet been set for the testing of molecular markers. This raised the question of how to find an experimental design that could provide molecular information on endocrine disruptors both rapidly and reliably, and could also be integrated into existing, standardized ecotoxicological test protocols. In Elke Muth-Köhne's opinion, the answer is the investigation of the expression of genes involved in endocrine, i.e. hormonal, processes. The genes serve here as molecular biomarkers. Studies of the expression of such genes fulfil the criteria for integration into an AOP, as they are directly affected by the initial action of an endocrine disruptor, react very rapidly to such events and can be detected using standard molecular biological methods. Based on previously obtained data and an intensive literature search, a shortlist of about 30 genes was created that fulfilled the criteria for biomarkers. The selected genes play a role in various processes involved in steroid biosynthesis, and steroids in turn activate a signaling pathway that maintains the normal functioning of the hormonal system. The Fish Sexual Development Test was chosen as a standard fish test, covering the sexual development of fish up to sexual maturity. This test has been validated under the OECD guidelines program. The species selected for the tests was the zebrafish *(Danio rerio),* a model organism used in ecotoxicological testing. This test was refined for the investigation of gene expression patterns, and messenger RNA levels were measured at different stages of development such as embryonal and larval development, and early and late juvenile growth. Messenger RNA is the transcript of genetic information and is directly translated into protein expression. Gene expression was thereby determined in addition to the standard endpoints evaluated in the Fish Sexual Development Test, such as hatching, growth and sex ratio.

Genes involved in hormonal processes as biomarkers – important information on adverse effects by hormonal interaction

The test substance selected for this task – the aromatase blocker Fadrozol – is an ideal candidate as it acts specifically as an endocrine disruptor and exerts its action during steroid biosynthesis. It blocks the functioning of the enzyme aromatase. Uninhibited, aromatase triggers the conversion of androgens to estrogen, that is, of male to female

The 'key player' in the study: the zebrafish *(Danio rerio)* is the ideal candidate for the Fish Sexual Development Test, as it is especially sensitive to endocrine disruptors during sexual maturation.

The study was performed in a flow-through system, which allows precise and stable dosing of the test substance.



hormones. A well-balanced hormonal system is of particular importance for zebrafish, as both female and male juveniles first possess ovary-like gonads. When the level of male hormones rises, the fish will eventually develop into a male, regardless of the genetic sex. As Muth-Köhne points out, this illustrates the highly specific effect of Fadrozol treatment on the whole organism, which most probably arises through a series of alterations in gene expression at the molecular level.

Zebrafish are especially sensitive to androgenising substances – Fadrozol leads to an increased number of males

As expected, treatment with Fadrozol during development led to an increased number of males. This particular effect was accompanied by a change in the pattern of gene expression. Many of the genes reacted during at least one of the stages of development investigated, thereby confirming the sensitivity of zebrafish development to endocrine disruptors. The effects were already noticeable 48 hours after fertilization, when the zebrafish embryo is still inside the egg shield, obtaining nutrients from the yolk sac. These results show that the zebrafish reacts to hormonal disturbances a long time before sexual development. Expression of the gene encoding the yolk sac protein vitellogenin, for instance, was already impaired, although this is first needed when the female begins to produce eggs. Fadrozol interfered with the expression of five genes at more than one time point. These genes are the most promising candidates for aromatase inhibition. One of these processes is the regulation of transcription factors – proteins that bind directly to the DNA and thus regulate the transcription of DNA into messenger RNA. A further example is cholesterol transport and subsequent steroid synthesis. Furthermore, some of the identified genes are directly controlled by estrogen receptor activation and are thus directly affected by decreased levels of the female reproductive hormone.

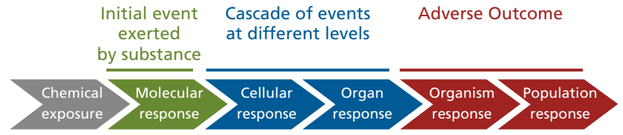
Dr. Elke Muth-Köhne, Department Ecotoxicology: "Environmental pollutants can have highly specific effects on organisms, which most probably arise through a series of alterations in gene expression at the molecular level."

The diversity of steroid biosynthesis processes that are covered by the genes identified highlights their suitability as molecular biomarkers of aromatase inhibition. Their integration into existing test protocols thus offers excellent opportunities to obtain a very early warning of possible negative actions of substances harmful to fish and whole fish populations. This could save time, lower costs and, importantly, reduce the number of test animals needed for the registration of a chemical of interest.

Molecular data extend a standard test – in parallel to the investigation of effects we analyze the cause

The project was funded by the German Federal Ministry for Environment, Nature Conservation, Building and Nuclear Safety (BMUB) (FKZ 371263418).

AE Ecotoxicology



The *Adverse Outcome Pathway* (AOP) concept: The AOP describes a cascade of events triggered on treatment with a chemical with a specific mode of action and with a negative outcome for a living organism or population. Each event should be a direct consequence of the previous and should be measureable by common methods.

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IME International

USA:
Malaria transmission blocking vaccine advances

Chile:
National Innovation Award for biological coal

Malaria transmission blocking vaccine advances

The Fraunhofer USA Center for Molecular Biotechnology (CMB) in Newark, Delaware is developing a new vaccine that is showing promise in the fight against malaria. Funded by the world-renowned Bill & Melinda Gates Foundation, CMB's candidate vaccine is progressing in clinical trials.

Malaria is a mosquito-borne infectious disease of humans and animals caused by parasitic protozoans, a group of single-celled microorganisms, belonging to the genus Plasmodium. Malaria causes symptoms that typically include fever, fatigue, vomiting and headaches. In severe cases it can cause yellow skin, seizures, coma or death. The disease is transmitted by biting mosquitos and symptoms usually begin ten to fifteen days after being bitten.
The disease is widespread in tropical and subtropical regions that are present in a broad band around the equator. This includes much of sub-Saharan Africa, South America and Asia and malaria has a major negative effect on economic development in those regions.

Bill & Melinda Gates Foundation funds CMB research

Although some vaccines are under development, no vaccine is currently available that provides a satisfactory level of protection against this disease. The Pfs25 antigen of *Plasmodium falciparum*, a leading candidate for transmission blocking vaccine development, has been shown to induce high levels of transmission reducing antibodies in animal models. The plant based expression system used at the CMB has proven to be particularly suitable for the production of a potent Pfs25 antigen.

Under a grant from the Bill & Melinda Gates Foundation, CMB has generated a Pfs25 virus-like particle (VLP) displaying multiple copies of Pfs25. The purified Pfs25 VLPs do not contain infective genetic material, are highly immunogenic and elicit complete transmission blocking activity in immunized mice for prolonged periods of time following a single administration.

To accomplish the goals of this project, CMB established international partnerships with organizations that have detailed expertise and knowhow in protein engineering and production, as well as in subunit vaccine development, pathology, immunology and vaccine candidate evaluation, in parasitology and the development of vaccine formulations, and also in guiding vaccine candidates through evaluation in human clinical trials.

Clinical Phase 1 study: Excellent safety and tolerability

CMB received clearance from the US Food and Drug Administration (FDA) for an investigational new drug, Fraunhofer's plant-derived malaria transmission-blocking vaccine Pfs25 VLP, which targets the Pfs25 antigen, to proceed into the clinic in a Phase 1 safety and immunogenicity study. The results of the Phase 1 study showed excellent safety and tolerability and will be published in 2016.

Center for Molecular Biotechnology

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Fraunhofer CMB's process involves the automated placement of seeds in specially designed growth trays. This ensures the consistency in the process.

Using an automated system, the seeded trays are placed in stainless steel growth racks in a strictly climate controlled room. The plants are grown for 4–5 weeks until they are mature enough to undergo vacuum infiltration.

Trays of plants are inverted for immersion in the vacuum infiltration tank. In this part of the process, CMB's target of interest is inserted into the plant. Following several days of protein production, the plants will be harvested and further processed to obtain the target protein.

Chilean National Innovation Award for biological coal from waste

Researchers of the Fraunhofer Chile Research Center for Systems Biotechnology (CSB) address the needs of the pharmaceutical, medical, agricultural and aquaculture industry in a new biotechnology laboratory to develop new products and processes. One of these - Hydrothermal Carbonization - was recognized with a Chilean National Innovation Award 2015 for the development of biocoal using industrial and domestic waste biomass.

The new biotechnology laboratory of Fraunhofer CSB in Santiago de Chile offers additional dedicated facilities for contract research.

Biocoal pellets produced by Hydrothermal Carbonization can be used in industry and in households to provide a clean burning fuel.

In order to expand its range of innovative products and services, Fraunhofer CSB opened a new biotechnology laboratory with specialized equipment and facilities. "This new laboratory allows Fraunhofer Chile Research to offer additional dedicated facilities to industry for contract research and expand the range of services we can provide in the field of genetics, pharmaceuticals, food ingredients, and waste management," says CSB Director Wolfgang Schuch.

Alzheimer's drug discovery: A Chilean rodent provides clues for research

The Biocomputing and Applied Genetics research line has facilities for next generation DNA sequencing and analysis that complement its computing capabilities. Genomic selections are being used to shorten the development for the new varieties of plants for the agroforestry industry.

A platform for Alzheimer's drug discovery and testing was implemented by the Biomedicine research line. The platform is based on *Octogon degus*, a rodent found only in Chile which develops Alzheimer´s symptoms naturally. This offers unique opportunities for pharmaceutical companies during preclinical research. The Renewable Resources research line is developing the supercritical fluid CO_2 extraction and encapsulation technology, which will provide new ingredients for the food industry.

Fraunhofer CSB is also applying 'Hydrothermal Carbonization' (HTC), a novel technology developed in Germany, in a unique technology offering in Latin America to local companies. This technology allows the transformation of organic biomass waste into high-quality biocoal and other added-value products. This process offers a sustainable solution for the use of waste materials which otherwise have no value to local companies. The solid fuel generated can be used in industry as well as households to provide a clean burning fuel. It can make a significant contribution to air quality: Wet wood is used extensively in many rural regions of Chile to provide heat. The consequence of this is a high load of particles in the air. In addition, the HTC process allows the recovery of water from the used biomass.

Hydrothermal Carbonization: Transforming organic waste into valuable products while recovering water

For its work in this field Fraunhofer CSB was recognized and awarded the Chilean National Innovation Award 'Avonni 2015' in the Environmental category. This year more than 700 proposals were submitted and a group of 90 industry leaders selected the most innovative and high-impact projects.

CSB Director Schuch: "This award is a recognition of the work that we have been doing in Chile for more than four years, to contribute through applied research to the development of novel products and services that support the competitiveness of the local industries."

MB Center for Systems Biotechnology

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In Dialogue with Andreas Vilcinskas

Andreas Vilcinskas has coined the term ‘Yellow Biotechnology’, a field of research aiming to tap the enormous potential of the insect world for science and research: maggots for the treatment of wounds, ladybugs in the fight against malaria, burrying beetles for the bioconversion of organic waste, antibiotics derived from insect molecules. Vilcinskas is pioneering this young discipline on an international level. He bridges two worlds: Originally specialized in zoology, he has worked in nature conservation and is a biotechnologist of international standing. As leader of the IME Project Group Bioresources he is in high demand as a specialist in Germany and further afield on issues of biodiversity, and for consultations at the highest political level.

Personal background
Prof. Dr. Andreas Vilcinskas is Professor of Applied Entomology at the Justus-Liebig University in Gießen. He leads the Fraunhofer IME Project Group Bioresources. Since 2014 he has also acted as Coordinator and Spokesman for the LOEWE Center for Insect Biotechnology and directs the very first institute worldwide for insect biotechnology, set up at Gießen University in 2015.

Insects, bacteria, fungi: Successful survival artists serving science

Professor Vilcinskas, have moths and maggots fascinated you since childhood?
I have been fascinated by zoology and particularly entomology for as long as I can remember. I began a butterfly collection at the age of 12 and went on adding to it until I started studies at university.

And what makes insects so interesting for science and research?
Insects are experts in survival. They flourish in places like cesspits or carcasses where other creatures cannot survive. And why? They are unbelievably adept at combating micro-organisms, making them the most successful class of organism on the planet. With a total of 1.2 million species, more than every second species known to us is an insect. This manifest biodiversity at species level reappears at the biochemical and molecular level. Taken together, I regard the insects as a gigantic library of natural products that we strive to explore for the benefit of humankind.

'Unique selling point' is a term used in marketing - in your research field, what is it that only Yellow Biotechnology can offer?
We see our market niche as the harnessing of bioresources for the bio-economy. Groups of organisms with extremely high biodiversity such as the insects with their many species are of great interest here. And we are the only operational unit in Europe covering the complete value chain from basic research through targeted identification of natural products up to the development of products and services.

Where do you see the greatest potential for Yellow Biotechnology?
When you consider the quantities of food products they destroy on farmland and in warehouses, insects can be seen as man's greatest competitors for food. Furthermore, insects are the most important transmitters of infectious diseases. From malaria through to plague and even Zika viruses – the pathogens that kill millions of people are carried by insects. The development of innovative, environmentally friendly procedures for the control of harmful insects and so-called disease-carrying vector insects is a central task in insect biotechnology. Then there are the novel active agents for new drugs based on molecules from insects. And last but not least, 'Yellow Biotechnology' can supply natural enzymes that are highly attractive for industrial applications such as bioconversion of organic waste into valuable raw materials. Making a mint out of manure, you could say.

What have been your key successes in this promising young discipline?
We have managed to establish Yellow Biotechnology as a trademark and in this field have built up one of Germany's most successful research alliances.

In a joint Natural Product Center of Excellence, Sanofi and the Fraunhofer-Gesellschaft work on new therapies against infectious diseases. The Fraunhofer scientific expert is the IME's Prof. Dr. Andreas Vilcinskas.

The LOEWE Center for Insect Biotechnology in Gießen has a wide impact. At the research level, for instance, we are developing a wound ointment with active substances extracted from the wound maggot. Tiny amounts of the respective molecules operate like a team of biosurgeons: there are enzymes in the maggot that remove necrotic tissue without harming healthy tissues. Some facilitate wound healing while others promote blood clotting or kill pathogens. Imagine packing all that into a cream or onto a bandaid … we would then have wrapped up a whole package of natural products for wound healing.

How intensive are efforts worldwide to exploit insects for research?
Researchers in Korea, Japan and China have been working in this field for some time. However, Yellow Biotechnology is still a global market niche. There are locations focusing on the topic, but only in certain specialist fields. One institute in China, for instance, is focusing exclusively on insect-derived cellulases. There are similar centers in Europe too but with its comprehensive approach in Yellow Biotechnology, Gießen has a unique position worldwide.

Together with the international healthcare company Sanofi, the Fraunhofer Society founded a joint Natural Product Center of Excellence in 2014. What is the key factor here and what do you aim to achieve with this collaboration?
One key point here is that scientists from Sanofi and Fraunhofer are working side by side at

The burying beetle could be a valuable worker in the bioconversion of biological waste.

“The world of insects and micro-organisms is like a gigantic repository of natural materials and building blocks. We want to tap these bioresources for the bio-economy.”

the bench and in one laboratory. We have the expertise to carry out a targeted search for new active substances while Sanofi has the competence to bring them to the market. By combining skills and resources, we have a better chance of reaching our goal. And we can involve other companies, but not as competitors. Dow AgroSciences, for example. This is really a win-win-win situation: sharing can reduce the soaring costs of research. And if one partner cannot use a natural compound identified for development of antibiotics, another may use it to develop new plant pesticides. This provides an enormous opportunity to develop synergies.

Before the G7 Summit 2015, Chancellor Merkel spoke to you and leading scientists from Sanofi about the current state of antibiotic research. How would you describe the state of play here?
With regard to development of new antibiotics, it is clear that the low-hanging fruits have been harvested. At this point innovative technologies need to be applied to unearth new natural products. Thousands of tricks can be devised to get bacteria to produce potential candidates. You just need to know how.

Scientific research often yields unexpected results. What has been one of the biggest surprises for you in your scientific career?
When I looked at the hemolymph of the Asian ladybug for the first time, it was full of parasites that the beetle itself apparently tolerated. I have never seen anything else like that in 20 years of research into the immune system of insects. Looking at how this species of beetle defends itself against parasites, we discovered harmonine in the hemolymph. Because laboratory experiments showed that this substance can suppress the pathogens that cause tuberculosis and malaria, it is now being used to develop drugs against those diseases.

Among other places, you’re planning another trip to Indonesia in 2016. What draws you to this country in particular?
Up to now we have worked exclusively on indigenous and immigrant insects such as the Asian ladybug. Indonesia is a hotspot with one of the highest levels of biodiversity in the world, one of the countries with the greatest variety of species. The German Federal Ministry of Education and Research is financing the program ‘Biodiversity and Health’ and this funding will enable us to screen insects of the rain forests for compounds that might be effective against pathogens. Until now, hardly any research has been carried out on those insects. Opening up this treasure-trove of new natural products is a thrilling task.

What are your long-term aims for Yellow Biotechnology?
That brings us back to the beginning of our conversation: We want to tap bioresources for the bio-economy. Groups of organisms with great biodiversity allow us to take things a step further: First there are the insects. And now through our joint Natural Product Center we can access Sanofi’s strain collection of micro-organisms – one of the largest in the world.

Interview: Sabine Dzuck

MB Bioresources

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Bridges between two worlds: Prof. Dr. Andreas Vilcinskas is a zoologist as well as a biotechnologist. He pioneers the young discipline of insect biotechnology and is in high demand globally as an expert in this field.

In Focus

An article by Dr. Matthias Kotthoff

The ‘radio kitchen’ at Fraunhofer IME:
What is lurking in processed food?

The ‘radio kitchen’ at Fraunhofer IME: What is lurking in processed food?

Our author

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A new laboratory is being set up as a ‘kitchen’ at the Fraunhofer IME in which foodstuffs can be processed under close-to-normal conditions and the transformation or breakdown products of their ingredients can be analyzed by means of radioactive labeling. What used to take years should now proceed faster.

Food safety: Processing alters material properties – revealing risks to the consumer

Most components of foodstuffs, such as carbohydrates, fats and proteins, and also vitamins and trace elements, are desired or at least harmless. Many food ingredients occur naturally and contribute to a balanced diet and well-rounded eating experience. Others, known as supplements or additives, are introduced intentionally to attain certain properties. Other substances get into foodstuffs by accident and are ingested by the consumer as contaminants and residues.
When foods are processed, however, their properties are altered. French fries become crispier; steaks become tender and give off an appetizing roasting aroma. The processing also produces new desirable ingredients while certain undesirable components are destroyed. But new and often unknown compounds may also be formed, posing uncertain risks. Thus processing procedures influence not only food quality but also food safety.

These processes are brought about by complex chemical reactions that often take years or decades to elucidate. Detailed knowledge of the reaction cascades is needed to assess the risks to consumers and to develop optimized products and procedures. We are interested not only in the technological processes used in the food industry but also in the everyday preparation and cooking of food at home and in restaurants.

Food quality: Processing alters aromas – optimizing recipes and procedures

Natural ingredients can be transformed through processing into substances that are harmful to health. Acrylamide serves as a good example to illustrate the challenges encountered when striving for food safety: Acrylamide is a small, highly reactive molecule that plays a key role in the production of plastics, paints and varnishes, and is also a basic ingredient of cosmetic products. It is currently classified as ‘probably carcinogenic’. Through an accident in 2002, a Swedish research team detected high concentrations of acrylamide in starchy roasted foods and discovered it was the end-product of the highly complex Maillard reaction. It is a derivative of the amino acid asparagine, which occurs naturally in almost every foodstuff.
Only in the last few years has it been possible to lower acrylamide levels through new procedural concepts and the modification of conditions, in particular, lowering of processing temperatures, and so improve consumer safety. Billions of euro have been invested in research and in the adaptation and supervision of processing procedures to this end.
Due to a lack of practical research approaches, there is still very little known about the behavior of chemical residues from agricultural production during food processing and the secondary metabolites produced. Critical source materials include pesticides, veterinary drugs and feed additives, as well as chemical environmental contaminants.

Coffee is a particularly interesting example for extensive chemical alterations during multi-stage processing.

Cutout of an HPLC/MS device for the analysis of metabolized components of foodstuffs (HPLC/MS: high pressure liquid chromatography coupled with mass spectrometry).

In technological processing also, many desirable substances are newly formed. Think of the aroma of freshly roasted coffee or a crisp cookie. To date, most formation pathways of these aroma-bearing substances have not been explained in detail. For optimization of recipes and procedures, however, it would be of great interest to know the exact formation pathway. Resource efficiency is currently the number one issue in food production – process changes such as lowering the temperature or process water consumption are becoming imperative, which implies that the influence on quality is known.

Visualizing new target substances is an analytical challenge. The solution: Radioactive nuclides

With the current technology used for food analysis it is scarcely possible to identify and quantify the metabolites of ingredients in processed foods. This is largely due to the complex matrices of foodstuffs in which unknown target substances remain hidden and cannot be visualized with the technology available. Little is therefore known about the reaction pathways underlying food-processing procedures at the molecular level.

Radioactive nuclides – in this case, the nuclide carbon-14 (^{14}C) – can be used to label source compounds of interest so that their fate can be determined and quantified with appropriate analytics. Their fate, be it degradation, reaction with other ingredients or a whole reaction cascade, can then be understood. Since breakdown products of the original labeled substance will also be marked, both the source compound and its residues can be tracked throughout the processing procedure and a balance taken.
Our laboratory has already acquired a nickname: The ‘radio kitchen’ is fitted with all the key processing equipment used in the food industry as well as that of a normal domestic kitchen so as to reproduce the following technological areas:

- Fruit processing/beverage technology
- Cereal crop processing/milling/baking technology
- Meat processing technology
- Restaurant and domestic cooking

This extension of our activities into the area of food quality and safety arose from our long-term expertise in chemical analysis at the Fraunhofer IME with a recent research focus on plant and animal metabolism. We can now cover the entire agricultural value chain – from environment to agricultural product and finally to the fork of the consumer. Thus research on animal and plant metabolism, established over many years at the IME and relevant to registration tests, can now be supported and usefully extended.
In this context, the Fraunhofer IME has since 2016 collaborated with the Fraunhofer Institute for Process Engineering and Packaging IVV in an internal Fraunhofer research program. The aim here is to track pesticides and their transformation or breakdown products from plant cultivation through to ready-to-eat foods and finally to minimize the formation of harmful products during the manufacturing process.

Outlook: Simultaneous optimization of resource efficiency and food quality

In food quality research, modified food processing procedures can be geared towards the formation of specific reaction products. Thus changes can be made to the temperature profile and recipe so as to improve resource efficiency and simultaneously observe what effect this has on the reaction pathways underlying the aroma profile. At the same time, undesirable metabolites formed during processing can potentially be broken down into uncritical degradation products by longer retention times.

AE Environmental and Food Analysis

The process cascade from raw material to consumer is often long.




Six Selected Publications from 2015

Plant Biotechnology

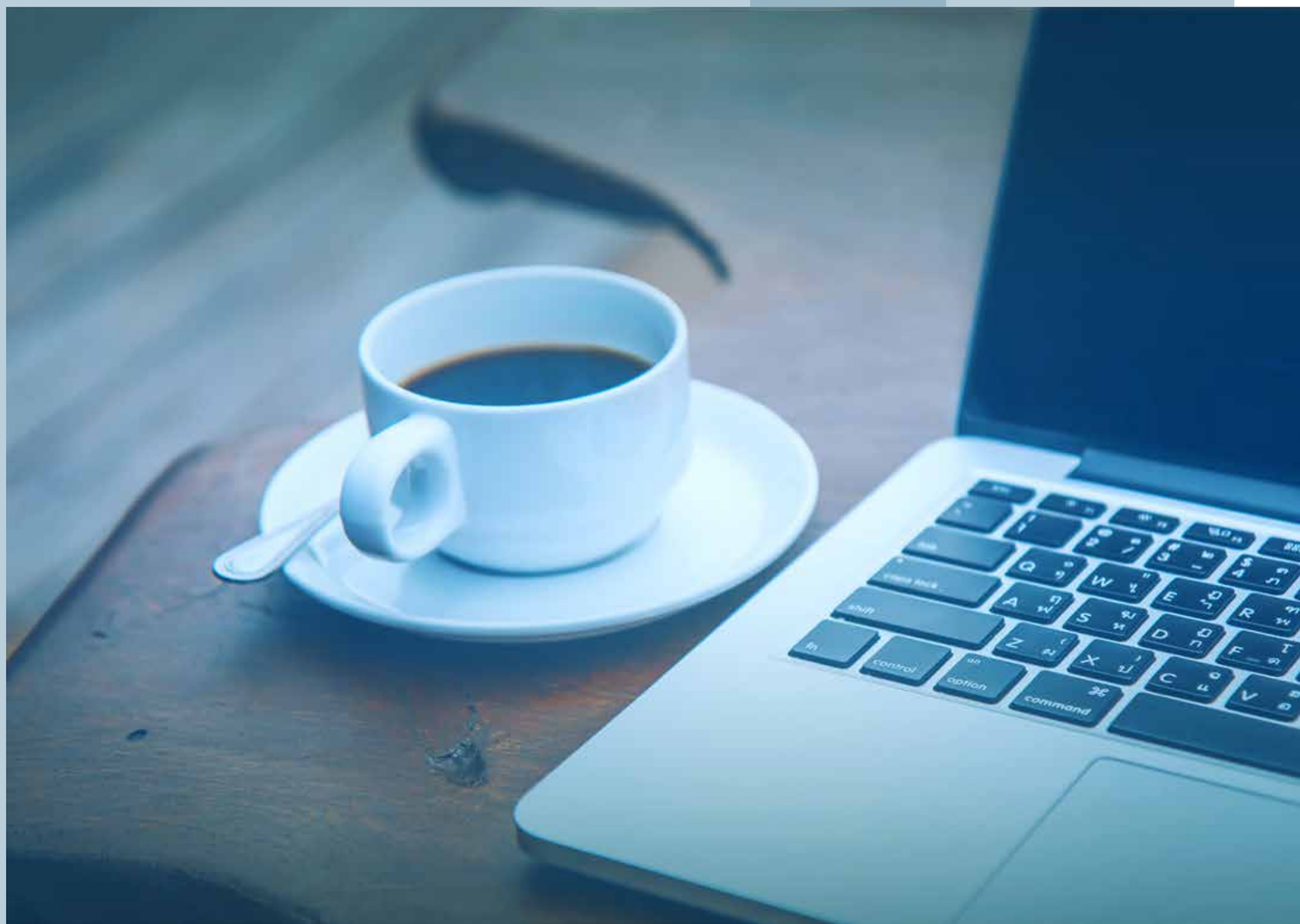
Pharmaceutical Product Development

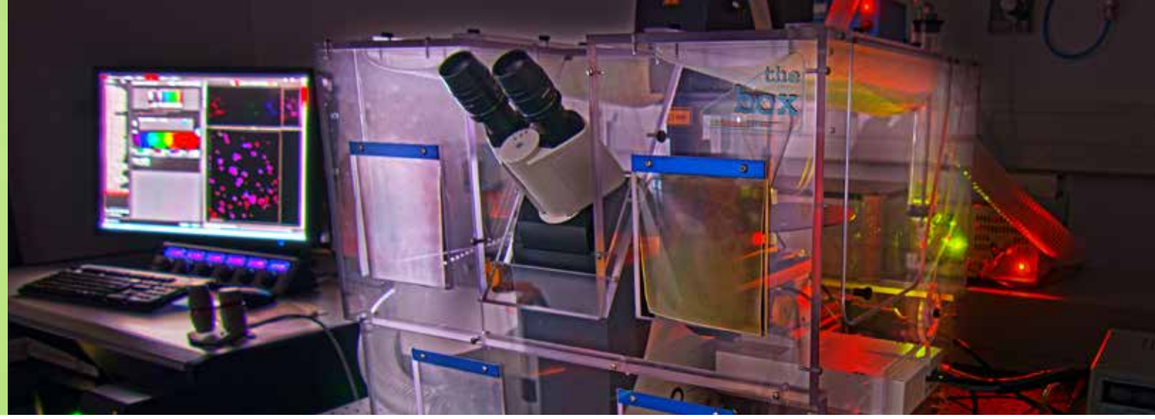
Translational Medicine and Pharmacology

ScreeningPort

Ecotoxicology

Bioaccumulation and Animal Metabolism





Malaria research: New plant-based vaccine cocktail

Alexander Boes,
Plant Biotechnology
New approaches to malaria vaccine development are needed. The plant-based production of vaccine cocktails is promising.

Despite many years of intensive research there is still no approved vaccine for malaria. The complex life cycle and high genetic variability of the pathogen *Plasmodium falciparum* presents a huge challenge for vaccine development. The combination of important antigens representing different parasite stages in a vaccine cocktail is a promising approach. Plants are ideal for cost-effective, large-scale production of vaccine components. At IME, we are therefore using our established plant-based production platform for the production of multistage malaria vaccine components.

In the framework of this study we have produced and characterized a vaccine cocktail from four recombinant fusion proteins. They contain a total of ten antigens representing the three key stages in the parasite's life cycle: the pre-erythrocyte, blood and sexual stages. All fusion proteins can be produced in tobacco plants at low cost, in sufficient amounts and with adequate purity. In *in vitro* experiments with immune sera we have been able to demonstrate a marked inhibition of up to 90% in all three development stages, and also provide quantitative data concerning the inhibitory action of the induced antibody responses. Thus we have a basis for targeted optimization of this and other multistage or multicomponent malaria vaccines.

MB Plant Biotechnology

Boes, A., Spiegel, H., Voepel, N., Edgue, G., Beiss, V., Kapelski, S., Fendel, R., Scheuermayer, M., Pradel, G., Bolscher, J.M., Behet, M.C., Dechering, K.J., Hermsen, C.C., Sauerwein, R.W., Schillberg, S., Reimann, A., Fischer, R.: Analysis of a multi-component multi-stage malaria vaccine candidate tackling the cocktail challenge.
PLoS One, Online journal 10 (2015), Nr. 7, Art. e0131456
(DOI:10.1371/journal.pone.0131456)

New drug candidate against leukemia – reducing side-effects

Christoph Stein,
Pharmaceutical Product Development
Our antibody-based fusion protein will extend the therapeutic options for personalized therapy in leukemia patients.

Each year more than 10, 000 individuals are newly diagnosed with leukemia in Germany. This includes various forms of the disease affecting not only children and adolescents but mostly older people. As a result of the overall increase in life expectancy, the number of new cases is set to rise further in coming years.
The standard therapy for leukemia causes considerable side-effects in most patients. Research is therefore focused on alternative forms of therapy.
One highly promising approach is the use of antibodies specifically targeting leukemic cells. These molecules not only serve to recognize abnormal cells but to deliver toxic substances that will eliminate the cancer cells. This form of treatment spares healthy cells and greatly reduces undesired side-effects. We have developed a candidate molecule of this sort, which attacks certain structures on the surface of the cancer cells. Moreover, it has been successfully tested against primary leukemia cells derived from the blood of leukemia patients. These structures had been described before in the literature but it was as yet unknown that they are suitable as targets for an antibody-based therapy. We are now a step closer to obtaining a new, effective and also less harmful medication. Further preclinical studies on the efficacy of the new active agent are planned for the near future. In addition, we plan to further increase tolerability of the drug candidate by using a toxic substance of human origin. Preliminary clinical trials will commence soon.

MB Pharmaceutical Product Development

Mladenov, R., Hristodorov, D., Cremer, C., Hein, L., Kreutzer, F., Stroisch, T., Niesen, J., Brehm, H., Blume, T., Brummendorf, T., Jost, E., Thepen, T., Fischer, R., Stockmeyer, B., Barth ,S., Stein, C.: The Fc-alpha receptor is a new target antigen for immunotherapy of myeloid leukemia. Int J Cancer (2015)
(DOI: 10.1002/ijc.29628)

Repositioning of established drugs – targeted development of new painkillers

Gerd Geisslinger,
Translational Medicine and Pharmacology
We identify novel uses for approved medications. This saves time and money.

In recent years, evidence has accumulated that supports the use of existing drugs, approved as antibiotics, antidepressives and antidiabetics, as novel treatments for chronic and neuropathic pain. In the article 'Drug Repurposing for the Development of Novel Analgesics' we show how the principle of drug repositioning can be applied to the targeted development of new agents for pain relief. We discuss the mechanisms of action of the compounds and their application to pain control. Surprisingly, some agents such as the antibiotic minocycline can activate astrocytes and microglia in the spinal cord and thereby counteract neurogenic inflammation. Other drugs such as ceftriaxone reduce levels of the pain-relevant neurotransmitter glutamate in the spinal cord or inhibit calcium release in sensory neurons, thereby relieving peripheral pain. The article also highlights the considerable benefit of bioinformatic analysis in connection with drug repurposing.
Using a similar approach, we have identified a novel drug candidate for the treatment of multiple sclerosis and are the first Fraunhofer unit to bring a candidate drug to the Phase IIa stage of clinical trials.

MB Translational Medicine and Pharmacology

Sisignano, M., Parnham, M.J., Geisslinger, G.: Drug repurposing for the development of novel analgesics. Trends Pharmacol Sci (2015) pii: S0165-6147(15)00242-4
(DOI: 10.1016/j.tips.2015.11.006)

Advancing screening technology – for faster drug discovery

Philip Gribbon, ScreeningPort
Close cooperation between academia and industry opens up additional opportunities to identify starting points for difficult drug research.

Together with international pharmaceutical company AstraZeneca (AZ), the Fraunhofer IME aims to improve the overall efficiency of early drug discovery, by making use of enhanced technologies and innovative operating models in the area of small molecule screening. At Fraunhofer IME and AZ, bottlenecks in chemical synthesis requirements are removed by the use of acoustic droplet ejection for compound handling, while advanced disease models based on stem cells allow for better decision making during hit-to-lead drug discovery projects. Both organisations recognise the critical need for the optimal design of compound screening collections, and how the formation of public-private partnerships provides access to additional opportunities to identify chemical starting points for difficult therapeutic targets. It is also recognized that in order to improve the overall success of drug discovery, novel collaborative strategies must be put into practice, in particular embracing the idea of 'open innovation', where partners from industry and academia make their libraries and screening technologies available to each other and share target and disease knowledge. AstraZeneca and Philip Gribbon of IME ScreeningPort have published a joint comment on these two topics in the leading scientific journal 'Nature Reviews Drug Discovery', under the heading 'Towards a hit for every target'.

MB ScreeningPort

Rees, S., Gribbon, P., Birmingham, K., Janzen, W.P., Pairaudeau, G.: Towards a hit for every target. Nature Reviews Drug Discovery aop (2015)
(DOI: 10.1038/nrd.2015.19)

Effect modeling for ecological risk assessment of pesticides

Udo Hommen, Ecotoxicology
Good mechanistic effect models allow realistic risk assessment of the influence of pesticides on the environment.

Before pesticides are officially approved, the risks they pose to non-targeted organisms are analyzed in detail in order to draw up requirements for their safe application, if indicated. This type of analysis usually comprises standardized laboratory tests with various classes of organism. For a more realistic risk assessment, further, more complex, studies can be carried out. However, the multitude of possible situations in the field can scarcely be tested empirically. This is where computer simulations come into play, where effects at organism, population and community level are described in mathematical models. In their most recent directives on risk assessment for pesticides, the European Food Safety Authority (EFSA) discusses the use of such effect models and has put together a document with recommendations for 'good modeling practice'. But guidance on how to use these models in the regulatory framework is still lacking. Together with scientists from research institutes, industrial enterprises and regulatory authorities, we therefore organized an international workshop MODELINK on this subject. The results have now been published as a summary of the first general recommendations for the use of such models in the European approval process. Case studies with models for fish, birds, small mammals, soil-dwelling organisms, aquatic invertebrates and aquatic plants supplement the series.

AE Ecotoxicology

Hommen, U., Forbes, V., Grimm, V., Preuss, T. G., Thorbek, P., Ducrot, V.:
How to use mechanistic effect models in environmental risk assessment of pesticides: Case studies and recommendations from the SETAC workshop MODELINK.
Integr Environ Assess Manag, 12 (2016) 21–31
(DOI: 10.1002/ieam.1704)

Pesticides in fish feed: A consumer risk?

Christian Schlechtriem, Bioaccumulation and Animal Metabolism
Bioaccumulation of pesticides in farmed fish can be tested experimentally. This allows us to identify risks for the consumer.

Fish reared by aquaculture constitute around 50% of current fish consumption worldwide. In order to guarantee sustainable levels of aquaculture production, large amounts of plant matter are incorporated into aquaculture diets. This raises the risk of the transfer and accumulation of pesticides in farmed fish – and consequently the danger of pesticides ending up in the stomachs of consumers.
Where pesticides are used on plant crops with raw or processed products usable in fish feed, the EU pesticide authorization process requires fish metabolism studies to be carried out. Metabolic studies quantify and characterize the accumulated levels of pesticides in edible animal tissue after the consumption of contaminated feed. They also provide a basis for the setting of maximum permissible concentrations. We performed laboratory studies on rainbow trout and carp to demonstrate the effectiveness of a specially developed procedure for fish metabolism studies. This allowed us to determine the total residue levels and metabolic profile, in fillets and liver tissue, of a test substance previously used in the experimental feed for both fish species. Our new test design for fish metabolism studies can thus be used within the framework of the regulatory testing of pesticides to investigate the transfer, accumulation and characterization of pesticide residues in fish after the ingestion of contaminated feed.

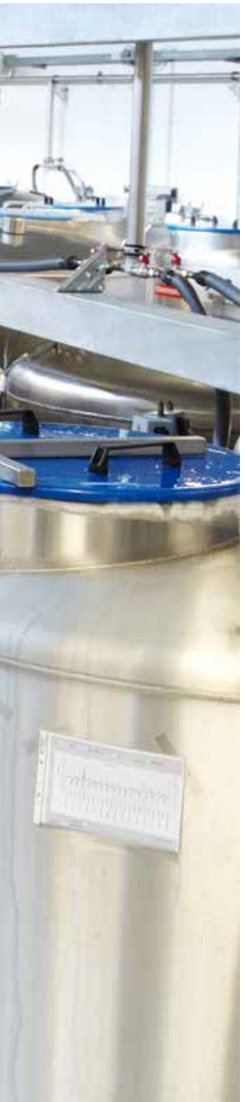
AE Bioaccumulation and Animal Metabolism

Schlechtriem, C., Bischof, I., Atorf, C., Bergendahl, E., Seymour, P., Whalley, P.:
Development of a regulatory testing procedure to study the metabolism of pesticides in farmed fish. Pest Management Science, 72 (2016) 362-270
(DOI 10.1002/ps.4007)

People and Events

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

International cooperation: Tracking down the smallest particles

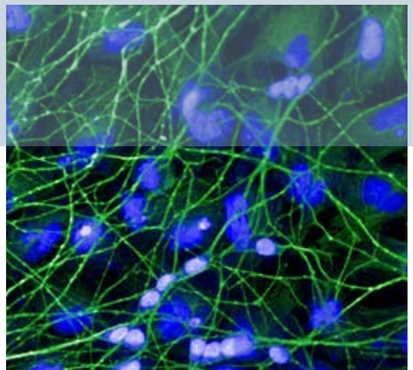


FENOMENO is a European project aiming to understand the impact of manufactured nanomaterials on the environment. Nanomaterials are increasingly used to optimize a wide range of everyday products such as sun cream products containing nanostructured titanium dioxide (TiO_2) or nanosilver-optimized functional sportswear. Nanomaterials are released from textiles by washing or reach wastewater treatment plants as a result of body care. Even though they are mostly removed during wastewater treatment, the remaining levels in the effluents are significant and nanomaterials may become more toxic towards aquatic organisms due to their modification during wastewater treatment. FENOMENO is jointly executed by University of Siegen and the team of Christian Schlechtriem, Fraunhofer IME Schmallenberg (Germany) as well as project partners in Austria and Portugal. Cutting edge approaches to analyze and monitor the biological impact of TiO_2 and silver nanomaterials on different trophic levels within a relevant food chain (algae – Daphnia – fish) are used at different levels of investigation, from behavioral to biochemical, from laboratory to complementary field studies. The 36-month project started in April 2015 and has received more than 1.1 million euro funding. (http://www.fenomeno-nano.de/). AE

Antibiotics research: German Chancellor Merkel discussed with Sanofi and IME scientists

Multidrug-resistant pathogens increasingly threaten the health of people both in the developing world and in industrialized countries. The fight against pathogens is therefore at the top of the political agenda: German Chancellor Angela Merkel had made antibiotics and thus the fight against resistant germs a topic on the agenda of the G7 meeting in Germany, June 7 and 8. In the run-up to the meeting she met scientists of the global health care company Sanofi and Fraunhofer IME at Sanofi's site in Frankfurt, to discuss the status of their joint antibiotics research. After the academic exchange, the Chancellor and Sanofi's CEO, Olivier Brandicourt, inaugurated a new facility for the sterile filling of biologics.
In 2014, Sanofi and the Fraunhofer-Gesellschaft founded a Natural Product Center of Excellence: Scientists representing both partners work as a team and in joint laboratories to explore and optimize naturally occurring chemical and biological substances, mainly for the treatment of infectious diseases. Moreover, Sanofi shares its culture collection with Fraunhofer. It is one of the largest in the world with more than 100,000 micro-organisms. Angela Merkel praised this cooperation between Fraunhofer and Sanofi as a groundbreaking step forward to keep innovation in Germany. On the part of the IME, Rainer Fischer, Senior Executive Director, and Andreas Vilcinskas, Head of the Project Group Bioresources at IME, participated in the meeting (please also see our interview with Andreas Vilcinskas pp. 44-49). MB

Stem cell research: Ensuring the quality of human iPS cells – cooperation with US partners



'Induced pluripotent stem cells' (iPS cells) are made by taking a mature cell, such as a skin cell, and dialing back its developmental programming so it becomes a stem cell, capable of differentiating into virtually any cell type in the body. Scientists now routinely create iPS cells. They have enormous potential for regenerative medicine, research, and the development of new therapeutic agents. The demand for high-quality iPS cells is constantly growing. "If we use human iPS cells for the testing of possible therapeutic agents, we are able to draw more reliable conclusions with regard to the reaction in the human body. This way, we might lower failure rates in drug development – and thus also diminish the costs," says Ole Pless of the IME ScreeningPort. "But this requires that the iPS cells function in the way they are supposed to. They must be of the highest quality." And exactly here is the starting point for the team of three German and US partners: They have joined forces to advance the quality control of human stem cells for research and clinical use. Together, they will develop new genomics-based methods to analyze the cells. The new software will be called 'PluriTest2'. Involved in the project are The Scripps Research Institute in California, USA, the Center for Integrated Psychiatry Kiel and the Fraunhofer IME. The project is jointly funded by the California Institute for Regenerative Medicine and the German Ministry of Education and Research. MB

Change in the management of Quality Assurance at the Schmallenberg site

After ten years as Head of Quality Assurance at Schmallenberg, Gerd Wasmus took partial retirement on 31 July 2015. He began work at the Fraunhofer IME in 1986 as a scientist in the Departments of Chemistry and moved to Quality Assurance in 1994. From October 2005 he led the Quality Assurance Unit, directing its expansion in terms of structure and personnel in line with the growing importance of GLP and accreditation projects. By this means, the revenue, largely generated through GLP projects and closely dependent on the quality of the studies, has been tripled over the last ten years, reaching around 6.8 million euro in 2015. For this, Director of the IME Schmallenberg Christoph Schäfers extends his warmest gratitude. Gerd Wasmus' successor is his long-term colleague Cornelia Bernhardt. AE

Major building works at Schmallenberg

For the IME Applied Ecology Division in Schmallenberg, the year 2015 was one of planning and construction preparations for the approved building and conversion projects. Completion is scheduled for 2021 with a projected cost of 24.5 million euro. These large-scale building projects will provide laboratory units and offices for the Departments of 'Ecological Chemistry', 'Bioaccumulation and Animal Metabolism' and 'Ecotoxicology'.

The year 2015 also saw completion of a service and disposal yard with a new chemical storage unit, waste disposal point, vehicle depot and central materials store in the workshop area, with direct access for deliveries via a new entrance gate. A further building was erected for soil preparation close to the environmental specimen bank. A new central power plant, designed to supply both existing and new buildings, will go into operation in early 2016. The existing laboratory facilities have been fitted with new ventilation systems for the major construction period and for future use by the analytical departments. As the building for ecotoxicological testing had to make way for construction of the new block, temporary facilities will be erected in 2016 in addition to an annex for a novel flow-through facility. These measures will allow operations to be continued throughout the construction period 2017 - 2020, despite extensive demolition of some smaller buildings. The consortium Meyer-KSG was awarded the contract for the building work in the major construction period. Besides laboratory facilities, the institute will have a central section with seminar rooms, a canteen and a library. Costs for preliminary works in 2015 and 2016 were close to 4.2 million euro, around 3.7 million euro of which was supplied by the Applied Ecology Division of the institute. AE

Environmental risks of biocides – research findings presented at the Fresenius Conference

Researchers from the Fraunhofer IME were invited to present their findings at the 4th Fresenius Conference on Environmental Risk Assessment of Biocides. Heinz Rüdel presented a project performed for the German Federal Environment Agency, on prioritizing of biocides for environmental monitoring. He called for a specific monitoring of biocides identified as relevant in order to determine their influence on the environment and the definitive consequences of the EU biocide regulation. Michael Klein gave a talk on exposure modeling and demonstrated the suitability of FOCUS methodology for assessment of the leaching of biocides from building materials. This method was first developed for the assessment of pesticide concentrations in groundwater. Aquatic mesocosms are a suitable tool to investigate the effects of biocides on populations of aquatic organisms under field conditions. Udo Hommen demonstrated the use of such artificial ponds in his presentation. In 2014, after many mesocosm studies had been performed in the context of pesticide risk assessment, the IME was contracted – in collaboration with gaiac, Aachen – to carry out a specific biocide study, which was presented at the conference. AE

International workshop: Environmental monitoring of biocides in Europe

In the context of a three-year project on biocide monitoring conducted on behalf of the German Federal Environment Agency (UBA), Fraunhofer IME was contracted to organize an international workshop. The event, held in Berlin in June 2015, was hosted by UBA and the NORMAN association and attracted more than 70 workshop attendees from about a dozen European countries, representing authorities, research institutes, industry and non-governmental organizations. Discussions focused on compartment-specific approaches to biocide monitoring and covered aspects such as prioritization, sampling strategies, measurements and databases. The workshop report is available online at: http://bit.ly/1I8tIqk. AE

Insects of the Indonesian Jungle: BMBF funds opening of molecular treasure trove

Insects and the substances they produce offer enormous potential for therapeutic and diagnostic purposes. In 2015, the joint project ‘Insect-derived anti-Infectives from Indonesia’ was launched, in short: ‘Triple-In’. Funded by the German Federal Ministry of Education and Research (BMBF) ‘Triple-In’ is one of eight joint projects. The common goal is to identify and make use of natural products that are indigenous to Indonesia and that may help to fight infections. Together with Indonesian and German partners, Andreas Vilcinskas, Head of the IME Project Group Bioresources and project manager of ‘Triple-In’, will search particularly for small molecules and peptides, which will be tested, for example, against the pathogens of tuberculosis or malaria. Indonesia is of great interest to insect biotechnologists like Vilcinskas, because it is one of the countries with the highest number of species worldwide, like a molecular treasure trove. In order to fully document it over the next decade, three partners have joined forces, amongst them the IME with Andreas Vilcinskas as project coordinator: Also BMBF-funded, the Berlin ‘Museum für Naturkunde’, the Indonesian Institute of Sciences and the IME are building up a biodiversity inventory. The project’s aim is to provide information on all described Indonesian species, to serve as a platform for the description of species that are yet to be discovered and as a basis for the intelligent screening of organisms for new bioactive substances (please also see our interview with Andreas Vilcinskas pp. 44-49). MB

Edible Innovations

Can high-tech products hope to compete with Grandma’s lovingly baked apple pie? Public mistrust of innovations in the food industry and an implied rejection of the increasingly technological nature of food processing are highlighted in the study ‘Edible innovations: Food in the crossfire between technological progress and consumer resistance to technology’. This is a study conducted by Fraunhofer Food Chain Management Alliance (FCM) on behalf of *Die Lebensmittelwirtschaft e.V.* (The Food Industry Association). At a joint press conference prior to a symposium on 4 November 2015 in Berlin, Mark Bücking, Spokesman for the FCM Alliance at Fraunhofer IME, innovations expert Meiert J. Grootes, CEO Veripan AG and Stephan Becker-Sonnenschein, Managing Director of *Die Lebensmittelwirtschaft e.V.*, presented this representative consumer study and discussed the findings with participants. The aim of the study was to draw up precise recommendations, based on consumer attitudes towards technical innovations, to help companies and trade associations gain public acceptance of innovative food products and processes. Link to the study (in German): http://www.fcm.fraunhofer.de/de/presse/studie-essbare-innovationen.html. AE

Great job: IME Aachen runners successful in corporate run 2015

An IME Aachen team of runners joined the local corporate run 2015 – 7000 starters, 462 companies or institutions, and track racing over 5 and 10 kilometers. After a brief photo-shoot for the two groups of runners, the ‘IME Runners’ and the ‘Wild Researchers’, the team started out determined and was not even discouraged by missed shuttle buses, rush-hour traffic and a last-minute arrival at the starting line. “The sunny autumn weather and a great atmosphere made this an amazing event for us,” says IME team captain Nadja Voepel. “IME supporters along the race course also did a fantastic job. They spurred us to good personal finishing times.” Matthias Buntru, Postdoc in IME’s Plant Biotechnology Department, even finished second best in the overall ranking. – Congratulations to all runners! Ambitions are awakened. And participants already plan to improve the training for the next run. MB

Reducing loss of harvest with the ‘plant doctor’

Plant pathogens cause major economic losses in the agricultural industry because late detection delays the implementation of measures that can prevent their dissemination. Sensitive and robust procedures for the rapid detection of plant pathogens are therefore required to reduce yield losses and the use of expensive, environmentally damaging chemicals. In a paper published in the scientific journal ‘Applied Environmental Microbiology’ scientists of the Fraunhofer IME describe a simple and portable system for the rapid detection of viral pathogens in infected plants based on immunofiltration, subsequent magnetic detection, and the quantification of magnetically labeled virus particles. Grapevine fanleaf virus was chosen as a model pathogen. MB

TRIP: Doctoral colloquium on translational drug discovery is a success

Front row from left to right: Prof. Dr. Dr. Gerd Geisslinger (Head of the IME Project Group TMP and Speaker of TRIP), Prof. Dr. Birgitta Wolff (President Goethe University Frankfurt/Main), Volker Bouffier (Prime Minister of Hesse), Prof. Dr. Josef Pfeilschifter (Dean of the Medical Faculty Goethe University Frankfurt/Main).

As an interface between university research and the Fraunhofer IME Project Group Translational Medicine and Pharmacology, the international doctorate program 'Translational Research Innnovation - Pharma' (TRIP) has proven to be a success. The graduate program was jointly launched in 2012 by the Goethe University, Frankfurt/Main, and the Else Kröner-Fresenius-Stiftung (EKFS). After a positive interim evaluation, the program will receive further funding. The EKFS will continue to support the colloquium with 1.4 million euro over the next three years, with the university contributing the second half of the costs. TRIP persues an innovative, hands-on training concept for young executives in the field of patient-oriented biomedical research. One new feature of TRIP is that among other things, that several graduate students work together in interdisciplinary project teams. In July 2015, the first PhD students successfully completed their dissertations: More than 20 young women and men received their doctoral degrees of the Goethe University, Frankfurt/Main. Hessian Prime Minister Volker Bouffier congratulated the young researchers. MB

Novel IME technology for protein expression in plant cells – workshop in South Africa

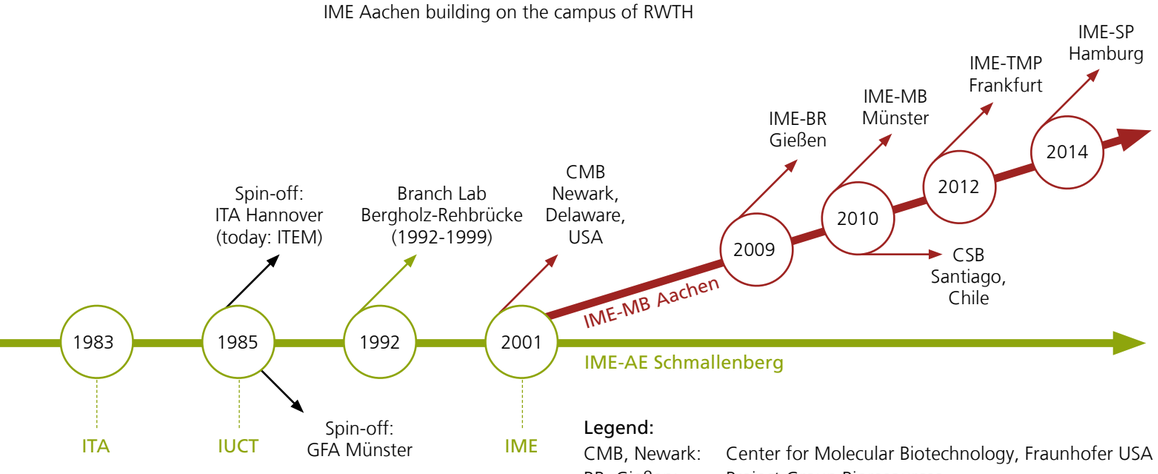
The focus was on innovations in 'Molecular Biopharming' at the one-week workshop organized by the Fraunhofer IME in cooperation with the BioPharming Research Unit of the University of Cape Town in South Africa, November/December 2015. The workshop entitled 'Plant cell packs (PCP) for transient expression: Innovating the field of molecular biopharming' was held during the 'Virology Africa Conference' in Cape Town. The aim of the workshop was first to strengthen ties with the research team of Ed Rybicki, Professor of Microbiology at the University of Cape Town, and second, to introduce the new PCP technology developed at the Fraunhofer IME. This is a novel system the rapid generation of recombinant proteins, based on plant cell cultures, in which cells are applied not in the form of a suspension but as multilayer cell packs. The new method is currently the only technique combining the advantages of a plant-based suspension culture and transient protein expression. Researchers from the Rybicki Group are scheduled to visit the IME in early summer 2016, in order to further familiarize themselves with the PCP method in the laboratories at Aachen. MB

Vaccine against rheumatoid arthritis: Funded by the German Ministry of Education and Research

With the 'GO-Bio' initiative, the German Ministry of Education and Research (BMBF) supports research teams in the life sciences on their way from an academic idea to a sustainable business foundation. The Fraunhofer IME Project Group Translational Medicine and Pharmacology has been successful in the highly competitive selection process: With 3.4 million euro, the BMBF will support an interdisciplinary team around Harald Burkhardt and Frank Behrens over two and a half years. The overarching goal is to develop a vaccine against rheumatoid arthritis, a chronic and so far incurable disease. Now the focus is on preparing the launch of 'AIDCure GmbH', which will develop the new therapeutic approach. In this project, the IME works closely together with Professor Rikard Holmdaal of the Karolinska Institute in Stockholm. MB

Dedicated organizer – Head of Administration Franz-Josef Albers retires

Franz-Josef Albers took over administrative management of the Fraunhofer Institute for Toxicology and Aerosol Research ITA at Schmallenberg in 1983 with a staff of 176 across three sites. Mr. Albers was very committed in the shaping of the institute from its foundation to the present Institute for Molecular Biology and Applied Ecology IME, with six sites and a staff of 477 (at the end of 2015) in Germany and overseas branches in the USA and Chile. He was closely involved in the spin-off of the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM in Hanover, completed in 1985, and the strategic reorientation of the Schmallenberg site into an environmental research institute renamed Institute for Environmental Chemistry and Ecotoxicology IUCT. In addition, as Head of Administration, he assisted in the setting up of the Division of Molecular Biology, initiated in 1998 by Rainer Fischer, and the construction of the new IME Aachen building on the campus of RWTH Aachen University. Executive Director of the IME, Rainer Fischer, and Director of the Applied Ecology Division in Schmallenberg, Christoph Schäfers, extend their warmest thanks to Mr. Albers for his support over the last three decades, without which this development of the IME would not have been possible.
Since 1 January 2016 Franz-Josef Albers' post as Head of Administration of the Fraunhofer IME has been taken by his representative for many years at the Aachen site, Dietmar Douven. The Administrative Manager of the Applied Ecology Division at the Schmallenberg site is now held by his former colleague, Katharina Schaff. Mr. Albers remains closely associated with the institute, and the institute management will appreciate his support in future as advisor and consultant. AE



Legend:

CMB, Newark:	Center for Molecular Biotechnology, Fraunhofer USA
BR, Gießen:	Project Group Bioresources
CSB, Santiago:	Center for Systems Biotechnology, Fraunhofer Chile
MB, Münster:	Department Functional and Applied Genomics
TMP, Frankfurt:	Project Group Translational Medicine and Pharmacology
SP, Hamburg:	Department ScreeningPort

With seriousness and playful instinct: Awards ceremony 'Jugend forscht'

With a lot of intellectual curiosity and motivation, 190 schoolchildren over ten years and teenagers set out to enter the regional competition of Hamburg Volkspark and bring their ideas to life. The regional rounds are the first phase of 'Jugend forscht', Germany's best-known mathematics and science competition. Together with the Hamburger Sportverein (HSV), Hamburg-based IME ScreeningPort acted as host for the young participants. The result of the regional competition was 82 projects from the areas of professional life, biology, chemistry, geo and space sciences, mathematics/informatics, physics and technology. The many research topics included the musical preferences of bean plants, zippers based on magnetism, six-legged salvage robots and fossil discoveries from Cyprus. Thirteen first prizes were awarded. A project by Florentine Mostaghimi-Gomi (18) and Ole Keim (17) on hippopotamus fossils from Cyprus later also won the German Chancellor's special award for the most original work throughout Germany.
Together with a team of pupils and students Mira Grättinger of the IME ScreeningPort organized this regional science competition with great commitment for the third year in a row. MB

Summer School and training days on ecotoxicology and hazardous chemicals

The IME in Schmallenberg held their first Summer School as part of their teaching program at the Universities of Münster and Siegen. Researchers from the Applied Ecology Division set up seminars and field studies on the subject of 'Aquatic Eco(system)Toxicology'. From 24 August to 4 September 2015 course participants had the opportunity to perform short standard tests for risk assessment of chemicals and to gain insights into the use of higher-level test systems.
Participants of the course 'Basic Principles of Ecotoxicology' were given the opportunity to learn about test facilities for regulatory testing procedures. In July, as part of their specialist training as qualified toxicologists of the German Society for Experimental and Clinical Pharmacology and Toxicology (DGPT), they made a one-day excursion to the IME in Schmallenberg.
In the spirit of social responsibility and community involvement, IME Schmallenberg also offered advanced training in the handling of hazardous chemicals to members of the local fire brigade in 2015. AE

Joseph von Fraunhofer Prize: Natural rubber from dandelions – successful cooperation with Continental

Dandelions are robust plants that provide an excellent alternative source for a raw material of high demand: natural rubber, the fundamental ingredient in rubber products. In a joint project of the Fraunhofer IME, the Department of Biology and Biotechnology (IBBP) at the University of Münster and the tire manufacturer Continental, car tire prototypes made of dandelion rubber have been developed and produced. For their work on the Russian dandelion and its application as a source of natural rubber, Dirk Prüfer and Christian Schulze Gronover of IME and IBBP as well as Carla Recker of Continental received one of three Joseph von Fraunhofer Prizes 2015. The awards were presented in the presence of Federal President Joachim Gauck and Hesse's Prime Minister Volker Bouffier.

In the rubber processing industry, there are numerous potential applications for this alternative and sustainable raw material. Not only car tires, also mattresses, gloves, adhesives and many other products are conceivable. At the International Motor Show IAA 2015 in Frankfurt, Continental has already presented another prototype: engine mounts based on dandelion rubber. The industrial manufacture of these product should be possible in a few years (please also see our article pp. 26-29). MB

New young investigator group: Faster and more cost-effective biopharmaceutical development

The development and manufacturing of biopharmaceuticals involves high costs. To bring them to the market in a faster and more cost-effective way is the aim of young researcher Johannes Buyel. Since April 2015 he has led the new young investigator group 'FAST-PEP', supported by Fraunhofer Attract funding. His idea: by closely integrating the testing of product candidates with the development of corresponding efficient manufacturing processes, it should become possible to decide early on, if those innovative substances will also work in practice. This way, failure rates in drug development could be significantly reduced – and hence also the costs. In addition, since November 2015 and together with Jürgen Drossard Johannes Buyel heads the Department Integrated Production Platforms as the successor of Stephan Hellwig. As a promising young researcher Buyel was selected to take part in the 'Lindau Nobel Laureate Meeting 2015'. In summer, 650 selected young scientists came together to share knowledge with 65 Nobel Laureates from the fields of physics, physiology or medicine, and chemistry. "I will certainly not forget this meeting with Nobel Laureates. They have all turned their hobby into a profession, like me, and have persued their research with incredible passion. This is very inspiring for the future," says Buyel. MB

4th Annual Conference of the House of Pharma & Healthcare – bringing all players together

The 'House of Pharma & Healthcare' brings together stakeholders from health and pharmaceutical industries in Germany to jointly discuss solutions to the challenges facing the healthcare system. Two key objectives are to build up social and political acceptance of the biosciences and to close current innovation gaps in drug development. Despite myriad advances in medicine, many diseases can still not be cured or adequately treated. And the demand for disease prevention and personalized medicine continues to rise. House of Pharma & Healthcare is therefore forging links between business, science, politics, patient organizations, physicians, pharmacists and health insurance companies. The 4th Annual Conference of the House of Pharma & Healthcare in 2015 brought 400 participants to Frankfurt/Main, making it the largest forum for the pharmaceutical and biotechnology sectors in the Rhine-Main metropolitan area. Among the issues debated were ways to set a fair price for key pharmaceutical innovations and the role of big data in the health sector.

The House of Pharma & Healthcare is an initiative of the LOEWE Center for Translational Medicine and Pharmacology in Frankfurt. The Center's Spokesman Gerd Geisslinger also heads the Fraunhofer IME project group of the same name. MB

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